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The Efficacy of Cannabis as a Substitute Addiction for Opiates.

Clark Furlong

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Background: Approaches to opiate addiction focus on abstinence and/or a harm reduction model that often utilizes substitute medications. Methadone and suboxone are the most prescribed drugs for opiate maintenance therapy. The long-term side effect profile and health consequences are undesirable. Research is looking for healthier alternatives.

Purpose: Opiate maintenance therapy participants have a mortality rate greater than twelve times that of the normal population, we seek to discover if cannabis can be a useful/safer alternative.

Methods: Following a comprehensive literature review a 7-question online survey was designed with SurveyMonkey to gauge current Augsburg students' perception of cannabis as an alternative to opiates. This class-based project was designated IRB-Exempt from Augsburg University IRB, #2023-06-04. The survey was sent to current Augsburg students via mass email titled "Augsburg A-mail". To qualify participants must have been current Augsburg students, age eighteen or older, and be living within the United States. Data was collected via survey monkey for approximately 5 weeks.

Conclusions: Upon review of the literature, it is reasonable to conclude that cannabis has some efficacy in the setting of opiate maintenance, as well as other therapeutic uses. Based upon this study's research, cannabis perception among students was positive and reflected the themes of the literature. Putting this all together, cannabis is likely effective in harm reduction, however perceptions and knowledge vary. More research and work around awareness is recommended to establish this as viable therapy.

Key Words: Cannabis efficacy, chemovar, buprenorphine, methadone, opioid, opiate, opiate use disorder, opiate maintenance therapy, substitute addictions, heroin, harm reduction, long term effects, endocannabinoids, marijuana, and cannabis.

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Introduction

It is estimated that approximately the same number of people have died from opiate overdose as have died in the entire Vietnam war and numbers are continuing to rise. Currently there are efforts to help decrease the mortality rate associated with the opiate epidemic. Harm reduction has been implemented in several forms, but are our current substitute addictions/maintenance therapies as efficacious as possible alternatives? The National Institute on Drug Abuse has released a list of the top 10 potentially beneficial mechanisms to research in response to the opiate epidemic, among them were cannabinoid CB1 antagonists.¹ Cannabis has been shown to reduce pain and there is growing evidence of a symbiotic relationship between cannabis and opiate receptors (CB1/CB2 and mu receptors respectively). This is in line with the theory that CB1 receptors have interplay with opiate receptors and some potential benefit in addiction/pain management. Hence, the purpose of this study is to understand if cannabis may have some potential in harm reduction as an opiate alternative and to gain understanding of the perception of cannabis in lieu of opiates amongst university students.

To determine the efficacy of cannabis/chemovars (chemovars are blends of CBD, THC and terpenes, each defined by their unique properties and ratios) as a substitute addiction for opiate maintenance therapy (OMT), we must first understand substitute addictions and the role they play in harm reduction. Harm reduction as a concept is a relatively new idea, first noted to be conceptualized in the nineteen twenties. Literature notes harm reduction for substance abuse being implemented in the nineteen seventies and eighties with the rise of heroin and the

HIV/AIDS epidemic.² Harm reduction has been shown to be effective, and while the ethics remain intensely debated (abstinence vs moderation/substitution etc.), that is for another time. One thing is for sure, there are ways to reduce harm to those that do not agree or cannot comply with the abstinence model. There have been many successful implementations of harm reduction regarding the opiate epidemic: clean needles, safe injection rooms, opioid agonists /partial agonists serving as substitute addictions and prevention programs are some of the attempts that society has made to thwart this epidemic.

Harm reduction is a public health approach to creatively combatting high-risk behaviors, like drug and alcohol addiction. Harm reduction has taken a while to gain public and political acceptance. One critique of the current idea is that more harm reduction services will result in a more humane society, but without addressing the systemic avenues that create harm we are sustaining systems of harm in a much larger sense.³ Examples of current large-scale harm are lack of social services, marginalization of populations, and the pharmaceutical industries grip on healthcare. That said, micro applications of harm reduction on the user level could create an impetus for greater systemic (macro) change. An example of this is the pandemic, it had a positive effect on harm reduction; telehealth proved successful for many people with substance use disorders.³ Home medical deliveries skyrocketed and through the media, issue awareness increased for the management of SUDs (and mental health overall) during the pandemic.⁴ This supports the idea that systemic changes can have long lasting improvements in the realm of harm reduction.

Harm reduction focuses on reducing the negative outcomes of the action and historically has valued abstinence as a goal, but not a requirement. There have been numerous studies showing that moderation and/or replacement therapies work well in adherent populations.^{4,5} For

instance, heavy drinkers who have identified the need to change and are motivated, yet not ready to abstain may benefit from controlled moderation (e.g., drinking every other day).⁵ If adherent, they could experience fewer comorbidities and chronic diseases as well as have an easier time achieving abstinence (if desired). Another well documented harm reduction technique is substitute addictions like that of methadone and/or suboxone for heroin/prescription opioids, which over time has shown decreased harm/overdose and less crime related to drug procurement.⁴

However, is better than bad good enough? Many of the programs that offer support for opiate addiction do not always result in recovery. Often individuals who start opiate substitution therapy (OST) on suboxone or methadone spend the rest of their lives on the drug. In the USA the minimum recommended amount of time on substitute medications is 12 months, and more often it is years.⁶ Attempts to quit are either thwarted by relapse or an inevitable return to maintenance therapy. Which begs the question, are there other options or new ways to reduce harm? One possibility on the horizon for harm reduction enthusiasts is the legalization/re-scheduling of cannabis. Cannabis has many medical uses currently (pain management, anti-emetic, PTSD, and it is even being trialed in some places as substitution therapy). The research being done is limited because of restrictions on cannabis, but it's re-scheduling should allow it to be researched more freely and thoroughly. Current research is focusing on the interplay between CB and mu receptors as well as the modification of the endocannabinoid system; reporting benefits in numerous areas of health/disease like cancer, mental health, pain, thermoregulation, and digestion.

Long term use of opiates and even maintenance with pharmaceuticals can lead to poor outcomes and adverse events (obesity, diabetes, and heart arrhythmias to name a few).⁷

Methadone is currently the most prescribed drug for OST, but it does not have universal efficacy.⁸ Would long term cannabis therapy provide better outcomes, including less long-term addiction/reliance on opioids? While cannabis has a wide range of effects that vary based on the individual, there are many reports in the literature of patients utilizing cannabis to get off opiates. There are also many examples of patients using cannabis for pain as an adjunct to opiates.⁹ In fact, many cancer patients use cannabis for their ailments and cannabis is now being prescribed for chronic pain in certain areas.¹⁰ The research suggests the mechanism of action of cannabis could be beneficial in reducing pain, so how about the other symptoms of heroin withdrawal? While we may have not figured out the science yet, anecdotally cannabis is a tool that is being used for withdrawal symptoms and a bridge back into the community by many. The purpose of this paper is to determine if cannabis has enough potential efficacy as an opiate alternative to warrant further exploration in the realm of harm reduction and create a survey based on themes with the literature to explore student/public perception of cannabis to determine if current research reflects reality.

Background/Literature Review

Current Models of Substitute Addictions

Society benefits most when those with a problem are promoted to live a better life rather than be punished, and it is theorized that in the case of opiate addiction this can be accomplished with education and access to harm reduction services instead of incarceration.² Opiate addiction is a chronic and often debilitating disorder that is often accompanied by periods of remission and relapse. Treatment and recovery are long complicated processes often managed with

pharmacotherapy in the form of suboxone and methadone. The age and duration of use are longer in methadone using patients when compared to that of suboxone¹¹, however relapse occurs at similar rates regardless of pharmacotherapy. Replacement therapy has been shown to reduce criminal activity associated with drug obtainment. Also, substitution therapy tends to reduce comorbidities and mortality (HIV, overdose, infectious disease etc.).⁴ The majority (92.8%) of OST participants believed their treatment caused significant changes in their lives and it is estimated that only 11.2% of participants felt like OST caused significant side effects.¹² However, most of the participants in this study about OST felt judged by friends and family for their use of substitute medications. Almost 61.8% of participants felt like clinicians weren't educated enough about OST and participants were split on whether OST was considered a treatment or a drug. Generally, research has found methadone to be more efficacious than suboxone for reasons including compliance, ease of access, less associated illegal use, and its approval among patient populations. However, many methadone users experience side effects such as constipation, sweating, dry mouth, malaise, joint pain, and decreased sexual desire/performance, yet it is still proposed to be preferred over suboxone as it is a full opiate agonist whereas suboxone is a partial opiate receptor agonist.¹³ However, options outside of methadone/suboxone are being explored because it does not work for everyone, and the long-term side effects are often unfavorable (diabetes, obesity, QT prolongation, etc.) in those who experience them.

Pros and cons of opiate substitution therapy

There is an ever-increasing rise of opiate related deaths and a continuing epidemic, yet the treatment has not changed nor has there been much effort into pharmacological advancement with opiate addiction interventions. Even opiate addicts undergoing treatment face a mortality

rate that is 12 times greater than that of the average public.⁶ Studies have claimed that longer term OST has favorable benefits when examining relapse, however the long-term physical impacts seem to have been overlooked. Many users of methadone experience sleep difficulties, problems with sexual performance, and cardiovascular incidents. It is theorized that many of those receiving OST should be detoxified and tapered off the drug, which is how it was designed to be used in maintenance programs. However, intention does not always reflect practice and the reported improvements in quality of life from long term OST participants often cause researchers and policy makers to overlook adverse events and side effects.¹⁴ For many individuals long term OST and psychosocial support is currently the best option.

Many acknowledge the benefits of opiate maintenance therapy but suggest improvements could be made regarding the populations increase of alcoholism and depression.¹¹ After a 5-year longitudinal study on long term effects of OST, Zippel-Schultz et al concludes that long term OST may enable the reduction of comorbidities and a drug-centered lifestyle, but how could further improvements be made? One shortcoming of OST is that it really is a just a substitute for the drug itself, other supports are often limited, and acquisition of those supports is placed upon the client. Nonetheless research by Ellefsen et al and many others have supported the idea that users of opiate maintenance therapy are generally satisfied with the treatment.¹⁵ In a relatively short-term follow-up study by Smyth et al, psychosocially assisted OST appears to be associated with improved psychological well-being in heroin-dependent adolescents, especially in the areas of depression and anxiety.¹⁶ This data supports the idea that improvements can be made to OST and that previously suggested theories of improvement (psychosocial support) are turning out to be successful with real time results.

The endocannabinoid system

Melamede suggests a cannabinoid-based approach to modifying the endocannabinoid system to promote survival of the fittest (in other words making ourselves more fit for survival through the use of synthetic exogenous cannabinoids).¹⁷ The idea is that humans and other animals make use of internally produced cannabis-like products known as endocannabinoids. The endocannabinoid system (ECS) helps regulate homeostasis within all body systems.¹⁷ Therefore, the health of an organism is interdependent on the endocannabinoid system. Endocannabinoids have many intricate and unknown effects on system regulation throughout the lifespan. The ECS plays a key role in the pathogenesis of many neurological diseases, including multiple sclerosis (MS), epilepsy, Alzheimer's disease (AD), Parkinson's disease (PD), and Huntington's disease (HD).¹⁸ Cannabis has the potential to alter endocannabinoid levels in those seeking to modify or maintain homeostasis. It is currently believed that endocannabinoids downregulate anxiety, pain, and satiety signals while upregulating appetite, mood, and lipogenesis.¹⁸ While the science is not yet fully understood, a vast amount of research is aimed at exploring the potential uses for cannabinoids. Cherkasova, Wang, Gerasymchuk & Fiselier make note that much cancer treatment is designed around this ECS theory when prescribing cannabis as a medicine. In fact, cannabis has been used for medicinal purposes for thousands of years until the 1940s when authorities made it illegal.¹⁹ While cannabis has anti-tumor properties like the induction of autophagy/apoptosis and it can prevent proliferation/metastasis, its immunosuppressive effects can have negative effects on healthy cells (although this is uncommon).¹⁹ Therefore, cannabis should be used with caution, and a great deal of research is needed to better understand future applications and implications.

Much like cancer, with opiate withdrawal there is pain. Pain is the number one reason that opiates are prescribed and a big precipitating factor for this epidemic. Cannabinoid and

opioid receptors have similar neural transduction systems and CB1 and μ -opioid receptors colocalize in afferent pain neurons. CB2 receptors have also been observed to indirectly stimulate opioid receptors in afferent pathways, both of which can increase the analgesic effects of opiates. This research suggests that cannabinoids can help reduce the quantity of opiates being taken, this is known as the opioid sparing effect. Multiple systemic reviews have found that those using cannabis in conjunction with opiates for various types of pain (diabetic neuropathy, spinal cord injury, neuropathic pain, cancer pain, etc.) have found a 30% reduction in pain when compared to a placebo.¹⁹ However, research has been limited by cannabis access, small sample sizes, difficulty with dose adjustment, and participant withdrawal. There is also a theory that there is a biphasic effect of THC where low doses reduce pain, and high doses can actually make it worse. Future cancer research is looking at the effects of CB1 and CB2 receptors in conjunction with the endocannabinoid system and how modifying effects can influence cell behavior among other downstream effects.

Cannabis uses/benefits

Multiple states have authorized cannabis as an opioid substitution agent and as a treatment for posttraumatic stress disorder (PTSD). De Aquino , Sofuoglu, Stefanovics & Rosenheck sought to investigate the relationship between cannabis use, non-medical opioid use, and PTSD symptoms among U.S. veterans. From 1992–2011, veterans admitted to specialized intensive PTSD treatment participated in a national evaluation with assessments at intake and four months after discharge. At follow-up, substance use or PTSD symptoms did not significantly differ. Cannabis use was not associated with a substantial reduction of non-medical opioid use, or either improvement or worsening of PTSD symptoms in this population. The group using cannabis was found to have worse PTSD symptoms overall but use less opiates.²⁰

Use was also recorded via self-report and all substances were procured outside of the study. The study was limited to veterans, and it could benefit from a repeat with improved controls. One acknowledgement is that it is possible that cannabis did not make PTSD worse, but in the populations with worse PTSD cannabis was used as an “off-label” medication. What is promising is that states are recognizing the potential benefits of cannabis, and the approved uses could be beneficial for harm reduction purposes in the setting of opiate addiction. This research is important because it showcases an approved use of cannabis for PTSD (efficacy may be person dependent) which can often be experienced by those overcoming opiate addiction.

While the science is starting to blossom, there is an overwhelming amount of anecdotal evidence based on user experience supporting the use of cannabis for harm reduction. Among samples of people who use drugs (PWUD) studied, use of cannabis for harm reduction was a common strategy, reported by approximately 1 in 4 respondents at least once during the study period.²¹ The most frequent reasons included substitution for stimulants or for illicit opioids. Often users are not consciously substituting cannabis for other drugs, but this passive act may have benefits as cannabidiol (CBD) has been shown to reduce opiate cravings and drug related anxieties.²¹ Shapira et al found that self-substitution of one illicit substance for another is a highly prevalent behavior among treatment-enrolled patients with SUD. Changes in drug availability appear to have the highest impact on the decision to substitute. In cannabis and heroin preferers substituting for other substances is often for improved effects, reduced ADRs, self-medicating, or managing withdrawal symptoms.²² Through this a reoccurring theme presents in those self-medicating; they experiment with varieties of substances in an ongoing effort to achieve personal benefit of the highest level (or consume whatever is available, and cannabis is usually quite prevalent).

One study found that smoking cannabis did not reduce heroin withdrawal symptoms, a very important component to harm reduction. It is important to note that the study was small and that only 46 of the 107 participants in the study had ever used cannabis and that withdrawal symptoms were captured in two-day windows once per week. Yet it was deemed plausible that opioid-withdrawal symptoms could be relieved by individual cannabinoids, such as cannabidiol 21 or by inhibitors of endocannabinoid system.²³ A large survey designed to assess marijuana substitution for opiates with 9,003 respondents suggests that even if objective measures do not support marijuana as a substitutive option for opioid use, patients perceive that marijuana use has reduced their opioid use. As 41% of respondents reported a decrease or cessation of opiate use due to cannabis use, 46% reported no change and 8% saw an increase of use.²⁴ One large fear of those who oppose cannabis as a substitute for opiates is the lack of research of potential harms and the lack of overall knowledge about the substance. Nonetheless cannabis has been used by humans for centuries and whether the claims can be supported objectively is yet to be determined to due lack of research.

Researchers have looked at social media apps/sites like Reddit (and its respective sections titled “subreddits”) to better understand current opiate users’ naturalistic cannabis use compared to those using in recovery. When comparing the active use group to the recovery group, cannabis related posts were twice as common in the recovery subreddit. Many users referred to cannabis as treatment and made specific note of managing withdrawal symptoms.⁹ Other research sought out to understand the epidemiology behind the self-reported use of cannabis for medical purposes. The study found that among 27,169 participants that self-reported cannabis use for medical purposes was around 27%. The most common physical reasons for use were pain management, sleep, headaches, appetite assistance, and nausea relief. The most common mental

health symptoms that were alleviated by those self-reporting cannabis use were depression and anxiety (both of which are common comorbidities of opiate addiction/withdrawal).²⁵ The research also found self-report cannabis use to be higher in recreational states than in states that did not have legal recreational cannabis. While these benefits have been found to be difficult to replicate or define via objective constructs, one recurring theme is that anecdotally people seem to enjoy cannabis and find many benefits from it.

Lucas et al found that about 36.1% of respondents use cannabis as a substitute for illicit substances (including opiates) (*n* = 137), and 67.8% use cannabis as a substitute for prescription drugs (*n* = 259). The three main reasons cited for cannabis-related substitution are “less withdrawal” (67.7%), “fewer side-effects” (60.4%), and “better symptom management” suggesting that many patients may have already identified cannabis as an effective and potentially safer adjunct or alternative to their prescription drug regimen.²⁶ These findings suggest that medical use of cannabis may indeed play a harm reduction role and may have a place in abstinence-based substance use treatment approaches (or perhaps a bridge to these approaches).²⁶

Cannabis pharmacology

Cannabis is highly lipophilic and therefore it is a good candidate for nanosized drugs available via many routes of administration. Pharmacokinetic investigations by Abrams et al revealed no significant change in the area under the plasma concentration–time curves for either morphine or oxycodone after exposure to cannabis. Pain was significantly decreased (average 27%, 95% confidence interval (CI) 9, 46) after the addition of vaporized cannabis. The conclusion was that vaporized cannabis augments the analgesic effects of opioids without significantly altering plasma opioid levels.²⁷ Cannabis has been shown to be effective for treating

nerve pain without the risk of fatal poisoning and as such seems like a reasonable adjunct to opioids in severe pain settings. Some experts in harm reduction suggest that physicians who treat neuropathic pain with opioids should evaluate their patients for a trial of cannabis and prescribe it when appropriate prior to using opioids.²⁸ Many proponents of this approach recommend whole plant cannabis rather than derivatives because of the potential beneficial effects of other compounds in whole plant cannabis (many of which are still not fully understood). The research also refers to the theory that there are synergistic effects between cannabis and opiate receptors. Carter et al writes “from a pharmacological standpoint, using cannabinoids is much safer than opiates” these researchers go on to state that the compelling evidence can help reclassify marijuana, and eventually reduce opiate related morbidity and improve outcomes in patient care.²⁹

The study By Gibson examines the effects of three different cannabis chemovars with different THC ratios to assert whether differing levels of CBD content produce different effects. 159 cannabis users were included, they were assessed before, immediately after and one hour after the administration of their assigned chemovar. Those that used a split THC & CBD chemovar that was CBD dominant had greater levels of CBD plasma levels and reduced levels of THC present in their serum. The CBD dominant chemovars provided all of the anecdotal benefits of the more THC heavy varieties but with less paranoia and anxiety. The patients experienced positive mood effects with lower levels of serum THC when using CBD dominant chemovars. This is intriguing for harm reduction as chemovars have potential for use in substitute addictions with less potential for psychoactive effects than current options.³⁰ Future research can look at appropriate ratios of CBD and THC in various chemovars while attempting to differentiate ratios for their respective medical purposes.

Potential harms associated with cannabis

While cannabis may be beneficial from a physical standpoint and pharmacological level, for some there may be risks that are greater than the benefits. One population that comes to mind is those suffering from mental health issues. Looking at bipolar disorder, consumption of cannabis can worsen psychotic, manic, and depressive symptoms. Therefore, conditions with substantial evidence suggesting cannabis as harmful should avoid use of the drug. However, consumers with mental health conditions generally perceive cannabis to have a positive impact on their lives. The relationship between cannabis and mental health is disorder specific and may include a combination of perceived benefits and harms.³¹ However, the contents of cannabis vary, and the study suggests that increased amounts of CBD may offset the negative effects of THC in this instance. Currently there is a need for longitudinal studies of participants that begin before the onset of cannabis use disorder (CUD) or a mood disorder. To date, studies have excluded those with comorbidities outside of mood disorders and CUD. This research is interesting because it contradicts previously cited anecdotal evidence, but it is specific to vulnerable populations. Cannabis use, particularly heavy and dependent use, is likely bidirectionally associated with the onset and course of depression, with evidence that some depressed individuals may initiate cannabis to self-medicate while cannabis use may precede depression in others.³² Therefore, we need to learn more about the drug and its nuances. For some cannabis may be beneficial but to others it may be incredibly detrimental, clearly more research is needed.

Chronic cannabis users often experience deficits in verbal episodic memory, but no difference in special working memory or response inhibition.³³ While evidence exists for the progression to lung disorders in chronic tobacco smokers, the effects from habitual(smoked)

cannabis use are less clear. The carcinogens and respiratory toxins in cannabis and tobacco smoke are similar but smoking cannabis results in higher exposures to inhaled tar and gases on a “per-puff” basis.³⁴ Currently the biggest risk posed to the public by cannabis are the psychoactive effects of delta 9 THC and societies glorification of the drug (let us not forget that all drugs have some risk of harm). However, while literature hints at these possible harms, there needs to be controlled comprehensive research looking at various concentrate levels of cannabis products performed longitudinally in both the short and long term.³⁵

Potential efficacy of cannabis as an opiate alternative

This review has covered the history of harm reduction and the current state of the opiate epidemic. Approaches to this problem seem reasonable, yet improvements to them can be made. This review has supported the theory that cannabis has some potential to be efficacious in the setting of opiate harm reduction. Cannabis is a drug that humans have a complex relationship with. Throughout this review the benefits and potential uses of cannabis have been highlighted in a way that showcase its potential uses in harm reduction and the treatment of opiate addiction. In addition to providing pain relief, less cravings, reduced anxiety/depression, PTSD relief, increased appetite, and better sleep, cannabis can provide a legal high (in some states) for patients suffering from an opiate affliction. Cannabis may have some harms associated with it, however, there appear to be far less than with opiate use. It is therefore possible that cannabis can improve lives and provide better outcomes when compared to the current model of opiate substitution/maintenance therapy. Keeping in mind the role of cannabis in harm reduction, the challenges with SUD stigma, and the rescheduling of marijuana, there is a distinct possibility that cannabis use in harm reduction models will increase. Given that possibility, this study seeks to understand student/public perception of cannabis as an opiate alternative. Understanding current

perceptions can inform the drug re-classification scheduling process, shift standards of care in SUD management, and direct focus of future research. To this end, a survey about cannabis perception was conducted to provide valuable insight into America's education and opinions regarding cannabis and the perception of cannabis as an opiate alternative.

Methods

This class-based project was designated IRB-Exempt from Augsburg University IRB, #2023-06-04. A 7-question online survey was designed with SurveyMonkey using a dichotomous approach to gauge current Augsburg students' perception of cannabis as an alternative to opiates. Each question was to incorporate a theme from the literature including; overall harm of the substances in question, substance effects on mental health, cannabis's effects on pain, management of withdrawal, and prevalence of cannabis/legality. The survey was sent to current Augsburg students via mass email titled "Augsburg A-mail". The survey was also announced to the Augsburg 2025 PA cohort verbally. To qualify to complete the survey participants must have been current Augsburg students, age eighteen or older, and be living within the United States. Participants were presented with an informed consent form prior to proceeding with the Survey. Data was collected via survey monkey and the study was open for approximately 5 weeks. All information was kept confidential on a locked laptop and not released on any public servers. Questions had only two possible answers, as such data was analyzed based on percentages and majorities. Responses were directly compared to themes and trends within the literature to understand how well public perception reflects our current understanding of cannabis.

Research Results

From 5/25/24 to 7/3/24 a total of 125 survey responses were recorded via SurveyMonkey. The survey took an average time of 2 minutes to complete. Overall, the results of the survey reflect the trends found within the literature. Most interesting were the mixed views on the mental health effects of cannabis and that most participants answered that cannabis can aide in opiate withdrawal. Student/public perception of cannabis and its potential uses reflect recent research findings.

Do you believe that there are more harms associated with opiates or cannabis?

Answered: 125 Skipped: 0

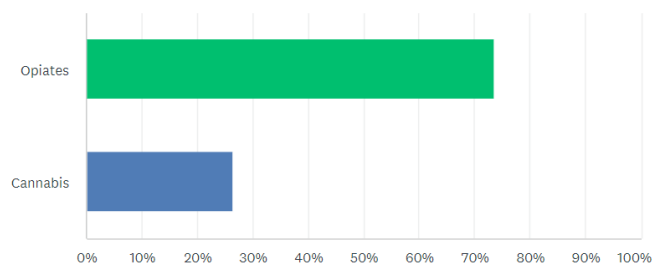


Figure 1

Do you believe that cannabis has a positive effect on mental health?

Answered: 124 Skipped: 1

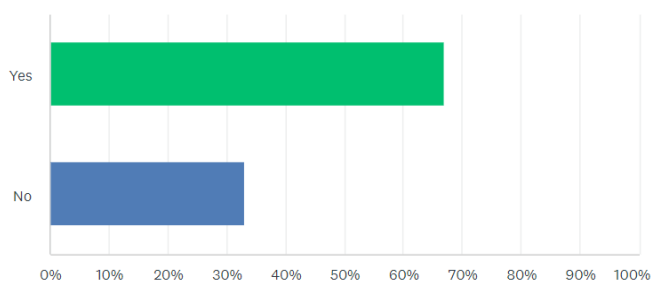


Figure 2

Do you believe that cannabis has a negative effect on mental health?

Answered: 124 Skipped: 1

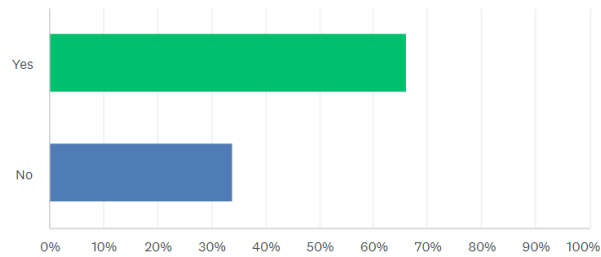


Figure 3

Do you believe that cannabis can be used to manage pain?

Answered: 125 Skipped: 0

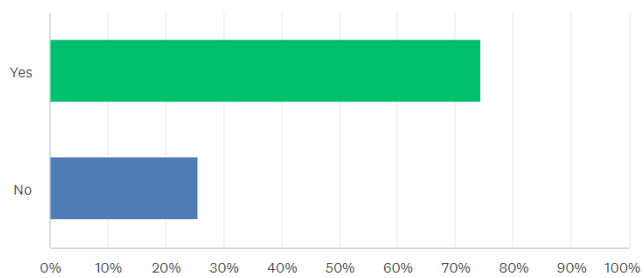


Figure 4

Do you believe that cannabis can be used as a tool to manage withdrawal symptoms of opiates?

Answered: 123 Skipped: 2

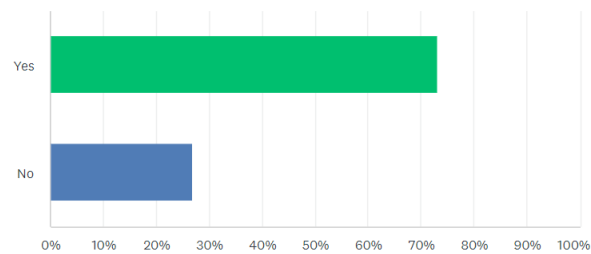


Figure 5

In the last 12 months has anyone you know used cannabis for an “off-label” medical purpose?

Answered: 124 Skipped: 1

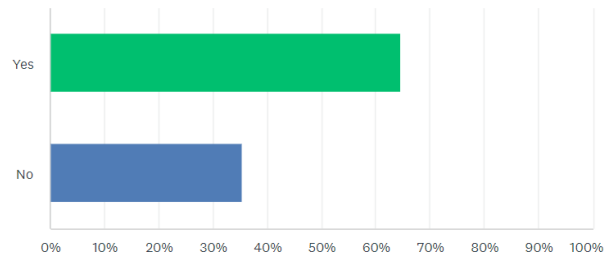


Figure 6

Do you think cannabis should be legalized?

Answered: 125 Skipped: 0

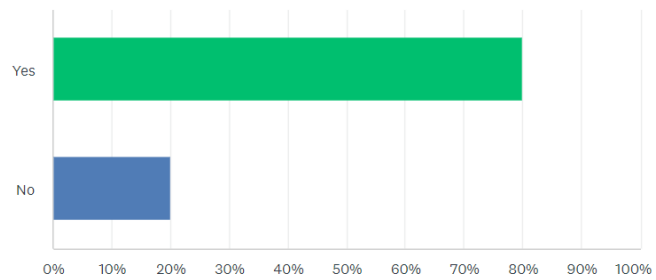


Figure 7

Discussion/Analysis

Trends in the literature suggest cannabis has a better side effect profile and less severe long-term health effects than opiates. Most participants felt as if more harms were associated with opiates, this was an impetus of this study and the survey results reflect the conclusions of the literature.^{7,11,14,16,29} However, this is based on our current understanding of cannabis and opiates are better researched, meaning more harms could be associated with cannabis as research becomes available. What is interesting about the data is the lack of understanding about cannabis's effects on mental health, two thirds of participants answered that cannabis has positive effects on mental health and yet two thirds of the participants answered that it has negative effects on mental health. The literature showcases this through mixed results based on user experience, comorbidities (certain mental health disorders, vulnerable populations etc.), and subjective self-reports of user effects.^{25,31,32} Simply put some people's mental health may benefit from cannabis while others experience a detriment. It will be interesting to see how science can objectively define these measures going forward and whether specific strains of cannabis or chemovar blends may have different effects.

Cannabis has been shown to reduce pain and there is growing evidence of a symbiotic relationship between cannabis receptors and opiate receptors. The student population seems to be educated about cannabis's use in a pain setting, this reflects the literature as it has many applications in cancer settings¹⁹, chronic pain²⁷ and even palliative care²⁹. Most respondents answering that cannabis can help withdrawal symptoms is interesting. Anecdotally this is referenced in the literature, students seem to have similar knowledge or beliefs about cannabis's potential in that setting. Perhaps the general population has made the connection that cannabis is being used for many symptoms of opiate withdrawal but in other settings. For example; cannabis

is used to prevent nausea and be an appetite stimulant for patients receiving chemotherapy, both of which it could be used for in opiate withdrawal. Knowing someone who was using cannabis for an off-label use was prevalent in the survey responses, this implies that people are using cannabis to self-medicate or treat themselves⁹.

Cannabis has also been shown to aid in the regulation of the ECS, an area of study getting attention in both pain and cancer research. By externally moderating our ECS via cannabinoids there is potential to alter the function of many human systems, from tumor suppression to mental health. The literature review supports the idea that cannabis has potential as a harm reduction agent because it is currently being used for purposes that could have a direct application in harm reduction settings and currently it is believed to be less harmful than opiates. The results of the survey showcase this potential as most respondents felt that cannabis could help with opiate withdrawal symptoms. However, given the current restrictions on cannabis and the vulnerable populations in question this may be very difficult to implement going forward. Implications include but are not limited to; differing cannabis laws from state to state, current models/stigma of substitute addictions, current federal scheduling of cannabis, cannabis's wide range of subjective effects, overall lack of cannabis research and the amount of time to perform necessary research. The results of the survey favor legalization, which seems to reflect national polls and trends as we enter a period of "public comment". As such researchers and cannabis enthusiasts remain hopeful.

Prior to conducting the research, the author acknowledged bias and finds it necessary to disclose that prior to this literature they believed cannabis was far less harmful than opiates. This literature review utilized expanded search criteria to include research and articles up to ten years of age, this was different than the original goal of five years. This limitation showcases the need

for more research about cannabis and specifically harm reduction. The scheduling of cannabis as a schedule 1 substance on the federal level is an ongoing limitation to research. Other limitations included lack of funding for this study and selection bias/convenience sampling (the survey may better reflect the perception of the public if it were made available to them). This study was limited to Augsburg students as a measure of control and convenience. A larger scale study conducted with a team could have created a more cohesive survey with greater validity by using scales and previously constructed survey questions. In theory this could have led to more digestible responses with meaningful implications for a better-defined construct. Off-label medical uses could have been defined within the survey providing insight into more common applications that could guide future research.

Unfortunately, cannabis studies are often small and performed with many limitations. Many studies cited within this literature were often based on self-report as the objective effects of cannabis have yet to be fully defined. Future research should look at external cannabinoid consumption and its modifying effects on the endocannabinoid system when facing detriment, while also exploring other potential benefits and risks. Further research should also investigate secondary metabolites of cannabis and their synergistic effects as well as the mechanism of action of phytocannabinoids (cannabinoids that occur naturally in the cannabis plant) to create target specific drug delivery systems. Understanding the mechanisms at the neurotransmitter level and its symbiotic relationship with opiate receptors will prove useful in pain management and addiction settings.

Most researchers believe that there will be an explosion of data in the coming years with the changing public perception of cannabis and the potential rescheduling of cannabis on the federal level. Nonetheless the proven efficacy of cannabis in pain management and cancer,

coupled with its other uses/benefits and rather safe side effect profile make it an excellent candidate for further exploration in substitute addiction research. While substituting is not appropriate for everyone, drug replacement or supplementation may exacerbate poor outcomes in certain populations. Many researchers believe that opiates are overall more harmful than cannabis²⁷ and some clinicians even believe that prescribing cannabis in place of opioids for pain may reduce the morbidity and mortality rates associated with prescription pain medications and as such may be an effective harm reduction strategy.^{28,30} There is a strong body of evidence that supports the theory that cannabis may be efficacious in opiate related harm reduction settings.

Conclusion

Cannabis can be rather challenging to study because of different plant species/strains, inconsistencies in the routes of administration, variations of systemic effects, metabolism and extraneous variables related to the research subjects. Current research suggests that cannabis has a great deal of potential for opiate related harm reduction and substitute therapies. Cannabis has been shown to improve opioid analgesic effects while reducing patient tolerance and dependence. There is well documented research on the efficacy of cannabis for the substitution of illicit drugs (opiates) and pharmaceuticals (opioids). In animal models' cannabinoids have been shown to reduce the effects of opiate withdrawal (and anecdotally in humans). As such cannabis could have the potential to decrease adverse outcomes and reduce drug seeking behavior in patients battling with opiate addiction.

Cannabis products are being explored for various medical conditions, including chronic pain, epilepsy, anxiety, nausea, and various mental health conditions. The administration of cannabis requires healthcare professional consultation and adherence to the prescribed dosages, as the effects of THC can vary significantly from person to person.¹⁸ As cannabis regulation evolves, so will the safety and availability of cannabis products. Unregulated cannabis products present a concerning aspect of the cannabis industry and more will be understood about dosing and route of administration in the future. Therefore, more research is needed, and the current findings are limited. Cannabis is further complicated by each country/state having different laws and regulations applying to it. As such, it is difficult to objectively determine appropriate use and application of cannabis (let alone scientific construct). It does appear that certain cannabinoid properties and even THC could be used to treat various conditions with improved knowledge of the endocannabinoid system (if proposed theories hold up as research progresses). However, precautions need to be taken with certain mental health disorders as cannabis should be avoided in patients prone to psychosis.

Future efforts should also investigate cannabis access, the overall effects of cannabinoids (positive and negative), standardized dosing of cannabis, and the methods of consumption as they pertain to overall health and dependence. Researchers should also seek to understand the role of cannabis and cannabinoids in both the affective and somatic components of opiate withdrawal as well as other psychiatric purposes. Future harm reduction models could differentiate between biomedical substitution for prescription pharmaceuticals and psychoactive drug substitutions. Regardless, a clear evidence base detailing potential harms of various cannabis compositions and concentrates as well as their neurobiological and behavioral mechanisms is paramount to harm reduction efforts. The literature and results of the research

performed supports the theory that cannabis may be efficacious in the setting of opiate substitution therapy and less harmful than current options. Nonetheless, more research is needed to confirm the trends found within literature. Research of greater scope and validity should be repeated on larger scales to better gauge public perception/education.

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Appendix A

The Survey questions were as follows:

1. Do you believe there are more harms associated with opiates or cannabis?
2. Do you believe that cannabis has a positive effect on mental health?
3. Do you believe that cannabis has a negative effect on mental health?
4. Do you believe that cannabis can be used to manage pain?
5. Do you believe that cannabis can be used as a tool to manage the withdrawal symptoms of opiates?
6. In the last 12 months has anyone you know used cannabis for an “off label” medical purpose?
7. Do you think cannabis should be legalized?