Featured Articles

...And What a Year it Was! ........................................4
N. el-Guebaly

Marijuana and the Workplace ..................................5
C. Els, A. Amin, S. Straube

Treatment of Cannabis Dependence with Synthetic Cannabinoids: A Systematic Review ...............8
A. Bahji, M.N. Mazhar

Culturally Specific Treatment Programs and the Muslim Community in Canada .........................13
S. Ahmed, N. Doukas

Naloxone Infusion in the Setting of an Unknown Ingestion: a Case Report ..............................19
R. Zivanovic, E. Wood, S. Nolan

25 Abstracts from CSAM-ISAM Montreal 2016 ...... 25
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...And What a Year it Was!

As we complete the fourth issue of our Journal for 2016, I cannot help but reflect on the extraordinary year our field has experienced in Canada. A major societal preoccupation has been the pending regulation of marijuana. An editorial by Els et al provides insight into the impact on the workplace of the use of marijuana. We look forward to feedback from the readership on this thoughtful piece with widespread implications. We also have an update by Bahji & Mazhar about the evidence behind the use of synthetic cannabinoids to address cannabis dependence.

The second national preoccupation started with concerns about the prevalence of opioid misuse, some of it iatrogenic. Soon, the tragic deaths of so many Canadians from fentanyl overdoses ensured daily coverage by our media, countless committees at all levels of government and promises of comprehensive remedial strategies. So far, the tangible result is that naloxone kits are now more accessible to deal with potential lethal crises. Some of the clinical complexities that may be involved in an “overdose” presentation are reported in Zivanovic’s et al paper. However, clinicians are still awaiting promised adequate resources to deal with lengthy waitlists for treatment beyond crisis intervention and ability to address the major physical and mental comorbidities involved. A naloxone kit is a critical band-aid but it does not substitute for adequate treatment to minimize relapses.

This year we were fortunate to host 550 attendants in a joint meeting of the International Society of Addiction Medicine (ISAM) and Canadian Society of Addiction Medicine (CSAM) in Montreal, October 20-23. We have selected 25 abstracts (10%) for your perusal, with implications for the Canadian context. They together outline future promises. The future of comprehensive opioid management was on full display with many Canadian investigators in the lead, with a panoply of measures under investigation that are complementary to the naloxone kits. Other abstracts addressed the need for an integrated approach to the management of opioid misuse with infectious diseases and psychiatric comorbidities.

We were also reminded that other substances continue to cause major societal burdens as well and should not be forgotten. Alcohol, nicotine, and stimulants among other drugs continue their detrimental consequences and should not be ignored. Evidence supporting progressive programs for the hospital and in the community was presented. Meeting the special needs of several groups were also highlighted including our aboriginal communities, LGBT groups as well as our gender and age specific requirements. Intriguing cannabinoid properties were also presented.

Further, we are proud to include a paper by Ahmed & Doukas addressing the rarely mentioned related needs of our Muslim communities; we hope to see more of these articles featuring the needs of our culturally diverse communities.

This editorial is a reminder that while the current limelight is on opiates and cannabis they should be viewed in the context of the wide spectrum of substances. Interventions must also be much more comprehensive than dealing with overdoses.

Lastly, our Journal is about to undergo a major structural change for 2017. We are in the final stages of negotiations with a well-known medical publisher, which should guide us towards a higher profile and eventual Impact Factor. Stay tuned hopefully for these exciting amendments in the next issues.

Very best of the New Year,

Nady el-Guebaly, MD
Editor-in-Chief, CJA-JCA
Marijuana and the Workplace

Charl Els a MBChB, FCPsych, MMed Psych, Aditi Amin MPH, MD, Sebastian Straube BM BCh, MA (Oxon), DPhil

ABSTRACT

The legal sale and consumption of marijuana for recreational purposes will likely become a reality in Canada in 2017. It remains the most commonly encountered substance in workplace drug testing, and given the substance’s impairing effects, the impact of its legalization will have on safety sensitive workplaces remains an insufficiently explored occupational risk issue. By extrapolating crash risk data, the authors conclude that single or recurrent marijuana consumption is not recommended for persons who perform safety sensitive tasks. Although further epidemiological research is needed, current evidence allows for an argument of precluding marijuana use, irrespective of source of procurement, in safety-sensitive jobs. A formal guideline development process should be initiated to provide evidence-based guidance on the issue of marijuana use in safety sensitive settings.

La vente et la consommation légales de marijuana à des fins récréatives deviendront vraisemblablement une réalité au Canada en 2017. Elle demeure la substance la plus couramment rencontrée dans le dépistage des drogues en milieu de travail et les effets de la légalisation sur les lieux de travail sensibles à la sécurité demeurent une question de risque professionnel insuffisamment explorée. En extrapolant les données sur les risques d’accidents, les auteurs concluent que la consommation de marijuana unique ou récurrente n’est pas recommandée pour les personnes qui effectuent des tâches sensibles à la sécurité. Bien que d’autres recherches épidémiologiques soient nécessaires, les données actuelles permettent d’exclure l’utilisation de la marijuana, quelle que soit la source de l’approvisionnement, dans les emplois sensibles à la sécurité. Un processus formel de développement des lignes directrices devrait être lancé pour fournir des conseils factuels sur la question de la consommation de marijuana dans des contextes sécuritaires.

After a century of prohibition, marijuana remains the most commonly used illicit substance in Canada, and the single most commonly encountered substance in workplace drug testing. In 2000 the Ontario Court of Appeal ruled that the total prohibition of marijuana possession was unconstitutional. Following this, and with arguably only low- and moderate-quality evidence supporting effectiveness of cannabinoids for medical use, Canada became the first country-wide jurisdiction in which marijuana could be authorized for medicinal use, with several other jurisdictions following suit.

The regulatory and legislative environment continues to change along with public attitudes toward marijuana - a more permissive approach appears to have developed. As per the Government of Canada’s expressed intent, Canada may become the first of the G7 group of countries with countrywide regulations in place to allow for use of both medicinal and recreational marijuana. To date, only Uruguay has fully legalized marijuana. The end of prohibition and the regulated, but legal sale and consumption of marijuana may become a reality in 2017 in Canada. However, several salient challenges have emerged, among others the anticipated impact this may have on occupational health, specifically as it pertains to safety-sensitive duties in workplaces. The term “safety-sensitive” (or “safety-critical”) refers to concerns that a performance error may result in the injury of a worker, coworkers or the general public, and/or disruption of equipment, production or the environment.

Marijuana contains more than 100 cannabinoids, some of which are centrally acting and which can result in adverse effects including cognitive and performance impairment. With consumption occurring via various routes, there currently exists no reliable method of controlling dose. Marijuana’s potency has increased over time, rising by an estimated factor of three in the last few decades, and there is also a rise in consumption of Butane Hash Oil (BHO, or “shatter”), containing 80 to 90 percent tetrahydrocannabinol.

Marijuana consumption has been demonstrated to have an adverse impact on a range of cognitive functions as well as be associated with performance deficits. In contrast to existing large-scale epidemiological evidence, and following limited testing in cannabis users (n=77) and controls (n=53), the COMPASS study found no difference in neurocognitive function after 1 year between these groups after adjustment for confounders. Of note, this finding is different from that found in other studies, i.e. systematic
reviews and a meta-analysis of fifteen studies, suggesting a broad range of impairments in various cognitive domains. It has been established that the cognitive skills required for safety-sensitive work tasks overlap to varying degrees with those required to safely operate a vehicle. Driving can be viewed as a proxy for determination of levels of impairment for other safety-sensitive duties. The required cognitive skills and capacities include unimpaired alertness, attention, concentration, coordination, reaction time, memory, ability to multi-task, perceptual abilities, thought processing, judgment, and insight. There is compelling evidence in support of the notion that marijuana, like alcohol and like opioids, can impair skills required for safe driving. A substantial body of epidemiological evidence demonstrates that cognitive impairments result in an increased risk for motor vehicle crashes. Two meta-analyses suggest that marijuana use is associated with an increased risk of motor vehicle crashes, and one of these suggests that is especially the case for fatal collisions. These two meta-analyses quantify the risk of motor vehicle crashes with marijuana use as roughly doubled, reporting statistically significant odds ratios of 2.66 and 1.92, respectively. There is also evidence for a dose-response relationship.

Extrapolation from crash risk data has been widely used to perform risk assessments in other settings, and it was the use of such extrapolation methods that resulted in the American College of Occupational and Environmental Medicine's guideline suggesting that the use of opioids is incompatible with working in safety-sensitive settings. Given that single or recurrent marijuana exposure can result in both cognitive and performance deficits, and is associated with an increased crash risk, the extrapolation of risk to safety-sensitive occupational settings appears reasonable.

Despite the established evidence that cannabis use prior to driving is an independent risk factor for motor vehicle accidents, the advice regarding the duration of such impairment following consumption appears inconsistent. The College of Family Physicians of Canada suggest that patients taking medical marijuana in the form of dried cannabis should be advised not to drive for at least four hours after inhalation, six hours after oral ingestion, and eight hours after inhalation or oral ingestion if the patient experiences euphoria. Yet, Health Canada states that the ability to drive or perform activities requiring alertness may be impaired for up to 24 hours following a single consumption. Other evidence suggests that some cognitive impairment may persist for longer post-consumption and may continue to exert impairing effects in executive functions even after 3 weeks of abstinence. Although occasional cannabis consumption can result in acute impairment of a range of cognitive functions, the long-term cognitive impact of cannabis is best demonstrated in chronic, heavy cannabis consumers, as opposed to occasional or light users. It is noted that a person consuming marijuana may be impaired despite feeling well, and also that an individual may test positive from past use but may not necessarily be impaired. Workplace drug testing does not measure impairment, but only the presence of the parent compound or its metabolite(s). Further, the degree of impairment following concurrent consumption of marijuana and alcohol is cumulative, and although users may be aware of deficits it has been suggested that they may only partially compensate for such decrements.

By extrapolation, we conclude that single or recurrent marijuana consumption is not recommended for persons who perform safety-sensitive tasks. This recommendation is extended beyond operation of motor vehicles to include any task that may require high levels of cognitive function and judgment, and may, furthermore, not be restricted to so-called safety-sensitive workers. In decision-critical settings, also, the cognitive and performance impairment resulting from marijuana use may pose a foreseeable threat to occupational safety.

On the contrary, it could be argued that reliance on motor vehicle crash data alone, and without supportive evidence specific to safety-sensitive workplaces may be insufficient to make the proposed extrapolations. It is the case that sufficient epidemiological evidence of non-driving activities in all safety-sensitive jobs is lacking. However, it is not feasible to wait to obtain direct data for each and every safety-sensitive position or task where marijuana consumption by workers may be anticipated. It is the norm for occupational health and safety guidelines to utilize evidence from other relevant populations when there exists a dearth for research for the target population. Creating the expectation that empirical studies have to be completed for every single safety-sensitive position, and that no extrapolation is allowed before we can assume that impairment caused by substance consumption may pose a risk, is unreasonable. It places an impossible burden of proof on adopting steps to ensure occupational safety. Adopting such approach could be considered a dereliction of duty, if argued from the opposing side. For example, what if a marijuana consuming person in a safety-sensitive position, involved in a serious accident, launches a tort case against a health provider or occupational health physician who authorized the use of marijuana, or declared the person (using marijuana) as fit for duty, while evidence suggested marijuana impairs driving capacity and increased risk? If it is reasonably foreseeable that if marijuana consumption impairs cognition, performance, and increases crash risk, it would also foreseeably increase risk in other safety-sensitive tasks. To date, the totality of evidence does not support the viewpoint that cognitive impairments related to marijuana use are not a problem in safety-sensitive positions. The burden of proof that consumption of potentially impairing substances under such circumstances is not hazardous would arguably be with the cultivators and distributors of the marijuana products. With the legalization of marijuana, the duty of
the Government of Canada in this regard has not been sufficiently explored. As of this writing, unsurprisingly most of the provincial medical regulatory authorities advise their members to caution workers on risks as well as benefits of consumption of marijuana. Such risks include working in safety-sensitive positions and operating a vehicle.

A weakness of this analysis of extrapolating crash risk data to safety-sensitive workers is the potential for unnecessary restrictions on persons who are not necessarily impaired, and who may not be at occupational risk. Further, there may emerge the increased potential for stigmatization of substance using individuals. The addicted population is already heavily stigmatized and this approach may result in lower levels of access to treatment.

The impact on specific safety-sensitive occupations and the threshold for determining impairment, as well as the duration of such, remain unclear. Further epidemiological research investigating this issue is needed. Despite the uncertainty, evidence would allow for an argument of preclusion of marijuana use, irrespective of source of procurement, in safety-sensitive jobs, unless absence of impairment could be demonstrated. The expansion of this analogy to other decision-critical positions, where consumption may also pose a potential risk, requires more in-depth analysis. The authors believe that following this preliminary analysis, a more formal guideline development process should be initiated, including a comprehensive literature review, identification of the relevant evidence, assessment of the quality of this evidence, and evidence synthesis, followed by application to practice by a multidisciplinary expert panel to develop guidance on the use of marijuana by workers with safety-sensitive duties.

REFERENCES:


Treatment of Cannabis Dependence with Synthetic Cannabinoids: A Systematic Review

Dr. Anees Bahji, MD, Dr. Mir Nadeem Mazhar, MBBS, FRCP, ABAM

ABSTRACT:

Introduction: The purpose of this systematic review is to assess the efficacy of synthetic cannabinoid preparations for the treatment of cannabis dependence. The authors reviewed literature on the use of synthetic cannabinoids in treating patients with cannabis dependence.

Methods: A search of five databases yielded eligible studies. We extracted information pertaining to study setting and design, demographic information, diagnostic criteria, the type of synthetic cannabinoid preparation used, and the efficacy of the treatment. Treatment outcomes were cannabis use, cannabis withdrawal, and patient retention in treatment.

Results: There is some evidence that dronabinol and nabiximols reduce cannabis withdrawal and improve retention in treatment, but these findings were not consistent across all studies. There is no definite evidence that synthetic cannabinoids decrease cannabis use.

Conclusion: The use of synthetic cannabinoids for cannabis dependence should still be considered experimental due to limited evidence of efficacy. Further research should compare the efficacy of different synthetic cannabinoid preparations at different doses and for longer durations of treatment.

INTRODUCTION:

Tetrahydrocannabinol (THC) is the primary psychoactive ingredient found in the cannabis plant1. THC is a partial agonist of the cannabinoid receptors, CB1 and CB21. The discovery of these receptors in 1988 led to the discovery of the endocannabinoid system – a series of naturally produced cannabinoids that stimulate the same receptors as THC, but in a far more selective manner1. Although we are capable of synthesizing our own endogenous cannabinoids, the psychoactive properties of THC have led to the criminalization of cannabis in many countries2. Despite being illegal, cannabis continues to be the most widely cultivated, produced, trafficked and consumed illicit drug worldwide3. In fact, the estimated cumulative, lifetime incidence of cannabis use among different countries varies from 0.3 to 42.4%4. But when does cannabis use become problematic?

According to the Fourth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), cannabis dependence is defined as a maladaptive pattern of cannabis use leading to significant impairment and distress, manifested by tolerance, withdrawal, using cannabis in larger amounts or durations than desired, and having a persistent desire or unsuccessful efforts to cut down or control cannabis use5. The lifetime prevalence of cannabis dependence is estimated to be 1.3% in the United States, and it is estimated that roughly one in eleven cannabis users will develop cannabis dependence6. Cannabis users are also more likely to use other substances, and to have comorbid mood and anxiety disorders5,6.

In recent years, much research has been done on developing effective non-pharmacologic and pharmacologic treatments for cannabis dependence, the latter focusing...
mostly on the modulation of known neurotransmitter systems – the serotonin, dopamine, and norepinephrine pathways\(^7,8\). Studies have examined existing psychotropic medications for their ability to reduce cannabis withdrawal symptoms or decrease actual cannabis use, but none of these drugs have shown significant potential for treating cannabis dependence to date\(^8\).

In the past, there has been success using agonist replacement therapies for other substance use disorders, such as nicotine replacement for tobacco use disorder, methadone for opioid use disorder, and more recently, benzodiazepines for benzodiazepine dependence\(^9,10\). In theory, agonists of the endogenous cannabinoid receptors (CB1 and CB2) could treat cannabis withdrawal symptoms, and possibly, cannabis dependence\(^11\). Currently, several different THC agonists are available, and have been tested for their potential for treatment of cannabis dependency, including dronabinol (Marinol), nabilone (Cesamet), and nabiximols (Sativex). While these have shown some promise in reducing cannabis withdrawal symptoms in monitored laboratory settings, it is unclear if these results will translate to clinical settings\(^12\).

In this systematic review, we explore the existing scientific literature for an answer to a very simple question: can synthetic cannabinoids be helpful in the treatment of cannabis dependence?

**METHODS:**

**DATA SOURCES AND TERMS USED:**

A literature search was conducted of EMBASE, Medline, PsychInfo, PubMed and Cochrane Systematic Reviews databases for eligible studies. Search terms included nabilone/cesamet, dronabinol/marinol, nabiximols/sativex, cannabis use disorder, cannabis dependence, cannabis abuse, marijuana addiction, mental and behavioural disorder due to use of cannabinoids, treatment, efficacy, effectiveness. Mental and behavioural disorder due to use of cannabinoids was included as a search term because it is the ICD-10 equivalent of cannabis use disorder. The search included all studies until March 15, 2016. Please refer to Figure 1 for details of our search strategy in pictographic form.

**STUDY SELECTION:**

Studies fulfilling the following criteria were included in this review: 1) randomized controlled trials; 2) inclusion of synthetic THC/treatment/intervention with synthetic cannabinoids; and 3) diagnosis of cannabis dependence/ cannabis use disorder/mental and behavioural disorder due to use of cannabinoids using valid diagnostic criteria. The inclusion criteria were developed by the first author and reviewed by the co-authors.

Studies with the following characteristics were excluded from the systematic review: 1) no synthetic cannabinoid used (e.g., antidepressants, antipsychotics); 2) psycho-social intervention as a primary intervention; 3) non-randomized controlled trials; 4) lack of valid diagnostic criteria (e.g., those who simply used cannabis).

**DATA EXTRACTION:**

The following data were extracted from each study: country of study, publication year, number of participants, study setting (inpatient, outpatient), study design, study duration, gender distribution, mean age and age range of the participants, diagnostic criteria applied for cannabis use, intervention applied, controls used, primary and secondary outcomes, and commentary on treatment adherence and adverse effects if available. The supervising author conducted data extraction. A meta-analysis could not be conducted due to heterogeneous characteristics of selected studies.

**RESULTS:**

The EMBASE, Medline, PsycInfo, PubMed, and Cochrane Systematic Reviews database searches identified 13, 17, 15, 42, and 2 studies, respectively. Both authors reviewed study titles and abstracts independently, and 66 studies were identified as potentially relevant after removal of duplicates. These studies were reviewed in full by the first author, and 47 were excluded, as they were clearly off-topic during the abstract and title screen. Of the remaining 19, further review of the full-text articles found that 7 studies did not use a randomized control trial format, and 9 studies did not use a synthetic cannabinoid as a primary intervention. Ultimately, 3 studies were found to be eligible for analysis in the systematic review. It was agreed that the supervising author’s decision would prevail in case of any potential disagreements. The first author subsequently conducted a hand search of the references of the three eligible studies, identifying no additional relevant studies.

Table 1 lists the characteristics of studies assessing the use of synthetic cannabinoids in patients with cannabis dependence. All three studies used DSM-IV criteria for the diagnosis of cannabis dependence\(^5\).

The 2015 study by Levin et al. evaluated the use of...
lofexidine and dronabinol for the treatment of cannabis dependence in 156 people, finding that the concurrent administration of lofexidine and dronabinol was not more effective than placebo for promoting abstinence, reducing withdrawal symptoms, or retaining individuals in treatment.

The 2011 study by Levin et al. evaluated the use of dronabinol for the treatment of cannabis dependence in 122, finding dronabinol to be superior to placebo in promoting retention in treatment and in reducing withdrawal symptoms; however, the overall proportion of patients achieving sustained abstinence was low, and there was no evidence for an advantage of dronabinol over placebo on the outcome of cannabis use.

The 2014 study by Allsop et al. evaluated the use of nabiximols for the treatment of cannabis dependence in 51 people, and they found that nabiximols attenuated cannabis withdrawal symptoms and improved patient retention in the treatment; however, placebo was just as effective as nabiximols in promoting long-term reductions in cannabis use following medication cessation.

DISCUSSION:

Cannabis dependence can be divided into two separate, but related, concepts: physical dependence and psychological dependence. The former can be thought of as a cannabis-specific adaptation associated with a specific withdrawal syndrome that can be produced by abrupt discontinuation or decreasing the blood levels of THC. The latter is consistent with the traditional description of addiction, as a primary, chronic, neurobiological disease with multiple genetic, environmental, and psychosocial contributions leading to impaired control, compulsive use, and cravings. It is this pattern of psychological dependence that most closely fits the idea of cannabis dependence as described by the DSM-IV; however, the term cannabis use disorder, as used by DSM-V, is more comprehensive, and includes the physical dependence component of cannabis use.

In our systematic review, we explored the medical literature to determine if synthetic cannabinoids were effective treating cannabis dependence. Although our review did not find overwhelming evidence for synthetic cannabinoids in reducing cannabis use or cannabis withdrawal, we found that there is potential for nabiximols and dronabinol in lowering cannabis withdrawal symptoms. This makes logical sense when we realize that nabiximols and dronabinol target the same CB1 and CB2 receptors that bind THC, and function as agonist substitutes for THC. However, reducing cannabis withdrawal symptoms only addresses the physical dependence component of cannabis dependence: what about the psychological dependence?

Unfortunately, our systematic review was unable to address this issue because we excluded studies that included psychological therapies. We know from the existing literature that non-pharmacologic interventions are essential in addressing psychological cannabis dependence. Thus, to determine if synthetic cannabinoids can effectively treat cannabis dependence, studies that combine pharmacologic and non-pharmacologic approaches are needed. Additionally, studies that involve a longer duration of treatment would be helpful; of the studies included in this review, the longest duration of treatment was only 12 weeks. Longer studies would provide more data about the efficacy of synthetic cannabinoids, would enable better follow-up and monitoring of participants. Furthermore, two studies were done in an inpatient setting, while the other was done on an outpatient patient, so we are unable to comment on the efficacy of community treatment settings. In reality, most cannabis dependence is treated in the community, as it is rare that someone would get hospitalized for cannabis use or related issues.

Future directions may consider exploring how different cannabinoid preparations compare to each other. In our review, each study only looked at single preparations versus placebo, we could not find studies comparing different preparations (e.g., nabilone versus dronabinol versus nabiximols). Unfortunately, the current legal climate has limited the availability of different synthetic cannabinoid preparations in different countries, and has by extension restricted the types of research that could be conducted. For example, dronabinol is no longer available in Canada, and nabiximols is only approved in Canada for neuropathic pain in patients with multiple sclerosis. Other barriers to recruiting participants for research of cannabis dependence mirror barriers to accessing treatment for cannabis dependence, and these include a general lack of interest in treatment, a lack of motivation and knowledge of treatment facilities, an overall lack of treatment facilities, the costs associated with treatment, and difficulty meeting treatment program eligibility criteria.

Studies with greater numbers of participants would be helpful in assessing efficacy of synthetic cannabinoids. In our review, the highest number of participants in a single study was 156. Given that legal factors are also of significance and that many people with cannabis dependence may fear seeking medical support if they run the risk of facing criminal charges for cannabis possession, this may be a barrier in recruiting high numbers of participants in studies. This warrants the question: what role does the legal status of cannabis play in the prevalence of cannabis dependence?

In recent years, recreational, or non-medical use of cannabis has become legal in several American jurisdictions,
including Washington, Colorado, and California\textsuperscript{24-26}. There are also formal discussions underway regarding legalization of non-medical cannabis in Canada\textsuperscript{2}. Some argue that decriminalization of non-medical cannabis possession may eliminate some of the harms of prohibition, however, there are also significant concerns that ongoing policy changes in favour of legalization may increase use of cannabis by young people\textsuperscript{27,28}. Although there is a lack of evidence to support a causal effect between cannabis policy changes and actual cannabis use, policy changes in favour of legalization have been associated with reduced risk perception; thus, a nuanced understanding of the impact of legal status is needed in order to build evidence for future policy options\textsuperscript{28}. A recent Canadian study found that the second most commonly abused substance involved in emergency department visits was cannabis\textsuperscript{29}. This finding suggests that cannabis use continues to be a significant driver for emergency room visits and legalization may increase the number of emergency room visits related to cannabis use in the future.

Despite popular depictions of recreational cannabis as a safe, innocuous, and sometimes health-promoting substance\textsuperscript{30,31}, cannabis remains a potent psychoactive substance, with numerous effects on the central nervous, cardiovascular, cerebrovascular, respiratory, gastrointestinal, immune, and reproductive systems\textsuperscript{16,32,33}. Particularly, there is some evidence that sustained cannabis use in adolescence can contribute to early presentations of psychosis and can worsen established psychosis\textsuperscript{34,35}. Overall, epidemiologic evidence has warranted a message that cannabis can increase the risk of psychotic disorders; however, a causal relationship has yet to be established\textsuperscript{33,34}. Additionally, further studies are required to determine the magnitude of this effect, to determine the effect of different strains of cannabis on risk, and to identify high-risk groups particularly susceptible to the effects of cannabis on psychosis\textsuperscript{35}.

Overall then, there is insufficient data to evaluate the effectiveness of synthetic cannabinoids in the treatment of cannabis dependence and it warrants further investigation. More research is needed to find effective treatments for cannabis dependence, and particular clinical targets could include achieving abstinence, reducing cannabis use, and reducing withdrawal in dependent patients seeking treatment for their cannabis use.

**FIGURE 1: LITERATURE SEARCH STRATEGY**

- **PSYCHINFO**
  - Until Mar 15, 2016
  - 13 citation(s)

- **EMBASE**
  - Until Mar 15, 2016
  - 17 citation(s)

- **MEDLINE**
  - Until Mar 15, 2016
  - 15 citation(s)

- **PUBMED**
  - Until Mar 15, 2016
  - 42 citation(s)

- **COCHRANE SYSTEMIC REVIEWS**
  - Until Mar 15, 2016
  - 2 citation(s)

- **66 Non-Duplicate Citations Screened**

- **Inclusion/Exclusion Criteria Applied**
  - 7 Articles Excluded
    - During Data Extraction: did not use synthetic cannabinoid as primary intervention

- **19 Articles Retrieved**

- **Inclusion/Exclusion Criteria Applied**
  - 9 Articles Excluded
    - After Full text Screen: did not use synthetic cannabinoid as primary intervention
  - 3 Articles Included

- **19 Articles Excluded**
  - During Data Extraction: non-RCT
### REFERENCES


### TABLE 1: CHARACTERISTICS OF STUDIES INCLUDED IN SYSTEMATIC REVIEW

<table>
<thead>
<tr>
<th>Author</th>
<th>Country</th>
<th>Year</th>
<th>Participants</th>
<th>Setting</th>
<th>Gender</th>
<th>Mean Age</th>
<th>Interventions</th>
<th>Treatment Outcomes</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levin et al</td>
<td>USA</td>
<td>2015</td>
<td>156</td>
<td>Outpatient</td>
<td>68.8% male</td>
<td>35.1 years</td>
<td>Lofexidine and dronabinol versus placebo</td>
<td>No reduction in cannabis use. No reduction in cannabis withdrawal. No improvement in retaining individuals in treatment.</td>
<td>11 weeks</td>
</tr>
<tr>
<td>Levin et al</td>
<td>USA</td>
<td>2011</td>
<td>122</td>
<td>Outpatient</td>
<td>82.1% male</td>
<td>37.6 years</td>
<td>Dronabinol versus placebo</td>
<td>No reduction in cannabis use. Some reduction in cannabis withdrawal. Some improvement in retaining individuals in treatment.</td>
<td>12 weeks</td>
</tr>
<tr>
<td>Allsop et al</td>
<td>Australia</td>
<td>2014</td>
<td>51</td>
<td>Mixed</td>
<td>76% male</td>
<td>35.4 years</td>
<td>Nabiximols versus placebo</td>
<td>No reduction in cannabis use. Some reduction in cannabis withdrawal. Some improvement in retaining individuals in treatment.</td>
<td>4 weeks</td>
</tr>
</tbody>
</table>
ABSTRACT

Objective: Despite Islam's prohibition against substance use, alcohol and illicit drug use is a growing concern among Muslims. This will place a burden on North American substance use treatment agencies when considering that the Muslim population continues to grow in Western society, as does the growing rate of alcohol and drug consumption among this population.

Method: The researchers reviewed each Canadian province and territory’s substance use treatment registry in order to identify agencies that provide a culturally specific provision of care to meet the treatment needs of Muslims residing in Canada.

Results: After a careful review of all provincial and territorial substance use treatment registries it was found that all provinces provide extensive Aboriginal specific programming, but Ontario and Alberta were the only two provinces to provide ethno-specific services other than Aboriginal services. None of the ethno-specific services accommodated Canada’s Muslim population.

Conclusion: Substance use treatment services tailoring to the diversity of a Canadian mosaic will need to seriously consider allocating significant funds toward culturally specific services.

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Aboriginal services. None of the ethno-specific services accommodated Canada’s Muslim population.

Conclusion: Substance use treatment services tailoring to the diversity of a Canadian mosaic will need to seriously consider allocating significant funds toward culturally specific services.

Objective: Malgré l’interdiction de l’usage de la drogue par l’Islam, l’alcool et la consommation de drogues illicites sont de plus en plus préoccupants parmi les musulmans. Cela représentera un fardeau pour les agences nord-américaines de traitement de l’alcoolisme et les toxicomanies quand on considère que la population musulmane continue de croître dans la société occidentale, tout comme le taux croissant de consommation d’alcool et de drogues chez cette population.

Méthode: Les chercheurs ont examiné chaque registre canadien de traitement de la toxicomanie de la province et du territoire afin d’identifier les organismes qui fournissent une prestation de soins adaptée aux besoins culturels afin de répondre aux besoins de traitement des musulmans résidant au Canada.

Résultats: À la suite d’un examen minutieux de tous les registres provinciaux et territoriaux de traitement de la toxicomanie, on a constaté que toutes les provinces
for several decades, Canada has been seeing a rapidly changing landscape of ethno-cultural and religious diversity in which many non-Westerners who have migrated to North America are adopting and acculturating to Westernized values and customs. Among these adopted customs is consuming fast food and pop-culture media, as well as the consumption of mind altering substances, even though many non-Western communities have prohibited the intake of drugs and alcohol based on their religiosity. For example, despite Islam’s prohibition against substance use, alcohol and illicit drug use is a growing concern among Muslims. This will place a burden on North American substance use treatment agencies when considering that the Muslim population continues to grow in Western society, as does the growing rate of alcohol and drug consumption among this population. In fact, a report released by the Pew Research Center on, The Future of The Global Muslim Population, estimated a growth from 940,000 in 2011 to 2.7 million Muslims in Canada by 2030, comprising roughly 6.6% of the total Canadian population.

While seeking treatment for substance use may seem like a prudent decision, the stigma associated with drug and alcohol use has traditionally resulted in barriers to seeking treatment among Muslims. Another possible barrier to treatment seeking among non-Westerners is the belief that Western, Anglo-based treatment services may not cater to one’s cultural needs. Muslims residing in North America are more recently beginning to enroll themselves in treatment for problematic substance use, which highlights the need for Muslim specific services. This changing landscape among Canada’s population demands appropriate treatment services for its multicultural community. Fortunately, provinces and territories across Canada provide easy access to substance use treatment registries that allow both professionals and the general public to access. This allows people to view these treatment registries in order to locate tailored services.

In order to understand the extent to which Canada can meet the treatment demands of a growing diversified Muslim population, it is necessary to identify appropriate treatment programs across Canada. The authors searched all provincial and territorial substance use treatment registries in Canada to identify services that provide an Islamic provision of care to its clientele.

LITERATURE REVIEW

When searching for available studies conducted on substance use and the Muslim population the literature is limited, but there is a growing trend that points to college students as an area of interest. Alcohol consumption among U.S Muslim rates is higher when compared to students in predominantly Muslim countries, specifically Egypt and Jordan. In Egypt, a study conducted amongst a sample of 687 college students to examine awareness and practice of risk behavior among university students showed that 18% engaged in risk behavior such as tobacco, substance and unprotected sexual activity. In Jordan, a study conducted amongst 5064 university and college students to examine the impact of substance use among students and their attitude towards substance use showed that 12% of students reported using alcohol and 29% reported using tobacco. Compared to 46.6% of U.S Muslim students, only 18% of students in Egypt reported to engage in risk behaviors such as tobacco, substance use and unprotected sexual activity, and even lower in Jordan, with 12% of students having reported the use of alcohol. Other studies on substance use conducted in Arab countries reveal that alcohol and drug use is on the rise in Lebanon and Kuwait, which may be attributed to social and economic factors. However, these factors have not been further investigated due to the stigmatization of substance use in the Middle Eastern. In the study conducted in Kuwait researchers reviewed 747 clients admitted to a psychiatrist ward and found that 9.5% of patients were diagnosed with alcohol and drug use disorders. In a more recent study researchers reviewed a sample of 1394 adults from the UAE in where substance use was included as a variable and found that only 1% of participants reported substance use to be a concern on an individual level. However, when these participants were asked about substance use in relation to their behavior at home such as interpersonal issues, the rate of substance use rose from 1% to 5.2%. As evident, the literature demonstrates increasing rates of substance use among Muslims on a global level. Research on substance use among Muslims has been accumulating over the last two decades and showing a significant need to develop appropriate treatment services.
CULTURAL DIFFERENCES IN THE ISLAMIC WORLD

Islam involves peoples of many different races, ethnicities and cultures, many literatures and languages, with many histories, and a myriad of interpretations some of which may conflict with each other. Islam spread beyond the Middle East into many different regions, ranging from China to Bosnia to Zanzibar, and came to be understood in many different cultural ways. This diversity was the result of the core set of religious beliefs interacting in complex ways with the many different contexts including history, cultural traditions, social, economic, political structures, and geography and physical location in the world. Despite the multitude of cultural differences in Muslim majority counties, one of the main fundamental concepts of Islam is protecting and promoting life and good health in all circumstances during all stages of life. This is why Islamic scholars agree that any substance that causes intoxication and harm to the body is not permissible and considered forbidden (haram). Therefore, Muslims can internalize feelings of guilt and shame due to the stigma associated with substance use which is spread from the teachings of the Islam.

STRENGTHS AND LIMITATIONS OF PROVIDING CULTURALLY SPECIFIC TREATMENT SERVICES

Canada's diversity has important implications for treatment programs, which is why administrators should consider the strengths and limitations when developing culturally appropriate services for Muslims residing in Canada. Below are some reasons for pursuing this effort that has been compiled by the Center for Substance Abuse Treatment (2006):

- Individuals from minority groups can be a significant—even majority—sector of potential clients.
- Understanding and appreciating a client's cultural background expand treatment opportunities. Every culture has specific values that can be used in treatment, such as the support of extended families and of religious or spiritual communities.
- Enhancing the sensitivity and capacity to treat clients from other cultures improves a program's ability to treat all clients.
- Cultural competence is increasingly a requirement of funding and accreditation bodies.
- The ability to attract and serve ethnic clients is a financial issue. Improvements in cultural competence may contribute to improved client retention.

When reviewing the literature that investigates cultural competence, three positions have been articulated after researchers conducted meta-analysis on the topic. First, researchers have concluded in their meta-analysis that cultural competency interventions have a moderate positive effect. In the second study, researchers take a more cautious position because of the lack of adequate tests for cultural competency effects. Nevertheless, these researchers' position is that: "In the absence of efficacy studies, the combined use of protocols or guidelines that consider culture and context with evidence-based care is likely to facilitate engagement in treatment and probably to enhance outcomes" (p. 20). In the third study researchers concluded that overall treatment effects of their analysis showed medium magnitude. In light of the varying results on this topic that range from moderate to likely to medium, further research is needed. A strong support regarding methodologies for tailoring evidence-based interventions for specific populations would be extremely helpful. Because culture is continually evolving, the ability to identify factors that are amendable to adaptation, while maintaining the critical ingredients of care, would provide a methodology for continually ensuring that care is sensitive to the needs and concerns of any client group (p.20). In addition, properly assessing the effectiveness of interventions regarding treatment retention and abstinence from substance use for example, may improve with clinical trials using control groups.

PROCEDURE

The researchers reviewed each Canadian province and territory's substance use treatment registry in order to identify agencies that provide a culturally specific provision of care to its clientele. Please refer to Appendix A.

RESULTS

After a careful review of all provincial and territorial substance use treatment registries it was found that all provinces provided extensive Aboriginal specific programming, but Ontario and Alberta were the only two
provinces to provide ethno-specific services other than Aboriginal services.

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Based on the results of this study’s search, locating a Muslim specific program was explored on a global level through a Google search using key words Muslim, addiction, treatment, program. This search generated only one Muslim specific program. This search was conducted to review any previously developed programs that can serve as guideline towards developing future tailored substance use treatment programs for Muslims residing in Canada. Below is an example of a treatment program developed for Muslims residing in Sydney, Australia:

**Hayat House** (Hayat, the Arabic word meaning ‘life’) is designed to be a culturally appropriate, community-based drug and alcohol addictions rehabilitation program that meets the needs of Sydney’s diverse Muslim community. Hayat House provides community-based substance abuse assessment, counselling (individual, couple, family and group), casework and rehabilitation to Muslim individuals and their families. Below are the services provided in this program:

**Assessment and Counselling** - Individual counselling will be provided 2 days per week. Some after-hours counselling will be available depending on availability.

**Weekly Group Therapy** - All groups will run for approximately 2 hours and will incorporate both the Millati Islami principles as well as a psychological topic revolving around wellbeing and self-care. Groups will be facilitated by trained counsellors.

**The Millati Islami 12-step Program** - Millati Islami is a fellowship of men and women, joined together on the “Path of Peace”. They share experiences, strengths and hopes while recovering from an active addiction to mind and mood altering substances.

The spiritual and religious intentions behind the initiation for this project to meet the ultimate objectives of the maqasid al-shariah which are necessary (al-daruriyah) for humans to function and live peacefully in this world according to the Qur'an and Sunnah. These include protection of life, protection of religion, protection of human generation or procreation, protection of intellect or mind, and lastly protection of wealth or resources.

Hayat House hopes to reach these ultimate objectives by assisting Muslims from further harming their health and lives from addiction with the aim to guide them towards abstinence from drugs and alcohol.

**DISCUSSION**

Among the hundreds of agencies available across Canada that provide a substance use component of treatment, only three programs other than Aboriginal, were identified as having a specific cultural element to their provision of care. It was found that many Canadian agencies particularly in major cities do their best to provide a diversified array of languages to converse in with clients whose first language is not English. Language centres primarily provide basic translation services for multi-service agencies, and mental health and health clinics. However when one considers the intensity of a structured full-time treatment program, where clients will spend the good part of their day in treatment, or even residing in the treatment centre for a few weeks, then one has to go beyond just language to accommodate diversity in a client’s therapeutic journey.

Treatment providers need to be careful not to make assumptions about a client’s culture and values based on race or ethnicity. When trying to avoid stereotyping, clinicians must be mindful that each client is a unique individual, and that culture is complex and not easily reduced to a simple description. Having an observation that appears accurate and helpful when applied to a large group of people may be misleading and harmful if applied to an individual. It is hoped that the utility of offering broad descriptions of cultural groups outweighs the potential misunderstandings. We are reminded that counselors need to find a balance between understanding clients in the context of their culture and seeing clients as merely an extension of their culture. Culture is only a cultural issue that will affect acceptance and treatment. How strongly individuals share the dominant values of their culture varies and depends on numerous factors, including their education, socioeconomic status, and level of acculturation to U.S. society.

Substance use treatment services tailoring to the diversity of a Canadian mosaic will need to seriously consider allocating significant funds toward culturally specific services, and be mindful that staff composition influences the increase in treatment initiation and retention. Canadian treatment agencies also need to consider sociocultural issues that will affect acceptance and treatment outcome. Involving family and community is another
component that should be considered when delivering treatment to those of a non-Western background because restorative efforts to repair an individual’s familial and social network can buffer the effects of alcohol or drug abuse. This familial/community involvement in recovery makes all the more sense when considering the importance of what Abbott calls cultural recovery: “Cultural recovery involves regaining a viable ethnic identity and acquiring a functional social network committed to the person’s recovery; making religious, spiritual, or moral recommitment; re-engaging in recreational or vocational activities; and gaining a social role in the recovering community, society at large, or both. Those individuals who fail to make a satisfactory recovery are at risk for re-addiction.” It is not within the scope of this paper to create a more comprehensive list of things to consider when developing programs to meet the substance use treatment needs of Canada’s Muslim population, but the paper has provided a few essential examples that should be considered among program developers.

CONCLUSION

This paper raises awareness on the growing North American Muslim population and those seeking substance use treatment despite the extreme stigma associated with Islam’s prohibition against the consumption of mind altering substances. This paper alerts researchers, policy makers, program developers, front line staff and the Canadian population about the lack of cultural diverse substance use treatment programs available in Canada. It is time that Canada weaves the mosaic tapestry of cultures that it is comprised of into its substance use treatment programs.

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APPENDIX A

These sites were accessed on the worldwide web between March 18, 2016 and March 29, 2016.


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Naloxone Infusion in the Setting of an Unknown Ingestion: A Case Report

Rebecca Zivanovic, MD, Evan Wood, MD, FRCP©, Seonaid Nolan, MD, FRCP©

ABSTRACT

Drug-related overdoses and deaths are a major public health concern in Canada. Reasons for this include high rates of opioid and benzodiazepine prescribing in addition to a surge of high potency opioids, such as fentanyl, in Canada’s illicit drug markets. The vast majority of opioid-related overdose deaths are accidental in nature and require emergency resuscitation with naloxone, a pure mu opioid receptor antagonist. Though established as an effective antidote for opioid overdose, there is some literature to suggest naloxone may also be an effective intervention for a variety of non-opioid toxicities. Here we report a case of a patient who presented to the emergency department of an urban hospital located in downtown Vancouver, Canada due to an overdose after intentionally ingesting multiple unknown illicitly purchased pills. Despite empiric treatment with a naloxone infusion, which was associated with clinical improvement, the patient’s urine mass spectrometry collected over 40 hours after initial presentation was negative for all opioids and their metabolites. This case reinforces the importance of prompt urine drug screen collection and emphasizes the complexity in detecting a potential high-potency opioid overdose. Furthermore, it highlights the potential difficulty in differentiating the clinical presentation of a benzodiazepine from opioid induced overdose and considers what role, if any, naloxone might play in the management of a non-opioid toxicity.

INTRODUCTION

Drug-related overdoses and deaths are a major public health concern in Canada. Though comprehensive national data is lacking, provincial trends clearly demonstrate an alarming increase in overdose deaths attributable to illicit drugs. In British Columbia, for example, approximately 465 illicit drug overdose deaths occurred in 2015, a 27% increase from just one year prior. The recent emergence and increased availability of fentanyl in illicit drug markets has contributed substantially to the increasing number of drug overdoses and deaths and, as a result, have become an increasing public health concern. Furthermore, prescription drug overdoses, of which opioids and benzodiazepines are major contributors, are widely recognized to be responsible for a significant number of preventable deaths. The role of naloxone

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Key words: overdose — naloxone — drug use — opioid toxicity — benzodiazepine toxicity
(Narcan) in treating opioid overdoses has previously been well described. In brief, naloxone is a pure mu receptor antagonist that reverses opioid-induced depression of both the respiratory and central nervous system by displacing bound opioids from the mu receptors and preventing new opioid binding at these sites. The half-life of the drug is approximately 60-90 minutes requiring infusion or repeat administration in instances where longer acting opioids are responsible for opioid toxicity. Naloxone is a well-established antidote for opioid overdose and should be given empirically to any patient suspected of opioid toxicity. Beyond its typical role in the treatment of opioid overdose, however, studies have suggested naloxone to be an effective intervention for a variety of non-opioid toxicities including clonidine, valproic acid or ramipril intoxication or ethanol-induced coma. Though limited by its small sample size, one study demonstrated clinical improvement among patients presenting with a benzodiazepine overdose after the administration of naloxone. Additionally, the beneficial role of naloxone in the treatment of concurrent benzodiazepine and opioid overdose has also previously been described. Here, we report a case of a patient who presented to the emergency room of an urban hospital located in downtown Vancouver, Canada due to an overdose after intentionally ingesting multiple unknown illicitly purchased pills in an attempt to commit suicide. Despite empiric treatment with a naloxone infusion, which was associated with clinical improvement, the patient’s urine mass spectrometry was negative for all opioids and their metabolites.

CASE REPORT

A 55-year-old Indigenous woman was found to be unresponsive by support workers in her housing facility at approximately 13:30 on the day of hospital admission. Drug paraphernalia including previously used needles and other injecting equipment were also found in proximity. At the time of emergency health services (EHS) arrival, the patient was briefly rousable to painful stimuli only and had a Glasgow coma scale (GCS) score of 10. No further history could be obtained. On physical examination she was afebrile, her blood pressure (BP) was 112/56 mmHg, heart rate (HR) 121 beats per min (bpm), respiratory rate 18 breaths per min with noted periods of apnea, her oxygen (O₂) saturation was 90% on room air (RA) and her blood glucose level was 5.8 mmols/Litre. Her pupil size was documented as being difficult to assess. Given the high index of suspicion for an opioid overdose, 0.8 milligrams (mg) of naloxone was administered intramuscularly (IM) at 14:07. Almost immediately, the patient’s level of consciousness improved, her GCS increased from 10 to 13 and her oxygen saturation increased to 97% on RA. She was subsequently transferred to an urban hospital located in downtown Vancouver, Canada.

On admission, though no further history could be obtained from the patient, old hospital records noted a past medical history significant for a stimulant use disorder, chronic obstructive pulmonary disease, hypertension, hyperlipidemia and non-ischemic cardiomyopathy with an implantable cardioverter-defibrillator in-situ and last known ejection fraction of 45%. A review of the patient’s Provincial prescription database revealed recent prescriptions for the following medications: atorvastatin, clopidogrel, escitalopram, ferrous gluconate, furosemide, metoprolol, ramipril, topiramate, spironolactone and fluticasone/salmeterol, ipratropium and salbutamol metered dose inhalers. Her admission examination revealed a temperature of 36.9 degrees Celsius, BP of 140/71 mmHg, HR of 78 bpm, respiratory rate of 16 breaths per minute and O₂ saturation of 99% on 2L nasal prongs. Her pupils were 4mm bilaterally. She was drowsy but irritable, moving all four extremities and responded to painful stimuli. Her cardiovascular, pulmonary and abdominal examinations were all normal. Initial blood work including a complete blood count, electrolyte profile, calcium, magnesium, phosphorous, urea, creatinine, liver enzymes, international normalized ratio, lactate, troponin, anion and osmolar gaps were all normal. The patient was found to have a mildly low albumin at 32 grams/Litre as well as a respiratory alkalosis (pH 7.43, bicarbonate 21) (likely secondary to recent naloxone administration). Serum toxicology screening for acetaminophen, salicylic acid and ethanol were negative. A urinalysis collected during the first night of admission was positive for red blood cells and white blood cells; this sample was cultured and later confirmed to be positive for >100 million CFU/L of E. coli. Blood cultures were sent and later reported to be negative. An electrocardiogram (ECG) revealed a sinus tachycardia with a rate of 121 bpm and a QTc of 514 milliseconds. Imaging revealed a normal chest x-ray and computed tomography scan of the head. Unfortunately no urine drug screen (UDS) was sent at the time of hospital admission.

Approximately 2 hours after her initial naloxone dose, the emergency physician noted a decrease in the patient’s level of consciousness. Her pupils were noted to be miotic. Over the ensuing 2 hours a total of 3.2 mg of naloxone was administered intravenously in 6 separate doses with the patient’s level of consciousness temporarily responding after each dose. Of note, there was no significant change in her respiratory rate or O₂ saturation throughout this time. Following this, the patient’s BP was 115/80 mmHg, HR 99 bpm, she remained afebrile and had a respiratory rate of 12 breaths per minute with an O₂ saturation of 99% on 2 litres by nasal prongs. She was responding only to painful stimuli. The emergency physician initiated a naloxone infusion at 0.6mg/hour (hr) at 18:00. No
change in vital signs or GCS were observed initially and so the rate of infusion was slowly increased to 1.5mg/hr at which point her level of consciousness improved to where she was confused but could verbally communicate. Additionally, her respiratory rate increased to 16 breaths per minute and remained stable overnight. At 04:30 the following morning the patient’s respiratory rate increased to 20 breaths per minute and so the naloxone infusion was decreased to 1mg/hr. The remainder of her vitals were stable. At 07:00 the patient was observed to be fully alert, oriented and sitting up spontaneously with a GCS of 15. Her respiratory rate had decreased to 18 breaths per minute and her O2 saturation was 91% on RA.

Further history revealed the patient had purchased what she was told were “narcotics” off the street and ingested an unknown quantity of unidentified pills in an attempt to commit suicide. The inpatient Psychiatry and Addiction Medicine teams were consulted to see the patient. A UDS was ordered by the Addiction Medicine Consult team that morning and, given the improvement in her clinical status, the naloxone infusion was discontinued at 13:00 the day following admission.

Approximately 4 hours after discontinuation of the naloxone infusion, the patient’s level of consciousness deteriorated whereby she became rousable only to loud verbal stimuli, was confused and would only provide 1-2 word answers. Throughout this 4-hour interval, the patient did not leave her bed in the emergency department nor had any documented visitors. A naloxone infusion was restarted at 0.5mg/hr with good clinical response. The next morning (almost 40 hours after initial presentation to hospital) the patient was reassessed by the Addiction Medicine Consult team and was found to be alert and oriented with a GCS of 15. Her vital signs were stable including a respiratory rate of 18 breaths per minute and O2 saturation of 96% on 2L by nasal prongs. A second order for a UDS was written (as the order from the previous day had not been completed) and a naloxone infusion taper was initiated. This was tolerated well by the patient who was subsequently transferred to the hospital ward.

The UDS, which was not collected until almost 40 hours after presentation to hospital, was positive for cocaine, benzodiazepines and marijuana but was negative for all opioids including oxycodone, fentanyl, buprenorphine and methadone. The sample was sent to the provincial lab for mass spectrometry testing which confirmed this result. The mass spectrometry results are detailed in Table 1. Escitalopram and topiramate were found in the patient’s urine, both of which were prescribed to her, in addition to temazepam, oxazepam and quetiapine, which were not prescribed.

**DISCUSSION**

We have described a case of an individual who presented with decreased level of consciousness after reportedly ingesting unknown “narcotics” with suicidal intent. Little history was available at initial presentation. However, based on the clinical presentation, drug paraphernalia at the scene and suspicion for an opioid overdose, naloxone IM was administered by EHS. The patients’ clinical response to the initial dose of naloxone suggested opioid overdose to be a potential contributing cause for the patient’s drowsiness. Furthermore, beyond benzodiazepine and antipsychotic ingestion, a full medical work up did not provide any alternate explanation for her presentation. The patient was managed with a naloxone infusion with the dose being titrated according to level of consciousness and respiratory rate. There was a significant delay in both the ordering and collection of a UDS that was ultimately found to be negative for opioids and their metabolites; this was confirmed with mass spectrometry. This UDS result presented a perplexing picture of a patient that appeared to be successfully treated for an overdose with a naloxone infusion despite no opioid metabolites detected in her urine.

Despite the negative UDS, opioid use is still a possible explanation for this patient’s clinical presentation and response to the naloxone infusion. Our mass spectrometry analysis only tested for the substances detailed in Table 1, and therefore may be limited. It is possible this patient ingested an opioid not tested for such as Tapentadol or a non-pharmacologically produced fentanyl analogue. The UDS may not have tested positive for any opioids or associated metabolites because of the delay in specimen collection (approximately 40 hours after initial presentation to hospital), as we know the sensitivity of a UDS decreases as time elapses from drug ingestion. Though urine mass spectrometry detection can depend on many factors including differences in urine specific gravity, creatinine clearance and individual drug metabolism, fentanyl is usually only detectable in the urine between 24-48 hours after ingestion. Norfentanyl however, a fentanyl metabolite, should remain detectable by urine mass spectrometry for up to 96 hours after ingestion. Our patient’s urine mass spectrometry was negative for both fentanyl and norfentanyl. Furthermore, the need for such a prolonged naloxone infusion, which would suggest ingestion with a long-acting opioid such as methadone.
with an elimination half life of 8-59 hours (and should theoretically still test positive on the UDS at the time of collection), makes the use of common opioids a less convincing cause for the patient’s presentation.

Alternatively, perhaps this patient ingested a high-potency opioid that escaped UDS detection. W-18 is an example of such a compound with a potency originally cited to be approximately 100 times stronger than fentanyl (which is also already known to be roughly 100 times more potent than morphine). W-18 is a synthetic opioid-like molecule originally discovered at the University of Alberta in 1982, which, until only recently (when it was added as a Schedule I drug to Canada’s Controlled Drugs and Substances Act) could be manufactured and bought freely. As a consequence, the compound is starting to emerge within Canada’s illicit drug market, with some fentanyl pills being found to contain W-18 in Alberta last year and British Columbia more recently. To our knowledge, no confirmed overdose case involving W-18 has yet been described in Vancouver and research is scant regarding its classification as a true opioid, the drug’s duration of action or the efficacy of naloxone to reverse its effects. As a consequence, more research regarding the drug itself and its potential for toxicity is urgently needed.

Given the findings of both temazepam and oxazepam in the patient’s urine, another explanation may be that the patient’s UDS was a true negative for opioids, and her clinical presentation was more consistent with benzodiazepine toxicity. One randomized clinical trial involving 116 patients sought to evaluate the effect of naloxone treatment compared to supportive therapy among individuals presenting with a benzodiazepine overdose involving either diazepam, clonazepam, alprazolam or lorazepam. The study showed that all case subjects had an increased level of consciousness at reassessment after naloxone administration for their benzodiazepine toxicity compared to no one in the control group. They also reported improvement in other symptoms including weakness, ataxia, hyporeflexia and dysarthria in the case groups compared to control. The authors of this trial allude to a possible action of naloxone at gamma-aminobutyric acid (GABA) neurons and GABA receptors that mediated the observed effect. Naloxone may also act on the endogenous opioid system to increase one’s level of consciousness. Furthermore, a combination of these hypotheses may explain this patient’s clinical presentation and response to naloxone as we know the use of opioids, benzodiazepines and antipsychotics such as quetiapine may lead to complex drug interactions and significantly increases one’s risk for overdose. In supra-therapeutic doses quetiapine in particular can cause hypotension, tachycardia, and drowsiness due to its alpha-adrenergic receptor and histamine receptor blockade. The ingestion of quetiapine in this case, as evidenced by the positive result on mass spectrometry, may certainly have contributed to the patient’s clinical presentation.

Finally, the possibility exists that ingestion of an alternate, unidentified substance contributed to the patient’s presentation and time, as opposed to the naloxone infusion, resulted in the patient’s clinical improvement - though this explanation is made more curious by the patient’s decompensation following the initial discontinuation of the naloxone infusion.

This case emphasizes the importance of a timely UDS after hospital admission and highlights the complexity in detecting, differentiating and managing an overdose of unknown etiology. Given its relatively safe side effect profile, clinical judgement should prevail when considering treatment for a suspected opioid overdose. Furthermore, as high potency opioids continue to emerge in Canada’s illicit drug market more sophisticated and accurate methods for detection will need to be developed to aid clinical management. Lastly, further research is needed evaluating the role of naloxone for the management of non-opioid toxicity and the potential mechanism of action in this regard.
REFERENCES


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ISAM-CSAM Montreal 2016 Abstracts

OPIOID MANAGEMENT

LONG-ACTING FORMULATIONS TO IMPROVE SUBSTANCE ABUSE TREATMENT ADHERENCE

Ivan D. Montoya, M.D, M.P.H.
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Low treatment adherence is prevalent across all medical conditions and a major barrier to achieving the benefits of effective therapeutic interventions. This is especially relevant among patients with Substance Use Disorders (SUD) whose clinical condition make them more prone to have poor treatment adherence. Multiple strategies to improve treatment adherence among SUD patients have been evaluated. For example, intensive counseling, contingency management techniques, prescribed pill counts, biomarkers in urine (e.g., riboflavin, quinine and acetazolamide), electronic tools, etc. but they have not been completely successful. Long-acting formulations of medications have greatly helped to improve the treatment adherence in many areas in medicine. They include long-acting antipsychotics (e.g., paliperidone palmitate) and removable depots of contraceptive agents (e.g., Norplant). Similarly, long-acting formulations are expected to improve medication adherence and help patients with SUDs. A long-acting formulation of naltrexone approved by the FDA has demonstrated better adherence than the oral formulation. Recently, the FDA approved an implantable formulation of buprenorphine that delivers stable blood levels of this medication for six months and showed non-inferiority as compared to the oral formulation. Furthermore, several research groups are developing long-acting formulations of medications to treat SUDs. Although they seem to be well tolerated, and improve pharmacokinetic coverage and treatment outcomes, complexities around their safety, tolerability, and starting/stopping protocols require careful consideration. The purpose of this presentation is to review the risks and benefits of long-acting formulations of medications as tools to improve the adherence to and outcomes of SUD treatments.

POSTER: A RANDOMIZED TRIAL OF PROBUPHINE IMPLANTS IN ADULTS STABILIZED ON SUBLINGUAL BUPRENORPINE

Sonnie Kim, PharmD

Email: Sonnie@braeburnpharma.com

Background: Long-acting buprenorphine implants (BI) were noninferior to daily sublingual buprenorphine 12–16 mg (SL BPN) in opioid-dependent treatment-naïve users. Purpose/Hypothesis: This was a randomized, double-blind, noninferiority study in opioid-dependent adult outpatients clinically stabilized for ≥3 months on ≤8 mg SL BPN who were randomized 1:1 to daily SL BPN tablets plus 4 placebo implants or daily SL placebo tablets plus four 80-mg long-lasting BI. Procedures/Data/Observations: Urine was tested at 6 scheduled monthly and 4 random visits. The primary efficacy variable was responder rate (subjects without evidence of illicit opioid use in >4 of 6 study months). Safety was assessed throughout the study. Responder rates were greater for long-acting BI (96.4%; 84/89) relative to SL BPN (87.6%; 81/84); the 2-sided 95% confidence interval (0.009, 0.167) of the proportion difference was above the predefined noninferiority margin (P<0.001 for noninferiority; p=0.034 for superiority). Of subjects receiving SL BPN, 28.1% (25/89) showed evidence of illicit opioid use compared with 14.3% (12/84) receiving BI. Study completion rates were similar (94.4% SL BPN; 93.3% BI). Of subjects receiving SL BPN, 10.1% had ≥1 severe treatment-emergent adverse event vs 3.4% receiving BI (p>0.05). Conclusion: BI maintained treatment efficacy in clinically stable opioid-dependent adults. BI may provide superior relapse prevention relative to SL BPN in this population.
Modelling the Effectiveness of Subdermally Implanted Buprenorphine, Injectable Naltrexone, and Sublingual Buprenorphine for Clinically Stable Adults with Opioid Dependence

John A Carter, Ryan Dammerman, Walter Ling, Michael Frost

Objective: To assess subdermally-implanted buprenorphine (SI-BPN) versus injectable-naltrexone (XR-NTX) or sublingual-buprenorphine (SL-BPN) for opioid dependence.

Methods: A Markov model simulated cohorts for 6-12 months (1 month/cycle, clinically-stable patients at baseline). A network meta-analysis of the aforementioned treatments was undertaken to generate probabilities for state transitions governed by treatment effectiveness. Treatment effectiveness was defined as the cumulative proportion of patients without evidence of illicit opioid use. Risks of the following outcomes were modeled with literature estimates specific to Canada in the base case and specific to the United States for comparison: nPatients diverting/misusing, nPatients relapsing, pediatric exposures, detox utilization, suicides/drug-related deaths. Univariate and probabilistic sensitivity analysis assessed the impact of underlying model uncertainty on outcomes.

Results: The Markov model illustrated SI-BPN's effectiveness over XR-NTX (+10%) and XR-NTX over SL-BPN (+5%). Non-oral treatment benefits were driven by reduced rates of diversion/misuse. A greater risk of overdose associated with the XR-NTX versus SI-BPN (+2-6%) drove benefits of the latter.

Conclusions: Investigational SI-BPN may reduce patient- and societal-level burdens of opioid dependence. Although generalization of these findings may be limited by use of indirect comparisons (some using secondary outcomes), this model suggests improved morbidity and mortality with SI-BPN treatment relative to XR-NTX and SL-BPN.

Slow Release Oral Morphine (SROM): Closing the Gap Between Methadone and Diacetylmorphine in OST

Robert Haemmig
University Psychiatric Services Bern, Switzerland

In a prospective, multiple-dose, open label, randomized, non-inferiority, cross-over, multi-center study over two 11-week periods and an additional 25-week observation period slow release oral morphine (SROM) was tested against methadone in patients on stable methadone doses of 50mg/d or more. Patients were switched from oral methadone solution to SROM capsules in a ratio 1:6 to 1:8. Both treatments were well tolerated. The methadone induced prolongation of QTc disappeared after a switch to SROM. Patients reported a higher treatment satisfaction, fewer cravings for heroin, and lower mental stress under SROM. Additionally, the metabolism of SROM is independent from liver function.

SROM was registered as a substitution medication based on the above mentioned study in May 2013. Since then more than half of the patient in our treatment center wished to switch from methadone to SROM. Clinical experience shows that a too rapid switch to SROM results in an unpleasant histamine reaction. We developed a scheme that avoids this AE.

The SROM formulation releases the morphine slowly in the intestines, so the SROM does not cause a rush. All the characteristics and effects taken together, SROM is to position somewhere in between methadone and diacetyl-morphine.

Opioid Abuse and Dependence Among Patients with Chronic Non Cancer Pain: A Training Challenge in Pain Management for Québec Family Physicians

Elise Roy, Christiane Thibault, Pierre-André Dubé, Denis Hamel, Maud-Emmanuelle Labesse, Richard Coté
Addiction Research and Study Program, Faculty of Medicine and Health Sciences, Université de Sherbrooke, Longueuil, QC, Canada; Institut national de santé publique du Québec, Montréal, QC, Canada.

Objective: To assess concerns, practices and training needs of family physicians (FP) who prescribe opioids for chronic non cancer pain (CNCP) with respect to risks of abuse and dependence among patients.

Methodology: An online survey was carried out from 10/14/2016 to 11/16/2016. Concerns were assessed asking “To what extent do you agree or disagree that the following factors cause you to avoid prescribing or hesitate to prescribe opioids for CNCP?” Among the suggested factors, four were about risks of adverse effects. Practices were assessed asking how often participants applied each of the Collège des médecins du Québec recommendations. Regarding training needs, participants had to rank their three most important topics out of eight suggestions. For analyses, frequency distributions were calculated, weighted according to the age and gender distribution of the Québec FP population.

Results: Of 636 respondents (43.8% men; 55.3% ≥ 50 years old), 15.2% and 70.9% felt very or somewhat confident that they could properly prescribe opioids for CNCP. Concerns related to abuse (72.5% strongly agree/somewhat agree), dependence (73.2%) and lack of support should these
complications occurred (75.4%) were the main barriers reported. Yet only 19.7% always/often screened their patients for risks of abuse and dependence. Almost half (46.4%) identified training on abuse and dependence risks assessment and management as one of their three top priorities, but only 13.7% ranked it first.

Conclusions: Although risks of opioid abuse and dependence are major concerns among FP, screening practices are suboptimal, suggesting that many FP need training in this area.

UNDERSTANDING OPIOID USE DISORDER: HIGHLIGHTING THE HETEROGENEITY IN PATTERNS OF USE AND METHADONE MAINTENANCE THERAPY OUTCOMES

Dr. Caroline Brunelle
Email cbrunell@unb.ca

Objective: The prevalence of prescription opioid use (POU) has been increasing steadily in North America, along with a concerning number of opioid-related mortalities (Fischer et al., 2015). This presentation will integrate findings from two separate studies, with different goals. Study 1 aims to determine whether distinct homogenous subgroups of opioid misusers exist in order to gain a better understanding of the treatment needs of these individuals. Study 2 focuses on identifying predictors of continued illicit opioid use in Methadone Maintenance Treatment (MMT) clients.

Methodology: Two separate samples (n= 60 & n=52) of MMT clients were recruited. In study one, clinical records were examined to code for physical and mental health indicators at entry into treatment, six months, and one year post onset of MMT. In study 2, MMT clients completed a number of questionnaires assessing substance use and personality.

Results: In study 1, two clusters of MMT clients emerged using a latent class cluster analysis. The first, composed of one third of the sample respond poorly to treatment, display higher levels of psychiatric comorbidity and substance use severity while the second cluster are younger, have less severe substance use history, report greater frequency of pain conditions and respond better to MMT. In study 2, a regression analysis indicated that impulsivity is the only personality trait predictive of continued illicit opioid use while receiving MMT.

Conclusions: Taken together, these findings highlight individual differences in opioid misusers and the importance of matching opioid misusers to their specific treatment needs.

PSYCHIATRIC COMORBIDITY AND TRAMADOL ABUSE

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Objective: Opioid use disorders attributed to tramadol (OUD-T) is a public health problem in Egypt. The objective of this study was to assess the psychiatric comorbidity among patients with opioid use disorder attributed to tramadol.

Methods: This study included 100 patients with opioid use disorders attributed to tramadol (according to DSM-IV-TR) and 100 control persons (matched for age, gender and education) who were recruited from Zagazig university hospital, Egypt. The participants were interviewed using Structured Clinical Interview for DSM disorders (SCID-I & SCID-II), Addiction Severity Index scale (patients), and urine screening for drugs.

Results: Twenty-four percent of the patients used tramadol only while 76% of the patients used other substances in addition to tramadol (polysubstance group). Most (91%) of the patients had tramadol dependence. Forty-nine percent of the patients had psychiatric comorbidity especially mood disorders (59.2%) while only 24% of the control persons had psychiatric comorbidity especially anxiety disorders (83.3%). The most common personality disorders among patients were borderline (24%) and antisocial (22%) while in control persons, the most common Personality disorders were obsessive compulsive (8%) and the avoidant (7%). Cluster B (76.6%) was the most common category among patients (compared to 25.8% in control persons) while Cluster C (51.6%) was the most common category among control persons (compared to 15.6% in patients).

Conclusions: Most of the patients were dependent on tramadol and approximately three out of four used many substances. Almost half of the patients had psychiatric comorbidity and approximately three out of four had cluster B personality disorders.
PERSONALITY TRAITS AND METHADONE DOSE AND COMPLIANCE INDEPENDENTLY PREDICT CONCURRENT SUBSTANCE USE IN CLIENTS UNDERGOING METHADONE MAINTENANCE TREATMENT FOR OPIATE ADDICTION

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Objective: This study aimed to examine the relationship of personality and methadone dose/compliance to concurrent substance use in a sample of methadone maintenance therapy (MMT) clients.

Methodology: Sixty-eight clients (63.2% male; mean age = 38.5 years, SD = 9.8) were recruited from a low-threshold MMT clinic in Halifax, Canada (mean methadone dose = 105.4 mg, SD = 41.1). Substance use was assessed using an adapted version of the Drug List Questionnaire (Barrett, Gross, Garand, & Pihl, 2005). Demographic variables and methadone dose/compliance were collected via self-report. Personality dimensions were measured using the Substance Use Risk Profile Scale (Woicik, Stewart, Pihl, & Conrod, 2009).

Results: Prescription opioid misuse was predicted by lower methadone compliance (B = -.606, OR= .545, 95% CI [.342-.869], p = .01), higher hopelessness (B= .259, OR= 1.30, 95% CI [1-1.67], p = .048) and anxiety sensitivity (B= .568, OR= 1.77, 95% CI [1.13-2.75], p = .012). Injection drug use (n=51) was predicted by lower methadone dose (B= -.043, OR=.96, 95% CI [.93-.98], p =.003), higher impulsivity (B=.398, OR= 1.49, 95% CI [1.04-2.14], p = .031) and hopelessness (B=.426, OR= 1.53, 95% CI [1.04-2.25], p = .03). In contrast, neither personality nor methadone variables predicted alcohol, cannabis, cocaine or benzodiazepine use.

Conclusion: In sum, methadone variables and personality independently predicted opiate use and injection drug use patterns within a clinical sample of clients at a later stage of addiction. Results caution that personality may be targeted in treatment as a supplement to MMT.

References:

INFECTIOUS DISEASES

THE PROMISE OF A CURE: TAKING ADVANTAGE OF HEPATITIS C CARE TO REACH OUT AND IMPROVE THE HEALTH AND WELLBEING OF PERSONS WHO INJECT DRUGS

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The economic, health and social consequences of drug use disorders are devastating worldwide. Injection drug use is a major public health concern as it is, nowadays, the main factor contributing to hepatitis C virus (HCV) transmission worldwide. Timely HCV detection and a combination of harm reduction interventions are required to reduce HCV transmission among PWID, albeit not enough to achieve elimination.

Significant decreases in HCV incidence and prevalence and in the corresponding disease burden can only be accomplished by reducing transmission rates among high-risk persons and enhancing treatment access for those at the greatest risk of disease progression or of transmitting the infection.

Compounding the health impacts of drug use and HCV disease are the myriad of other adverse health outcomes faced by PWID. It is imperative to better leverage and intervene on barriers to linkage and engagement in care. Enhanced HCV care and treatment could also lead to more appropriate health services and improved health outcomes, including for addiction and mental health.

In this new era of short all-oral effective direct acting antiviral HCV treatments, there is a unique opportunity to focus on the needs of persons with drug use disorders while in treatment, to achieve HCV cure, reduce HCV reinfection rates and overdose deaths.

This presentation will discuss individual-centered and systemic approaches for bridging addiction, HCV and primary care disciplines in order to address the health and wellbeing of drug users, and reduce the health and social burden associated with these syndemic epidemics.
A HEPATITIS C TREATMENT PROGRAM FOR HOMELESS PATIENTS
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Being homeless increases the risk that a substance user will become infected with hepatitis C. Moreover, people who experience residential and social instability are less likely to access health care and to comply with medical recommendations if they do seek care. Given these unique characteristics of homeless people, investigation and treatment of hepatitis C in this population requires an approach tailored to their needs.

We established a hepatitis C treatment program for homeless patients in collaboration with the Old Brewery Mission (OBM) shelter in downtown Montreal. OBM houses clients in a 14 bed “medical” unit and each person has a bed in a cubicle with a locker and access to a shared living room and kitchen. As part of the multifaceted program, a counsellor from the Mission offers psychosocial services. Also, a nurse from the service de médecine des toxicomanies (SMT) is present 30 hours per week and art classes and other activities are offered. Finally, when patients complete the intervention and transition to stable housing a 500$ bursary is given to them. Comprehensive health care including psychiatric services are offered at the SMT outpatient clinic, which established a hepatitis C clinic in 2010 targeted at patients with substance use disorders.

The first patient entered the treatment program in May 2014. Since then, 93 homeless patients have been evaluated and 54 were admitted into the program for different periods of time. Descriptive data on the participants and their treatment episode will be presented and discussed.

C-EDGE CO-STAR: RISK OF REINFECTION FOLLOWING SUCCESSFUL THERAPY WITH ELBASVIR (EBR) AND GRAZOPREVIR (GZR) IN PERSONS WHO INJECT DRUGS (PWID) RECEIVING OPIOID AGONIST THERAPY (OAT)
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Background: The fixed-dose combination of EBR/GZR 50mg/100mg (NS5A inhibitor/NS3/4A protease inhibitor), is a highly effective, well-tolerated, all-oral, once-daily regimen utilized in diverse populations of HCV GT1/4/6-infected patients, including PWID on OAT. Data on reinfection rates after successful HCV therapy will help inform the development of treatment programs in this population.

Methods: The double-blind, placebo-controlled CO-STAR study evaluated the efficacy of EBR/GZR for 12 weeks in treatment-naïve HCV GT1/4/6-infected patients ± cirrhosis ± HIV receiving OAT. Patients were randomized 2:1 to an immediate (ITG) or deferred (DTG) treatment group. Recurrent viremia was evaluated among patients with undetectable HCV RNA at end of treatment (EOT). If this was detected, population sequencing and phylogenetic analysis were performed to distinguish relapse from reinfection.

Results: Of 301 randomized patients, 201 were in the ITG (76% male; 15% black; 76% GT1a, 20% cirrhotic; 8% HIV+). Baseline OAT included methadone (81%) and buprenorphine (19%); 62% had detectable drugs on urine drug screen. 197/200 patients had undetectable HCV RNA at EOT. Recurrent viremia was detected in 14 patients, with 7 virologic relapses, and 7 probable reinfections; 5 through follow-up week (FW)12 and 1 at FW24. Three subjects with documented reinfection had subsequent clearance of HCV RNA.

Conclusion: Reinfection following successful therapy was seen in some patients as early as FW8. Although subsequent spontaneous clearance occurred in 3/7 cases, further work is needed to identify correlates of reinfection and develop strategies to reduce its occurrence.
CANNABIS

CANNABIS: PRESCRIBE, CONTROL, BAN OR SET FREE? HOW AND WHY?
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Approved medical indications for cannabis or Δ-THC are still widely limited to relief of neurogenic pain, nausea and vomiting due to chemotherapy, and appetite stimulation in AIDS and cancer patients. Newer studies provide fairly good evidence of usefulness in epilepsy, multiple sclerosis, Crohn's disease, various sleep disorders, and possibly psychosis. However, much of this evidence relates to CBD, which is free of unwanted psychoactivity seen with THC or cannabis. Several other claimed therapeutic uses still lack sufficient evidence in humans or are rejected by clinical experience. Cannabis is not the best drug for any indication because its low selectivity carries high risk of adverse side effects. More selective developments are most likely to come from highly specific modulators of different components of the endocannabinoid system.

Non-medical use is typically at much higher doses of THC, and adverse effects are common, especially in adolescents and young adults. There is growing pressure for abandonment of prohibition, because of harm to those acquiring criminal records solely for possession for personal use, but there is need to prevent access to cannabis by youth. Selecting the best policy option requires accurate knowledge of the magnitude of problems caused both by cannabis and by the law, and the probable effects on both by each option. Much of this information is not yet available. The most rational approach is therefore to decriminalize possession now, closely monitor consequences of legalization where it is already being tried, and defer decision on legalization until the necessary information is available.

CANNABIS INDUCED PSYCHOTIC DISORDER AND CANNABIDIOL’S PURPORTED ANTI-PsyCHOTIC PROPERTIES: THE STATE OF THE EVIDENCE
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Introduction: This presentation will review the effect of cannabidiol (CBD) in regards to psychosis, schizophrenia, and it’s plausibility as a treatment for psychosis.

Methods: We reviewed the literature that proposes the mechanisms of cannabis induced psychotic disorders and hence increases the risk of early onset schizophrenia. A PubMed search was completed from 2000 to present for english language articles.

Results: There have been recent studies showing psychosis is secondary to the THC in marijuana, more striking is that 69 studies were found showing CBD may be protective and actually have antipsychotic properties equal in efficacy to atypical antipsychotics such as amisulpride, including 8 clinical trials. One of the most worrisome risks is the contribution to the onset of schizophrenia in children and adolescents using marijuana. This leads to a significantly poorer prognosis than adult onset. The percentage of THC is much higher today than in the past and certain formulations have been able to even further concentrate THC such as ‘shatter’, ‘wax, ‘honey oil’, etcetera. Complicating this is that CBD is almost nonexistent in street marijuana. Due to Mendelian genetics, as THC concentration is increased CBD concentration is inversely reduced. This eliminates the protective factors of CBD while increasing the risk of psychosis. THC and CBD seem to have opposite physiologic effects on endogenous anandamide levels and cannabinol receptor binding, the mechanism likely leading to CBD’s antipsychotic effect.

Conclusions: Early evidence shows that CBD may be a novel and viable treatment of psychosis. This may have an effect on the regulation of CBD and THC percentages in regards to the prevention of early onset schizophrenia.
OTHER DRUGS

ALICE RAP – OVER 200 SCIENTISTS, 21 PROJECTS, 5 YEARS OF RESEARCH ON PSYCHOACTIVE SUBSTANCES AND GAMBLING PREVENTION AND POLICIES: LESSONS LEARNED?

Jürgen REHM
Centre for Addiction and Mental Health (CAMH), Toronto

ALICE RAP was an EU funded large project to reframe addictions, winning a special competition on reframing addictions. Its results has been summarized in a series of five books of Oxford University Press (see Anderson et al., 2016 for a final summary of all findings), numerous peer-reviewed journal articles, and a series of policy briefs (http://www.alicerap.eu/). We will give a succinct overview of main results and then discuss parameters of success, in particular, whether the project achieved what is was set out to do, namely achieve a reframing of addictions in Europe. We will separate three dimensions of impact: a) the academic discourse, b) impact on funder and European Union bodies, and c) wider impact on the debate of substance use policies; and present empirical indicators of dissemination up to September 2016.


CAN ALCOHOL DEPENDENT PATIENTS RETURN TO REDUCED DRINKING LEVELS: WHAT DO THE DATA INDICATE?

Prof. Karl Mann, MD
Central Institute of Mental Health, University of Heidelberg, Germany

Around 80 to 90% of alcohol dependent individuals who perceive a need for treatment do not get involved mainly because they are not willing or not able to subscribe to the goal of complete abstinence. For this reason harm reduction strategies such as a reduction in alcohol consumption have been tested both in psychotherapy and in pharmacotherapy. Observational studies and controlled trials conclude that abstinence remains the best option. However, reduction of consumption for alcohol dependent patients is possible. Stability of remission seems more likely in subjects reporting less severe forms of the disorder. Evidence based treatment guidelines as well as the guidance papers of US and European authorities have taken note of these developments and accept low-risk drinking limits (FDA) or intermediate harm reduction (EMA) as valuable trial endpoints.

POSTER: EFFICACY OF PSYCHOSTIMULANT INTERVENTIONS FOR AMPHETAMINE AND METHAMPHETAMINE USE DISORDERS: A SYSTEMATIC REVIEW & META-ANALYSIS

Meha Bhatt, Laura Zielinski, Lola Baker-Beal, Neera Bhatnagar, Zainab Samaan

Background: Psychosocial interventions are used to manage amphetamine and methamphetamine use disorders (AMD) but it remains difficult to retain patients in treatment (1). Psychostimulant maintenance interventions have been investigated, in combination with psychosocial interventions, to improve treatment outcomes.

Objectives: Summarize evidence for the efficacy and safety of psychostimulant drugs for management of AMD.

Methodology: We searched MEDLINE, EMBASE, PsycINFO, Cochrane Central, and CINAHL for RCTs examining the efficacy of psychostimulant drugs for AMD, in comparison to placebo. No restrictions were placed on age and studies within sub-populations were included. Screening and data abstraction were conducted in duplicate. Meta-analyses were performed, when possible, and risk of bias was assessed for individual studies and overall quality of evidence.

Results: Seventeen trials were included in the review (6 studies of bupropion, 6 of methylphenidate, 3 of modafinil and 2 of dexamphetamine). Psychostimulant treatment showed no significant difference compared to placebo for amphetamine and methamphetamine use measured as mean negative urine screens (mean difference -0.16, 95% CI -1.96 to 1.64), or treatment retention (odds ratio 1.11, 95% CI 0.73 to 1.68). Incidence of serious adverse events did not differ between treatment and placebo groups.

Conclusions: The findings do not support the use of psychostimulants for managing AMD. The quality of evidence for all outcomes was very low. It remains challenging to conduct trials in this area due to difficulties in ensuring medication adherence and trial completion.

References:
Despite overwhelming evidence documenting the positive health and social benefits associated with harm reduction practices these practices have limited reach inside acute care settings. Consequently, hospitals are considered high-risk environments for patients with substance use disorders because individuals are often unable to access evidence-based interventions such as sterile injection supplies or naloxone kits. This results in additional morbidity and mortality, as well as placing individuals at risk for premature discharge. Instead of abstinence only policies, a focus on reducing harm during hospitalization is a more ethical approach. The Addiction Recovery and Community Health (ARCH) Team is a specialty consult service based out of an inner city acute care hospital. Since 2014, this team has been integrating a harm reduction approach into routine patient care. Interventions provided by the team include: evidence based treatment recommendations for problematic substance use (including the initiation or maintenance of opioid agonist therapy); treatment of acute pain and withdrawal; provision of sterile injection supplies to patients with ongoing injection drug use during hospitalization; overdose prevention and naloxone training; health promotion interventions (including sexually transmitted infection and blood borne virus screening); and intensive social stabilization (including housing, income and identification). In addition, targeted educational programs have been deployed including rotating inservices, Grand Rounds series, symposia, and the development of local champions. The team is also exploring the feasibility of a managed alcohol program and supervised injection services. This presentation will outline the benefits and challenges associated with incorporating harm reduction strategies into an acute care setting.
CONCURRENT SUBSTANCE USE DISORDERS AND PTSD IN AN INPATIENT ADDICTION TREATMENT PROGRAM IN CANADA
James MacKillop, Wendi Woo, Christopher Ryan, Sarah Sousa, Isabella Romano, Courtney Ropp, Roy Cameron, Harry Vedelago
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Objective: To characterize concurrent substance use disorders and post-traumatic stress disorder (PTSD) among individuals being admitted to an inpatient addiction treatment program toward improving treatment quality.

Methodology: Patients were 142 (66% male) treatment-seeking individuals who completed an assessment battery at admission to the Addiction Medicine Service at Homewood Health Centre in Guelph, Ontario. The battery comprised the following: World Health Organization (WHO) Alcohol, Smoking, and Substance Involvement Screening Test; WHO ICD-10 Alcohol Use Disorder Symptom Checklist (adapted to include all symptoms in DSM-5); Drug Use Disorder Identification Test; PTSD Checklist for DSM-5 (PCL-5); Life Events Checklist for DSM-5 (LEC-5).

Results: Overall, 76% and 37% of patients had severe alcohol and drug use disorders, respectively. More than half used only one substance regularly (excluding tobacco), while 45% reported regular use of two or more substances. Close to half (43%) met the PCL-5 screening criterion threshold for PTSD. Although exposure to any of the traumatic events on the LEC-5 significantly increased the odds of the PTSD threshold (ps <.05-.0001), effect sizes varied substantially between individual events. Significant associations were present between level of use of alcohol, marijuana, sedatives or prescription sleep aids in relation to specific PTSD symptom clusters.

Conclusions: The results reveal high rates of concurrent substance use disorders and PTSD in this treatment setting and suggest quality improvement strategies should focus on addressing this comorbidity. These data provide valuable directions for treatment planning and program development to promote positive patient outcomes.

Prize: Best Poster Award

POSTER: IMPLEMENTATION OF A STANDARDIZED CLINICAL SCREENING BATTERY FOR AN INPATIENT AND OUTPATIENT CONCURRENT DISORDERS PROGRAM: INITIAL FINDINGS
Holly Raymond, Michael Amlung, Prabjhot Saini, Jodi Younger, Iris Balodis, and James MacKillop
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Background and Objective: Epidemiological studies consistently reveal high rates of comorbidity between addictive disorders and other psychiatric disorders (i.e., concurrent disorders, CD). Given the substantial heterogeneity in CD, comprehensive screening of symptom profiles is critical for focused and efficient treatment. The objective of this study was to implement a standardized clinical screening battery to aid diagnosis and treatment of individuals with CD. Methodology: Inpatient and outpatient clients in the CD program at St. Joseph's Healthcare Hamilton completed a computerized questionnaire battery during an intake assessment. The battery comprised validated measures of substance use (e.g., alcohol, drugs, tobacco) and a range of psychiatric disorders (e.g., depression, bipolar disorder, psychosis, borderline personality, etc.). Each client's responses are automatically scored to generate a one-page clinician report summarizing substance use and mental health status. Results: We will present findings from an initial cohort of clients from the inpatient and outpatient CD clinics. At present, data are available for 101 outpatients. Preliminary analyses indicated significant correlations between elevated drug use severity and higher scores on each of the psychiatric scales examined, including symptoms of depression, bipolar disorder, psychosis, PTSD, and borderline personality. Multiple regression analyses indicated that depression and bipolar disorder scales accounted for unique variance in drug use severity. Conclusions: These preliminary results may offer useful strategies for other mental health programs that seek to address CD. In addition, this approach represents a bench-to-bedside partnership between academic researchers and treatment providers that is consistent with a growing emphasis on translational research in psychiatry.
Suicidal ideation, attempts, and completed suicides involve alcohol in over 80% of cases in this sub-arctic region. Binge and chronic drinking are closely associated with suicidal behaviors in our studied populations. Established treatments such as AA, counselling, and acute detox appear to have little impact in these isolated and small communities.

With the suicide rate 34% above the Canadian average, several newer treatment modalities were introduced between 2010-2015: 1) Native Healing Programs 2) Brief Intervention in the ER and SBIRT 3) Help telecommunication and messaging 4) contagion containment 5) courses in effective intervention skills and prevention network development. Our 3 year brief intervention study shows a 30% reduction in binge drinking. Other findings are similar to studies done in various international settings.

While reduction in medical morbidities and ER utilization can be associated with decreased alcohol intake, a reduction in suicidal behavior and completed suicides in the studied communities correlates with a reduction in binge drinking.

Autopsy data suggests a gradual downward trend in suicidal behaviors and completions in the studied communities.

TRAUMA, MENTAL HEALTH AND SUBSTANCE ABUSE IN PREGNANT ABORIGINAL WOMEN: RESULTS FROM THE “VOICES AND PHACES” STUDY

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Background: Depression during pregnancy is a serious health issue. Among its correlates is substance abuse, which carries devastating health consequences for both mother and fetus. Very little research has examined prenatal depression specifically in Aboriginal populations.

Objectives and methods: “Voices and PHACES” was a community-based, qualitative constructivist grounded theory study conducted in Calgary (2012-2014). It sought to understand the risk factors, the protective factors and the societal context of prenatal depression in Aboriginal populations. Data stemmed from personal and focus-group interviews with pregnant Aboriginal women, service-providing professionals, and stakeholders.

Results: Chronic life stress and trauma were identified as key causes of depression, and were influenced by negative life events and circumstances, negative relationships, and socioeconomic factors. Driving these determinants were upstream, systemic factors related to historical and present-day societal context, including colonization and continued marginalization in Canadian society. Substance abuse was found to be a common coping mechanism for stress, trauma, and depression, indicating that mental health issues need to be addressed in order to effectively manage addiction. Social support and traditional Aboriginal healing practices were identified as protective, and thus may be key intervention strategies.

Conclusion: The links between trauma, mental health issues and substance abuse are well-recognized, and form the basis of calls to take a trauma-informed approach to addiction. Aboriginal women experience particularly severe and unique sources of trauma. Culturally-appropriate, culturally safe and trauma-informed approaches to addiction are warranted, as are interventions that address the broader determinants of mental health in Aboriginal women.

HOPE AND DESPAIR – CULTURALLY SENSITIVE COMMUNITY LED OPIATE MAINTENANCE PROGRAMS IN REMOTE FIRST NATIONS IN NORTHWESTERN ONTARIO

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Perhaps nowhere in Canada is the impact of Prescription Drug Abuse (PDA) as devastating as amongst Canada’s First Nations (FN) communities. Physical isolation and lack of road access result in illicit drug costs ten times those of urban centres, adding to the negative social and community impact experienced elsewhere due to PDA.

In respond to the PDA/opiate crisis, a number of grass-roots, community driven, culturally sensitive treatment programs have been initiated in 16 remote, fly-in communities in Northwestern Ontario. The first program began in 2013 and they have been highly successful, with retention rates in excess of 90%. Working collaboratively, consultant addiction physicians, northern primary care physicians/ nurse practitioners, community mental health
workers and community leaders, all working together, have created a network of opiate maintenance programs, using a variety of models, as designed by the community. Over 500 patients have been successfully treated using Buprenorphine/Naloxone and traditional healing practices. Multiple indicators of ‘community wellness’ reflect the extremely positive influence that these programs have had. Communities have gone from desperation to hope, as families remain intact, child poverty and health improve, as patients in these programs, who are parents and grandparents, begin to heal and re-engage in life.

THE LGBT COMMUNITY

GATHERING USERS’ PERSPECTIVE, CLINICIANS’ AND COMMUNITY STAKEHOLDERS’ EXPERIENCE TO INCREASE ACCESS TO ADDICTION SERVICES IN MEN WHO HAVE SEX WITH MEN
Mathieu Goyette, Jorge Flores-Aranda

Men who have sex with men (MSM) use less addiction services than other men. This is especially true for MSM who live outside urban centers or who don't already have a connection with addiction or sexual health services. It is therefore necessary to rethink the strategies used to reach MSM to raise their awareness about risks and harms related to their substance use. In order to reach these men, "MON BUZZ" project was developed. MON BUZZ is a French speaking webbased screening and brief intervention on substance use and misuse designed by potential users, clinicians and researchers to reach MSM. The current presentation aims 1) to describe strategies developed by different stakeholders (potential users, clinicians and researchers) to reach MSM that have been used in MON BUZZ and 2) to put in relation the target population and the strategies used related to MSM reached in the current project. In a community based participatory research perspective, strategies used to reach this population (format, content and communication and diffusion strategies) are described related to the contribution of each groups of stakeholders. Then, preliminary data related to user’s profiles (severity of substance use, geographical area and current and past addiction services used) on the first weeks of MON BUZZ deployment are presented. Results are discussed related to the reaching out achievement of the target population and the Conceptual framework of access to health services (Lévesque et al., 2012). The strategies used are discussed related to their potential transposition in others addiction’s field.

EXPERIENCES OF DRUG ABUSE AMONG MEN WHO HAVE SEX WITH MEN: ISSUES AND CHALLENGES FOR THE IMPLEMENTATION OF COMPREHENSIVE SERVICES
Jorge Flores-Aranda, Karine Bertrand, Elise Roy

Gay and bisexual men present more substance use problems compared with their heterosexual peers. However, they delay seeking addiction services, and when they do, the services do not always meet their needs. The objective of this presentation is to describe issues and challenges regarding the implementation of addiction services which take into account gay men needs. A qualitative study based on symbolic interactionism was carried out. Semi-structured interviews were conducted with 35 gay/bisexual men aged 18 years and over who had substance use problems, were born in Canada and lived in Greater Montreal. A thematic analysis was performed. The majority of participants had already used addiction services, but almost half of them had been referred to such a service. For some, their problematic substance use had not been detected at the right time. The factors triggering a request for help with addiction services were sometimes associated with the gay life-course experience and the substance use trajectories. Indeed, an increase in substance use and introspection leading to a request for help thus occurred when participants were having difficulties accepting their sexual orientation, during sexual experimentation or when they were diagnosed with HIV. According to some participants, sexuality is not sufficiently addressed in addiction services. Offering comprehensive services, including substance use and sexuality represents a challenge for caregivers.
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