Workplace Safety and Insurance
Appeals Tribunal

Tribunal d'appel de la sécurité professionnelle
et de l'assurance contre les accidents du travail

Addiction

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This medical discussion paper will be useful to those seeking general information about the medical issue involved. It is intended to provide a broad and general overview of a medical topic that is frequently considered in Tribunal appeals.

Each medical discussion paper is written by a recognized expert in the field, who has been recommended by the Tribunal's medical counsellors. Each author is asked to present a balanced view of the current medical knowledge on the topic. Discussion papers are not peer reviewed. They are written to be understood by lay individuals.

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Every Tribunal decision must be based on the facts of the particular appeal. Tribunal adjudicators recognize that it is always open to the parties to an appeal to rely on or to distinguish a medical discussion paper, and to challenge it with alternative evidence: see *Kamara v. Ontario (Workplace Safety and Insurance Appeals Tribunal)* [2009] O.J. No. 2080 (Ont Div Court).For more information about these papers, please consult the *WSIAT Guide to Medical Information and Medical Assessors*.

Introduction

Addiction is defined as the adverse consequences associated with compulsive drug- seeking behaviours. In Canada, the economic toll associated with drug and alcohol addiction, and co-morbid mental illnesses, is estimated to be $40-52 billion dollars[1], and in the United States such estimates are approximately $700 billion per year[2]. At the same time, addiction assessment and treatment services are greatly lacking in Canada, with specialized treatment services often available only in large urban centers, and with demand greatly exceeding treatment capacity. Complicating this reality, only about 10-12% of people with addictions actually seek treatment[1], so this lack of treatment capacity is a considerable challenge for successful addiction treatment, and recovery. Fortunately, there is increasing appreciation of alcohol and drug addictions as chronic medical illnesses, worthy of medical treatment and insurance and disability coverage[3]. To this end, alcohol and drug addictions are classified as disabilities under the Ontario Human Rights Code.

This medical discussion paper presents a brief overview of the principles behind the assessment and treatment of substance use disorders, describes addiction diagnostics, and reviews selected topics commonly encountered in cases before the Workplace Safety Insurance Appeal Tribunal (WSIAT).

Definitions

The latest version of the diagnostic criteria for psychiatric and addictive disorders, the Diagnostic and Statistical Manual, 5th Edition (DSM-5), was published in 2013 by the American Psychiatric Association[4]. With this publication, the terms “abuse” and “dependence” were be eliminated in preference of the term Substance Use Disorder (SUD) (e.g. Alcohol Use Disorder (AUD), rather than Alcohol Abuse or Alcohol Dependence). A review of current terminology is given below:

Substance Use Disorder (SUD): This includes a cluster of cognitive, behavioural and physiological symptoms indicating that the affected individual continues using the substance despite significant substance-related problems. The diagnostic criteria for SUDs are listed below:

> **Criterion A**: A problematic pattern of substance use leading to clinically significant impairment or distress, manifested by at least two of the following eleven criteria over the past 12 months:

1. The substance is often taken in larger amounts or over a longer period than was intended.
2. A persistent desire or unsuccessful efforts to cut down or control substance use.
3. A great deal of time is spent in activities necessary to obtain the substance, or to use and recover from its effects.

4. Craving, or a strong desire or urge to use the substance.
5. Recurrent substance use resulting in failure to fulfill major obligations at work, school or home.
6. Continued substance use despite recurrent social or interpersonal problems caused or exacerbated by substance effects.
7. Important social, occupational or recreational activities are curtailed or reduced because of substance use.
8. Recurrent substance use in situations in which it is physically hazardous.
9. Substance use is continued despite knowledge of having a psychological or physical problem that is likely to have been caused or exacerbated by the substance.
10. Tolerance, as defined by: a) a need for markedly increased amounts to achieve substance intoxication or desired effect; b) a markedly diminished effect with continued use of the same amount of the substance.
11. Withdrawal, as manifested by: a) The characteristic withdrawal syndrome for the substance upon discontinuation or reduction of use; b) the substance (or related compound) is taken to relieve or avoid withdrawal symptoms.

Remission Criteria:

a) Early Remission – Have not met above criteria in past 3-12 months;

b) Sustained Remission – Have not met above criteria for 12 more or longer.

Severity Criteria:

- Mild – Presence of 2-3 symptoms;
- Moderate – Presence of 4-5 symptoms;
- Severe – Presence of 6 or more symptoms.

It is notable that with the DSM-5, most of the previous criteria from the DSM-IV from “abuse” and “dependence” were combined in “substance use disorders”, with the exception that “legal” issues were excluded, and craving was added as a new feature.

Description of Pathophysiology

a) Causation: Drug addiction is a complex biological process that is thought to be mediated by long-term changes in the mesolimbic dopamine system located in the midbrain of the human brainstem, which is modulated by higher brain centers such as

the prefrontal cortex. Several other transmitter systems converge on these midbrain dopamine projections, including endogenous opioid peptides (e.g., enkephalins and endorphins), GABAergic, glutamatergic, and endocannabinoid systems. The final common pathway related to the effects of misused substances appears to be activation of mesolimbic dopamine systems (See **Figure 1**). Ultimately, the causes of drug addictions are thought to be multifactorial (e.g., related to the interplay of biological, social, psychological and cultural factors).

However, the recent view of addiction as a brain disease does not negate the importance of social determinants of health or societal inequalities. For example, neuroimaging research has been shown the impact of the social environment on brain functioning in people with SUDs. Moreover, social determinants of health/societal inequalities impact the biology of the brain and provide a further understanding of how this occurs, which may lead to advancement in the areas of prevention and treatment for SUDs[2].

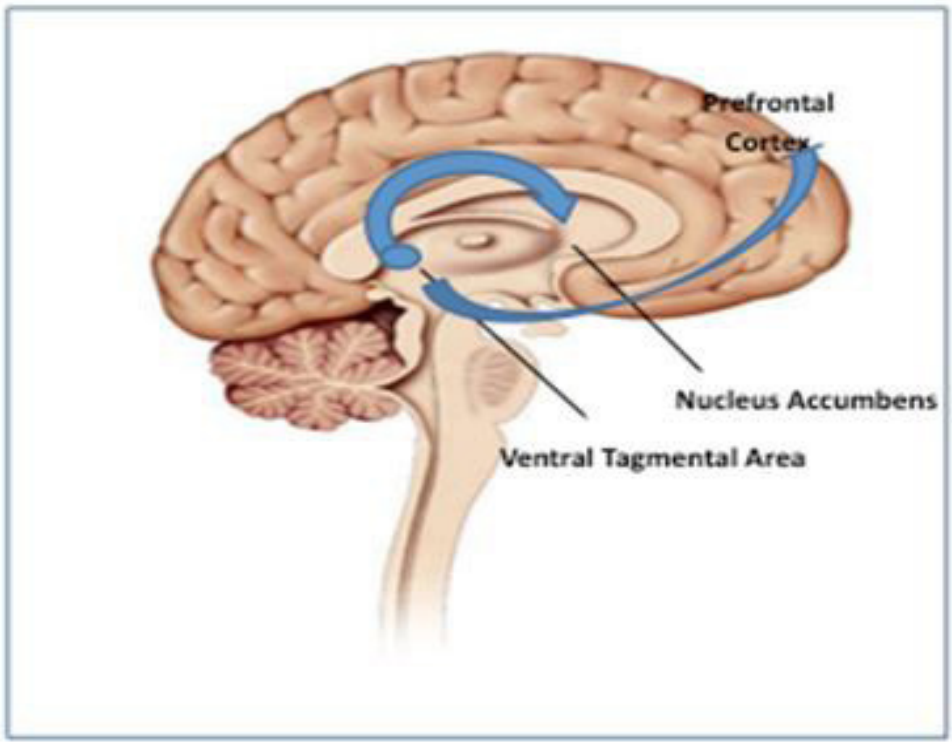

Figure 1 - Dopamine Mesolimbic Pathway

b) Clinical Profile: Drug addiction often progresses from experimental, non-dependent use to a rapid profile of compulsive drug-seeking and loss of control which progresses to substance use disorders (SUDs). Presumably, such progression is mediated by long-term changes in mesolimbic dopamine and related neurotransmitter systems in the brain reward system.

c) **Natural History:** Drug addiction is generally a clinical disorder with an onset in teenage years to early adulthood, with peak expression in middle adulthood. In later years, the course of most drug dependence tends to wax and wane, although in alcohol and other sedative-hypnotic addictions, onset may be in later years (e.g. age range of 30- 50s) and be manifest by rapid progression (e.g. “telescoping”).

d) **Effects of Treatment on Brain Systems Involved in SUDs:** There is evidence to suggest that with treatment and abstinence from SUDs, many of the changes in brain function described above in section “3a” will eventually reverse, but the time course for this reversal to normal function is unknown. However, studies use of drug cue presentation (e.g. exposing drug dependent persons to people, places or things that remind them of previous drug use to stimulate drug craving) suggest that after chronic drug exposure, the brain becomes “hard-wired” to respond to drug cues, which leads to craving, which is a proximate mediator of substance use relapse.

Diagnosis: How is it made?

a) **Diagnostic Tests:** Typically the presence of drug misuse is detected using objective drug screens in urine, blood or saliva. The clinical diagnosis of SUDs is based on clinical history, according to diagnostic schedules such as the DSM-5 or ICD-11. Point of care (rapid) testing offers the advantages of getting results immediately, which can reinforce drug reductions or abstinence. However, many hospitals rely on definitive testing which follows “chain of custody” sample handling procedures, and are definitive, confirmatory tests performed by accredited tests with higher costs and results only obtained in 3-7 days and are required for clinical and legal purposes.

b) **Differential Diagnosis:** The clinical presentations associated with SUDs can mimic several medical and psychiatric disorders, therefore use of urine and blood toxicology can be quite informative to narrow the differential diagnosis to SUD.

Risk Factors

It is important to note that both genetic and environmental factors confer vulnerabilities to the initiation and maintenance of SUDs. The best example of these dual contributions comes from the Vietnam Twin Registry Studies[5] where American troops who were identical twins (adopted away at birth) serving in the Vietnam war were followed after they returned from Vietnam (where they were first exposed to heroin and other drug use). The highest concordance rates of heroin use were found in the order monozygotic twins > dizygotic twins >> non-twin siblings, suggesting the importance of genetic contributions to SUDs. However, even amongst monozygotic twins the concordance rates were 50-60%, suggesting that environmental factors also contribute towards substance use initiation and maintenance.

Several characteristics have been shown to increase the risk for prescription narcotic use, including male gender, age <41, a history of SUDs or psychiatric co-morbidity, a history of legal problems and motor vehicle accidents, and a history of adverse childhood events[6]. Moreover, the increasing availability of prescription drugs over the internet has further contributed to rapid and easy access to these agents, which has also compounded the problems in monitoring their use and misuse. As described later, the COVID-19 pandemic has only exacerbated this situation.

Indigenous Health and Substance Use Disorders

It is well-known that indigenous people have poorer health, on average, than non-indigenous people and carry disproportionate burdens of harm related to substance use, resulting from structural and systemic disadvantages caused by colonization. Moreover, connection to indigenous culture has been shown to play a role in reducing disparities in health, including substance-related harms. To this end, evidence from prospective studies shows that people who identify as Indigenous are less likely to receive treatment for substance use and, if they do access treatment, they are more likely to drop out[7]. Thus, It is critical to take an approach to SUD and pain evaluation that embraces the needs of persons with an indigenous background, e.g. “two-eyed seeing”[8]. Unfortunately, the published literature in this area is limited. Nonetheless, one study suggested that a focus on family and social supports is critical especially in indigenous women[9]. Further work in the implementation of established and novel treatment and evaluation protocols that are sensitive to the needs of indigenous patients suffering from chronic pain and SUDs, including traditional indigenous healing practices[10], is clearly warranted.

Controversies that Surround Addiction: Sorting the Hype from the Facts

This section will focus on several important clinical controversies related to the prescription of narcotic analgesics.

A) Non-Medical Use of Prescription Narcotic Analgesics

Despite reductions in the rates of alcohol, tobacco and illicit drugs, rates of prescription narcotic analgesics continue to rise sharply[11]. In the United States, approximately 5% of the population is reported to have used non-prescribed psychotropic medications in the past month, and about two-thirds of this use was of narcotic analgesics. In fact, from 1995 to 2005, the number of Americans misusing controlled prescription drugs jumped from 6.2 to 15.2 million. The most commonly used prescriptions in the USA are hydromorphone drugs (e.g. in combination with acetaminophen), exceeding 100 million in 2005, far exceeding other commonly prescribed drugs such as atorvastatin (63 million) and amoxicillin (52 million). A similar pattern of use appears to be occurring in Canada. Therefore, the economic and social burden of prescription drug misuse is significant, and these persons appear to have much higher (8 to 9-fold) associated healthcare costs as compared to persons who do not misuse prescription drugs[12].

Many persons who go on to misuse prescription narcotic pain medication have undiagnosed or under-treated pain syndromes. Despite concerns by physicians and other health care providers that it is undesirable to prescribe larger doses or narcotic pain medication over long periods of time, it is highly recommended that analgesic medications should be prescribed in sufficient doses and for a sufficient length of treatment to adequately control acute or chronic pain[12]. However, in cases of insufficient pain relief, patients may escalate their use in an attempt to self-control their pain. The term "pseudoaddiction" has been used to describe such cases. Moreover, it has been observed in such cases that: 1) patients are using higher doses to achieve pain relief, NOT to achieve a "high"; 2) with sufficient increases in the narcotic analgesic dose by the treating physician, these aberrant behaviours will subside. Importantly, the key to success in treating such patient with chronic pain syndromes with narcotic analgesics is careful monitoring and follow-up by the treating physician.

B) Physicians encountering patients needing acute and chronic pain control who have histories of substance use disorders (SUDs)

In pain treatment settings, >90% of patients reported receiving opioids for the management of chronic pain syndromes. Rates of SUDs in these settings have been estimated to be between 18-41%[11], with one study in chronic lower back pain patients suggesting a specific prevalence of 36-56%[13]. While the presence of a history of drug or alcohol misuse should be noted in any patient to whom narcotic medication prescription is being considered, the presence of such a history should not be considered an absolute contraindication, as these medications can have clear benefits for pain management in such individuals. Careful monitoring of such patients (as with any patient prescribed these medications) is warranted, and the frequency and quantity of such prescriptions should be minimized, with more frequent visits to the prescribing physician. The use of frequent urine drug testing (UDT) is also an important part of the treatment planning for such patients, and evidence of drug relapse can be quickly obtained. In such cases, the patient can be advised that unless they agree to stop abusing illicit substances or enter drug treatment with evidence of no continuing drug use by UDT, the analgesic pain control treatment may be interrupted, especially in light of concerns about overdoses or drug interactions. The use of screening tools such as the opioid risk tool (ORT) allows prescribers to estimate risk of opioid use disorder prior to the initiation of therapy. During treatment, the use of tools such as the Current Opioid Misuse Measure (COMM), which is a tool designed to monitor for aberrant opioid-associated behaviours in patients receiving chronic opioid maintenance analgesic therapies is recommended[14]. It is important that clinicians treating co-morbid pain and SUDs employ an integrated approach which combines appropriate pharmacotherapeutic principles with psychosocial and behavioural therapies.

C) Protocols for prescribing narcotics to persons with a history of SUDs

It is frequently perceived that use of narcotic pain medications in persons with SUDs is contraindicated. However, in many cases use of these agents in acute pain settings is

necessary and consistent with compassionate treatment. Strategies to minimize the chance of drug diversion and initiation of narcotic pain addictions are also important.

In cases where such prescriptions are required, careful monitoring of prescriptions and usage should be a priority. Agents with longer half-lives and less propensity for misuse potential (e.g. methadone and buprenorphine) should be considered over short-acting, short half-life narcotic agents such as oxycodone and hydrocodone. The use of an opioid treatment agreement (OTA) is highly recommended, as it outlines the therapeutic goals of opioid therapy, responsibilities of both patient and physician, and designation of a single pharmacy source for obtaining prescriptions; such plans have been shown to increase treatment compliance and decrease the risk of illicit drug use or relapse.

The use of accepted pharmacological and behavioural treatments should be strongly considered in such individuals, under close medical supervision. Pharmacological treatments for opioid addiction include naltrexone (opioid antagonist used as a relapse-prevention strategy), and agonist-maintenance treatments (an agonist is an agent which stimulates a drug receptor, mimicking the effects of the endogenous neurotransmitter) including methadone and buprenorphine. Behavioural treatments include drug counseling (both individual and group), motivational interviewing (to engage patients, and build insight into their drug problems), and cognitive-behavioural and social skills training (to teach patients to manage cravings, and reduce exposure to high-risk situations associated with drug relapse). In addition, therapeutic interventions directed to dysfunctional relationships in the patient's life should also be addressed such as that with the spouse and/or family.

D) Issue of Drug Dependence Entitlement that is the Sequelae of Narcotic Pain Medication Treatment for a Compensable Injury: The Need for Accommodation in the Workplace and Appropriate Compensation

Addiction to narcotic analgesics is unfortunately a common complication of the treatment of chronic pain, and not easily predictable. In fact, the current state of the science in predicting who will become a narcotic misuser after a therapeutic trial of prescription opioids for analgesia is far from accurate, and there is a need for better predictive tests[12]. Nonetheless, the occurrence of narcotic addiction is a predictable sequela of pain treatment for workplace injury, and when it does occur, it is a problem that requires professional treatment and monitoring, particularly in the following circumstances:

1. There is evidence of compulsive drug-seeking with resultant psychological and physical dependence, and significant functional impairment in daily life is present;
2. Attempts by the patient and physician who prescribed the narcotics to reduce the severity and consequences of the narcotic addiction have failed.

Drug treatment (both pharmacological and psychosocial) is a mandatory part of the evaluation process, and should be done by experienced treatment professionals working in the setting of an accredited treatment facility.

Frequently Asked Questions

1. Are addictions a "personal choice"?

While it is clear that in many cases people who misuse drugs and alcohol can make the decision to stop using addictive substances, in many cases of more severe presentations of SUDs, these addictive behaviours become involuntary[15], and the personal choice element is circumvented. In such cases, professional assistance is often needed. This likely relates to the observation that chronic drug and alcohol (mis) use can cause permanent changes in the brain's reward and reinforcement centers based on neuroimaging studies in people with SUDs[16] (see Figure 1).

2. What are the signs and symptoms of drug-seeking behaviours, and their relationship to SUDs?

Prior to the onset of SUDs, there is often a history of impulsivity, pre-morbid novelty/drug-seeking behaviours and drug use experimentation, which typically begins in adolescence[17]. The "gateway hypothesis" suggests that early use and experimentation with drugs such as alcohol, tobacco and cannabis leads to use of illicit drugs such as heroin, and cocaine. However, this hypothesis has been criticized, and is perhaps better accounted for by common genetic, neurobiological and environmental factors for the initiation and maintenance of SUD.

3. What is the relationship between addictions and Posttraumatic Stress Disorder (PTSD)?

There is strong evidence that SUDs are highly co-morbid with PTSD [50-70%[18]], and that drug and alcohol misuse may occur as a "self-medication" response to acute traumatic experiences which qualify for the PTSD diagnosis. However, it is important to note that not all people exposed to a traumatic event develop PTSD, and not all people who develop PTSD in response to a traumatic event initiate and maintain a co-morbid SUD. This speaks to the issue of resilience, and that there are complex biological, psychological and social determinants of health which lead to the expression (or not) of PTSD and/or co-morbid drug and alcohol addictions, in response to traumatic stress.

4. At what point, if any, can addiction be considered a permanent condition? How would this be determined?

There has been much criticism of addiction as a brain disease[2,19]. This concern largely focuses on the assertion that addiction is a chronic and relapsing condition. Epidemiological data demonstrates that a large percentage of individuals achieve remission, often without any formal treatment, and at times resuming low-risk substance use. Thus, it has been asserted that these spontaneous remission rates invalidate the concept of a chronic, relapsing disease.

However, it should be noted that people who appear to remit spontaneously may actually do so because of limited test-retest reliability of the diagnosis. Commonly used diagnostic criteria alone tend to be over-inclusive for a reliable, clinically meaningful SUD diagnosis. For example, the DSM-5 requires that only 2 out of 11 symptoms is sufficient for a diagnosis of SUD, and this would classify individuals as belonging to the mild category. This diagnosis is likely to have low test-retest reliability and these individuals would therefore fail to exhibit a chronic relapsing course. Moreover, although a significant number of individuals diagnosed with SUDs exhibit a chronic relapsing course, a large proportion of people with SUD do not. Many individuals achieve longstanding remission and among the population of individuals with the highest prevalence of SUDs – young adults – the majority age out of excessive substance use.

Thus, it may not be beneficial to define addiction as having a chronic relapsing course as a defining feature. However, the course of SUDs is clinically significant because it indicates the need for long-term disease management instead of expecting a timely recovery[19]. Accordingly, a more accurate definition of addiction may be that it is a condition characterized by *"clinically significant impairment or distress resulting from substance use, with substantial variability in course, ranging from full remission to a chronic relapsing profile"* [2].

5. Broadly speaking, what are the risk factors for the development of a substance use disorder?

Several key factors that contribute to increased risk to SUDs are discussed below:

i. **Early life experiences:** Early life stressors (e.g., adverse childhood events) including physical, emotional, and sexual abuse; neglect; household instability (parental substance misuse and conflict, mental illness, or incarceration of family members); and poverty. Stress induced by these risk factors may act on the same stress circuits in the brain that addictive substances impact, which may explain the increased addiction risk. During adolescence, individuals are extremely vulnerable to substance misuse. In addition to a higher prevalence of risk-taking and experimentation during this period, the brains of adolescents undergo significant changes which make them vulnerable to substance exposure. For example, the frontal cortex (which includes the prefrontal cortex) does not fully develop until the early to mid-20s and heavy drinking/drug exposure during adolescence impacts the development of this critical brain region. Individuals who begin substance use during adolescence frequently experience more chronic and intensive use and are at an increased risk of developing SUDs. Moreover, adolescents who experiment with substances that go on to develop a SUDs may have pre-existing differences in their brains. For example, the volume of the frontal cortex was found to be smaller in young people who transitioned from no/minimal drinking to heavy drinking over the course of adolescence than individuals who did not drink during adolescence.

ii. **Genetic and molecular factors:** Genetic factors account for 40-70% of individual differences in risk for SUDs. Some gene variants that have been discovered to predispose individuals to or protect them from addiction are involved in the metabolism of alcohol and nicotine (e.g. aldehyde dehydrogenase and CYP 2A6), or are receptors/proteins associated with key neurotransmitters and molecules that participate in the addiction cycle. Others are involved in strengthening the connections between neurons and in forming drug memories.

iii. **Psychiatric and Substance Use Co-Morbidity:** Many individuals with SUD also have a mental health condition. For example, there is a 3-4-fold higher rate of tobacco smoking among patients with schizophrenia and approximately 30-60% of patients seeking treatment for alcohol use disorder also have PTSD. Although establishing the relationship between SUDs and mental disorders is difficult, there are several explanations for why this occurs. It is possible that having a mental illness increases ones vulnerability to SUD because certain substances may be able to alleviate symptoms. It is also possible that substance use disorders may increase an individual's vulnerability to mental disorders or trigger a mental disorder that would otherwise not have occurred. For example, alcohol tends to increase the risk for PTSD by impeding the brain's ability to recover from traumatic experiences. Moreover, in individuals with genetic vulnerabilities, cannabis may increase the risk of psychosis and schizophrenia. Finally, it is possible that both SUDs and mental disorders derive from shared, overlapping factors like a genetic predisposition, neurobiological deficits, and exposure to traumatic/stressful events[20].

iv. **Sex/Gender:** Men are at a higher risk of AUD than women, although gender differences in alcohol use are declining. Men are also more likely to have other SUDs, but women who use cocaine, opioids, or alcohol progress from initial use to a disorder at a more rapid rate than men (e.g. telescoping). Women exhibit increased symptoms of withdrawal from certain drugs like nicotine and cannabis, and maintain higher levels of cortisol and more severe negative affect during withdrawal.

v. **Race and Ethnicity:** African American smokers have been shown to exhibit greater activation of their prefrontal cortex upon exposure to smoking-related cues and have slower rates of nicotine metabolism than White smokers, both which may reduce their risk and severity of tobacco use disorder[21]. Moreover, 36% of East Asians carry a gene variant in the enzyme alcohol dehydrogenase, that alters the rate at which alcohol is metabolized. This causes a buildup of acetaldehyde, which in turn produces symptoms of flushing, nausea, and rapid heartbeat. Having this genetic variant may protect some individuals of East Asian descent from AUD.

6. What are the possible effects of a work-related injury on the development or exacerbation of a substance use disorder? What factors are contributory, protective, etc.?

High physical job demands, low skill discretion, and high decision authority have been found to be positively associated with SUDs. Adverse physical and psychosocial working conditions may increase the risk of OUD. Occupational injuries and pain are treated more often with opioids as analgesics and for longer periods compared to non-occupational injuries. Chronic opioid therapy for non-cancer pain is associated with earlier OUD onset. In addition, psychosocial work stressors such as job strain, may increase the risk of OUD through contributing to mental disorders. Depression and anxiety disorders are associated with higher dose and long-term opioid treatment and therefore OUD. Working under stressful conditions may provoke some individuals to self-medicate their negative emotions with opioids. Moreover, the risk of opioid overdose deaths is greatest among the working population[22].

It is not uncommon for workers to use opioids to get high. In fact, 20-30% of opioid overdose fatality cases used prescription painkillers for the purpose of a good feeling or getting high. Workers may use opioids to meet their high physical and emotional job demands and doing so increases their risk of work-related injuries. The prevalence of OUD was found to be highest among female workers who reported frequent heavy lifting on their jobs[23]. Women may be at a greater risk of back injury from heavy lifting tasks than men. Additionally, the incidence of long-term opioid analgesic use for non-cancer pain treatment has been found to be greater in women than men. Interestingly, job strain was more strongly associated with OUD in men. Therefore, addressing adverse working conditions in terms of biomechanical and psychosocial work hazards may significantly contribute to OUD prevention. Despite the fact that the maximum weight to be lifted with two hands is recommended to be 20 kg, 7% of participants were required to lift loads weighing greater than 20 kg for most or all of their work time.

In the case of chronic disabling occupational spinal disorders, these individuals had a partial or total work disability for at least 4 months. A significant association was found between patients with chronic disabling occupational spinal disorders and SUDs. Patients were 4.9 times more likely to suffer from SUDs and 2.2 times more likely to suffer from any SUD compared to the general population[23].

7. What is the relationship between pain and addiction? What is the relationship between pain, mental health and addiction?

Pain is the most common presenting complaint to primary healthcare workers, and is a potent stressor that increases the risk of substance relapse. As described previously, “pseudoaddiction” describes a pattern of maladaptive narcotic analgesic use that is driven by inadequate treatment of pain. A diagnosis of pseudoaddiction is made retrospectively. If aberrant behaviour is reduced or eliminated with appropriate treatment of pain, pseudoaddiction may be the more appropriate diagnosis[24].

If a patient expresses that their aberrant behavior is due to inadequate analgesia, the clinician should carefully review the treatment plan and if appropriate, titrate the prescribed medication upward to decrease pain and improve function. An increase in dose should be accompanied by a reduced prescribing interval and an assessment of whether drug misuse, pseudoaddiction, or OUD is a possibility. Pain and addiction can exist as co-morbid conditions but also as a dynamic continuum. In certain situations, the drug may be the problem and the solution. In other cases, such as when pain co-occurs with cocaine or alcohol use disorders, the SUD is the more likely diagnosis. With chronic pain, the appropriateness of prolonged opioid use should be periodically assessed, particularly when there is a lack of objective evidence of improvement in pain relief or function. When pain and addiction co-exist, failure to treat both conditions will most likely lead to poor outcomes. A patient suffering from addiction may be both addicted to and physically dependent on a drug, but the majority of pain patients taking opioids are physically dependent but are not addicted to these drugs. Thus, physical dependence is not necessary or sufficient for a diagnosis of addiction to be made

Chronic pain and psychiatric diagnoses have a bidirectional relationship[25]. Many individuals may develop a psychiatric disorder as a result of chronic pain. Moreover, a history of mental illness is a risk factor for chronic pain. In pain populations, 30-60% have co-occurring depression. Patients with pain and comorbid depression suffer from increased pain severity, poorer functioning, and more disability compared to non-depressed pain patients. Interestingly, 50% of patients diagnosed with depression report experiencing physical pain symptoms. Moreover, the presence of a psychiatric diagnosis increases the chance of being prescribed an opioid and developing OUD. When pain persists for longer than 6 months, it is considered chronic. Psychosocial factors increase the risk of transition from acute to chronic pain. Compared to acute pain, chronic pain exceeds the normal healing time, lacks a biological purpose, and is more strongly associated with psychological factors. Previously, it was believed that chronic pain was due to ongoing peripheral nociceptive input from peripheral tissues. It is more likely that both the peripheral and central nervous system play a role in determining which nociceptive input detected by sensory nerves in the peripheral tissues will lead to the perception of pain. Many with significant peripheral nociceptive input will not experience pain and some without any identifiable peripheral nociceptive input will experience severe pain.

Central pain describes any CNS pathology or dysfunction that may contribute to the development or maintenance of chronic pain. Centralized pain has been predominantly associated with idiopathic or functional pain syndromes like fibromyalgia, headache, and irritable bowel syndrome. The physiological hallmark of fibromyalgia – centralized pain is augmented central pain processing. When there is a lack of identifiable, diffuse, peripheral inflammatory process involving body tissues, the central nervous system is likely causing augmented pain processing. There is evidence of decreased μ-opioid receptor availability in fibromyalgia patients – possibly due from an increased release of endogenous opioids (e.g. enkephalins). Together with the finding of increased endogenous opioids in the cerebrospinal fluid, these results contribute to

the understanding of why opioid analgesics do not appear efficacious in patients with fibromyalgia. There are increases in concentrations of glutamate in the pain processing regions like the insula in patients with fibromyalgia. Gabapentin likely alleviates pain in these patients by reducing glutaminergic activity. In fibromyalgia patients, it has been demonstrated that the level of depressive symptomatology did not influence the degree of neuronal activation in the primary and secondary somatosensory cortices which are responsible for the coding of sensory intensity of pain. However, depressed individuals displayed increased activation in the amygdala and insula which are responsible for the affective or cognitive processing of pain.

Patients with chronic pain benefit from a combination of pharmacotherapy and behavioural interventions. The CDC in the United States recommends against using opioids to treat chronic pain and that they should only be employed if all other treatment options have been exhausted. Certain antidepressants have at least moderate analgesic effects and are recommended as first line treatment for some pain conditions. Pain processing and mood are controlled by common neurotransmitters: serotonin, norepinephrine, glutamate, and GABA. Therefore, pain and depression should respond to similar pharmacological treatments. There is limited evidence that selective serotonin reuptake inhibitors (SSRIs) for example can successfully treat pain specifically, but they are recommended in the case of comorbid symptoms of depression. Tricyclic antidepressants (TCAs) and serotonin and norepinephrine reuptake inhibitors (SNRI's) most likely improve pain by enhancing activity down descending antinociceptive pathways that use norepinephrine and serotonin as key neurotransmitters. These drugs do not make pain better by improving depression, but because the same neurotransmitter serves different functions in different brain regions. Gabapentinoids such as gabapentin and pregabalin act in the CNS by reducing glutamatergic activity in ascending pain pathways.

It is important to note that pain and mental illness should not be treated with a one-size fits all approach. Medications should be considered for their individual efficacy on pain and mood. CBT for chronic pain focuses on the relationship between cognitions, emotions, and behaviors and how these interact with pain and functioning. CBT for pain primarily targets symptom relief and increasing physical functioning. Although the focus of CBT in the context of chronic pain management does not directly address depression, mitigating pain or increasing physical activity may also improve mood. In addition, CBT may also be helpful in patients with comorbid substance use disorder. Chronic pain management should focus on the biopsychosocial model and target functional improvement and quality of life as opposed to just symptom elimination. Needless to say, failure to address co-occurring mental health issues will impede pain management.

8. Is there a relationship between a history of drug use or alcohol use and the subsequent development of a substance use disorder after a work-related injury? What are some of the risk factors?

A history of SUDs is the most robust predictor of opioid misuse in people with chronic pain. Polysubstance use also increases the risk of opioid misuse. Moreover, surgical procedures are the primary reason for exposure to prescription opioids[26]. Inadequate postoperative pain management is associated with increased risk of chronic pain which warrants the need for long-term opioid utilization. Individuals who are prescribed opioids within a week of a low-risk surgical procedure are 44% more likely to become prolonged opioid users within one year after the surgery compared to individuals who did not receive prescription opioids. In the study by Lawal and colleagues[26], prolonged opioid use after surgery was found to be increased in females; among individuals with a high school degree versus a college degree or higher; among individuals using antidepressants, opioids, benzodiazepines, alcohol, cocaine, or tobacco before surgery (with preoperative use of opioids, tobacco, or cocaine having the strongest association with prolonged opioid use after surgery). In addition, individuals who had filled at least one opioid prescription in the year before surgery had a 5.3-fold risk of prolonged opioid use after surgery. Finally, prolonged opioid use after surgery was also found to be increased among participants with anxiety, depression, and mood disorders. Prolonged opioid use after surgery was strongly associated with a history of back pain and fibromyalgia.

9. What are the short-term and long-term health consequences of addiction?

Many physical health problems are associated with problematic drug and alcohol use, which can impact the functioning of many organ systems directly and indirectly. Alcohol can damage almost every tissue and physiological system which can subsequently lead to disability or disease. In outpatient (67%) and inpatient (33%) populations seeking addiction treatment, Keaney et al.[27] the majority of the SUD group were addicted to opioids (91.5%) and of those, the majority (96%) were addicted to heroin. Moreover, 75% of participants were cigarette or other tobacco smokers. 76% of the sample had at least 1 physical health problem upon admission. Gastrointestinal and liver disorders were the most commonly identified problems, and occurred in 36%, cardiovascular problems in 28%, respiratory problems in 30%, and dental problems in 23% of the overall sample. Physical health problems were more common among patients with AUD. Among individuals with SUD, respiratory disorders were the most common health problem, but there were no significant differences between SUD and AUD patients on this domain. In both groups, physical health was worst among those treated in inpatient settings. Commonly diagnosed gastrointestinal disorders included gastric bleeding, peptic ulcers, pancreatitis, and liver disease (such as cirrhosis), while the most commonly diagnosed cardiovascular disorder was hypertension. Moreover, AUD patients had more severe physical health problems than patients with SUD. Physical health problems were exacerbated by poor nutrition, limited health care, unemployment, or homelessness.

The leading cause of accidental injury and death among adolescents are related to SUDs[28]. Behaviours associated with drinking and drug use in adolescence lead to an increased risk of injury and violence. These behaviors include driving under the influence of alcohol or being driven by someone under the influence of alcohol. Approximately 1/6 of college students have reported driving while under the influence of drugs. Importantly, substance use among adolescents is associated with risky sexual behaviors, which are associated with STDs among teens. Unprotected sex and a history of sex with multiple partners is more common among substance misusers.

Teens with SUDs are three times more likely to make a suicide attempt compared to teens who do not use drugs. Moreover, there is a high rate of comorbid SUD and mental health/psychiatric disorders among adolescents. Rates of depression are higher for girls than boys with SUDs and anxiety symptomology is highly prevalent for both adolescent boys and girls with SUDs.

10. What are recognized treatments for substance use disorders? What is their typical duration, format, etc.?

In this section, the focus will be on the pharmacological and behavioural treatments of opioid[29] and alcohol use disorders[30].

Opioid Use Disorders (OUD): Methadone, Buprenorphine (in combination with naloxone, as Suboxone) and Naltrexone are the FDA and Health Canada approved medications for the treatment of OUD.

Methadone is long-acting synthetic opioid agonist which can prevent withdrawal symptoms and reduce craving among individuals addicted to opioids. It can also block the effects of other opioids. It is taken orally and was approved for the treatment of OUD in the 1960's and is a long-acting opioid receptor agonist, that is the mainstay of OUD treatment. However, it is associated with significant side effects (constipation, sedation and respiratory depression).

Buprenorphine is a synthetic opioid that acts as a partial agonist at μ-opioid receptors, and an antagonist at κ-opioid receptors. It does not produce the euphoria and sedation characteristic of heroin and other opioids and can reduce or eliminate withdrawal symptoms. There is a low risk of overdose when taking this drug. Buprenorphine is available in 2 formulations that are taken sublingually – a pure form of the drug and a more commonly prescribed formulation called Suboxone (combination of buprenorphine with naloxone – the short-acting opioid receptor antagonist). Naloxone has no effect when Suboxone is taken as prescribed but if an individual tries to inject Suboxone, naloxone will produce severe withdrawal symptoms which decreases the likelihood the drug will be misused. Buprenorphine can be provided in office-based settings by qualified physicians, and is also available as an implant (Probuphine) and injection (Sublocade).

Finally, **naltrexone** is a synthetic μ-opioid antagonist. It prevents the euphoric effect of opioids. By taking naltrexone, the repeated absence of the desired effects from opioids will eventually diminish craving and addiction. Naltrexone has no potential for misuse and is not addictive. It is normally prescribed in outpatient medical settings; however it should begin after medical detoxification in a residential setting to prevent withdrawal symptoms. It is taken orally, either daily or 3 times a week, however noncompliance is a frequent problem. A long-acting injectable version of naltrexone (Vivitrol) only needs to be delivered once a month which can facilitate increased compliance; however, it is not available in Canada.

Alcohol Use Disorder (AUD): There are three Health Canada and FDA-approved medications for AUD: Naltrexone (ReVia), acamprosate (Campral) and disulfiram (Antabuse).

As with OUD, **naltrexone** antagonizes μ-opioid receptors and endogenous opioid function, which are also involved in alcohol craving and the reinforcing effects of drinking.

The newest anti-alcohol agent **acamprosate** acts to enhance gamma-aminobutyric acid (GABA) and inhibit glutamate neurotransmitter systems and reduces symptoms of protracted withdrawal. This drug may be more effective in patients with severe alcohol dependence.

Finally, **disulfiram** is an aldehyde dehydrogenase inhibitor which interferes with the degradation of alcohol which causes acetaldehyde to accumulate. This causes an unpleasant reaction involving flushing, nausea, and palpitations if an individual drinks alcohol. Compliance is often poor when taking disulfiram, but it still may be effective in patients who are highly motivated. Patients may only use it for high-risk situations, and it can be administered in a monitored fashion to improve compliance.

Other off-label medications that can be used to treat AUD include the anti-convulsant agents gabapentin, topiramate and lamotrigine.

Behavioural Treatments:

Motivational Interviewing (MI): MI is a counseling approach that assists people in resolving their ambivalence about engaging in treatment and abstaining from drug use. This strategy aims to promote rapid and internally motivated change as opposed to guiding the patient in a stepwise fashion through the recovery process. The effects of MI depends on the drug used and goal of the intervention. It is successful with people addicted to alcohol for improving their engagement in treatment and reducing their problematic drinking. MI (or when combined with personalized scenarios, motivational enhancement therapy) can also be used successfully in SUD adults when combined with CBT[31].There are mixed results on the efficacy of MI/MET for individuals misusing

other drugs like heroin, cocaine, and tobacco. In general, MI is more effective for engaging drug misusing people in treatment rather than promoting changes in drug use.

Cognitive Behavioral Therapy (CBT): CBT is based on the theory that learning plays a critical role in the development of maladaptive behavioral patterns like substance misuse. Individuals undergoing CBT learn to identify and correct problematic behaviors, for example dealing with drug cues, triggers and high-risk social situations that promote substance use relapse. The patient is taught to anticipate likely problems and strengthening their self-control through the development of effective coping strategies. Techniques include exploring the positive and negative consequences of continued drug use, self-monitoring to recognize cravings early, identifying situations that put one at risk for relapse, and developing strategies to manage cravings and avoid high-risk situations.

Contingency Management (CM): CM involves giving patients tangible rewards to reinforce positive behaviors like abstinence. In both methadone programs and psychosocial counseling treatment programs, incentive-based interventions are highly effective at increasing treatment retention and promoting abstinence. Two examples are described below:

Voucher-Based Reinforcement (VBR): In VBR, patients receive a voucher for every drug-free urine sample provided. These vouchers have monetary value that can be exchanged for food items, movie passes, or other goods or services consistent with a drug-free lifestyle. VBR has been demonstrated to be effective in promoting abstinence from opioid and cocaine in patients undergoing methadone detoxification.

Low Cost CM: This method uses cash prizes instead of vouchers. Programs last at least 3 months and involve participants supplying drug-negative urine or breath tests in exchange for drawing from a bowl for the chance to win a prize worth between $1-$100. The number of draws start at one and increases with consecutive negative drug tests and/or counseling sessions attended but resets to one after a drug-positive sample or unexcused absence.

Twelve-Step Programs: Twelve-step programs (e.g. Alcoholic Anonymous) involve an engagement strategy used to promote substance users becoming affiliated with and involved in 12-step self-help groups. They have been proven to be effective in treating AUD, and there is preliminary but promising research that suggests it is also helpful for helping people with other SUDs maintain abstinence.

11. How might the use of pharmacological treatment modalities (e.g. methadone) influence the other medications a worker can use for the work-related injury?

At the correct dosage, medications used in methadone-assisted treatment (MAT) have minimal adverse effects on intellectual function, mental capability, physical functioning, or employability. However, side effects of the medications used in MAT may hinder a person's ability to drive, operate heavy machinery, or perform other functions safely.

Typically signs of excessive MAT dosing are sedation (e.g. “nodding”) and constipation. In addition, medications that are CYP 3A4 inhibitors (e.g. phenytoin, carbamazepine, ritonavir, fluvoxamine) may increase (or decrease) the circulating levels of methadone, causing these MAT-related adverse or withdrawal effects[32].

Individuals who work in safety-sensitive jobs may require restrictions or limits on their duties while taking these medications. Reasonable accommodations by the employer should be considered. When starting MAT, people should avoid driving and hazardous work activities until their dosages are stabilized, side effects are managed, and impairment risks related to their work are properly assessed. It is also important to note that side effects of these medications often diminish over time (e.g. tolerance).

12. Has the COVD-19 pandemic had an impact on the development of substance use disorders? How? Are there certain workers who are more affected?

Mental health impacts of the COVID-19 pandemic include increased symptoms of anxiety, depression, and suicidal ideation. Moreover, both alcohol and cannabis use has increased. Before the pandemic in 2019, Statistics Canada found that 67% of Canadians reported excellent or very good perceived mental health. Moreover, 14% of respondents reported severe depression symptoms. In 2015-2016, the Canadian Community Health Survey found that 2% of Canadians reported moderately severe/ severe symptoms of depression, and 24% of respondents reported moderate to severe anxiety symptoms. In addition, 5% of respondents seriously contemplated suicide since March of 2020. This is compared to a Statistics Canada finding in 2019 that 3% of Canadians reported seriously contemplating suicide in the past 12 months. They also found that 30% of respondents who use alcohol reported greater consumption during the pandemic. More than 20% of respondents who use alcohol reported problematic use. In addition, 40% of respondents who use cannabis reported increasing their use during the pandemic. 40% of respondents who use cannabis reported problematic use.

Respondents’ financial status, social isolation, and health concerns were found to be the most significant stressors during the pandemic; 30% of respondents reported less exercise and social interaction in late November/early December 2020.

In addition, another study found that confinement at home due to the sustained lockdown, and detrimental financial burdens have led to psychological difficulties and excessive substance misuse[33]. People with SUDs are at a higher risk for pulmonary infections due to substance misuse related pre-existing cardio-pulmonary morbidities, compromised immunity, altered health-seeking behavior and inadequate access to health care resources, failure of rehabilitation strategies due to social distancing and housing instability. Moreover, smoking is an adverse prognostic indicator of COVID-19. Alcohol consumption can lead to a dysfunctional immune system, vitamin deficiency, aspiration pneumonia, liver and cardiometabolic diseases, and thrombosis which can all lead to poor health outcomes after contracting COVID-19. Opioids can cause respiratory depression and hypoxemia which can lead to cardiopulmonary and neurological complications and poorer COVID-19 outcomes. Behaviours associated with substance

use that increase the risk of viral spread, including vaping and smoking, spitting (in the case of tobacco-chewers) and sharing cigarettes, alcohol, and needles.

The COVID-19 pandemic led to chronic social isolation, physical distancing, and sustained lockdown which resulted in widespread deterioration of health and well-being. Many individuals dealt with psychosocial stressors including prolonged home confinement, depression and panic, fear, vulnerability, work from home, unstable financial situation, unemployment, lack of job prospects, and uncertainty about the future. Sudden unemployment is particularly distressing for individuals in low-income groups such as migrant works, daily earners, and small businessmen. Distressed individuals may cope through addictive substances which can trigger the development of SUD. Thus, there has been a widespread increase of alcohol, tobacco, and electronic cigarette use during the pandemic.

The prolonged travel-ban limited the supply of recreational substances in the market which paved the way for adulterated and toxic substitutes at cheaper prices. Moreover, prompt medical attention during the pandemic for this population has also been much more difficult to obtain. In terms of behavioural addictions, internet usage and in particular, pornography and video gaming, significantly increased during the pandemic. In addition to compromised mental health, increased screen time reduces physical activity, and leads to poorer eating habits and disrupted circadian rhythms, all of which can contribute to cardiometabolic disorders, obesity and diabetes. SUDs are already highly prevalent amongst the homeless, migrant workers, prisoners and other marginalized communities. These groups are also at an increased risk of contracting COVID-19. Health care workers have been found to be particularly vulnerable to behavioral addictions to cope with the stress of the pandemic. Addiction is often referred to as a disease of isolation and many treatment strategies for substance users involve family support, socialization, and CBT.

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