

Canadian Guidelines on Opioid Use Disorder Among Older Adults 2019

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Canadian Guidelines on Opioid Use Disorder Among Older Adults

Scope

The Canadian Coalition for Seniors Mental Health (CCSMH) received a grant from the Substance Use and Addictions Program (SUAP) of Health Canada to create a set of guidelines on the prevention, assessment, and management of **substance use disorders** among older adults. This guideline on opioid use disorder (OUD) in older adults (age ≥ 65) is one in a series of four that also includes [alcohol](#), [cannabis](#), and [benzodiazepines](#). Primarily, these guidelines are targeted to primary care clinicians and specialists serving older adults. In addition, these guidelines are meant to inform patients, caregivers, and care facility administrators.

The GRADE approach was utilized in the creation of these guidelines. The methodology can be found in a separate document at ccsmh.ca.

An introduction which highlights issues of relevance to all four guidelines can be found at ccsmh.ca.

These guidelines are not intended to provide a comprehensive guide on the use of opioids either by medical prescription or recreationally. Rather, the goal of this document is to provide useful guidance for clinicians on preventing the development of **OUD** and optimally assessing and treating older individuals who have developed such a disorder.

Although our guidelines are described in four separate documents, multiple substance use is common. Clinicians are encouraged to utilize all of the guidelines when relevant.

Summary of Recommendations and Grades

We used the GRADE approach (Grading of Recommendations, Assessment, Development and Evaluation) as a method of grading the quality of evidence and the strength of recommendations. In following the GRADE process, the initial step was to grade the quality of available evidence supporting each recommendation. Subsequently, we identified the overall strength of the recommendation taking into account both the quality of the evidence and other factors such as the potential to do harm, the cost and feasibility.

We developed a separate category for recommendations which are not primarily based on empirical evidence; but have agreement that they represent best clinical practice. Examples would include: optimal assessment processes and those related to education and/or policy. These recommendations have been categorized as “C” for consensus. We did not use the GRADE process for these recommendations. Other guideline groups have used a similar approach e.g. British Association for Psychopharmacology Guidelines (2012). While such recommendations lack empirical evidence, we believe they are also useful and important.

GRADE

| QUALITY OF EVIDENCE | STRENGTH OF RECOMMENDATION |
|---|---|
| The quality of evidence for each recommendation is determined through an examination of the following factors: (1) Study design and the quality of the studies that were included, (2) the directness of the evidence (generalizability or applicability) and (3) the confidence that patients will benefit from the treatment. | The strength of each recommendation is determined through an examination of the following factors: (1) The balance between benefits and undesirable effects/risks, (2) uncertainty or variability of patient values and preferences and (3) the resources associated with management options. |

****High quality evidence doesn't necessarily imply strong recommendations, and strong recommendations can arise from low quality evidence.*

QUALITY OF EVIDENCE

| | |
|-----------------|--|
| HIGH | Further research is unlikely to change confidence in the estimate of effect |
| MODERATE | Further research is likely to have an important impact on the confidence in the estimate of effect and may change the estimate |
| LOW | Further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate |

Note: Meta analyses and Randomized Controlled Trials are considered high quality vs. Observational studies which are considered low quality

STRENGTH OF RECOMMENDATION

| | |
|---------------|---|
| STRONG | Strong recommendations indicate high confidence that desirable consequences of the proposed course of action outweigh the undesirable consequences or vice versa. |
| WEAK | Weak recommendations indicate that there is either a close balance between benefits and down sides (including adverse effects and burden of treatment), uncertainty regarding the magnitude of benefits and down sides, uncertainty or great variability in patients' values and preferences, or that the cost or burden of the proposed intervention may not be justified. |

(Adapted from Guyatt et al, 2008)

QUESTION A: In older adults, what measures can reduce the risk of developing an OUD?

RECOMMENDATION #1:

In order to avoid the risk of developing an OUD, older adults with acute pain in whom opioids are being considered should receive the lowest effective dose of the least potent immediate release opioid for a duration of ≤ 3 days and rarely > 7 days.

[GRADE Quality: Moderate; Strength: Strong]

RECOMMENDATION #2:

In most circumstances, avoid prescribing opioids for older adults with CNCP. For severe pain that is not responsive to non-opioid therapy in patients without a history of substance use disorder and without active mental illness, a trial of opioid treatment may be considered. Consider obtaining a second opinion before prescribing long-term opioid therapy. After explaining the risks and benefits to the patient, prescribe only in accordance with published guidelines for adults, initiate and maintain opioids at lower doses than for younger adults, and discontinue if function does not improve or if adverse effects arise. [GRADE Quality: Moderate; Strength: Strong]

RECOMMENDATION #3:

Patients and their families should be advised to store opioids safely, never to share their medication, and to return unused medication to the pharmacist for disposal. [GRADE Quality: Low; Strength: Strong]

RECOMMENDATION #4:

Pharmacists and nursing staff are advised to inform the prescriber if there are concerns with co-prescribing, adherence to treatment, or intoxication. [GRADE Quality: Low; Strength: Strong]

QUESTION B: In older adults with or at risk for an OUD, what preventive measures can reduce the risk of opioid overdose?

RECOMMENDATION #5:

In older adults with polypharmacy or comorbidities that increase the risk of opioid overdose (e.g., benzodiazepine use, renal failure, sleep apnea), the lowest effective opioid dose should be used and tapering the opioid and/or other medications should be considered.

[GRADE Quality: Moderate; Strength: Strong]

RECOMMENDATION #6:

Once the decision is made to reduce the opioid dose, a slow outpatient tapering schedule (e.g., 5% drop every 2-8 weeks with rest periods) is preferable to more rapid tapering.

A faster taper schedule may be attempted under special circumstances of medical need, if the patient is in a treatment setting with medical supervision.

[GRADE: Quality: Low; Strength: Weak]

RECOMMENDATION #7:

Dispense naloxone kits to anyone using opioids regularly for any reason (CNCP, OUD, etc.), and train household members and support staff on use. [GRADE Quality: Low; Strength: Weak]

RECOMMENDATION #8:

Include skilled pharmacists and/or nurses on teams to educate patients on appropriate use of opioids and other medications.

[GRADE Quality: Low; Strength: Weak]

RECOMMENDATION #9:

Older adults with or at risk for an OUD should be given advice on strategies to reduce the risk of opioid overdose and information on supervised consumption sites, if available in the community.

[GRADE Quality: Moderate; Strength: Strong]

QUESTION C: In older adults, when and how should one screen for an OUD?

RECOMMENDATION #10:

Older adults should be screened for an OUD using validated tools, if appropriate (e.g., CAGE-AID, ASSIST, PDUQp, ORT, POMI, COMM). Medication reviews and urine drug screens should be utilized if the patient is taking opioids for CNCP or an OUD.

[GRADE Quality: Low; Strength: Strong]

QUESTION D: In older adults at risk for an OUD, what are the elements of assessment?

RECOMMENDATION #11:

Identify a diagnosis of an OUD through completion of a comprehensive assessment, including substance use, medical, pain, psychiatric, cognitive, and psychosocial history within a cultural context, and conduct a brief functional assessment. The use of validated assessment tools may be useful in this process. In addition, a detailed physical examination must be conducted, with an emphasis on signs of intoxication or withdrawal and the sequelae of substance use. Laboratory and other investigations (including urine drug tests) should be performed as appropriate for the medical conditions identified. Reassessment is essential and should be conducted episodically throughout long-term care.

[GRADE Quality: Moderate; Strength: Strong]

QUESTION E: In older adults with or at risk for an OUD, what considerations are important to patients during the assessment process?

RECOMMENDATION #12:

A full explanation of findings and diagnosis must be shared with the patient and, if appropriate, caregivers. Therapeutic optimism should be provided (i.e., hope given that addiction is a treatable disorder and that older adults, and especially older women, typically have better treatment outcomes than younger adults). [Consensus]

QUESTION F: In older adults with an OUD, what approaches and medications are safe and effective for opioid withdrawal management?

RECOMMENDATION #13:

Opioid withdrawal management should only be offered in the context of connection to long-term addiction treatment. [GRADE Quality: Moderate; Strength: Strong]

RECOMMENDATION #14:

Induction onto an opioid agonist is recommended over a non-opioid treatment withdrawal management in older adults with an OUD. If a trial of tapering is attempted, there should be the option to initiate longer-term opioid agonist therapy or opioid antagonist therapy. [GRADE Quality: Moderate; Strength: Weak]

RECOMMENDATION #15:

Buprenorphine-naloxone should be considered first line for opioid withdrawal management in older adults. Methadone is an alternative that may be used, however consider the added risk of adverse events. [GRADE Quality: Moderate; Strength: Weak]

RECOMMENDATION #16:

For symptom control during opioid withdrawal management, adjuvant medications (see comments) can be used in a time-limited fashion but with caution due to medical comorbidities, side effect risk, and other concerns related to older age. [GRADE Quality: Moderate; Strength: Weak]

QUESTION G: What medications and protocol adjustments are safe and effective in the treatment of an OUD in older adults to improve outcomes?

RECOMMENDATION #17:

Buprenorphine maintenance should be considered a first-line treatment for an OUD in older adults. [GRADE Quality: Moderate; Strength: Strong]

RECOMMENDATION #18:

Methadone maintenance treatment may be considered for those older adults who cannot tolerate buprenorphine maintenance or in whom it has been ineffective. [GRADE Quality: Moderate; Strength: Strong]

RECOMMENDATION #19:

If renal function is adequate, daily witnessed ingestion of slow-release oral morphine may be considered with caution for those older adults in whom buprenorphine and methadone maintenance have been ineffective or could not be tolerated. Careful supervision of initiation onto short-acting morphine first is recommended, prior to transition to maintenance with the long-acting 24-hour formulation. [GRADE Quality: Low; Strength: Weak]

RECOMMENDATION #20:

For older adults with an OUD for whom opioid agonist treatment is contraindicated, unacceptable, unavailable, or discontinued and who have established abstinence for a sufficient period of time, naltrexone may be offered. [GRADE Quality: Moderate; Strength: Weak]

RECOMMENDATION #21:

Offer medications for an OUD in the context of connection to long-term addiction, mental health, and primary care treatment, where careful monitoring and dose titration can occur. [GRADE Quality: Moderate; Strength: Strong]

RECOMMENDATION #22:

Advise patients that the use of alcohol, benzodiazepines, and other sedative-hypnotics is hazardous when combined with opioid agonist treatment. If the older adult is living in the community and is already physiologically dependent on one of these substances, then slow tapering of the substance(s) (to elimination if possible) rather than abrupt cessation is recommended. If the patient is in hospital, residential treatment, or a long-term care setting and medically managed by an experienced provider, detoxification can progress more rapidly, concurrent with the initiation or stabilization on medications for OUD. [GRADE Quality: Moderate Strength: Strong]

RECOMMENDATION #23:

Early take-home dosing for buprenorphine maintenance treatment may be considered, including home induction in patients who are low risk, if they find it difficult to attend the office in withdrawal and if the patient has social supports at home. This approach should not be considered for methadone initiation unless supervised (e.g., reliable caregiver or medical personal administration). [GRADE Quality: Low; Strength: Weak]

QUESTION H: In older adults, compared with younger adults, what dose/protocol adjustments are needed when initiating or maintaining medications to treat an OUD?

RECOMMENDATION #24:

Reduce initial doses of medications for treatment of an OUD (e.g., by 25%-50%); slow dose escalation frequency (e.g., by 25%-50%); use the lowest effective dose to suppress craving, withdrawal symptoms; and drug use; and monitor closely (especially for sleep apnea, sedation, cognitive impairment, and falls with opioid agonists). [GRADE Quality: Low; Strength: Strong]

RECOMMENDATION #25:

The threshold to admit an older adult with social, psychological, or physical comorbidities to either residential or hospital care for opioid withdrawal management or induction onto medications for an OUD should be lower than for a younger adult. [GRADE: Quality: Moderate; Strength: Strong]

RECOMMENDATION #26:

In older adults on medication for an OUD requiring management of mild-to-moderate acute pain or CNCP, non-medication and non-opioid strategies are recommended. For those on an opioid agonist for an OUD who have severe acute pain that has been unresponsive to non-opioid strategies, a short-acting opioid may be considered for a short duration (1-7 days) along with a taper, if necessary (1-7 days). [GRADE Quality: Moderate; Strength: Weak]

QUESTION I: In older adults, what psychosocial interventions are effective in the treatment of an OUD to improve outcomes?

RECOMMENDATION #27:

Psychosocial interventions should be offered concurrently with medications for an OUD, at a pace appropriate for age and patient needs, but they should not be viewed as a mandatory requirement for accessing pharmacotherapy. [GRADE Quality: Moderate; Strength: Strong]

RECOMMENDATION #28:

Contingency management may be offered as part of opioid treatment programs and used if accepted by the patient. [GRADE Quality: Moderate; Strength: Weak]

QUESTION J: For older adults with an OUD, what are the treatment considerations for special populations (specifically indigenous peoples)?

RECOMMENDATION #29:

Traditional healing practices used by indigenous communities can be integrated with buprenorphine treatment to improve outcomes for an OUD. [GRADE Quality: Low; Strength: Weak]

QUESTION K: For older adults with an OUD, what specific treatment recommendations are suggested for non-community-based facilities?

RECOMMENDATION #30:

If experienced, clinicians may manage older adults with a mild-to-moderate OUD; however, for patients with more severe or complex disorders, it is recommended that personnel or teams with advanced substance use disorder management skills be accessible to support clinicians and to enhance their capacity to care for patients in all settings. The threshold for an admission to hospital or drug and alcohol treatment facility under the care of an Addiction Medicine Specialist is lower than for younger adults, and closer follow-up is needed on discharge to ensure appropriate community-based support. [GRADE Quality: Moderate; Strength: Strong]

RECOMMENDATION #31:

Older adults with an OUD who are admitted to a hospital, drug and alcohol treatment facility, or non-medical facility with access to medical care (e.g., prisons and shelters) should be offered opioid agonist treatment at the onset of withdrawal (advisable within 1-3 days), with bridging pharmacological treatment on discharge with confirmed transfer of care. [GRADE Quality: Moderate; Strength: Strong]

QUESTION L: For older adults with an OUD, what systemic factors support recovery?

RECOMMENDATION #32:

The cost of medically-recommended pharmacological and non-pharmacological treatment for an OUD in older adults should be covered by the public health plan. [GRADE Quality: Moderate; Strength: Strong]

Canadian Guidelines on Opioid Use Disorder Among Older Adults

Rationale

Opioids have been used for medicinal and religious purposes for thousands of years, and the addictive potential of this class of substance has been documented in the Western medical literature for centuries (Astyrakaki et al., 2010; Dormandy, 2012). The current opioid crisis began with the overprescribing of opioids for acute and chronic pain and has now grown to epidemic proportions, with the unchecked distribution of potent illicit opioids (Volkow et al., 2019).

Globally, according to the World Health Organization people over the age of 50 accounted for 27% of deaths from drug use disorders in 2000, a figure that rose to 39% by 2015. Of those deaths in older adults (age ≥ 65), approximately 75% were linked to the use of opioids (Degenhardt & Hall, 2012; UNODC, 2018). Despite these numbers, there is a paucity of data about the many ways opioids specifically affect older adults and about how to care for those who develop addiction, also referred to as an OUD (American Psychiatric Association, 2013).

The purpose of these guidelines is to highlight the issues facing older adults with, or at risk for, an OUD, and to provide recommendations for the prevention, screening, assessment, and treatment of an OUD in those ≥ 65 years of age. This guideline may also apply to those chronologically up to a decade younger but functionally aged by the consequences of their drug use (Bachi et al., 2017).

Opioid Pharmacology and Availability in Canada

The term “opioid” refers to any substance that binds to an opioid receptor. Endogenous opioid peptides (e.g., endorphins), natural or synthetic exogenous opioid receptor agonists (e.g., morphine), and opioid receptor antagonists (e.g., naloxone) are all, by definition, opioids (Inturrisi et al., 2018). For the purpose of this guideline, however, the term opioid will be restricted to the description of natural or synthetic exogenous full or partial opioid receptor agonists, unless otherwise specified.

Opioids bind allosterically to mu, kappa, delta, and/or NORpr opioid receptors found in the central nervous system, gut, and circulating immune system. Some opioid effects can be clinically beneficial, including analgesia, relief of diarrhea, respiratory calming in chronic obstructive lung disease, and assistance with end of life management (Inturrisi et al., 2018; Busse et al., 2018). Other short- and long-term effects of opioids are detrimental, including nausea and vomiting, constipation, sedation, mood changes, myocardial infarction, immunosuppression, and trauma, the latter of which includes falls, fractures, and motor vehicle accidents. Other harmful effects of opioids include hormone suppression leading to sexual dysfunction and osteoporosis, dry mouth leading to

tooth decay, respiratory depression leading to sleep apnea and/or overdose (sometimes fatal), and addiction (Baldini et al., 2012).

Most clinicians are aware that chronic opioid use can lead to both physiologic tolerance and dependence, and a withdrawal syndrome when opioids are discontinued (or when the doses are lowered quickly). Many health care providers and patients, however, are unaware that opioid use can also, paradoxically, cause a generalized increase in pain sensitivity (opioid-induced hyperalgesia) (Mao, 2002; Rivat & Ballantyne, 2016). During withdrawal, further pain sensitivity may arise as the hyperalgesia is unmasked (Hooten et al., 2015). As well, during opioid withdrawal, pain can return to old healed injury sites (called withdrawal-associated injury site pain), and it may take weeks to months for pain sensitivity to normalize after opioids are discontinued (Rieb et al., 2016; 2018). These issues are particularly important for older adults, since 30% to 40% of older adults suffer from chronic pain, a condition that becomes increasingly prevalent until the age of 85. As the baby boomer population ages, the use of opioids to treat pain rises (Johannes et al., 2010; Schofield, 2018).

There are four alkaloid opioids (also called opiates) derived from opium that can be extracted from the poppy plant (*Papaver somniferum*): morphine, codeine, thebaine, and papaverine. Semi-synthetic opioids include hydromorphone and diacetylmorphine (heroin). Synthetic mu opioid receptor agonists available by prescription in Canada for the management of pain include tramadol, oxycodone, meperidine, tapentadol, fentanyl, remifentanyl, sufentanyl, methadone, and buprenorphine. Opioids with mixed kappa receptor agonism and mu receptor antagonism that are available to treat pain include pentazocine, butorphanol, and nalbuphine.

Medications to treat OUD encompass both opioid agonists and antagonists. Several opioid agonist treatments are authorized for OUD in Canada. Liquid methadone is most common and has the longest history of use. Sublingual buprenorphine is also approved as opioid agonist therapy and is available as a sublingual formulation mixed with naloxone to discourage injection (BUP-NX). Other forms of buprenorphine will soon become available in Canada, including a monthly subcutaneous injection and an implantable capsule that releases medication over a period of several months. Slow-release oral morphine (SROM), a capsule opened and sprinkled onto applesauce or into liquid, taken once daily, is also available as opioid agonist therapy in some provinces.

Buprenorphine has some unique properties. It acts as a full mu opioid receptor agonist with respect to its analgesic effect, yet it is only a partial mu opioid receptor agonist with respect to its effect on mood (euphoria) and respiratory depression (Raffa & Pergolizzi, 2013). One systematic review found that in twenty-five of twenty-six studies, buprenorphine had clinical analgesic efficacy that was comparable or superior to morphine (Raffa et al., 2014). Also unique to buprenorphine is its affect as a kappa opioid receptor antagonist, which may positively affect mood (Falcon et al., 2016).

Mu opioid receptor antagonists available by prescription in Canada include injectable and intranasal naloxone, methylnaltrexone, naloxegol, and oral naltrexone, either alone or as an agonist/antagonist product where it is mixed with oxycodone. While naloxone is bioavailable in parenteral or intranasal forms, it is not efficacious when taken orally.

Naloxone is therefore used only for resuscitation purposes.

Naltrexone, however, is bioavailable in both oral and parenteral formulations and can be used for abstinence-based treatment of an OUD. At the time of this writing, the manufacturer of an injectable

extended release form of naltrexone (XR-NTX) has yet to apply to Health Canada for approval of its use. Physicians may prescribe XR-NTX to their patients, however, if their provinces or health authorities apply to Health Canada under a special authority based on exceptional need, such as that defined by the current opioid crisis.

Many of the prescription opioids mentioned above are obtainable through the illicit drug market in Canada, as are a number of highly potent and often lethal fentanyl derivatives, including carfentanyl.

Addiction and the Opioid Crisis

Addiction is a more complex process than simply the development of tolerance and withdrawal. An OUD involves an individual's pathological relationship with an opioid, leading to the compulsive use of the substance despite negative consequences, as well as negative emotional states during times of abstinence. These behaviors and affective states correspond to changes in brain chemistry and function, particularly in the mesolimbic system, hippocampus, amygdala, and prefrontal cortex (Volkow & Koob, 2018). Opioids can cause a type of Pavlovian conditioning, with a learned association between drug use and the physiologic and perceptual effects of the drug. This can lead to craving (or the urge for pain relief) and/or altered opioid use (Volkow & McLellan, 2016). Thus, the neurobiology of addiction can be summarized in a cyclic three stage framework: binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation (Uhl et al., 2019).

Historically, lack of education in medical schools and residency programs about pain and addiction has led to an under-prepared and under-skilled population of clinicians having to recognize and deal with these potentially fatal medical disorders (Rieb & Wood, 2014; Volkow & McLellan, 2016; Klimas et al., 2017).

In recent years, the opioid crisis has often made headline news in North America, however the impact on older adults is often missed. In Canada, from 2007 to 2015, hospitalizations for opioid overdose (referred to as poisonings) have been consistently higher in older adults than in any other age cohort. At over 20 per 100,000, these older-adult admissions are almost double that of 15 to 24 year old, and represent 30% of all admissions to hospital for opioid poisoning (Canadian Institute

for Health Information (CIHI), 2018b). Most opioid poisonings in older adults in Canada are accidental: 33% of those poisonings, however, are intentional (National Initiative for the Care of the Elderly (NICE), 2018). A recent study found that in older adults, opioid misuse was associated with increased odds of suicidal ideation (Schepis et al., 2019), and opioids are often the substance involved in both suicide attempts and completions when medications are used.

Other factors that may contribute to the high rate of opioid poisonings in older adults in Canada include addiction, prescriber error, patient confusion about medication instructions, dosing errors due to cognitive problems, drug-drug interactions, and metabolic changes. Also, polypharmacy may play a role in opioid poisonings in older adults, including fatal overdoses. The co-ingestion of alcohol and prescription medications (e.g. benzodiazepines, tricyclic antidepressants, and possibly gabapentinoids) can increase the risk of respiratory depression and death (Canadian Agency for Drugs and Technology in Health (CADTH), 2011). Adults accessing the illicit drug market and using drugs such as cocaine or other stimulants as well as potent opioids such as fentanyl and other derivatives, has been associated with the rise in coroner cases and increased street availability of those drugs in British Columbia (Baldwin et al., 2018).

Opioid Use Disorder in Older Adults

In Canada, by 2016, older adults outnumbered children for the first time, reaching 13% of the population. By July 1, 2018 that number had reached 17.2% (Statistics Canada, 2018). In the United States, persons > 65 years of age are projected to go from representing 15% of the population in 2014 to 21% of the population by 2030. Similar growth is expected in Canada (United States Census Bureau, 2018). Adults born between 1946 and 1954 are often referred to as the baby boomer generation. “Boomers,” as they are nicknamed, have had more permissive attitudes toward drug use, easier access to opioid medications, and a greater exposure to illicit drug use than any previous generation (Burgos-Chapman et al., 2016). As a result, there are two primary cohorts of older adults who develop OUD.

The first group with OUD is made up of those who have been exposed to opioids for many years through drug experimentation, often beginning in adolescence or early adult

life. Some have been identified with and treated for an OUD, and many have had adverse health consequences as a result of their drug use as well as for other reasons (Lofwall et al., 2005; Hser et al., 2007; Grella & Lovinger, 2011). The second group of older adults who may develop an OUD are those prescribed opioids by a health care provider for a pain condition and who may have continued taking prescription opioids for an extended period (Jinks & Raschko, 1990; Kalapatapu & Sullivan, 2010). Others may have turned to the illicit market in order to maintain an ongoing supply of opioids following discontinuation of their prescription by a health care professional.

In one study of 75 adults up to age 70 who were hospitalized for an OUD, 46% had begun their addiction with a “legitimate prescription” (Canfield et al., 2010). According to the 2005-6 US National Survey on Drug Use and Health (NSDUH), in the 10,953 people > 50 years of age surveyed, 1.4% had misused their opioid prescription medications in the past year (0.6% in those ≥ 65), and of these, 21% first did so after the age of 50 (Blazer & Wu, 2009). Based on these data, the authors estimated that 9% to 10% of those who misuse their medication go on to develop an OUD. Another US study found that a significant source of prescription drugs available on the street in Delaware were diverted from older adults, who tended to sell to a few trusted friends or a dealer who then resold the medication to others (Inciardi et al., 2009).

According to the latest NSDUH in 2016, 0.8% of adults surveyed met Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) criteria for OUD in the past year (Substance Abuse and Mental Health Services Administration (SAMHSA), 2017). In contrast, the prevalence of OUD in older adults for prescription and illicit opioids in Canada has been difficult to estimate using current survey information. This may be due in part to the hesitancy of participants to disclose illegal activity and to survey questions gathering information in a form which does not align with DSM diagnostic criteria (Canadian Centre on Substance Use and Addiction (CCSA), 2018). In Canada, 43.9% of adults > 55 years of age have used a prescription opioid and 1.1% of that group have done so daily (or almost daily) in the last year (Ibid). In the decades prior to 2015, the amount of opioid prescribed in Canada had risen substantially. In 2015 to 2016, however, while the average dose of opioid prescribed actually dropped, the overall number of opioid prescriptions written continued to rise (CIHI, 2018a). During that time, more than 20% of older Canadian adults had at least one opioid prescription,

the negative impacts of which are substantial (Ibid). Of the 128 older adults who died of opioid-related causes in Ontario between 2013 and 2016, 73 (57%) had an active prescription for an opioid at the time; the rest did not (Gomes et al., 2018), implying either stockpiling of a previous prescription or illicit opioid use.

In clinical interviews, OUD may present more subtly in older adults and require a more nuanced approach (Sullivan & Levin, 2016). OUD may overlap with physiologic tolerance alone and may be mistaken for or masked by other medical conditions. Consequences from opioid use may not be recognized in older adults who have stopped work and who have restricted social networks, thus limiting symptomatology in those domains. Obtaining a history from an older adult, especially one with cognitive impairment, can be challenging in a busy office or hospital setting. Confidentiality and the avoidance of stigmatization are important aspects of effective patient engagement and rapport with older adults in general, but they become essential in the context of a possible OUD. Patient engagement in the therapeutic process is one of the ways to ensure that all individuals with OUD, including older adults, are identified through screening and assessment and receive appropriate evidence-informed pharmacological and psychosocial treatment. Keep in mind that older adults who become addicted to opioids can exhibit some of the same behaviours as their younger counterparts, including seeking medications from multiple providers, stealing prescription pads from offices, and purchasing opioids from friends and/or drug dealers.

Adults entering older age are having an effect on the demographics of substance use and on the need for treatment, its utilization, and its cost. For example, one study from New York City found that, as of 2012, adults > 60 years of age comprised 13.1% of those in opioid treatment programs, up from 1.7% in 2006 (Han et al., 2015). This study also noted a shift from illicit drugs to those obtained by prescription as the primary type of opioid used. In 2003, it was estimated that the number of older adults in the United States needing treatment for OUD will rise 70% by 2020, to 4.4 million (Gfroerer, 2003). Additionally, when compared to their younger counterparts, older US veterans with OUD have higher rates of comorbid mood disorder, post-traumatic stress disorder, hepatitis C,

human immunodeficiency virus, and chronic pain, including neuropathy, which has notably increased the cost of care (Larney et al., 2015).

In Canada, the need for expanded resources for treatment of older adults with OUD will likely rise in the coming years proportional to the US estimates. Evidence-based treatment for OUD in adults in general is cost-effective and decreases both morbidity and mortality (Krebs et al., 2018). The lifetime savings to provincial and national health care based on this evidence-based model could be substantial. All components of the Canadian health care system must prepare to provide addiction treatment to older adults, including those affected by an OUD.

Prevention of Opioid Use Disorder Among Older Adults

According to the model proposed by George Vaillant, MD, there are host, agent, and environmental risk and protective factors that affect the development of a substance use disorder, including genetics, social role modeling, and drug exposure (Vaillant, 1995). Identified risk factors for OUD in older adults include being male, exposure to illicit opioids earlier in life, social isolation/loneliness, having a psychiatric disorder prior to OUD, and having pain (Burgos-Chapman et al., 2016). To curb opioid poisonings and OUD, measures need to be implemented for both primary prevention (before opioid initiation) and secondary prevention (when using an opioid but prior to experiencing problems indicative of an OUD). These issues are outlined in the questions (A-B) and addressed in the recommendations (1-9) listed below.

QUESTION A: In older adults, what measures can reduce the risk of developing an OUD?

RECOMMENDATION #1:

In order to avoid the risk of developing an OUD, older adults with acute pain in whom opioids are being considered should receive the lowest effective dose of the least potent immediate release opioid for a duration of ≤ 3 days and rarely > 7 days.

[GRADE Quality: Moderate; Strength: Strong]

A recent guideline from the United States recommends that opioids may be used as a last resort to manage acute pain, while the dose and duration of opioid therapy should be the lowest possible to avoid unnecessary exposure to longer opioid therapy (Dowell et al., 2016).

In Ontario, the 2018 Quality Standards recommend prescribing the lowest effective dose of the least potent immediate-release opioid, with a duration of ≤ 3 days and rarely > 7 days (Health Quality Ontario (HQO), 2018). Two fair-quality retrospective cohort studies found opioid therapy prescribed for acute pain to be associated with a greater likelihood of long-term opioid use (Alam et al., 2012). Another large, prospective cohort study found that the stronger predictor of continued opioid use at 1 year was the receipt of a first prescription supply that exceeded 10 or 30 days (Shah et al., 2017). These studies included adults and were not conducted specifically with older adult populations; however, the messages were consistent.

This recommendation is unlikely to have any adverse effects, provided other options to manage acute pain are available and successfully avoid unnecessary suffering, especially postsurgical pain (HQO, 2018). It has been previously recommended that older adults taking opioids for CNCP who do not meet criteria for OUD be tapered or switched to buprenorphine then tapered (Le Roux et al., 2016).

RECOMMENDATION #2:

In most circumstances, avoid prescribing opioids for older adults with CNCP. For severe pain that is not responsive to non-opioid therapy in patients without a history of substance use disorder and without active mental illness, a trial of opioid treatment may be considered. Consider obtaining a second opinion before prescribing long-term opioid therapy. After explaining the risks and benefits to the patient, prescribe only in accordance with published guidelines for adults, initiate and maintain opioids at lower doses than for younger adults, and discontinue if function does not improve or if adverse effects arise.

[GRADE Quality: Moderate; Strength: Strong]

There is consensus from three international recently published guidelines from Canada, the United States, and the United Kingdom that prescribing long-term opioid therapy for chronic non-cancer pain should be avoided (Abdulla et al., 2013; Dowell et al., 2016; Busse et al., 2017). The majority of the evidence included in these guidelines relates to adults, but these recommendations are even more important for older adults, in whom polypharmacy and multiple comorbidities are common. In a study of adults with chronic low back pain, hip or knee pain treatment with opioids was not superior to treatment with nonopioid medications for improving pain-related function over 12 months (Krebs et al., 2018).

This recommendation is unlikely to have any adverse effects; however, it is important to manage chronic pain using non-opioid therapies and non-pharmacological interventions in order to avoid unnecessary suffering and poor quality of life. Patient education, self-management strategies, movement based interventions, mind-body therapies, alternative therapies, and psychosocial support are all important in the ongoing long-term management of chronic non-cancer pain (HQO, 2018).

When choosing an opioid for cancer pain or chronic noncancer pain, a buprenorphine transdermal patch may be a lower-risk and efficacious option to consider even in those > 70 years of age, although cognitive impairment may still occur with any opioid (Griessinger et al., 2005).

RECOMMENDATION #3:

Patients and their families should be advised to store opioids safely, never to share their medication, and to return unused medication to the pharmacist for disposal.

[GRADE Quality: Low; Strength: Strong]

Some patients (and caregivers) may not know when their prescriptions include opioids. It is important to educate patients that certain medications (such as Tylenol#3®, Tramacet®, OxyIR®, etc.) contain opioids and have the potential to be used for non-medical purposes, e.g., “to get high”.

In Canada, pharmacies, hospitals, and transport companies are required to report to Health Canada every time controlled drugs are lost, whether through robbery, pilferage, or errors (Government of Canada, 2019). Health Canada data indicate that nine million doses of controlled substances—most of them opioids—were reported missing between January 1, 2012 and September 30, 2017. The annual number of pills, patches, and packages reported missing has climbed steadily since 2013 (Carman & Adhopia, 2018). The above-mentioned diversion does not include pills that are stolen or lost from the medicine cabinets of patients’ homes. This latter type of diversion is particularly relevant for older adults who have adolescents in their milieu, multiple caregivers, or who have cognitive impairment.

A recent Canadian guideline of opioids for CNCP recommends returning used fentanyl patches to the pharmacy prior to receiving the next prescription (patch-for-patch program) (Busse et al., 2017). This approach is mandatory in Ontario, and it might be good practice to generalize it to include any unused opioids (pills, tablets, liquid, patches, or topicals).

The implementation of this recommendation is unlikely to have any adverse effects; however, the prescriber and dispenser may need to take the time to explain this recommendation to patients and caregivers and answer their questions.

RECOMMENDATION #4:

Pharmacists and nursing staff are advised to inform the prescriber if there are concerns with co-prescribing, adherence to treatment, or intoxication.

[GRADE Quality: Low; Strength: Strong]

Although there is little direct evidence to support this approach, it is good practice for prescribers and dispensers to contact each other when there are concerns with the opioids being prescribed. This is especially true in the older adult population, in whom it is common to have polypharmacy, poor compliance, or higher risk for overdose (Canadian Pharmacists Association, 2016; Dowell et al., 2016).

The implementation of this recommendation is unlikely to have any adverse effects; however, the prescriber and dispenser may face challenges when seeking opportunities to contact each other for a discussion about these concerns.

QUESTION B: In older adults with or at risk for an OUD, what preventive measures can reduce the risk of opioid overdose?

RECOMMENDATION #5:

In older adults with polypharmacy or comorbidities that increase the risk of opioid overdose (e.g., benzodiazepine use, renal failure, sleep apnea), the lowest effective opioid dose should be used and tapering the opioid and/or other medications should be considered.

[GRADE Quality: Moderate; Strength: Strong]

Recent Canadian and American guidelines on opioid use for CNCP recommend reducing the opioid dose to the lowest effective dose to minimize risks of adverse events, including OUD, overdose, and death (Dowell et al., 2016; Busse et al., 2017; 2018). This is especially important in older adults, in whom polypharmacy and comorbidities are common.

The implementation of this recommendation is unlikely to have any adverse effects and may reduce unintentional deaths related to opioids. It is recognized, however, that tapering opioids can be challenging for the prescriber and the patient. It is important to mobilize resources that can assist in opioid tapering by increasing the knowledge, skills, and self-confidence of the prescriber. A number of educational initiatives across Canada (in-person or online) offer training for safe and effective opioid tapering for patients with CNCP (Busse et al., 2017; Rx Files, 2018).

RECOMMENDATION #6:

Once the decision is made to reduce the opioid dose, a slow outpatient tapering schedule (e.g., 5% drop every 2-8 weeks with rest periods) is preferable to more rapid tapering. A faster taper schedule may be attempted under special circumstances of medical need, if the patient is in a treatment setting with medical supervision.

[GRADE: Quality: Low; Strength: Weak]

The decision to taper and potentially discontinue either long-term opioid therapy for pain or opioid agonist treatment for addiction is complex and requires thoughtful assessment and consideration for each patient as an individual. Tapering opioids in older adults with pain (and without an OUD) may offer the advantage of increased cognitive alertness and lower the risk of potential adverse outcomes (e.g., falls, myocardial infarction, sleep apnea, overdose,). However, tapering opioids can also pose some risks if done inappropriately. Too great or too frequent a dose drop or abrupt cessation can lead to overwhelming withdrawal symptoms including pain, anxiety, insomnia, lowering of mood (including increasing suicide risk), craving, a move to use illicit or stockpiled opioids, and a dangerous drop in tolerance (Rieb et al., 2016).

Instead, a slow taper schedule (e.g., 5% drop every 2-8 weeks) may be needed with rest periods of 2 to 3 months when symptoms arise. Faster taper schedules can be employed if the patient is in a residential or hospital care setting under medical supervision and there is a medical indication for faster lowering of the opioid. There may be a point at which further lowering can be detrimental to the patient's health. In that case, stabilizing the dose and reviewing in 6 months may be appropriate. Clinical guidelines exist for tapering opioids in adults with CNCP (Berna et al., 2015), but not for older adults.

Generally, for patients with an OUD, opioid agonist treatment (without tapering) is recommended due to the very high opioid reinitiation ("relapse") rate when treatment is discontinued, and the subsequent elevated risk of death due to lack of tolerance (Bruneau et al., 2018).

However, lowering or discontinuation of opioid agonist treatment can be considered under the following circumstances: patient preference, adverse events, safety sensitive work or sport, dangerous co-use of other drugs/medications, or lack benefit. Tapering or discontinuation is more successful if the patient has good recovery capital and has remained free of drug- and alcohol-taking behaviors (aside from appropriate use of prescribed medications) for 1 to 2 years (HOO). In adults, patients who taper off buprenorphine

appear to fare better than those who taper off methadone, and slow taper schedules (e.g., 5% per 2-8 weeks) with rest periods (2-3 months when symptomatic) are more successful than fast tapers (10% per 1-2 weeks) (Nosyk et al., 2012). Again, if medically indicated, this process can move more rapidly under medical supervision, especially within an inpatient setting.

RECOMMENDATION #7:

Dispense naloxone kits to anyone using opioids regularly for any reason (CNCP, OUD, etc.), and train household members and support staff on use.

[GRADE Quality: Low; Strength: Weak]

In studies of younger adults, there is weak evidence that having an antidote at home may save some patients from dying if they face an opioid overdose (Walley, Doe-Simkins, et al., 2013; Walley, Xuan, et al., 2013). This practice is recognized as a safe public health strategy and is endorsed by many public health organizations.

Naloxone kits are free in many Canadian provinces, but they require some training to obtain and use properly, and often another person is needed to administer the naloxone to the patient. Providing naloxone is not a substitute for offering addiction treatment.

Be aware that the implementation of this recommendation by providing naloxone kits may occasionally have unintended consequences, such as false reassurance that all opioid overdoses can be reversed, and opioid users may feel emboldened to use higher doses (clinical experience).

RECOMMENDATION #8:

Include skilled pharmacists and/or nurses on teams to educate patients on appropriate use of opioids and other medications. [GRADE Quality: Low; Strength: Weak]

There is weak evidence from studies conducted with younger adults that the involvement of a skilled pharmacist or nurse in the multidisciplinary management of opioid therapy or OUD for patients with CNCP can be helpful (Costello & Thompson, 2015; Manworren & Gilson, 2015; Jukiewicz et al., 2017).

The implementation of this recommendation requires resources and funding for interprofessional and multidisciplinary teams to collaborate in the education, initial trial, monitoring, and tapering of opioids.

RECOMMENDATION #9:

Older adults with or at risk for an OUD should be given advice on strategies to reduce the risk of opioid overdose and information on supervised consumption sites, if available in the community.

[GRADE Quality: Moderate; Strength: Strong]

Individuals with an OUD require education on and access to harm reduction strategies, equipment, and facilities in order to reduce personal morbidity and improve the chances of survival, while decreasing the risk of spread of harm to others in society.

Supervised injection sites, needle exchange programs, and naloxone kit distribution are all examples of such strategies (Bastos & Strathdee, 2000; Kerr et al., 2005; Ng et al., 2017). Also, certain opioid prescribing practices may limit harms of OUD and overdose. For example, involving the pharmacist or family member to dispense and/or supervise medication, prohibiting early refills, limiting the dose or amount dispensed at any one time, using tamper-resistant medications and blister packing medications for take-home dosing, and implementing random callbacks for pill counts and urine drug screens.

Screening for and Assessment of Opioid Use Disorder Among Older Adults

Screening and assessment are the starting points for care of a person with an OUD, and many effective approaches to both exist for adults (Rieb, 2019). Table 1 provides an overview of some of the issues that may necessitate altering approaches screening and assessment for OUD to accommodate the unique needs of older adults, using the criteria in the DSM-5 (Kuerbis et al., 2014). Due to these issues, Kuerbis and colleagues suggest that further assessment be done if an older adult has just one positive feature for OUD (Ibid). The DSM-5 term “Unspecified Opioid Related Disorder” is used to describe simply the misuse or non-medical use of an opioid and may be an applicable diagnosis once addiction is ruled out.

Listed below are questions (C-E) along with recommendations (10-12) for screening and assessment of OUD specific to older adults (Kuerbis et al., 2014):

QUESTION C: In older adults, when and how should one screen for an OUD?

RECOMMENDATION #10:

Older adults should be screened for an OUD using validated tools, if appropriate (e.g., CAGE-AID, ASSIST, PDUQp, ORT, POMI, COMM). Medication reviews and urine drug screens should be utilized if the patient is taking opioids for CNCP or an OUD.

[GRADE Quality: Low; Strength: Strong]

Older adults often have atypical presentations of OUD, so timely recognition and identification can be challenging and may fail to occur. Although evidence of age-specific screening tools for OUD in older adults is limited, clinicians should use tools validated for the older adult population when appropriate (e.g., CAGE-AID, ASSIST, PDUQp). Screening can help to identify misuse that may not be obvious to clinicians and encourage early and appropriate

treatments. The ASSIST screening tool was successfully used in the Brief Intervention and Treatment for Elders (BRITE) program in health care and non-health care settings (Schonfeld et al., 2015). Medication reviews and urine drug screens should be utilized if the patient is taking opioids for any reason (Draper et al., 2015). One screening tool validated in older adults with pain who are already prescribed opioids is the Pain Medication Questionnaire (Park et al., 2011). Screening tools validated in adults in general prescribed opioids for pain include the Current Opioid Misuse Measure (COMM) and the Prescription Opioid Misuse Index (POMI), along with others like the Opioid Risk Tool (ORT) (Becker et al., 2013). National guidelines by the CCSA (2016) and the ASAM (2015) recommend routine screening, rescreening, and monitoring, particularly if the person has presented to the emergency department or has repeat presentations to primary care for pain medications.

Other presentations to keep in mind that might help distinguish the older adult with OUD from the one with pain alone may include one or more of the following (based on clinical experience): The patients with pain and an OUD tend to be on higher doses than is usual for their underlying condition; they sometimes run out of opioid medication early or have

Table 1 Opioid Use Disorder: This refers to a problematic pattern of opioid use leading to clinically significant impairment or distress, as manifested by at least two of the following occurring within a 12-month period.

| DSM-5 CRITERIA FOR OUD | CONSIDERATION FOR OLDER ADULTS |
|--|---|
| The opioid is taken in larger amounts or over a longer period of time than intended. | Cognitive impairment can prevent adequate self-monitoring. Opioids themselves may more greatly impair cognition among older adults than younger adults. |
| There is a persistent desire or unsuccessful efforts to cut down or control opioid use. | It is the same as for the general adult population. |
| A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects. | Consequences from opioid use can occur from using relatively small amounts. |
| There is craving, or a strong desire or urge to use an opioid. | It is the same as for the general adult population, but older adults with entrenched habits may not recognize cravings in the same way as the general adult population. |
| There is recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home. | Role obligations may not exist for older adults in the same way as for younger adults because of life-stage transitions, such as retirement. The role obligations more common in late life are caregiving for an ill spouse or family member, such as a grandchild. |
| There is continued use of the opioid despite persistent or recurrent social or interpersonal problems caused or exacerbated by their effects. | Older adults may not realize the problems they experience are from opioid use. |
| Important social, occupational, or recreational activities are given up or reduced because of opioid use. | Older adults may engage in fewer activities regardless of opioid use, making it difficult to detect. |
| There is recurrent opioid use in situations in which it is physically hazardous. | Older adults may not identify or understand that their use is hazardous, especially when using opioids in smaller amounts. |
| Opioid use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by drug use. | Older adults may not realize the problems they experience are from opioid use. |
| Tolerance as defined by either a need for markedly increased amounts of the opioid to achieve intoxication or desired effect OR a markedly diminished effect with continued use of the same amount of the opioid (note: criterion not felt to be met for an individual taking the drug under medical supervision). | Because of the increased sensitivity to substances as they age, older adults may seem to have lowered rather than increased tolerance. |
| Withdrawal as manifested by either characteristic withdrawal symptoms OR the opioid is taken to relieve or avoid withdrawal symptoms. | Withdrawal symptoms can manifest in ways that are more subtle and protracted. Nonproblematic users of opioids may develop physiologic dependence. |

Adapted from Kuerbis, A., et al. (2014). Substance Abuse Among Older Adults. *Clinics in Geriatric Medicine*, 30(3), 629-654.

other aberrant behaviours; they usually have underlying risk factors (e.g., anxiety, insomnia, depression, past history of a substance use disorder); they can have poor or deteriorating function and mood; they sometimes report significant withdrawal symptoms; they can show extreme resistance to tapering or cessation, even though they do not appear to get much analgesic benefit from the opioid; and family members have expressed concern about their opioid use.

QUESTION D: In older adults at risk for an OUD, what are the elements of assessment?

RECOMMENDATION #11:

Identify a diagnosis of an OUD through completion of a comprehensive assessment, including substance use, medical, pain, psychiatric, cognitive, and psychosocial history within a cultural context, and conduct a brief functional assessment. The use of validated assessment tools may be useful in this process. In addition, a detailed physical examination must be conducted, with an emphasis on signs of intoxication or withdrawal and the sequelae of substance use. Laboratory and other investigations (including urine drug tests) should be performed as appropriate for the medical conditions identified. Reassessment is essential and should be conducted episodically throughout long-term care.

[GRADE Quality: Moderate; Strength: Strong]

When a patient is deemed at risk for an OUD, a comprehensive assessment should be performed (Rieb, 2019). To confirm a diagnosis of OUD, the medical literature suggests that clinicians should use a systematic and age-appropriate approach that includes a functional assessment, history of substance use and medical comorbidities, as well as a history of pain and psychiatric, cognitive, and psycho-social-spiritual factors within a cultural context (Wu & Blazer, 2011; RCP, 2015; CCSA, 2016; Rao & Crome, 2016). The use of validated assessment tools may be useful in this process, and even screening tools can be used as a springboard for further exploration of the topic. In addition, a detailed physical examination must be conducted, with an emphasis on signs of substance intoxication and withdrawal, along with the sequelae of opioid and other substance use. Laboratory and other investigations (including but not limited to liver and kidney function and urine drug tests) should be performed, as appropriate to the medical conditions identified. Reassessment is essential and should be conducted episodically throughout long-term care.

A review conducted by the RCP (2015) identified risk factors relating to substance misuse in older people, including physical, psychological, and social factors. Rao & Crome (2016) provide details regarding specific assessment questions to ask. In TIP 63, SAMHSA provides screening and assessment tools for adults with substance use disorder, including opioid withdrawal measures and interpretation of urine drug screening (SAMHSA, 2018).

QUESTION E: In older adults with or at risk for an OUD, what considerations are important to patients during the assessment process?

RECOMMENDATION #12:

A full explanation of findings and diagnosis must be shared with the patient and, if appropriate, caregivers. Therapeutic optimism should be provided (i.e., hope given that addiction is a treatable disorder and that older adults, and especially older women, typically have better treatment outcomes than younger adults).

[GRADE: Consensus]

In a questionnaire-driven study of 197 individuals (Luoma et al., 2007) many of those interviewed stated that, as a result of having been diagnosed with a substance dependence disorder, they felt as if they had been stigmatized, both by others and by themselves, and that there had been negative consequences as a result of that diagnosis. This was particularly the case if they had accepted treatment for that illness.

Although randomized controlled trials of pharmacological and/or behavioural treatments for OUD in those > 65 years of age are lacking, some observational trials that include older persons demonstrate that older adults tend to do better in treatment than their younger counterparts, and older women do even better than men, providing reason to provide therapeutic optimism (Carew & Comiskey, 2018).

It is therefore essential that older adults who meet criteria for an OUD be reassured that such disorders are treatable illnesses and that they will receive comprehensive and effective care delivered in a timely and confidential fashion. Similarly, it is important that those involved with the patients' care—family members in particular—receive similar reassurances. This is best provided, initially, by clearly explaining both how the diagnosis was made and the methods of treatment recommended.

Treatment of Opioid Use Disorder Among Older Adults

Pharmacological Treatment:

Long-term medications for an OUD include opioid agonist treatment and opioid antagonist treatment. The options for opioid medications to treat an OUD that exist in Canada currently are provided in Box 1.

Issues related to pharmacological treatments are asked in questions (F-H) and answered in recommendations (13-26) listed below.

QUESTION F: In older adults with an OUD, what approaches and medications are safe and effective for opioid withdrawal management?

RECOMMENDATION #13:

Opioid withdrawal management should only be offered in the context of connection to long-term addiction treatment. [GRADE Quality: Moderate; Strength: Strong]

Recent guidelines and systematic reviews in older adults recognize OUD as a chronic disease that requires long-term management strategies (SAMHSA, 2004; *The ASAM Handbook of Addiction Medicine*, 2015; *The ASAM Essentials of Addiction Medicine*, 2015; ASAM, 2015; VA & DoD, 2015; Burgos-Chapman et al., 2016; CCSA, 2016; Le Roux et al., 2016; Loreck et al., 2016; Maree et al., 2016; Hassell et al., 2017; Bruneau et al., 2018). These sources base recommendations on observational studies of methadone patients and case series of those admitted to residential treatment, along with expert opinion. This clinical recommendation is well-established in younger adults, in whom retention in treatment is key for reduction in drug use, morbidity, and mortality. There is little potential harm in following patients long-term.

RECOMMENDATION #14:

Induction onto an opioid agonist is recommended over a non-opioid treatment withdrawal management in older adults with an OUD. If a trial of tapering is attempted, there should be the option to initiate longer-term opioid agonist therapy or opioid antagonist therapy.

[GRADE Quality: Moderate; Strength: Weak]

We did not identify any randomized controlled trials or observational studies on opioid withdrawal management in older adults. Thus, this recommendation is based on guidelines and systematic reviews from the adult literature as well as systematic and narrative reviews in older adults with lower age cut-offs (SAMHSA, 2004; *The ASAM Principles of Addiction Medicine*, 2009; *The ASAM Essentials of Addiction Medicine*, 2015; *The ASAM Handbook of Addiction Medicine*, 2015; ASAM, 2015; VA & DoD, 2015; Burgos-Chapman et al., 2016; CCSA, 2016; Gowing et al., 2016; Le Roux et al., 2016; Loreck et al., 2016; Maree et al., 2016; Hassell et al., 2017; Bruneau et al., 2018). Based on these sources, non-opioid medications used for withdrawal management carry significant risks in older adults (e.g., clonidine may cause postural hypotension, leading to falls). Also, opioid agonist medications have been shown to effectively manage opioid withdrawal (Wright et al., 2011) and more so than non-opioid medications in adults.

The adult literature clearly demonstrates that both relapse and overdose risk are greater among those who only undergo detoxification (tapering to elimination) than in those with an OUD who are maintained on agonist or antagonist treatment (Amato et al., 2013; Gowing et al., 2017). Users who attend abstinence-based treatment programs (without access to antagonist treatment) have a high drop-out rate, compared with those initiated on opioid agonist treatment (due to craving and withdrawal symptoms). They also have a higher rate of fatal overdose than patients who were never detoxified and continue to use because of loss of tolerance. Therefore, treatment providers have an obligation to offer opioid agonist treatment to patients who have failed or are likely to fail abstinence treatment.

For those in care facilities, or in other situations where access to self-administration of opioids is restricted, detoxification alone may be a viable option, when combined with general supportive counselling (working group consensus).

RECOMMENDATION #15:

Buprenorphine-naloxone should be considered first line for opioid withdrawal management in older adults. Methadone is an alternative that may be used, however consider the added risk of adverse events.

[GRADE Quality: Moderate; Strength: Weak]

A recent Cochrane meta-analysis in adults “was suggestive that buprenorphine and methadone have similar capacity to ameliorate opioid withdrawal, without clinically significant adverse effects ... and no difference in average treatment duration ... or treatment completion rates.” (Gowing et al., 2017). This review also found buprenorphine to be superior to clonidine or lofexidine protocols (Ibid).

Buprenorphine-naloxone has a better safety profile than other opioids used for withdrawal management and as such has been recommended as a first-line treatment option for use in detoxification, keeping in mind there are no trials in older adults (ASAM, 2015; VA & DoD, 2015; Le Roux et al., 2016; Bruneau et al., 2018). Buprenorphine may induce precipitated withdrawal from other opioids, so prescribing clinicians must have experience with induction techniques (Hess et al., 2011; Hämmig et al., 2016). Methadone carries a greater risk of overdose than buprenorphine at the time of induction due to its long half-life, its full mu opiate receptor agonist effect, variable response (including incomplete cross-tolerance), and the risk of medication interaction. Only experienced clinicians should prescribe methadone for older adults.

There is no medical literature to guide the use of morphine for OUD withdrawal management, although anecdotally it is used not infrequently in hospitals across the country, especially when experienced methadone and buprenorphine prescribers are not available. This is an area of potential future research and will not be commented on further here.

RECOMMENDATION #16:

For symptom control during opioid withdrawal management, adjuvant medications (see comments) can be used in a time-limited fashion but with caution due to medical comorbidities, side effect risk, and other concerns related to older age.

[GRADE Quality: Moderate; Strength: Weak]

In adults, there are a variety of non-opioid medications used to mitigate symptoms of opioid withdrawal. These include alpha adrenergic antagonists (e.g., clonidine), antidiarrheal medications (e.g., loperamide), sleeping medications (e.g., quetiapine, trazodone), anxiolytics (typically benzodiazepine receptor agonists), pain medications (e.g., acetaminophen, NSAIDS, gabapentin, pregabalin), and anti-nausea medications (e.g., dimenhydrinate). All of these medications carry risks of undesirable adverse effects in older adults and thus must be used with caution (ASAM, 2015; VA&DoD, 2015; RCP, 2015; Bruneau et al., 2018).

Withdrawal management is not as effective as opioid agonist treatment and should only be undertaken if the patient explicitly rejects opioid agonists or is in a controlled environment where access is restricted.

Although there have been anecdotal reports of benefit, the use of cannabis to detoxify from opioids is currently unsupported by evidence and cannot be recommended to older adults (Campbell et al., 2018; Caputi & Humphreys, 2018; Humphreys & Saitz, 2019).

QUESTION G: What medications and protocol adjustments are safe and effective in the treatment of an OUD in older adults to improve outcomes?

RECOMMENDATION #17:

Buprenorphine maintenance should be considered a first-line treatment for an OUD in older adults.

[GRADE Quality: Moderate; Strength: Strong]

In adults, there is high quality evidence that once initiated, buprenorphine maintenance at high doses is as good as methadone maintenance for retention in treatment, decreased drug use, and decreased mortality after nonfatal overdose (Mattick et al., 2014; Laroche et al., 2018). Also, buprenorphine maintenance has been shown to be superior to buprenorphine withdrawal for prescription opioid dependence (Fiellin et al., 2014). Although there are no randomized controlled trials, observational trials, or case series on

buprenorphine maintenance treatment in older adults, there is one adult treatment guideline that recommends it first-line, due to safety on initiation, maintenance, and take-home dosing, as well as availability and accessibility in Canada (Bruneau et al., 2018). One other adult treatment guideline and one systematic review recommend either buprenorphine or methadone maintenance first-line (VA & DoD, 2015; Hassell et al., 2017). Other guidelines and systematic reviews recommend buprenorphine maintenance treatment as one choice (ASAM, 2015; RCP, 2015; Le Roux et al., 2016; Loreck et al., 2016).

Burgos-Chapman et al. (2016) mention the decreased risk of respiratory depression with buprenorphine, compared with other opioids. As they summarize, “buprenorphine is the only opioid with a ceiling effect for respiratory depression. Respiratory rate rarely goes below 10 breaths per minute”. As mentioned above, the rate of suicide climbs with age. Thus buprenorphine would be the safest choice, due to reduced risk of completed suicide as well as unintentional overdose in older adults (Pergolizzi et al., 2008). Buprenorphine does not prolong QT interval and is safer for cardiac patients than methadone, which is especially important in older adults (Loreck et al., 2016).

Other advantages of buprenorphine over other opioids are its unique properties that may assist with mood and pain. As mentioned above, buprenorphine not only binds to the mu opioid receptor to produce pain relief, it also acts as an antagonist at the kappa opioid receptor, which can improve mood and potentially decrease opioid-induced hyperalgesia (Falcon et al., 2016). Patients who are opioid rotated to buprenorphine-naloxone often experience significantly less pain (Rieb et al., 2018; Daitch et al., 2014).

Controlled trials have shown that adult patients given buprenorphine-naloxone in the emergency department are more likely to participate in accessing medications for an OUD in the community and to report less drug use than those given counselling and referral alone (D’Onofrio et al., 2015). Buprenorphine can also be safely prescribed in non-medical settings with medical back-up, such as in prisons or on release from incarceration (Lee et al., 2012; Riggins et al., 2017; Bozinoff et al., 2018).

The form of buprenorphine currently available in Canada is a sublingual tablet with naloxone to act as a deterrent of abuse through injection. Soon, long acting formulations (monthly subcutaneous injections and an implantable form) will be available, although induction onto the sublingual tablet is recommended prior to using either of the two other formulations. The monthly subcutaneous injection has not

been trialed in older adults, however in studies of adults up to age 65 this formulation has been shown to be safe and effective for the treatment of OUD, and to be non-inferior to sublingual buprenorphine-naloxone (Lofwall et al., 2018; Haight et al., 2019). Also, the injectable formulation may have some patient-centred outcome advantages over placebo (Ling et al., 2019). In older adults, the depot formulation may be a consideration for convenience, when physical or cognitive issues make self-administration of daily tablets difficult, or when mobility issues prevent ready access to a pharmacy. In some provinces, special authority to prescribe buprenorphine for an OUD is no longer needed, although training is recommended (BCCSU, Provincial Opioid Addiction Treatment Support Program; CAMH, Buprenorphine-Naloxone Treatment for Opioid Use Disorder).

Practitioner comfort with induction can be a barrier, particularly with respect to concerns about precipitated withdrawal, so training and supervision of clinicians when first learning about buprenorphine induction is helpful. Bridging techniques utilizing buprenorphine patches or microdosing in a crossover titration have been shown to reduce precipitated withdrawal in adults (Hess et al., 2011; Hämmig et al., 2016). It may be reasonable to extrapolate these induction techniques for use in older adults. In TIP 63, SAMHSA outlines a comparison of buprenorphine, methadone, and naltrexone for use by clinicians to decide on medications in consultation with patients (SAMHSA, 2018).

RECOMMENDATION #18:

Methadone maintenance treatment may be considered for those older adults who cannot tolerate buprenorphine maintenance or in whom it has been ineffective.

[GRADE Quality: Moderate; Strength: Strong]

The most studied pharmacological treatment for an OUD is methadone maintenance. A systematic review of the medical literature in adults concludes that methadone is better for retention in treatment and reduction in heroin use than non-opioid treatments (Mattick et al., 2009). Patients initiated on methadone within a month of a nonfatal overdose have a decreased risk of mortality (Larochelle et al., 2018).

There are no randomized controlled trials on the use of methadone maintenance for an OUD in older adults. Nevertheless, all but one guideline and all systematic reviews on OUD in older adults recommend methadone as one first-line treatment choice (WHO,

2009; ASAM, 2015; VA & DoD, 2015; Han et al., 2015; RCP, 2015; CCSA, 2016; Le Roux et al., 2016; Loreck et al., 2016; Hassell et al., 2017; Carew & Comiskey, 2018; SAMHSA, 2018). One guideline recommends it as a second-line treatment (Bruneau et al., 2018).

In a systematic review by Carew in 2018, it was pointed out that older adults fare better in treatment with methadone than younger adults (Carew & Comiskey, 2018). The claim is based on findings by Crome (2015) and also a study (Firoz & Carlson, 2004), in which older adults > 55 years of age on methadone had 61% rate of no positive urine drug screens, compared with a 35% rate among younger adults. The review also referenced a 30-year prospective cohort trial conducted in New York City by (Han et al., 2015), which followed patients into their older adult age and demonstrated the efficacy of methadone maintenance treatment. The majority of those in treatment were 50 to 59 years of age at the time of publication, with the fastest growing cohort aged > 60 years. Another study of older veterans in the United States demonstrated that methadone maintenance therapy lowered addiction severity and reduced psychiatric, medical, and legal consequences of drug use (Fareed et al., 2009).

One observational trial that included very old adults up to age 99 who were former opium smokers and were given methadone dispensed by their children (with whom they lived) showed benefit of very low dose treatment—often just 6 mg/day (Guo et al., 2010). Methadone is the least expensive medication among those used for OUD. Its availability in liquid form makes titration easier and diversion more difficult when combined with witnessed ingestion. Women respond even better to methadone maintenance treatment than men [(Carew & Comiskey, 2018) quoting (Rosen et al., 2008; Grella & Lovinger, 2011)]. Unfortunately, there is a higher risk of death during induction with methadone than buprenorphine, and there are many more adverse drug interactions possible with methadone than with buprenorphine, thus we recommended it second-line for older adults.

RECOMMENDATION #19:

If renal function is adequate, daily witnessed ingestion of slow-release oral morphine may be considered with caution for those older adults in whom buprenorphine and methadone maintenance have been ineffective or could not be tolerated. Careful supervision of initiation onto short-acting morphine first is recommended, prior to transition to maintenance with the long-acting 24-hour formulation. [GRADE Quality: Low; Strength: Weak]

Although there are no randomized controlled trials or observational data on the use of slow-release oral morphine in older adults, there is one Canadian guideline that recommends this as a third-line approach in adults (Bruneau et al., 2018). Many older Canadians are already taking prescription opioids. There might be less perception of stigma with a medication like morphine that is more typically used for pain, rather than addiction treatment. In addition, most prescribers for older adults are more familiar with morphine dosing than methadone or buprenorphine dosing.

Some disadvantages of morphine include the risk of liver toxicity and the potential for rapid development of opioid-induced hyperalgesia. In addition, morphine has been shown to be the most immunosuppressive of all opioids [Bugos-Chapman quoting (Martucci et al., 2004; Pergolizzi et al., 2008)].

RECOMMENDATION #20:

For older adults with an OUD for whom opioid agonist treatment is contraindicated, unacceptable, unavailable, or discontinued and who have established abstinence for a sufficient period of time, naltrexone may be offered. [GRADE Quality: Moderate; Strength: Weak]

There are no randomized controlled trials or observational studies in older adults on use of naltrexone for treatment of an OUD. There are some inconsistencies in recent guidelines and reviews, although most favour its use as one option for adults of all ages (ASAM, 2015; Le Roux et al., 2016; Lee et al., 2016; Loreck et al., 2016; Hassell et al., 2017; Bruneau et al., 2018; Lee et al., 2018). In contrast, Burgos-Chapman et al. (Burgos-Chapman et al., 2016) recommend against naltrexone in older adult prescription opioid users if the opioid was being prescribed for pain. They do, however, support its use in heroin and other illicit opioid users.

Taking naltrexone precludes utilization of opioids to treat chronic pain and may present more of a challenge for acute pain treatment, although the blockade can be overcome in the urgent setting with anesthesiologist assistance. Due to the low drug interaction risk, lack of renal compromise, lack of respiratory depression, lack of cognitive impairment, and efficacy similar to buprenorphine in adults, we recommended naltrexone for the treatment of an OUD in older adults not requiring an opioid for pain treatment.

The oral formulation of naltrexone is not typically recommended long-term for an OUD, since it has not been shown to be superior to placebo (Minozzi et al., 2011) and non-compliance can lead to relapse and possibly increased risk of overdose, due to marked loss of tolerance. In contrast, among adults, extended-release injectable naltrexone (XR-NTX) has been shown to be non-inferior to buprenorphine maintenance treatment for lowering opioid use in two large randomized controlled trials (Tanum et al., 2017; Lee et al., 2018). Also, 153 post-incarceration patients given XR-NTX for 6 months and followed for two years have been shown to have less drug use than 155 participants randomized to treatment as usual, which included a choice of methadone, buprenorphine, and/or counseling (Lee et al., 2016). No deaths were reported in the XR-NTX group in this study, even after discontinuation; while seven deaths were reported in the treatment as usual group. In another study, mortality rates did not change with just one dose of XR-NTX among a small cohort followed post non-fatal overdose, retention being an issue (Larochelle et al., 2018). Thus, it is best to only offer naltrexone, especially XR-NTX, in the context of assured follow-up, for example when caregivers can ensure consistency of follow-up and dosing.

Another advantage of naltrexone is that it can treat alcohol use disorder by blocking the opioid pathway through which dopamine is released after alcohol ingestion. Thus, naltrexone is a reasonable consideration for those with concurrent active alcohol use disorder and an OUD.

A recent study found that over half of adults using opioids surveyed were interested in monthly XR-NTX for treatment (Kunøe et al., 2016). XR-NTX is more expensive than buprenorphine or methadone maintenance, if the payer only considers the cost of medication alone. However, injectable XR-NTX is quite cost-effective when considering the savings in overall health care costs (pharmacy, office, and hospital visits) and has improved outcomes for abstinence (Jackson 2014).

Some disadvantages of naltrexone treatment include injection site pain and abscesses. With the lowered immune response in older adults, this may be found to be more of an issue than with younger adults and may be a rationale for use of the oral formulation of naltrexone, if the injectable is not tolerated or desired. If the patient is not fully detoxified, there can be precipitated opioid withdrawal induced by initiation of naltrexone. This is why we recommend slow oral initiation first.

The primary disadvantage of XR-NTX currently in Canada is that it has yet to be approved by Health Canada and added to provincial formularies of medications covered for those on assistance. XR-NTX is currently only available through a special application process, and the patient must cover the cost of the medication and shipping from the United States, which can be prohibitive. We are hoping that by including XR-NTX in this evidence-based guideline that provinces and health authorities will be motivated to facilitate access (Rieb, 2018).

RECOMMENDATION #21:

Offer medications for an OUD in the context of connection to long-term addiction, mental health, and primary care treatment, where careful monitoring and dose titration can occur. [GRADE Quality: Moderate; Strength: Strong]

Many studies in older adults not on opioids stress the importance of continuity of care and a “medical home.” In adults, dropout rates are reduced and general patient care improved with addiction treatment embedded into primary care and mental health services (Kahan, 2016). A systematic review and meta-analysis has shown that psychotherapy is effective in treating concurrent mental health disorders in patients on opioid agonist treatment (Hassan et al., 2017). There is also evidence supporting the effectiveness of tricyclic antidepressants in patients on opioid agonist treatment in older adults (Ibid). Most guidelines and systematic reviews in older adults stress the importance of long-term integrated care that is integrated in multiple domains (VA & DoD, 2015; RCP, 2015; Kahan, 2016; Le Roux et al., 2016; SAMHSA, 2017).

Other health parameters may benefit from integrated addiction, mental health, and addiction treatment into primary care (Compton et al., 2015; Durbin et al., 2016). For complex polysubstance users, complex medical or psychiatric patients, and the frail elderly, participation of a multidisciplinary team that includes an addiction medicine specialist is advisable. Sometimes this team operates outside the primary care setting (e.g., rapid

access addictions clinic or geriatric psychiatry clinic). Availability of integrated services with the level of care required must be considered before making treatment recommendations.

RECOMMENDATION #22:

Advise patients that the use of alcohol, benzodiazepines, and other sedative-hypnotics is hazardous when combined with opioid agonist treatment. If the older adult is living in the community and is already physiologically dependent on one of these substances, then slow tapering of the substance(s) (to elimination if possible) rather than abrupt cessation is recommended. If the patient is in hospital, residential treatment, or a long-term care setting and medically managed by an experienced provider, detoxification can progress more rapidly, concurrent with the initiation or stabilization on medications for OUD.
[GRADE Quality: Moderate Strength: Strong]

The hazards of co-prescribing benzodiazepines and opioids in adults is well-documented (Sun et al., 2017; Hernandez et al., 2018). Due to these effects and others, OUD treatment guidelines and systematic reviews suggest tapering off benzodiazepines if co-prescribed with opioids (ASAM, 2015; HSE, 2016; Loreck et al., 2016; Bruneau et al., 2018). Our own benzodiazepine use disorder treatment guideline in older adults also recommends discontinuing benzodiazepines if co-prescribed with an opioid (X). The exact hazards of chronic, very low dose alcohol consumption (one drink per day or less) has not been clearly delineated, although refraining from all use is recommended as the safest practice when on opioid medication. Clinical practice in the United States includes instances where those on opioid agonist treatment for an OUD are transitioned to XR-NTX if they cannot curtail alcohol use. Due to the lack of availability and payment for XR-NTX in Canada and the risk of relapse and fatal overdose if opioid agonist treatment is stopped, the pros and cons of discontinuation of opioid agonist treatment should be assessed on a case-by-case basis.

RECOMMENDATION #23:

Early take-home dosing for buprenorphine maintenance treatment may be considered, including home induction in patients who are low risk, if they find it difficult to attend the office in withdrawal and if the patient has social supports at home. This approach should not be considered for methadone initiation unless supervised (e.g., reliable caregiver or medical personal administration).
[GRADE Quality: Low; Strength: Weak]

There is not clear evidence to support benefits of daily supervised dosing of buprenorphine (Saulle et al., 2017). Early take-home dosing of buprenorphine may help with initiation of maintenance treatment and decrease the likelihood of missed doses in adults, as outlined in a recent guideline (Bruneau et al., 2018). This practice is recommended as an option during treatment for adults (Ibid), and we believe it may be adapted for older adults. The fear of opioids causing harm is somewhat reduced in the case of buprenorphine, compared with other opioids, due to the ceiling effect for respiratory depression. Interestingly, diverted buprenorphine-naltrexone is sometimes used to help treat or detoxify opioid users accessing the illicit market. Patients can abuse non-witnessed doses: snorting crushed buprenorphine produces euphoria even in those opioid naïve and among those on maintenance therapy, so screening for such behaviour is important.

QUESTION H: In older adults, compared with younger adults, what dose/protocol adjustments are needed when initiating or maintaining medications to treat an OUD?

RECOMMENDATION #24:

Reduce initial doses of medications for treatment of an OUD (e.g., by 25%-50%); slow dose escalation frequency (e.g., by 25%-50%); use the lowest effective dose to suppress craving, withdrawal symptoms; and drug use; and monitor closely (especially for sleep apnea, sedation, cognitive impairment, and falls with opioid agonists).
[GRADE Quality: Low; Strength: Strong]

Although there are no randomized controlled trials to support the reduction of initial doses and slower escalation in older adults, it is reasonable to adopt this approach, given the metabolic changes of aging that affect the absorption, distribution, metabolism, and excretion of all medications, including opioids. These changes specifically include reduced

first-pass effect through the liver and reduced renal clearance. Further, the balance between medication benefits and adverse effects often differs in older adults, with increased risk of sedation, delirium, and falls with injury as potential harms resulting from too high an initial dose of medication or too rapid a dose escalation. For these reasons, multiple clinical practice guidelines support a cautious approach to prescribing medications for an OUD in older adults (American Geriatrics Society (AGS), 2002; 2009; Gupta & Avram, 2012; Malec & Shega, 2015; RCP, 2015; Hassell et al., 2017).

RECOMMENDATION #25:

The threshold to admit an older adult with social, psychological, or physical comorbidities to either residential or hospital care for opioid withdrawal management or induction onto medications for an OUD should be lower than for a younger adult.

[GRADE: Quality: Moderate; Strength: Strong]

Slow withdrawal management or induction onto medications for an OUD in the community is appropriate for an older adult who is stable, non-frail, and has supports available, including clinicians with experience managing OUD in the elderly. However, older adults often have a combination of multiple concurrent chronic conditions, frailty, low resource availability, and psychosocial vulnerability. Multimorbidity (multiple concurrent chronic conditions) is in fact the norm for older adults, with 60% of those > 80 years of age suffering from three or more chronic conditions (Denton & Spencer, 2010). Older adults are also more prone to the adverse effects of opioid withdrawal management or induction onto medications, including risk of delirium, which can be life-threatening.

For these reasons, the threshold to admit an older adult to residential/hospital care should be lower than for younger adults. Careful observation and interdisciplinary team support that is more likely to be available in a hospital setting can reduce the risk of harm particularly for frail, socially isolated individuals. As stated by the Canadian Centre on Substance Use and Addiction (CCSA, 2016): "Detoxification is particularly risky for older adults. 24-hours primary, psychiatric and nursing care in an intensive inpatient-setting is recommended. Once stable, the older adult can return to [the] community for ongoing treatment." Benefits of hospitalization must be weighed against risks, such as exposure to nosocomial infections and removal from social supports and a familiar environment. Also, there may be reluctance on the part of the older adult to go to a hospital or residential treatment setting.

RECOMMENDATION #26:

In older adults on medication for an OUD requiring management of mild-to-moderate acute pain or CNCP, non-medication and non-opioid strategies are recommended. For those on an opioid agonist for an OUD who have severe acute pain that has been unresponsive to non-opioid strategies, a short-acting opioid may be considered for a short duration (1-7 days) along with a taper, if necessary (1-7 days).

[GRADE Quality: Moderate; Strength: Weak]

Guidelines and reviews in adults indicate a stepped approach to the management of CNCP, beginning with non-pharmacological and non-opioid approaches, is prudent (Busse et al., 2016; Dowell et al., 2016; Busse et al., 2017; Busse et al., 2018). The Canadian guidelines on opioids for CNCP (Busse et al., 2017) recommend not offering opioid therapy to those with CNCP with a history of an OUD. However, this does not take into consideration those who require opioid agonist treatment for an OUD, those with unusual severe chronic pain disorders that are responsive to opioids, or those with severe acute pain needing hospitalization. Proceed with caution when prescribing a second opioid to those already on opioid agonist treatment (Furlan et al., 2010; ASAM, 2015; Dowell et al., 2016; HSE, 2016; Kahan, 2016; Guerriero, 2017; Bruneau et al., 2018). Since length of first prescription has been found to be a risk factor in longer than intended opioid use, many guidelines for CNCP in adults, older adults, and for acute pain post-surgery have recommended small prescription amounts with a taper schedule (Furlan et al., 2010; Dowell et al., 2016; Busse et al., 2017; Busse et al., 2018).

Although acute pain can typically be managed with non-opioid and non-pharmacological options, sometimes an opioid is the least toxic medication option when severe acute pain occurs in older adults with other health issues. Also, there may be older adults in whom opioids are the medication of choice for CNCP. For example, those who have been taking opioids for many years, who have not been successful with careful dose reductions in the past, and in whom benefits outweigh risks. Also, there may be those with acute pain who need longer opioid prescriptions than the example given in the recommendation (e.g., post major surgery or in a patient with systemic inflammatory arthropathy).

Other comments on medications for OUD:

In younger adults, for the palliative end of the OUD spectrum in whom all other modalities have been unsuccessful, there is currently available in Canada treatment with injectable diacetyl morphine (heroin) or injectable hydromorphone, collectively referred to as injectable opioid agonist treatment (iOAT). No data on iOAT in older adults were identified. The risk of adverse events with injectable medications rises with age, as does immunosuppression and mobility issues for accessing the three-times-daily visit to a clinic needed for iOAT. BC is currently the only province providing and paying for iOAT, and the cost is higher than with all other opioid agonist and antagonist treatments. Due to all of the above issues, we cannot endorse iOAT treatment in older adults at this time and thus have not included it in these guidelines.

Psychosocial Treatment:

Although robust data on behavioural interventions in older adults with OUD are lacking, an understanding of the importance of incorporating psychosocial supports is clear: Older adults may have an accumulation of losses (job, spouse, family, friends, role, home), and may struggle with lack of social support (White et al., 2009; Newson et al., 2011). The key question (I) regarding psychosocial interventions in older adults with an OUD is outlined below along with related recommendations (27-31). Also included is a question (J) on systemic features that may assist older adults in getting treatment for an OUD, along with a final recommendation (32).

QUESTION I: In older adults, what psychosocial interventions are effective in the treatment of an OUD to improve outcomes?

RECOMMENDATION #27:

Psychosocial interventions should be offered concurrently with medications for an OUD, at a pace appropriate for age and patient needs, but they should not be viewed as a mandatory requirement for accessing pharmacotherapy.

[GRADE Quality: Moderate; Strength: Strong]

A Cochrane review of 11 studies with 1592 participants concluded that adding psychosocial interventions to pharmacological treatment of adults (> 18 years of age, mean age 35 years, 67.45% male) was effective in terms of treatment retention, reduced opioid use during treatment and at follow up, and improved adherence to treatment. The psychosocial interventions were a mix of contingency management (CM), community reinforcement, psychotherapeutic counseling, intensive role induction with or without case management, counselling and education on high risk behavior, therapeutic alliance intervention, and family therapy (Amato et al., 2011). Although the evidence is based on a well-conducted review of at least a moderate quality, the results from this review are only indirectly related to older adults, and it is unclear which intervention beyond CM (discussed below in the following recommendation) is more effective than the others. Training and/or skilled providers of formal psychotherapy may be limited or unavailable. Despite these limitations, adding a psychosocial intervention is unlikely to have adverse effects on treatment outcomes (Dugosh et al., 2016).

In addition to psychosocial interventions, self-help and other peer groups are commonly seen as options for providing support to individuals with substance use disorders in general. The role of self-help programs was not evaluated in the above Cochrane review. One observational study that took place over two years in largely adult males with an OUD found similar improvement in retention and opioid use among those on methadone maintenance and those who attended Twelve-Step programs (Khodabande et al., 2012). Other authors have encouraged integration of Twelve-Step and pharmacological models (Galanter, 2018). Mindfulness meditation also was not included in the above Cochrane review but may have some affect in adults on lowering withdrawal/craving and health impacts (Grant et al., 2017). Self-help and mindfulness-based practices have not been investigated in older adults with an OUD, thus no direct evidence is available to support a recommendation currently.

RECOMMENDATION #28:

Contingency management may be offered as part of opioid treatment programs and used if accepted by the patient.

[GRADE Quality: Moderate; Strength: Weak]

CM is a method of behavioural modification using positive rewards for healthy behaviour change (e.g., medication carry home privileges, or a food voucher if urine samples are clear of unauthorized substances) and/or a negative consequence for undesirable behavior (e.g., loss of medication take home privileges if the urine sample has unauthorized substances). Evidence from systematic reviews and meta-analyses showed an overall reduction in opioid use among patients in CM interventions, compared with either methadone maintenance treatment alone or a control condition (Griffith et al., 2000; Prendergast et al., 2006). CM was also associated with increased short-term abstinence from opioids (Olmstead & Petry, 2009; Benishek et al., 2014). However, there was no additional effect of CM in decreasing opioid use among patients receiving buprenorphine maintenance treatment (Downey et al., 2000; Petry & Martin, 2002; Chopra et al., 2009; Ling et al., 2013).

The evidence related to CM is only indirectly related to older adults (since the above studies investigated CM in adults). Also, there were methodological limitations of the reviewed studies, for example, lack of quality assessment in the primary studies and potential confounding effects in these studies. When using CM, resources will be needed for the positive reinforcement incentive, which may add additional limitations to the use of CM in this population.

QUESTION J: For older adults with an OUD, what are the treatment considerations for special populations (specifically indigenous peoples)?

RECOMMENDATION #29:

Traditional healing practices used by indigenous communities can be integrated with buprenorphine treatment to improve outcomes for an OUD.

[GRADE Quality: Low; Strength: Weak]

Adults have been shown to benefit from an approach that integrates traditional indigenous healing methods and buprenorphine maintenance treatment. In a study of six First Nations communities in Ontario, combining buprenorphine and traditional practices maintained an exceptionally high retention rate along with urine drug screen results consistent

with lack of illicit opioid use (Mamakwa et al., 2017). There are no randomized controlled trials, systematic reviews, or observational studies specific to older adults on this topic. Little harm is likely to occur when combining traditional and medication approaches, even beyond buprenorphine. It is also possible that other cultural groups may benefit from an approach that integrates medication management and traditional healing practices. Some communities do not have access to either medication management or traditional healing services so may have barriers to actualize this recommendation.

Setting:

Setting can refer to treatment setting and also the living situation of the older adult.

QUESTION K: For older adults with an OUD, what specific treatment recommendations are suggested for non-community-based facilities?

RECOMMENDATION #30:

If experienced, clinicians may manage older adults with a *mild-to-moderate* OUD; however, for patients with *more severe or complex* disorders, it is recommended that personnel or teams with advanced substance use disorder management skills be accessible to support clinicians and to enhance their capacity to care for patients in all settings. The threshold for an admission to hospital or drug and alcohol treatment facility under the care of an Addiction Medicine Specialist is lower than for younger adults, and closer follow-up is needed on discharge to ensure appropriate community-based support.

[GRADE Quality: Moderate; Strength: Strong]

Data from best practice guidelines in healthier adults (and by extension older adults) suggest that if patients receiving opioid analgesics do not meet OUD criteria, they may be effectively slowly tapered off opioids in primary care or medical specialty care settings (Le Roux et al., 2016).

The integration of general health care and addiction treatment is lacking in many areas, making the treatment of an OUD in an aging population with greater clinical complexity inherently difficult (Rahul Rao & Roche, 2017). As patients age, treatment for the medical complications associated with substance use disorder (e.g., cognitive impairment, psychiatric disorders, organ failure, etc.) often becomes more clinically urgent than substance use

disorder treatment per se (Cicero et al., 2012). This issue may make it seem more economical and practical to treat the medical complications, but then often the underlying problem is not addressed. Comprehensive integration of addiction treatment services with primary, geriatric, and/or psychiatric services are necessary to effectively treat this population. In addition, understanding the factors that lead to OUD in older adults could assist with the development of early detection and/or interventions tailored specifically to address the opioid crisis in this population (Huhn et al., 2018).

RECOMMENDATION #31:

Older adults with an OUD who are admitted to a hospital, drug and alcohol treatment facility, or non-medical facility with access to medical care (e.g., prisons and shelters) should be offered opioid agonist treatment at the onset of withdrawal (advisable within 1-3 days), with bridging pharmacological treatment on discharge with confirmed transfer of care. [GRADE Quality: Moderate; Strength: Strong]

Several best practice guidelines provide strong support for treatment of adult patients with an OUD with addiction-focused medical management alone or in conjunction with other psychosocial interventions in a variety of settings (Mattick et al., 2003; Bao et al., 2009; Mattick et al., 2009; Fareed et al., 2012; Mattick et al., 2014; VA & DoD, 2015). Prescribing methadone can be restricted in various jurisdictions, whereas buprenorphine may be prescribed more readily by physicians in office-based settings, including primary care, outpatient specialty treatment, mental health clinics, and other treatment settings.

Based on the patient's needs and preferences (e.g., active duty military), individualizing treatment settings leads to optimal outcomes. Medications for an OUD have been shown to be effective in licensed opioid treatment programs, general medical settings, and a variety of community settings for different patient populations, including those who are homeless (Alford et al., 2007) or infected with HIV (Neri et al., 2005; Weiss et al., 2011).

Unfortunately, many individuals receiving medications for an OUD prior to arrest are made to withdraw from them

involuntarily once incarcerated, which is not advisable. Despite their established effectiveness, accessing medications for an OUD can be a challenge in correctional settings. Fewer than 40 of the 5,000 correctional institutions in the United States offer methadone or buprenorphine maintenance (Giftos & Tesema, 2018). Correctional Services Canada (federal) and most provincial correctional institutions allow for the provision of methadone and buprenorphine, while BC Corrections also offers slow-release oral morphine to treat OUD. Bridging prescriptions into the community are often lacking (Cheverie et al., 2010). Relapse rates and overdose risk is highest in the month immediately post discharge from jail or prison. Naltrexone has yet to be integrated as pharmacotherapy to treat OUD in Canadian correctional facilities, despite evidence for its benefit before and after discharge (Magura et al., 2009).

QUESTION L: For older adults with an OUD, what systemic factors support recovery?

RECOMMENDATION #32:

The cost of medically-recommended pharmacological and non-pharmacological treatment for an OUD in older adults should be covered by the public health plan. [GRADE Quality: Moderate; Strength: Strong]

Based on the principles of comprehensiveness and universality in the Canada Health Act, an individual has the right to fair and equitable treatment and timely access to publicly funded care when ill. OUDs are recognized as chronic medical illnesses categorized by well-defined symptomatology, and the treatment modalities for such have been proven effective. We are therefore advocating for the provision of care to those suffering from substance use disorders, and OUDs in particular, with such care funded by federal and provincial public health programs, as would be the case with any other chronic medical disorder (i.e., diabetes, chronic obstructive pulmonary disease, and coronary artery disease).

In Canada, substance use disorders are one of few chronic medical disorders that can require the patient to pay for some or all of their own treatment. For instance, funding can vary by patient age and by province, key medications are often not covered (e.g., naltrexone), and behavioural treatments (e.g., high quality residential care that is age-appropriate) often require the patient to pay out of pocket with no recourse for reimbursement from the provincial health care plan. The recommendation that Canada's public health care program should provide such funding has both financial (CCSA &

Discussion

Canadian Institute for Substance Use Research (CISUR), 2018) and ethical (VA & DoD, 2015; RCP, 2015; HSE, 2016; Bruneau et al., 2018) underpinnings.

In a recent document (CCSA & CISUR, 2018), it was noted that in 2014, substance use-related health care costs in Canada amounted to \$11.1 billion. Those costs were due to inpatient hospitalizations, day surgery episodes, emergency department presentations, specialist treatments for substance use disorders, the costs of physician time, and prescription drug costs. Although alcohol and tobacco use contributed over 90% of those costs, opioid-related health care costs accounted for the third-highest amount at \$313 million. In that older adults require more medical care and are more frequently admitted to hospital than younger individuals, the amount attributable to this demographic is likely to be considerable. Appropriately timed diagnosis and comprehensive treatment of an OUD (early diagnosis and intervention) would, as with any other chronic medical disorder, reduce the incidence of severe, late-stage illness and, therefore, of costly hospitalizations that are typically required for the management of advanced morbidity.

OUD has seen a significant demographic shift with the more liberal prescribing of opioids. The excess use of such medications has led to a new generation of patients with an OUD who were not well-described in the previous literature, namely older adults. Trends have shown that there is an increased rate of OUD and need for treatment in older adults for prescription and nonprescription opioids alike (Carew & Comiskey, 2018; Huhn et al., 2018). In Canada, for example, there were 21.5 million prescriptions for opioids issued in 2016, compared with 20.2 million prescription in 2002 (CIHI, 2018c). The same Canadian report indicated that 1 out of 8 older adults prescribed opioids were given a strong opioid (defined as oxycodone, hydromorphone, morphine, and fentanyl) on a long-term basis (more than 90 days) (Ibid).

The current literature reveals that a large proportion (44.2%) of patients with an OUD started using opioids through a prescription presumably for pain (Bawor et al., 2015). Older adults were more likely to be prescribed opioids than younger age groups, placing them at a significant risk for an OUD (CIHI, 2018c). A similar trend was also seen in US data showing older adults were prescribed opioids increasingly (27% annual use prevalence) and for a longer duration, based on insurance data of a large number of individuals aged ≥ 65 years (Jeffery et al., 2018).

Despite the increased numbers of older adults with an OUD, most previous guidelines for the management of OUD do not directly apply to this population, and there is an absence of clinical trials for the treatment of an OUD in older adults. In addition, the definition of “older adults” varied, making it challenging to identify studies that were specific to those aged ≥ 65 years. Therefore, most previous guidelines lacked relevance to older adults and left this age group and the health care providers who care for them without direction to guide management.

Given the growing number of older adults with an OUD and the current opioid crisis, the need for pragmatic and applicable guidelines for older adults is urgent. These newly-written guidelines are based on an extensive and systematic literature review and on existing opioid guidelines designed for adults, in addition to one that targeted older adults but without specific focus on opioid use.

Our guidelines represents a systematic effort to identify evidence from the medical literature, taking into consideration the context, the expertise of individuals working with older adults, the input from individuals with lived experience, and the multidisciplinary guidelines team. The guidelines provide 32 recommendations covering aspects of opioid management from prevention, screening, assessment, pharmacological treatment, psychosocial interventions, treatment setting, and steps to recovery. Each section is referenced, and each recommendation was evaluated using the GRADE framework. The strengths of the guidelines include the systematic approach, the pragmatic advice, and the encompassing management aspects of the disorder. Many of the recommendations are in alignment with the other two recent Canadian guidelines on OUD treatment in adults (Bruneau et al., 2018; Korownyk et al., 2019).

The challenges in writing these guidelines were many, most important of which was the lack of direct evidence to inform the guidelines of the efficacy or effectiveness of current treatment in this population. The existing evidence from randomized trials even for adults (defined as aged ≥ 18 years) often excluded patients with medical and psychiatric comorbidities (Dennis et al., 2015) both of which are likely conditions in individuals with substance use disorders (Druss, 2017). Older adults are more commonly susceptible to a combination of health and social adversities, hence are unlikely to be included in such trials for adults. Therefore, despite the best efforts to identify direct sources to inform the guidelines for the population of interest, what is recommended remains limited due to the lack of primary data.

Another limitation is the lack of a consistent definition for good or successful treatment outcome in OUD. There is also controversy over what age threshold should be used to define an older adult. Finally, there are limited data and empirical evidence for management of OUD in special populations related to sex, gender, and ethnic groups.

Future Directions

Studies with a focus on older adults are needed to provide empirical evidence for the effectiveness of pharmacological and psychosocial treatments in this group. The deliberate inclusion of subgroups in these studies will provide data for future guidelines to improve their external validity. Future studies to define meaningful and patient important treatment outcomes targets are needed. Also, the role of self-help groups is yet to be delineated. Canadian-based data are needed on the rates of opioid use and OUD in older adults as well as rates of overdose and mortality, in order to design targeted prevention strategies and test the effectiveness of OUD treatment and opioid overdose mitigation.

Conclusion

Older adults are susceptible to adverse health consequences of opioid use, and an increasing number of older adults are presenting with an OUD. There is a growing need for opioid management guidelines for older adults as the population in Canada ages. The current guideline is intended for use to prevent, screen, and assess for an OUD in older adults as well as to help treat those who are already suffering from the disorder. These guidelines are meant to provide evidence-informed, clinically relevant direction and advice on how to manage older adult patients with an OUD. We hope practitioners will find it a practical and useful clinical aide, and that the community at large will find it a helpful education resource.

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