

# Mental Health and Cognition in Older Cannabis Users: a Review



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## ABSTRACT

### Background

The impact of cannabis use on mental health and cognition in older adults remains unclear. With the recent legalization of cannabis in Canada, physicians will need up-to-date information about the mental and cognitive effects of cannabis use in this specific population.

### Method

A narrative review was conducted to summarize the literature on mental health and cognitive effects of cannabis use in older adults using Medline (OvidSP).

### Results

A total of 16 studies were identified, including nine cross-sectional studies on mental health comorbidities reported by older cannabis users. The self-reported prevalence of mental and substance use disorders is approximately two to three times higher in older adults who report past-year cannabis use, compared to older adults who report using more than one year ago or never using. The remaining seven clinical trials found that short-term, low-dose medical cannabis was generally well-tolerated in older adults without prior serious mental illness. However, mental/cognitive adverse effects were not systematically assessed.

### Conclusion

Although preliminary findings suggests that low-dose, short-term medical cannabis does not carry significant risk of serious mental health and cognitive adverse effects in older adults without prior psychiatric history, epidemiological studies find a correlation between past-year cannabis use and poor mental health outcomes in community-dwelling older adults. These findings may indicate that longer term cannabis use

in this population is detrimental to their mental health, although a direct causal link has not been established. Larger, longitudinal studies on the safety of medical cannabis in older adults are needed.

**Key words:** aged, frail elderly, cannabis, marijuana smoking, marijuana use, marijuana abuse, medical marijuana

## INTRODUCTION

Cannabis has recently been legalized for both recreational and medicinal purposes, and this may have important mental health and cognitive consequences for older Canadians. In Uruguay, where cannabis has been legalized, and certain U.S. states where it has been decriminalized, cannabis use has subsequently increased,<sup>(1-3)</sup> especially in the older adult population where it increased by up to 250%.<sup>(4)</sup> The most recent quarter of the Canadian National Cannabis Survey.<sup>(5)</sup> depicts a similar trend, with seniors showing the sharpest growth in consumption compared to all other age groups. An estimated 7% of Canadians aged 65 and older are now using cannabis. More than one quarter are new users, and most of them use for medicinal purposes.<sup>(5)</sup> This phenomenon is of particular concern given that older adults are at increased risk of developing adverse drug events compared to their younger counterparts.<sup>(6)</sup> Cannabis use specifically has been shown to cause more anxiety and panic attacks in older adults.<sup>(7,8)</sup> It can exacerbate existing mood disorders or psychosis, impair cognitive function, and increase the risk of motor vehicle accidents.<sup>(9,10)</sup>

Thus, with the recent legalization of cannabis in Canada, the need for up-to-date information about cannabis use in older adults will only become more apparent. In this review, we explore the growing literature on the mental health and cognitive correlates of cannabis use in adults aged 50 years

and over, including mental health and cognitive effects of medical cannabis use.

Cannabis refers to a group of three flowering plants known as *Cannabis sativa*, *Cannabis indica*, and *Cannabis ruderalis*. Each contains as many as 60 pharmacologically active components, the two most widely studied being  $\Delta^9$ -tetrahydro-cannabinol ( $\Delta^9$ -THC) and cannabidiol (CBD).  $\Delta^9$ -THC has been found to produce psychoactive effects, whereas CBD has been shown to exert anticonvulsive, anxiolytic, antipsychotic, anti-inflammatory, and neuroprotective effects.<sup>(11)</sup> These constituents, whose relative concentrations vary greatly from one strain to another, activate the human endocannabinoid system via CB1 and CB2 receptors, located in the central and peripheral nervous system, as well as the immune system.<sup>(12,13)</sup> Recent interest in the endocannabinoid system as a potential therapeutic target has led to an exponential growth of studies in this area. Currently, the evidence supports a benefit for the use of medical cannabis for chemotherapy-induced nausea and vomiting; bladder frequency, pain, and spasticity in multiple sclerosis; and glaucoma.<sup>(14)</sup> Some small, preliminary studies have suggested a potential benefit of using cannabis for the relief of symptoms associated with PTSD.<sup>(15)</sup> CBD extract may also be of benefit in certain psychiatric conditions such as Social Anxiety Disorder and schizophrenia,<sup>(16)</sup> although the data on efficacy and safety remains very limited and may not be applicable to older adults due, in part, to age-related changes in pharmacodynamics and pharmacokinetics.<sup>(17)</sup>

## METHODS

A Medline (OvidSP) search, from 1946 to December 2018, was conducted using the MeSH terms “aged” [Mesh] OR “aged, 80 and over” [Mesh] OR “frail elderly” [Mesh] combined with the MeSH terms “Cannabis” [Mesh] OR “Medical Marijuana” [Mesh] OR “Marijuana Smoking” [Mesh] OR “Marijuana Abuse” [Mesh]. An additional manual search of the bibliographic references of selected articles was also conducted to find relevant studies that were not captured by our original algorithm. A total of 594 non-identical abstracts were obtained.

To be eligible for review, articles were required to meet the following inclusion criteria: be published in English or French, include participants with a mean age of 50 years or older, report on current cannabis use (medical and/or recreational, smoked and/or ingested) and include mental health and/or cognitive outcomes. The 50-years-of-age cutoff was chosen to capture a wider array of preliminary findings, given that the literature on cannabis users aged 65 and over remains scarce. Only original research was considered, including randomized controlled trials (RCTs), prospective and retrospective observational studies, as well as epidemiological studies to widen the scope of our findings. Review articles were excluded. We also excluded studies looking at synthetic cannabinoids such as dronabinol and nabilone, and studies looking at individual cannabinoid extracts such as  $\Delta^9$ -THC or CBD.

Given that cannabis has so many constituents, the results of studies with individual cannabinoids and/or synthetic cannabinoids may not be applicable to whole cannabis and vice versa.<sup>(18)</sup> The risk of bias was assessed using the Cochrane Risk of Bias Tool 2<sup>(19)</sup> for RCTs, and the Grading for Recommendations, Assessment, Development and Evaluation (GRADE) handbook for observational studies.<sup>(20)</sup> The aforementioned review methods were established and approved by co-authors prior to conducting the review, but the protocol was not published in a registry in advance of the search.

## RESULTS

Forty-six articles were identified as relevant for full text review, of which 16 were retained for analysis. There were no duplicates. The main reason for exclusion was the lack of information regarding mental health and/or cognitive outcomes (Figure 1).

### Mental Health and Cognitive Correlates of Cannabis Use in Older Adults

The search strategy yielded nine studies providing information about self-reported mental health disorders in older, community-dwelling cannabis users. User status was defined as having used cannabis at least once in the past year, hence the term “past-year users”. The studies were all cross-sectional by design and mostly based on large, national U.S. databases. All reported on comorbid substance use and substance use disorders, and seven of them provided additional information regarding other mental disorders such as mood and anxiety disorders. None of them reported on cognitive function and/or disorders.

Compared to never-users, past-year cannabis users aged 50 years and older presented significantly higher rates of past-year mental disorders (33.23% vs. 18.86%) and lifetime mental disorders (48.78% vs. 27.26%), with  $p < .001$ .<sup>(21,22)</sup>

### Depression, Dysthymia, Bipolar Disorder, and Suicidality

Compared to non-users, past-year cannabis users aged 50 years or older reported significantly higher rates of past-year and lifetime depression, reaching proportions of 17.33% and 32.30%, respectively.<sup>(21,23)</sup> Controlling for age group, gender, race, marital status, educational level, employment status, income, health status, and alcohol and tobacco use, past-year use of cannabis and other drugs was associated with the highest odds of past-year (2.50, 95% CI = 1.66–3.76) and lifetime depression (2.75, 95% CI = 1.75–4.33), as compared to non-users, with  $p < .001$ .<sup>(24)</sup> Past-year cannabis use only was also associated with higher increased odds of past-year (1.73, 95% CI = 1.36–2.20) and lifetime depression (1.54, 95% CI = 1.17–2.03), albeit to a lesser degree. Only one study by Han *et al.*<sup>(4)</sup> found no significant association between past-year cannabis use and depression in adults aged 50 years and older, after adjusting for confounders. Dysthymia was also found to be significantly more prevalent in cannabis users

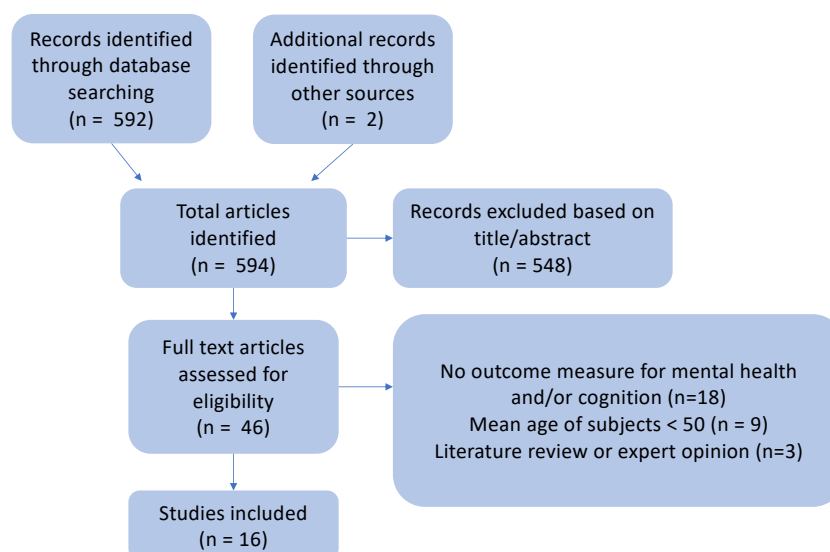


FIGURE 1. Study flowchart

aged 50 years or older compared to never-users (14.26% vs. 4.21%;  $p < .001$ ).<sup>(24)</sup> Similarly, the prevalence of past-year and lifetime Bipolar Disorder was significantly higher compared to never-users, although relatively less frequent, with rates of 3.82% vs. 1.15% with  $p < .001$ ; and 4.25% vs. 1.45% with  $p < .001$ , respectively.<sup>(21,22)</sup> As a measure of comparison, the weighed lifetime prevalence rate of Bipolar Disorder in Canada is estimated at 2.2% (95% CI = 1.94–2.37).<sup>(25)</sup> Moreover, Choi *et al.*<sup>(24)</sup> examined past-year suicidal ideation and the highest rates were found in those using cannabis combined with other drugs (13.64%), followed by cannabis-only users (5.0%) and never-users (2.21%), with  $p < .001$ . Among past-year cannabis users with depression, cannabis use frequency was significantly associated with increased odds of serious suicidal thoughts (OR 1.04, 95% CI = 1.01–1.07,  $p < .01$ ). Lifetime (but not past-year) suicide attempts were also more prevalent in older cannabis users vs. never users (10.75% vs. 2.86%,  $p < .001$ ).

### Anxiety, Anxiety Disorders and Post-Traumatic Stress Disorder (PTSD)

Five of the nine articles reviewed in this section examined Anxiety Disorders and PTSD in relation to cannabis use. Four studies found a significant association between past-year cannabis use and anxiety in older adults. Up to 22.98% of past-year cannabis users reported past-year diagnosis of anxiety disorders, and 29.61% reported a lifetime anxiety diagnosis.<sup>(23)</sup> These included specific phobia, social phobia, panic disorder, agoraphobia, and generalized anxiety disorder. When subgroup analysis was performed for the 50–64 and 65+ age groups, Salas-Wright *et al.*<sup>(26)</sup> found comparable rates of past-year anxiety for both groups (approximately 9%), but the adjusted odds ratio (AOR) was highest in the 65+ age group (2.87, 95% CI = 1.41–5.83), relative to older adults who did not use cannabis in the last year. As for PTSD, past-year cannabis users aged 50+ reported more past-year PTSD (9.44%

vs. 3.20%) and lifetime PTSD (11.57% vs. 4.08%) compared to never-users, with  $p < .001$ .<sup>(21,22)</sup>

### Personality Disorders

One study by Choi *et al.*<sup>(23)</sup> provided data on lifetime self-reported personality disorder diagnosis, which included borderline, schizotypal and/or antisocial personality disorders. They found that 34.82% of past-year cannabis users aged 50 years or older met criteria for a personality disorder. This was more than three times the proportion reported by never-users, which was 9.01%. After controlling for sociodemographic characteristics, past-year cannabis users remained at higher risk of having comorbid personality disorders (1.41, 95% CI = 1.07–1.85).

### Substance Use Disorders

All nine studies examined comorbid substance use. The majority of past-year cannabis users aged 50+ reported past-year substance use disorder (64.99%) and lifetime substance use disorder (82.13%), rates that were significantly higher than in the never-users subgroup (18.47% and 27.41%, respectively;  $p < .001$ ).<sup>(21,22)</sup> The most common past-year substance use disorder was nicotine use disorder (58–62%), followed by alcohol use disorder (29.26%), although a higher rate was reported for risky alcohol consumption (42.38–48.4%). Cannabis use disorder was relatively less prevalent, with 6.9–17.54% of adults aged 50+ meeting criteria in the past-year, and 26.88% meeting criteria in their lifetime.<sup>(4,21,22)</sup> Other drug misuse, such as cocaine, prescription opioids, sedatives, and tranquilizers, was less prevalent, affecting <12% of cannabis users aged 50–64, and <3.2% of those aged 65+.<sup>(27)</sup>

### Mental Health and Cognitive Side Effects of Medical Cannabis in Older Adults

A total of seven studies included secondary outcome measures on mental health and cognitive effects of medical cannabis use

in older adults. This included three prospective observational studies, one retrospective survey, and three double-blind randomized controlled trials (Table 1).

The most common psychiatric side effects were dizziness (5.4–12.8%), somnolence/drowsiness/sleepiness (3.3–52%), anxiety (14.2–17%), confusion (1.9–25%), and subjective worsening of memory (17.5%), followed by smaller incidences of hallucinations (0.8–17%), panic attacks (14.2%), paranoia (5.8%), and psychosis (2.1%). In the two trials that conducted preliminary studies, these psychiatric side effects led to treatment discontinuation in 14–21% of subjects. Of note, the preliminary dose escalation study conducted by Carroll *et al.*,<sup>(28)</sup> which included seven subjects and a four-week follow-up period, found an improvement in Mini Mental Status Examination (MMSE) scores following cannabis treatment ( $1.5 \pm 0.6$ ,  $p < .01$ ).

In the main studies, average THC doses ranged from 0.2 mg per day to 8.1 mg per day, and average CBD doses vary between 1 mg per day and 7.5 mg per day, although most subjects received <2.5 mg of both daily. Follow-up ranged from six weeks to six months. Participants had a variety of medical conditions for which cannabis was used, including chronic pain, cancer, Parkinson's disease, and Chronic Obstructive Pulmonary Disease. Eligibility criteria for cannabis treatment in all seven studies excluded participants with past history of psychosis, and five out of seven studies excluded participants with history of substance use disorder. Moreover, Carroll *et al.*<sup>(28)</sup> excluded subjects with MMSE scores < 26, and Pickering *et al.*<sup>(29)</sup> excluded subjects with high depression and/or anxiety scores at baseline assessment. Only two studies provided information as to whether or not participants experimented with cannabis in their lifetime. One of them included 2,736 patients aged 65 years and older, of which 25.4% reported previous experience with cannabis.<sup>(30)</sup>

The risk of bias for the three included RCTs was assessed with the revised Cochrane risk-of-bias tool for randomized trials.<sup>(19)</sup> They were rated as low risk on all of the tool's five domains (Table 2), with the exception of Strasser *et al.*,<sup>(31)</sup> which was rated as high risk in one domain due to missing outcome data. The risk of bias for the remaining four observational studies was assessed using the GRADE handbook,<sup>(20)</sup> where applicable. Issues regarding eligibility criteria, selection of participants, flawed measurements, failure to adequately control for confounders, and incomplete follow-up were noted. Specifically, selection of participants was based on pre-established tolerability to cannabis in two out of the four observational studies, with Balash *et al.*<sup>(32)</sup> requiring three-month cannabis use prior to study enrollment. Measurements of mental health and cognitive outcomes consisted of self-report measures and did not include standardized neuropsychological assessments and/or interviews. They failed to adequately control for confounders due to the lack of control groups. As well, incomplete follow-up was noted in Abuhasira *et al.*,<sup>(30)</sup> where 24% of subjects dropped out, 1.4% of whom citing intolerable adverse effects; however, these effects were not explicitly described. Potential conflict of interest was

also noted, as three out of the four studies concluding to the benefit and safety of medical cannabis were directly financed by Tikun Olan Co, a pharmaceutical company developing cannabis-based medical extracts.

## DISCUSSION

Despite the increasing prevalence of older cannabis users, few studies have examined the relationship between cannabis use and mental health in older adults. The epidemiological studies included in this review have found significantly higher rates of mental health and substance use disorders in older cannabis users compared to ex-users and never users. Specifically, older cannabis users appeared twice as likely to report past-year or lifetime mental disorder, and three times as likely to report past-year or lifetime substance use disorder, compared to older non-users. This association raises the question whether cannabis use plays a causal role in the development of mental disorders in older adults, as was demonstrated in younger populations.<sup>(33,34)</sup> Additionally, the high rates of concurrent use of cannabis and other psychoactive substances, namely alcohol, give cause for concern. This holds true for prescription opioids, sedatives and tranquilizers, as well. Despite relatively less concurrent misuse of these substances, compared to nicotine and alcohol, up to 16.5% of older Canadians report prescription sedative use.<sup>(35)</sup> The effects of these medications, in combination with cannabis, remain largely unknown.

With respect to mental health and cognitive effects of medical cannabis in older adults, the seven studies included in this review suggest that low-dose medical cannabis is generally well-tolerated in older adults, with few serious neuropsychiatric adverse effects, none of which resulted in death. This conclusion is in keeping with the data on safety of other cannabinoids such as dronabinol and cannabis oil, both studied for the treatment of Behavioral and Psychological Symptoms of Dementia and found to be well-tolerated.<sup>(36,37)</sup> It is also consistent with the Canadian Agency for Drugs and Technologies in Health's (CADTH) report which deems Sativex (a cannabis-based buccal spray) as safe for the treatment of chronic non-cancer pain in the adult population.<sup>(38)</sup> However, the reported cases of confusion, hallucinations and psychosis, albeit uncommon, invite caution.

### Limitations of the Literature

The main limitation of the epidemiological studies included in this review is that they cannot assess for causality due to their cross-sectional design. Moreover, the paucity of information with regards to patterns of use across the lifespan, frequency, and amount of current use, further limits interpretation. By grouping together participants that consumed cannabis once in the past year with participants who consume daily, under the category of active users, authors may have under-estimated the strength of the correlation between cannabis use and mental disorders in this specific population. Indeed, studies have consistently shown dose-related adverse effects of cannabis on mental health and cognition in younger adults.<sup>(39)</sup>

TABLE 1.  
Mental health and cognitive effects of medical cannabis in older adults

Authors	Name of Study	Methodology	Population	Comparator Group	Type of Cannabis	Mental Health / Cognitive Outcomes
Abuhaira <i>et al.</i> <sup>(30)</sup> 2018 (Israël)	Epidemiological characteristics, safety and efficacy of medical cannabis in the elderly	Prospective observational study	2,736 older patients (mean age: 75) being prescribed cannabis for a variety of medical conditions	None	Mostly Cannabis sativa	At 6 months: dizziness (n = 87, 9.7%), somnolence (n = 35, 3.9%), confusion/ disorientation (n = 17, 1.9%), hallucinations (n = 7, 0.8%)
Balash <i>et al.</i> <sup>(32)</sup> 2017 (Israël)	Medical Cannabis in PD: Real-Life Patients' Experience	Retrospective observational telephone survey	47 older adults with PD (mean age: 64.2 years)	None	Cannabis sativa 0.2 to 2.25 g/day	In subjects having used cannabis < 3 months (N=14): loss of consciousness (1) and hallucinations (1) In subjects having used cannabis > 3 months (N=47): Any kind psychotropic adverse effect (38.3%); subjective worsening of memory (17.5%), confusion (17%), anxiety (17%), hallucinations (17%), unsteadiness (15.6%), dizziness (12.8%), psychosis (2.1%),
Bar-Lev Schleider <i>et al.</i> <sup>(40)</sup> 2018 (Israël)	Prospective analysis of safety and efficacy of medical cannabis in large unselected population of patients with cancer	Prospective observational study	2,970 cancer patients (mean age: 59.5)	None	Mostly Δ9-THC-rich Cannabis indica	Dizziness (n = 96, 8.0%), sleepiness (n = 40, 3.3%), and psychoactive effect (34, 2.8%)
Carroll <i>et al.</i> <sup>(28)</sup> 2004 (U.K.)	Cannabis for dyskinesia in PD	Dose escalation study followed by double-blind RCT	19 PD patients with levodopa-induced dyskinesia (mean age: 67)	Within subject comparison (crossover design)	Cannabis sativa extract (2.5 mg THC/ 1.25 mg CBD)	In preliminary dose escalation study (N=7): 2 (28%) drop-outs including 1 (14.2%) for panic attacks. Improved pre vs. post MMSE (1.5 ± 0.6, p < .01) In main study: drowsiness /lethargy (9); detached (4); dizzy/light-headed (2); paranoia (1); confusion (1)
Lotan <i>et al.</i> <sup>(44)</sup> 2014 (Israël)	Cannabis (Medical Marijuana) Treatment for Motor and Non-Motor Symptoms of PD	Open label observational study	22 PD patients (mean age: 65)	None	Cannabis sativa	In preliminary study (N=28): dizziness and psychosis leading to 6 dropouts In clinical trial (N=22): dizziness, somnolence and drowsiness, as measured by the Medical Cannabis Survey NDARC questionnaire
Pickering <i>et al.</i> <sup>(29)</sup> 2011 (U.K.)	Cannabinoid effects on ventilation and breathlessness: a pilot study of efficacy and safety	Double-blind RCT	5 patients with moderate severity COPD, aged 66 to 68;	6 healthy controls, aged 51 to 67	Sublingual spray (2.7 mg THC/ 2.5 mg CBD), up to 3 sprays per treatment per subject	Confusion in 1 COPD patient Drowsiness in 1 healthy control No changes in Spielberger anxiety state test and the Thayer activation/deactivation scores in normal and COPD subjects, before and after drug or placebo administration
Strasser <i>et al.</i> <sup>(31)</sup> 2006 (Germany)	Comparison of Orally Administered Cannabis Extract and Delta-9-THC in Treating Patients With Cancer-Related Anorexia-Cachexia Syndrome	Double-blind RCT	61 patients with advanced incurable cancer (mean age: 61)	48 patients with advanced incurable cancer (mean age: 62)	Cannabis sativa extract (2.5 mg THC/ 1 mg CBD)	Cannabis extract was associated with a higher hazard rate for adverse events than placebo, but no difference was found between groups for cannabinoid-related toxicity and mood, as measured by the CannTox module of the EORTC QLQ-C30 scale

CBD = cannabidiol; COPD = Chronic Obstructive Pulmonary Disease; EORTC QLQ = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; MMSE = Mini Mental State Examination; NDARC = National Drug and Alcohol Research Center; PD = Parkinson's disease; RCT = randomized control trial; THC = Δ9-tetrahydrocannabinol

TABLE 2.  
Risk of bias according to the Cochrane Risk of Bias Tool 2<sup>(19)</sup>

	<i>Domain 1 Randomization Process</i>	<i>Domain 2 Deviations from Intended Interventions</i>	<i>Domain 3 Missing Outcome Data</i>	<i>Domain 4 Outcome Measurement</i>	<i>Domain 5 Selection of Reported Result</i>
Strasser <i>et al.</i> <sup>(31)</sup> 2006 (Germany)	Low Risk	Low Risk	High Risk	Low Risk	Low Risk
Pickering <i>et al.</i> <sup>(29)</sup> 2011 (U.K.)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Carroll <i>et al.</i> <sup>(28)</sup> 2004 (U.K.)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk

Other limitations from these epidemiological studies stem from the use of self-report measures, which renders them susceptible to social desirability bias and recall bias, and from their samples which included only non-institutionalized, community-dwelling subjects.

The seven clinical trials may also have under-estimated the strength of the correlation between cannabis and adverse mental and cognitive effects, given that three out of the seven studies conducted their trials on a selected patient population with pre-established tolerance to cannabis. The significant proportion of patients having already experienced with cannabis in their lifetime, as reported by Abuhasira *et al.*,<sup>(30)</sup> may also have contributed to a selection bias. Indeed, Bar-Lev Schieder *et al.*<sup>(40)</sup> have found that prior experience with cannabis is associated with a positive response to cannabis-based treatment in older patients with terminal cancer, as defined by significantly less endorsement of pain and nausea symptoms (1.32, 95% CI = 1.05–1.66). This highlights the importance of taking into consideration potentially confounding factors such as prior history of use. As such, it is unclear how the safety profile depicted in these studies would differ depending on patients' prior history of use, especially for those with past history of psychosis and/or substance use disorder, who may be especially at risk of experiencing adverse effects yet were systematically excluded. This was an important limitation as mental health conditions are among the most common self-reported reasons for medical cannabis use.<sup>(15)</sup>

Furthermore, the clinical studies included in this review did not formally assess the mental and cognitive side effects of medical cannabis. They were only reported as secondary outcomes, and methods to measure these outcomes varied widely, with some trials relying exclusively on spontaneous self-report. Systematic assessments pre- and post-treatment with validated mental health scales and/or cognitive function tests were not used in any of the studies. The lack of standardized cognitive assessment represents another important limitation since acute and chronic exposure to cannabis is known to impair cognitive function in the adult population, especially memory and verbal learning.<sup>(9)</sup> In relation to this topic, recent positive trials have sparked interest in using cannabinoids for the treatment of behavioral and psychological symptoms of dementia. A recent study by Herrmann *et al.*<sup>(41)</sup> on the use of

nabilone in the treatment of agitation in Alzheimer's disease found that nabilone was associated with a small improvement on the standardized MMSE, though it was deemed not clinically relevant. Interestingly, the study included in our review by Carroll *et al.*<sup>(28)</sup> did find an improvement in MMSE scores in their preliminary dose escalation study. They attributed this to a practice effect. However, in light of the recent findings described above, it may be possible that certain cannabinoids exert a differential—perhaps even beneficial—effect on cognition in older adults with cognitive impairment, compared to older adults with intact cognition.

The clinical trials included in this review present several other limitations. Namely, the relative short duration of follow-up possibly masked cannabis' long-term effects and addiction potential, the latter affecting as much as one in ten individuals who experiment with cannabis.<sup>(33)</sup> As well, the doses prescribed in these studies were relatively small compared to what is available in Canadian dispensaries and may not reflect the usual consumption habits of older adults. The term "medical cannabis" encompasses different formulations with varying concentrations of THC, CBD, and hundreds of other constituents about which we know very little. Certain formulations may carry starkly different risk and benefit profiles, which in turn interact with each individual's metabolism, comorbidities, and medication regimen. This may explain the wide spectrum of mental health effects reported by medical cannabis users. For instance, Brunt *et al.*<sup>(42)</sup> compared the effects of different concentrations of THC/CBD in older medical cannabis users and found that older adults using high THC/CBD strains experienced more feelings of dejection and anxiety compared to those using low THC/CBD strains ( $p = .02$  and  $p = .004$ , respectively). More research is needed to clarify who is at higher risks of developing adverse psychiatric reactions to a given cannabis strain, and whether that given risk outweighs its potential therapeutic value.

Taken together, these limitations are significant and indicate that the knowledge base in this field is in its infancy.

### Limitations of this Review

In interpreting these findings, one needs to take into consideration our decision to search only one database, which may have led to the exclusion of potentially relevant publications.

Furthermore, in an effort to report most accurately on what older Canadians are likely to consume at their local dispensaries, we decided to focus solely on whole cannabis products. In doing so, we grouped together studies looking at different cannabis strains with varying ratios of  $\Delta^9$ -THC and CBD. However, each may carry starkly different risk and benefit profiles. The different consumption methods, mainly inhalation and ingestion, may also play a key role in assessing safety of use. In fact, ingestion has been linked to an increased risk of accidental toxicity, due to delays in reaching peak concentration, leading patients to ingest more than the recommended dose.<sup>(14)</sup> Lastly, the physical adverse effects of cannabis use, including cardiovascular, pulmonary, and psychomotor effects, were not covered in our review. These would need careful consideration, especially in the older adult population, who often present with slower drug metabolism, polypharmacy, and multiple medical comorbidities.<sup>(43)</sup>

### Future Directions

At present, there are relatively few studies examining the impact of cannabis use on the mental health and cognition of older adults. Future prospective trials could follow never-users, ex-users, and active-users with no prior psychiatric history across time, to determine whether cannabis plays a causal role in the development of mental disorders in this specific subgroup of the population. As well, larger controlled trials assessing the safety and tolerability of medical cannabis must use validated instruments and scales in order to better quantify the mental health and cognitive adverse effects described in this review. Different strains of cannabis and varying methods of consumption could be compared against each other to better reflect what is currently available on the market, and hence better guide physicians when counselling older patient on cannabis use.

### CONCLUSION

This review aimed to provide physicians and allied health care professionals an update about mental health and cognitive effects of cannabis use in older adults. Epidemiological studies find that older cannabis users endorse higher rates of mental and substance use disorders. Although the direction of this association is still unclear, it highlights a potential need for more screening and treatment of mental and substance use disorders in this population. Conversely, initial studies of cannabis for medical purposes in older adults suggest treatment is relatively safe with regards to psychiatric side effects. However, none of these studies systematically measured mental or cognitive outcomes, leaving these effects in older adults largely unknown. These, and other major limitations, put into question the validity and generalizability of these conclusions. Larger, longer, adequately powered studies are warranted to further assess safety and tolerability in the long term. In the meantime, physicians should use caution when counselling older patients on the risks and benefits of cannabis use.

### CONFLICT OF INTEREST DISCLOSURES

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