EVIDENCE BRIEF

Canada's Lower-Risk Cannabis Use Guidelines for Psychosis (LRCUG-PSYCH)

Evidence-based recommendations for reducing psychosis-related risks when using cannabis

Cannabis use and psychosis

Cannabis is a commonly used drug, particularly among adolescents and young adults. Non-medical cannabis use was legalised in Canada in 2018, which has raised concerns about possible increases in cannabis-associated health risks. While most consumers use cannabis without experiencing serious related problems, cannabis consumption, especially when involving intensive use, has been shown to be one of the several risk factors for the development of psychotic disorders. Cannabis-induced psychosis affect relatively small proportions of the population but those affected may require long-term treatment and care. Cannabis use prevalence is also significantly higher among individuals who live with a psychotic disorder despite being associated with adverse related outcomes.

It is important to understand the factors that modulate risks and vulnerabilities for psychotic disorders when engaging in cannabis use.

What are the Lower-Risk Cannabis Use Guidelines for Psychosis (LRCUG-PSYCH)?

While only affecting a minority of consumers, psychosis is a serious health risk associated with cannabis use. Certain modifiable factors associated with cannabis use can influence the risks of cannabis-related psychotic outcomes. These outcomes can include:

- Psychosis-like symptoms and experiences,
- Development of a psychotic disorder,
- More severe positive symptoms, increased risk of relapse of symptoms, and treatment failure in individuals with a psychotic disorder.

The aim of the LRCUG-PSYCH is to provide evidence-based prevention and public health-oriented recommendations for cannabis consumers towards mitigating and reducing psychosis-related risks when using cannabis. The LRCUG-PSYCH aim to empower individuals to understand the applicable risks related to their cannabis use and to make choices about their consumption to help reduce their individual risk of adverse psychotic outcomes. These guidelines have been summarized into 11 recommendations clusters available for health promotion and psychosis-related prevention and care among cannabis users, and considered alongside interventions for those with psychotic conditions.

How were the LRCUG-PSYCH developed?

The LRCUG-PSYCH were developed by an international health and addiction expert team based on a comprehensive review and evidence grading of scientific literature on cannabis use and its associations with the development, course, and outcomes of psychosis. The conceptual approach for the LRCUG-PSYCH was informed by the general Lower-Risk Cannabis Use Guidelines for Canada (LRCUG) initially published in 2011, with the most recent version published in 2022 (Fischer et al.).

The description and critical appraisal that form the basis of the following guidelines can be found in the evidence review published in the Journal of Dual Diagnosis in 2023 (Fischer et al.).

Who are the LRCUG-PSYCH for?

The LRCUG-PSYCH serves as a public mental health resource for psychosis-related education, prevention and care, and harm reduction in contexts of non-medical cannabis use. These guidelines are for:

- Individuals who are thinking about using cannabis or actively using cannabis.
- Individuals who have a history of, or are at an elevated risk of developing psychosis.
- Clinicians, professionals, organizations, or government entities dedicated to improving the health of people who use cannabis.

Precautionary message for cannabis use and psychosis

There are many factors for reducing the risk of cannabis-related harms associated with psychosis. The only certain and reliable way to eliminate cannabis-related risks of psychosis outcomes is by abstaining from use. If abstinence is undesirable or unsustainable, other strategies such as controlling known risk factors associated with cannabis use can reduce the chances of experiencing harmful psychological effects and help safeguard the well-being of the consumers. Such strategies are summarized in the following recommendations.

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The LRCUG-PSYCH recommendations

Genetic risk factors

Genetics play a strong role in the development of psychosis and can have an effect on how cannabis use influences psychotic disorder and symptoms. While there is currently no easy practical way to assess a person's genetic risk for developing cannabis-related psychosis, individuals with a first-degree family history of psychosis (e.g. a parent, sibling or child) or with their own personal history of psychotic symptoms are at greater risk of developing psychosis-related harms associated with cannabis use.

Recommendation 1

Individuals with a family or personal history of psychosis should be advised about the elevated risks of psychosis if they are using or considering using cannabis. They should ideally not initiate or abstain from cannabis use. If they are using cannabis, they should reduce and minimize the intensity of use as the next best option.

Age of initiation/use

Adolescence

There is strong, consistent evidence that the risk of psychosis is greater when cannabis use is initiated at a younger age (e.g. age 16 years or younger). Adolescence is an important period for brain development, for which the endocannabinoid, dopaminergic and glutaminergic systems play essential roles. Cannabis use can interfere with these systems (e.g., disrupting processes such as synaptic pruning and myelination) in ways that increase the risk of psychosis. In addition, early cannabis use is associated with earlier onset of psychosis, more persistent psychotic experiences, and more relapses in people with psychotic disorders.

Older adults

There have been substantial increases in cannabis use in older adults (e.g. aged 60/65+), particularly in jurisdictions where the sale of cannabis is legal. Age-specific brain changes, other mental health conditions, and interactions with certain commonly prescribed medications in this age group may exacerbate the risk of cannabis-related psychosis outcomes. While data is more limited, people who use cannabis into their older age, especially those with a family history of schizophrenia, may also be more susceptible to psychosis-related consequences.

Recommendation 2

A **Cannabis use in adolescence should be avoided and accordingly delayed to reduce psychosis-related risks.**

B **Older age users, especially those with a family history of psychosis, should as a precaution avoid intensive use.**

High-THC/potency of cannabis

THC Content

Delta-9-tetrahydrocannabinol, also known as THC, is the main 'cannabinoid' constituent in cannabis responsible for both its euphoric and psychosis-related effects. The average THC-content of cannabis products has increased substantially over the past decade. There is strong evidence of a dose-response relationship between THC and psychosis, meaning that the higher the THC-content of the cannabis used, the higher the risks of experiencing psychotic symptoms or developing psychosis outcomes. There is also some evidence that high-potency cannabis is associated with more severe psychotic symptoms and increased risk of relapse in people with psychotic disorders.

CBD Content

Cannabidiol (CBD) is another main cannabinoid in cannabis. It is non-intoxicating, and at high doses may have some anxiolytic, antipsychotic and anticonvulsant properties. While limited, there is some evidence that using cannabis with high levels of CBD content may reduce the risk of THC-induced psychotic symptoms. Some studies have found evidence for pure CBD extracts having therapeutic use in patients with psychosis. However, the CBD-containing cannabis products available for non-medical use are generally not pharmaceutical grade and contain much lower doses of CBD than those used in clinical applications and are unlikely to produce therapeutic benefits for psychosis.

Recommendation 3

A **In order to reduce the risk of psychosis-related problems, THC-content of cannabis used should be as low as possible.**

B **While individuals are advised to use cannabis products with higher CBD levels, they should be aware that the evidence on CBD's potential to protect against psychotic symptoms,including those induced by THC, is limited, and that using high-CBD products is not a suitable substitute for following the other recommendations listed here.**

C **Where possible, regulated (ideally medical-grade) cannabis products should be used to increase product safety and ensure greater predictability of likely cannabinoid effects.**

Frequency of use

There is strong evidence that there is a dose-response relationship between frequency of cannabis use and psychotic outcomes. In other words, the more frequently cannabis is used, the greater the risk of both psychotic-like experiences and psychotic disorders. Evidence suggests that using cannabis at a frequency of once a week or more significantly increases the risk of developing psychosis, and the risk is substantially greatest with highly frequent (eg. daily) cannabis use. Risks may be considered

lower when cannabis is used occasionally (e.g., once a week) or less, and when other risk factors for psychosis are absent.

Recommendation 4

Reducing or keeping cannabis use frequency as low as possible, preferably less than once per week, is an important way to reduce the risks of related psychosis outcomes or problems.

Modes of use

Cannabis can be consumed in a number of different ways. The method of use can have a significant effect on the onset, expression and manageability of the effects, including psychotic symptoms or outcomes. Cannabis concentrates, waxes, and extracts typically used for 'dabbing', provide very high doses of THC, shown to increase the risk of psychosis-related outcomes. While edibles generally contain lower doses of THC than products for smoking or vaping, ingesting cannabis leads to both delayed and prolonged effects, making it difficult to titrate dosing and often resulting in over-consumption and/or unwanted psychosis-like effects. Alternatively, inhalation routes allow better control of dosing, however they may involve use of cannabis with high THC-content and so increase the risk of adverse psychosis ouctomes.

Recommendation 5

Cannabis users should be aware of the particular risk features of each use mode and avoid or limit their THC intake and exposure accordingly. Ingestion typically involves lower doses of THC, but the onset of effects and dosing are harder to predict, whereas inhalation is easier for managing dosing and related effects but THC content is typically elevated.

Other substance use

Other psychoactive substance use that commonly co-occurs with cannabis use can adversely affect the development and outcomes of psychosis. For example, tobacco is commonly mixed with cannabis (e.g., in 'joints'), but there is evidence that the mix of tobacco and cannabis or concurrent alcohol use may also contribute to psychosis development, particularly in adolescents. Individuals who use cannabis and develop psychosis are also more likely to use alcohol, tobacco, and other illicit drugs and are more likely to struggle with problematic substance use. These substances worsen outcomes in people with psychosis, such as worsening cognitive symptoms, increasing psychotic relapses, and worsening treatment or medication adherence.

Recommendation 6

Individuals who use cannabis should ideally avoid or reduce as much as possible the co-use of other psychoactive substances, including tobacco, alcohol and other illicit drugs, for overall improved health and reduced risk of cannabis-related psychosis outcomes.

Concurrent cannabis use with psychotic disorders

Cannabis use is linked to poorer outcomes in individuals with psychotic symptoms or psychotic disorders, including higher rates of symptomatic relapse and higher positive symptom severity. Higher-potency cannabis in particular may be associated with an earlier onset of psychosis, more symptoms and increased risk of relapse. The role of the frequency of cannabis use is not well studied but more intensive use is likely to increase risks of relapse. Some related evidence suggests that some of the neurobiological effects of cannabis use that adversely affect psychosis-related outcomes may be reversable. Substantially reducing or ceasing cannabis use may improve the course of illness and response to treatment in individuals with psychotic disorders.

Recommendation 7

A **People experiencing psychosis should ideally stop their cannabis use, if possible for that individual. Individuals with psychosis who are unable to stop using cannabis may experience improvements if they substantially reduce their intensity of use.**

B **People experiencing psychosis may benefit from switching to or increasing the use of lower-potency and CBD-rich cannabis products, instead of THC.**

Medication interactions and effects

Evidence suggests that individuals with psychosis who use cannabis are at increased risk of treatment non-adherence and are more likely to experience poorer treatment outcomes compared to non-users. Cannabinoids can inhibit or induce the metabolism of antipsychotics and sedatives, thereby reducing their efficacy or producing adverse effects. The addition of nicotine to cannabis consumption may amplify these effects, particularly decreasing the bioavailability of many antipsychotics such as clozapine and olanzapine.

Recommendation 8

A **Individuals living with a psychotic disorder who are receiving antipsychotic and other psychiatric treatment should reduce, or ideally cease their cannabis use to maximize beneficial therapeutic outcomes.**

B **Psychosis medication adherence and effect parameters should be carefully monitored among those who continue to use cannabis, and the treatment approach adjusted when necessary by professional care providers.**

Intermittent/suspended cannabis use

Reducing or ceasing cannabis use for a period of time is likely to improve the prognoses of cannabis users with psychosis and reduce psychotic symptoms. Effective treatment in the early stages of treatment is strongly predictive of a better

symptomatic course and outcomes. The early adjustment of clinical prescriptions and the use of alternative treatments, such as clozapine or long-acting depot injections, may improve the therapeutic prognosis of cannabis users with psychosis.

Some adverse neurobiological effects due to psychosis may also be reversible with cessation of, or a substantial reduction in cannabis use. The risk of psychosis relapse among those with discontinued cannabis use is similar to that among cannabis non-users and much better than that of persons who continue to use cannabis.

Recommendation 9

Individuals with psychosis who are unable to stop using cannabis should consider reducing the intensity of use or ceasing to use cannabis for a period of time to see improvements in their symptoms and course of their disorder. The benefits of these changes in use patterns may take some time to appear.

Combinations of risk factors

Many of the outlined cannabis-use related risk factors for psychosis outcomes may occur in combination, such as initiating cannabis use at a young age (e.g., adolescents) and engaging in frequent ("intensive") use of high- potency cannabis products. Such combinations of risk factors may adversely amplify the risks of psychosis and adverse outcomes. There is also evidence of interactions between cannabis use and other social and clinical factors, such as childhood trauma, as well as with gender, leading to further increased risks of psychosis-related outcomes.

Recommendation 10

A **For prevention purposes, those with multiple risk factors (e.g., familial psychosis or trauma history) are strongly advised to avoid the frequent use of cannabis and/or high- potency cannabis products, especially during adolescence.**

B **Those at high-risk of or who have developed psychoses should similarly avoid high-intense forms of cannabis use and follow other evidence-based risk reduction strategies.**

Other cannabis-related health risks and outcomes

Regular cannabis use can lead to other adverse health effects and is not limited to psychosis-related problems. For example, a cannabis use disorder (eg. dependence) can arise from intensive, long-term use of high THC cannabis products and lead to the compulsive, persistent use of cannabis, in turn increasing in psychosis-related or other health risks.

Cannabis use can also increase risks of motor vehicle crash involvement due to cognitive impairment. The smoking of cannabis, especially when mixed with tobacco, can result in pulmonary problems if mixing tobacco with cannabis. There is also emerging evidence that the use of high-THC products is associated with an increased risk of cardiovascular problems.

Additionally, pregnant women who use cannabis frequently, and especially during the first trimester of pregnancy, face increased risks of adverse fetus or neonatal health outcomes.

Recommendation 11

Individuals using cannabis who are at risk of psychosis should be informed on the multiple other cannabis-related risks and adverse outcomes for heath, such as cannabis dependence, motor vehicle crashes and related injuries, pulmonary and cardiovascular problems, and pregnancy-related health problems. They should be aware that regular, intensive use of cannabis should be avoided for general – beyond mainly mental – health protection.

References

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Endorsements

The LRCUG-PSYCH have been endorsed by the following organizations:

SSC SCHIZOPHRENIA SOCIETY OF CANADA

CANADIAN PUBLIC HEALTH ASSOCIATION

CANADIAN RESEARCH INITIATIVE IN SUBSTANCE MISUSE | INITIATIVE CANADIENNE DE RECHERCHE EN ABUS DE SUBSTANCE

Canadian Consortium for Early Intervention in Psychosis

Canadian Centre on Substance Use and Addiction

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A public brochure of the recommendations and a series of tools for clinical practice were created based on the original, scientific LRCUG-PSYCH publications. These resources are available online at cannabis-psychose.ca.