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Canadian Schizophrenia Guidelines: Schizophrenia and Other Psychotic Disorders with Coexisting Substance Use Disorders

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Abstract

Objective: Persons with schizophrenia and other psychotic disorders frequently have coexisting substance use disorders that require modifications to treatment approaches for best outcomes. The objectives of this review were to identify evidence-based practices best practices that improve outcomes for individuals with schizophrenia and substance used disorders.

Method: We reviewed guidelines that were published in the last 5 years and that included systematic reviews or meta-analyses. Most of our recommendations came from 2 publications from the National Institute for Health and Care Excellence (NICE): the 2011 guidance titled Coexisting Severe Mental Illness (Psychosis) and Substance Misuse: Assessment and Management in Healthcare Settings and the 2014 guidance titled Psychosis and Schizophrenia in Adults: Prevention and Management. We placed these recommendations into the Canadian context to create this guideline.

Results: Evidence supports the inclusion of individuals with coexisting substance use disorders in first-episode psychosis programs. The programs should integrate psychosis and substance use treatments, emphasizing ongoing monitoring of both substance use and patterns and symptoms. The best outcomes are achieved with combined use of antipsychotic medications and addiction-based psychosocial interventions. However, limited evidence is available to recommend using one antipsychotic medication over another or one psychosocial intervention over another for persons with schizophrenia and other psychotic disorders with coexisting substance use disorders.

Conclusions: Treating persons who have schizophrenia and other psychotic disorders with coexisting substance use disorders can present clinical challenges, but modifications in practice can help engage and retain people in treatment, where significant improvements over time can be expected.

Keywords

psychotic disorders, schizophrenia, substance use disorders, guidelines

Substance use disorders are frequent in persons who have schizophrenia and other psychotic disorders. Large epidemiologic surveys suggest that the prevalence of substance use disorders (excluding nicotine and caffeine use disorders) in persons with schizophrenia is 47% and 44.8%, respectively,[1,2] with the most frequently used substances being alcohol and cannabis. In addition, cigarette smoking has been reported in 60% to 90% of persons with schizophrenia and other psychotic disorders.[3,4]

Cannabis and stimulant use, in particular, appear to be associated with the development of psychotic symptoms; cannabis use appears to be an independent risk factor for the development of persistent psychotic disorders, particularly in those at genetic risk for developing schizophrenia and those who previously experienced psychotic symptoms.[5-7] Regular cannabis use in adolescence appears to significantly increase the risk of developing symptoms of psychosis, even after abstinence for a year, while the presence of psychotic symptoms does not appear to increase the risk of cannabis use.[8] A meta-analysis reported that persons who have used cannabis appear to develop psychosis 2.7 years earlier than those who have not used cannabis.[9]

Substance use not only appears to increase the risk of developing psychotic symptoms but also negatively affects the course of schizophrenia and other psychotic disorders,

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where persons have more positive symptoms, higher rates of treatment nonadherence, greater relapse rates, more depression and more service utilization.[10-13] However, the impact of substance use on the neurocognitive symptoms of psychosis is less clear, particularly for cannabis use.[14,15] Early substance use may induce overt psychosis in persons who are less cognitively vulnerable, resulting in the potential for improvement in cognitive functioning and decreased disability, especially with abstinence.[14,16]

Substance use can complicate the diagnosis of psychosis: Because substance use can produce psychotic symptoms, it can be unclear whether symptoms are substance-induced or representative of an underlying psychotic disorder. Many persons initially diagnosed with substance-induced psychosis are later diagnosed with a primary psychotic disorder.[17-19] Persons using substances may be reluctant to disclose their substance use, but when posed with a potential psychotic diagnosis these people may be more prone to attribute their symptoms to substance use, potentially to avoid having a diagnosis of a psychotic disorder and the need to take antipsychotic medications. Indicators of an underlying psychotic disorder being present include persistence of psychotic symptoms with abstinence, symptoms out of keeping with the type or amount of substance used, family history of schizophrenia, typical positive symptoms of schizophrenia (e.g., commenting auditory hallucinations) and/or presence of negative/cognitive symptoms.[20]

Methods

The methods for the Canadian Schizophrenia Guidelines are described in brief here; please see the Introduction and Guideline Development Process section for an in-depth description.

The guidelines were developed using the ADAPTE process.[21] Recognizing that the development of guidelines requires substantial resources, the ADAPTE process was created to take advantage of existing guidelines and reduce duplication of effort.

The first phase of ADAPTE, the set-up phase, involved preparing for the ADAPTE process. We assembled a national multidisciplinary panel from across Canada, including stakeholders with expertise in schizophrenia and mental health, health policy, patient advocacy and lived experience with schizophrenia. Endorsement bodies for the guidelines include the Canadian Psychiatric Association and the Schizophrenia Society of Canada, which were also heavily involved in the dissemination and implementation strategy.

The second phase of the ADAPTE process, the adaptation phase, involves identifying specific health questions; searching for and retrieving guidelines; assessing guideline quality, currency, content, consistency and applicability; making decisions regarding adaptation; and preparing the draft adapted guideline. We searched for guidelines on schizophrenia in guideline clearinghouses and on the websites of well-established guideline developers for mental health disorders, including the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), the American Psychiatric Association, the American Academy of Child and Adolescent Psychiatry and the European Psychiatric Association. A MEDLINE search was performed using the term *guideline* as publication type and *schizophrenia* as title or clinical topic. Inclusion criteria were that the guideline needed to be published after 2010, the guideline needed be written in English, and recommendations had to be developed using a defined and systematic process. We identified 8 current guidelines that were potentially suitable for adaptation. These guidelines were reviewed and evaluated in duplicate using the AGREE II tool,[22] an instrument to evaluate the methodological rigour and transparency with which a guideline is developed. Based on this evaluation, we determined that the 6 guidelines were of suitable quality and content for adaptation (Table 1). Recommendations from each guideline were extracted and classified based on content and then reviewed by the relevant working group. Following the ADAPTE process, working groups selected between guidelines and recommendations to create an adapted guideline. Each working group carefully examined each recommendation, the evidence from which the recommendation was derived and the acceptability and applicability of the recommendation to the Canadian context. After reviewing the recommendations from the guidelines, the working groups decided which recommendations to accept and which to reject and which recommendations were acceptable but needed to be modified. Care was taken when modifying existing recommendations not to change the recommendations to such an extent that they were no longer in keeping with the evidence upon which they were based.

Each working group developed a final list of recommendations from the included guidelines that were presented to the entire guideline panel at an in-person consensus meeting. Working group leaders presented each recommendation and its rationale to the panel. Anonymous voting by the entire panel using clicker technology was conducted for each recommendation. Recommendations required agreement by 80% of the group to be included in the Canadian guidelines. If a recommendation did not receive 80% agreement, the group discussed whether minor modifications to the recommendation would alter the likelihood that the recommendation would pass. In these situations, recommendations were modified (as described above) and the group revoted at a later date using an online anonymous survey. Whenever modifications in wording were made to original recommendations, the text "modified recommendation from" appears in the Canadian Schizophrenia Guidelines, and the source of each recommendation is noted after the recommendation statement. The strength or grade of the recommendation is provided if applicable, using the system which the recommendation came from. The strength of recommendation for each NICE guidance used in this section and their meaning are explained in brief in Table 2 (see the Introduction and

Table 1. Clinical Practice Guidelines Used for the Canadian Schizophrenia Guidelines.

Guideline Developer	Guideline Title	Year Published
National Collaborating Centre for Mental Health Commissioned by the National Institute for Health and Care Excellence (NICE)	NICE National Clinical Guideline Number 178. Psychosis and Schizophrenia in Adults: Prevention and Management	2014
National Collaborating Centre for Mental Health Commissioned by the National Institute for Health and Care Excellence (NICE)	NICE National Clinical Guideline Number 155. Psychosis and Schizophrenia in Children and Young People: Recognition and Management	2013
National Collaborating Centre for Mental Health Commissioned by the National Institute for Health and Care Excellence	NICE National Clinical Guideline Number 120. Psychosis with Coexisting Substance Misuse: Assessment and Management in Adults and Young People	2011
Scottish Intercollegiate Guidelines Network (SIGN)	SIGN 131. Management of Schizophrenia	2013
European Psychiatric Association	European Psychiatric Association Guidance on the Early Intervention in Clinical High Risk States of Psychoses	2015
American Psychiatric Association	American Psychiatric Association Practice Guidelines for Psychiatric Assessment of Adults	2016

Table 2. Strength of Recommendation System for NICE Guidance. [a]

Strength of recommendations

The wording used in NICE recommendations denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions that must (or must not) be used

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions that should (or should not) be used—a 'strong' recommendation

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm and will be cost effective.

Interventions that could be used

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and will be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation.

[a]NICE, National Institute for Health and Care Excellence.

Guideline Development Process section for a more detailed description). Once the voting and consensus process was completed, each working group created a separate report that contains all the recommendations adapted from the included guidelines, with accompanying text explaining the rationale for each recommendation.

During the finalization phase, the Canadian Schizophrenia Guidelines were externally reviewed by those who will be affected by their uptake: practitioners, policymakers, health administrators, patients and their families. The external review asked questions about whether the users approve of the draft guideline, strengths and weaknesses and suggested modifications. The process was facilitated through the *Canadian Journal of Psychiatry* and the Schizophrenia Society of Canada. The Canadian Psychiatric Association Clinical Practice Guidelines Committee reviewed and approved the guideline method process.

For this report, the following specific recommendations have been derived from NICE guidance[23,24] and adapted for the Canadian context by our working group. The terms *substance use* or *substance use disorder* have been used to be in keeping with DSM-5 terminology[25] instead of the term *substance misuse* used in the NICE guidance.[23,24]

Results

Recommendation 1

When working with adults and young people with known or suspected psychosis and coexisting substance use, take time to engage the person from the start and build a respectful, trusting, nonjudgmental relationship in an atmosphere of hope and optimism. Be direct in your communications, use a flexible and motivational approach and take the following into account:

- Stigma and discrimination are associated with psychosis and substance use.
- Some people will try to conceal either or both of their conditions.
- Many people with psychosis and substance [use] fear being detained or imprisoned, being given psychiatric medication forcibly or having their children taken into care, and some fear that they may be 'mad.'

[NICE Guidelines (Strong)]

Recommendation 2

When working with adults and young people with known or suspected psychosis and coexisting substance use, note the following:

- Ensure that discussions take place in settings in which confidentiality, privacy and dignity can be maintained.
- Avoid clinical language without adequate explanation.

- Provide independent interpreters (who are not related to the person) if needed.
- Aim to preserve continuity of care and minimize changes of key workers in order to foster a therapeutic relationship.

[NICE Guidelines (Strong)]

Recommendation 3

Health care professionals working with adults and young people with psychosis and coexisting substance [use] should ensure that they are competent to engage, assess and negotiate with service users from diverse cultural and ethnic backgrounds [including indigenous people] and their families, carers or significant others.

[Modified from NICE Guidelines (Strong)]

Recommendation 4

Work with local minority and ethnic [including indigenous people] organizations and groups to help support and engage adults and young people with psychosis and coexisting substance [use]. Offer organizations and groups information and training about how to recognize psychosis with coexisting substance [use] and access treatment and care locally.

[Modified from NICE Guidelines (Strong)]

Recommendation 5

Offer written and verbal information to adults and young people appropriate to their level of understanding about the nature and treatment of both their psychosis and substance use. Offer information and advice about the risks associated with substance [use] and the negative impact it can have on the experience and management of psychosis.

[Modified from NICE Guidelines (Strong)]

Recommendation 6

Encourage families, carers or significant others to be involved in the treatment of adults and young people with psychosis and coexisting substance use to help support treatment and care and promote recovery. When families, carers or significant others live with or are in close contact with the person with psychosis and coexisting substance use, offer family intervention.

[Modified from NICE Guidelines (Strong)]

Although there are currently few studies of family intervention specifically for persons with coexisting psychosis and substance use disorders,[26] the evidence for the benefit of family intervention for improving outcomes in schizophrenia is well established.[27,28]

Recommendation 7

Offer families, carers or significant others a carer's assessment of their caring, physical, social and mental health needs. Where needs are identified, develop a care plan for the family member or carer.

[NICE Guidelines (Strong)]

Recommendation 8

Offer written and verbal information to families, carers or significant others appropriate to their level of understanding about the nature and treatment of psychosis and substance [use], including how they can help to support the person. Written information should be available in the appropriate language or, for those who cannot use written text, in an accessible format (audio or video).

[NICE Guidelines (Strong)]

Persons with psychosis and coexisting substance use disorders can encounter barriers to their care, potentially worsening outcomes.[29]

Recommendation 9

Do not exclude adults and young people with psychosis and coexisting substance use disorder from age-appropriate mental health care because of their substance use disorder.

Recommendation 10

Do not exclude adults and young people with psychosis and coexisting substance use disorder from age-appropriate substance use disorder services because of a diagnosis of psychosis.

Recommendation 11

For most adults with psychosis and coexisting substance use disorder, treatment for both conditions should be provided by health care professionals in mental health care.

[Modified from NICE Guidelines (Strong)]

To date, the best evidence suggests that integrated substance use and psychosis treatment provided in a mental health care setting may lead to the best treatment outcomes compared with care provided in a parallel or sequential fashion.[30,31] While a specialized concurrent disorder program providing dual diagnosis enhanced services may be the ideal setting for treatment, these services are available only in some major urban centres. If a concurrent disorder program is present, it should be used; otherwise, the next best treatment setting would be a specialized psychosis treatment program.[30-32] Interestingly, for early psychosis populations, to date the evidence suggests that additional treatments beyond those involving assessment and monitoring of substance use on top of typical services provided in an early psychosis program have not been shown to be more effective.[32] It may be that the ability to demonstrate differences between usual early psychosis treatments and those with further specialized substance use treatment components is limited by several factors: the fact that many persons presenting for treatment

stop substance use on their own, while the most ill patients may persist in their use; commonalities between treatment as usual and specialized treatments (e.g., focus on engagement, motivational practices, etc.); substance use treatment not being matched appropriately to the stage of change for substance use; potential negative symptoms or cognitive deficits limiting psychosocial approaches; and/or overemphasis on group-based treatments that may have limited retention.

The management of all persons with psychosis and coexisting substance use disorders should be based on a comprehensive, multidisciplinary assessment.

Recommendation 12

Health care professionals in all settings should routinely ask adults and young people with known or suspected psychosis about their use of cigarettes, alcohol and prescribed and nonprescribed (including illicit) drugs. If the person has used substances, ask about all of the following:

- Particular substance(s) used
- Quantity, frequency and pattern of use
- Route of administration
- Duration of current level of use

[Modified from NICE Guidelines (Strong)]

Recommendation 13

Health care professionals in all settings should routinely assess adults and young people with known or suspected substance use disorders for possible psychosis. Seek corroborative evidence from families, carers or significant others where this is possible and permission is given.

[Modified from NICE Guidelines (Strong)]

Recommendation 14

Adults and young people with psychosis and coexisting substance use disorder attending mental health services should be offered a comprehensive, multidisciplinary assessment, including assessment of all of the following:

- Personal history
- Mental, physical and sexual health
- Social, family and economic situation
- Accommodation, including history of homelessness and stability of current living arrangements
- Current and past substance [use] and its impact upon their life, health and response to treatment
- Criminal justice history and current status
- Personal strengths and weaknesses and readiness to change their substance use and other aspects of their lives

The assessment may need to take place over several meetings to gain a full understanding of the person and the range of problems he or she experiences and to promote engagement.

[NICE Guidelines (Strong)]

It is also recommended that the following are assessed:

- Symptoms of psychosis and their duration
- Family history of psychosis or substance use disorders
- Correlation of psychotic symptoms to substance use patterns
- Review of prior psychosis treatments and their outcomes
- Assessment of relative severity of psychosis to substance use (to guide initial treatment focus)
- Safety-based issues: suicide, aggression/homicide/violence, physical health risks (e.g., withdrawal, overdose, seizures, blood-borne infections)

Recommendation 15

Review any changes in the person's use of substances. This should include changes in the way the use of substances affects the person over time:

- Patterns of use
- Mental and physical state
- Circumstances and treatment

Share the summary with the person and record it in the care plan.

[NICE Guidelines (Strong)]

The use of substances and/or the effects of psychosis can impair decision making.

Recommendation 16

If people with psychosis and coexisting substance use are parents or carers of children or young people, ensure that the child's or young person's needs are assessed.

[Modified from NICE Guidelines (Strong)]

Recommendation 17

If serious concerns are identified, a child protection plan should be developed.

[Modified from NICE Guidelines (Strong)]

Recommendation 18

When working with people with psychosis and coexisting substance use who are responsible for vulnerable adults, ensure that the home situation is risk assessed and that safeguarding procedures are in place for the vulnerable adult.

[Modified from NICE Guidelines (Strong)]

Recommendation 19

Ensure that the needs of young carers or dependent adults of the person with psychosis and coexisting substance use are assessed. Initiate safeguarding procedures where appropriate.
[NICE Guidelines (Strong)]

The consequences of substance use can include worsening of psychotic symptoms, treatment nonadherence, interaction with prescribed agents, medical comorbidity, increased service utilization (including emergency room visits and hospitalizations), increased suicides and violence and premature death.[10-13]

Recommendation 20

Monitor the physical health of adults and young people with psychosis and coexisting substance use. Pay particular attention to the impact of alcohol and drugs (prescribed and non-prescribed) on physical health. Monitoring should be conducted at least once a year or more frequently if the person has a significant physical illness or there is risk of physical illness because of substance use.
[Modified from NICE Guidelines (Strong)]

Persons with schizophrenia have been reported to die up to 20 years earlier than persons without this diagnosis, with the majority of this accounted for by cardiovascular factors.[33-35] While the focus in psychiatric practice often has been on mitigating the metabolic effects of antipsychotic medications, cigarette smoking remains the leading preventable cause of premature death and disease in Canada.[36,37] Cigarette smoking likely is the primary modifiable cardiovascular risk factor in those who have schizophrenia, as they are more frequent cigarette smokers, smoke more cigarettes and are more often nicotine dependent.[37-39]

Recommendation 21

Offer people with psychosis or schizophrenia who smoke help to stop smoking, even if previous attempts have been unsuccessful. Be aware of the potential significant impact of reducing cigarette smoking on the metabolism of other drugs, particularly clozapine and olanzapine.
[NICE Guidelines (Strong)]

Recommendation 22

Consider one of the following to help people stop smoking:

- Nicotine replacement therapy (usually a combination of transdermal patches with a short-acting product such as an inhalator, gum, lozenges or spray) for people with psychosis or schizophrenia
- Bupropion for people with a diagnosis of schizophrenia
- Varenicline for people with psychosis or schizophrenia

Warn people taking bupropion or varenicline that there is an increased risk of adverse neuropsychiatric symptoms and monitor them regularly, particularly in the first 2 to 3 weeks.
[NICE Guidelines (Strong)]

Strong evidence supports the benefit of smoking cessation interventions for persons who have schizophrenia.[40] Ideally, smoking cessation should occur when persons are psychiatrically stable and motivated for smoking cessation. If they are precontemplative or contemplative in their stage of change, a brief motivational intervention should be used (e.g., the 5 A's—Ask, Advise, Assess, Assist, Arrange) and their stage of change reevaluated in the future.[41]

For persons in preparatory or action stages of change, smoking cessation interventions should involve psychosocial counseling and support with pharmacologic interventions. Although nicotine replacement therapies (NRTs) are well tolerated, their evidence for benefit in persons with schizophrenia is limited, and there are no current placebo-controlled trials of NRT (Grade: Very Low, 7 open-label trials with $N = 650$).[40,42] Bupropion currently has the most evidence for benefit (Grade: High),[40,42] but persons should be warned about potential neuropsychiatric symptoms and monitor for them, including sleep impairment, suicidality and reemergence of psychotic symptoms. In persons without schizophrenia, varenicline appears to demonstrate the greatest efficacy for smoking cessation; however, only one randomized controlled trial (RCT) of varenicline in persons with schizophrenia is available, and varenicline is recommended second to bupropion (Grade: Moderate).[40,42-44] Data suggest limited evidence of an increased risk of adverse neuropsychiatric symptoms like suicidality or reemergence of psychosis, but it remains to prudent to warn about the potential risk for these and to monitor for them.[45]

Working with persons who have co-occurring substance use disorders and schizophrenia can be rewarding but also challenging. Practitioners should attempt to involve families, carers or significant others in the treatment plan.

Recommendation 23

Offer information to families, carers or significant others about local family or carer support groups and voluntary organizations, including those for psychosis and for substance use, and help families, carers or significant others to access these.
[NICE Guidelines (Strong)]

Practitioners should also collaborate with available local resources and seek appropriate support when possible.

Recommendation 24

Working with people who have psychosis and coexisting substance [use] can be challenging, and health care professionals should seek effective support [i.e., taking part in regular case conferences, consulting with substance use

services, working in a team-based setting, seeking supervision and/or using staff support groups].

[Modified from NICE Guidelines (Strong)]

Recommendation 25

Primary care providers should refer people with psychosis or suspected psychosis, including those who are suspected of coexisting substance use disorder, to mental health services for assessment and further management.

[Modified from NICE Guidelines (Strong)]

Recommendation 26

Health care professionals working within mental health services should ensure that they are competent in the recognition, treatment and care of adults and young people with psychosis and coexisting substance use disorder.

[Modified from NICE Guidelines (Strong)]

Recommendation 27

Health care professionals working within mental health services with adults and young people with psychosis and coexisting substance use disorder should consider having supervision, advice, consultation and/or additional training from specialists in substance use services.

[Modified from NICE Guidelines (Strong)]

Recommendation 28

Consider seeking specialist advice and initiating joint working arrangements with specialist substance use services for adults and young people with psychosis who are being treated in mental health services and are known to have any of the following:

- A severe substance use disorder
- Multiple substance use disorders of moderate severity or greater (i.e., alcohol and benzodiazepine use disorders)
- Intravenous substance use
- Serious social disruption (i.e., homelessness, family breakdown)

[Modified from NICE Guidelines (Strong)]

Recommendation 29

Delivery of care and transfer between services for adults and young people with psychosis and coexisting substance use should be coordinated to maintain engagement and ongoing care.

[Modified from NICE Guidelines (Strong)]

Treatment—General

Recommendation 30

Ensure that adults and young people with psychosis and coexisting substance use are offered evidence-based treatments for both conditions.

[NICE Guidelines (Strong)]

Recommendation 31

Ensure informed consent for treatment and, if there is doubt, assess mental capacity.

[Modified from NICE Guidelines (Strong)]

Treatment—Pharmacologic

Antipsychotic medication remains the mainstay of treatment for persons with schizophrenia and other psychotic disorders, whether or not they have a coexisting substance use disorder.[46]

Recommendation 32

Use antipsychotic medications according to the guideline on schizophrenia (NICE 2009) because there is no evidence for any differential benefit for one antipsychotic over another for people with psychosis and coexisting substance use disorder.

[Modified from NICE Guidelines]

Pharmacotherapy studies to date focusing on persons with schizophrenia and coexisting substance use disorders have been limited, leading to the NICE recommendation. However, the use of second-generation instead of first-generation antipsychotic medications may be preferred due to greater tolerability of second-generation antipsychotic medications and potentially decreased likelihood for developing extrapyramidal side effects in persons with substance use disorders (Grade: Low).[47-50] In the same vein, there is some evidence to suggest a potential preferred role of second-generation long-acting injectable (LAI) antipsychotic medications over first-generation LAIs,[51] but evidence for differences in substance use outcomes or psychotic symptoms with the use of second-generation LAIs compared with oral second-generation antipsychotic medications has not been demonstrated.[52,53] The benefits from using second-generation antipsychotic medications may be greater for those who discontinue illicit substance use compared with those who continue to use, according to a secondary analysis of data from the Clinical Antipsychotic Trial of Intervention Effectiveness (CATIE).[54]

Some literature has suggested a preferred role for clozapine in persons with schizophrenia and coexisting substance use disorders.[50,55,56] The lone RCT in this regard compared clozapine ($n = 14$) and ziprasidone ($n = 16$) in persons with schizophrenia and cannabis use disorder; investigators found that cannabis use equally decreased in both groups, but the clozapine group had fewer positive symptoms, more side effects and worse medication adherence.[57] No other RCTs

of clozapine compared with other antipsychotic medications are available, and all evidence is derived from retrospective case series that may be prone to selection bias. The limited evidence prevents clozapine from being preferentially recommended over other antipsychotic medications at this time. Future research is required in this area.

For persons with potentially substance-induced psychoses that do not resolve rapidly with abstinence, it is not clear what is the most appropriate duration of antipsychotic treatment. Following guidelines for a first episode of psychosis appears prudent, especially if risk factors for persistent psychosis are present, as many persons initially diagnosed with substance-induced psychosis are later diagnosed with a primary psychotic disorder.[17-19]

Currently, the 3 medications indicated for use in persons with alcohol use disorders are naltrexone, acamprosate and disulfiram; the best evidence is for naltrexone and acamprosate in persons without coexisting psychiatric disorders.[58] Although the NICE guidelines do not directly comment on known pharmacotherapies for alcohol use disorders in persons with schizophrenia and coexisting substance use disorders, there is some evidence of efficacy for naltrexone (Grade: Moderate, 2 double-blind RCTs, 2 open studies),[47,48,59] limited evidence for disulfiram (Grade: Low, 2 open-label retrospective studies)[47,48,59] and no current evidence for acamprosate (1 double-blind RCT, placebo = acamprosate).[47,48,59]

Pharmacotherapy for the treatment of cocaine use disorder is limited, with there being no currently indicated agents for cocaine use disorder despite multiple treatment trials.[47,48,59] In persons with schizophrenia and coexisting cocaine use disorders, limited data are available for desipramine (Grade: Low, 2 prospective studies vs placebo, no randomization)[47,48,59] and imipramine (Grade: Low, 1 positive study via secondary analysis, 1 with equivocal results).[47,48,59] Given the significant potential side effects of the tricyclic antidepressants and lack of indication for cocaine use disorder alone, the use of desipramine or imipramine in persons with schizophrenia and coexisting cocaine use disorder is not recommended.

Despite the frequency with which cannabis use is encountered in persons with schizophrenia, no evidence is available to support any potentially beneficial treatments pharmacologically or psychosocially.[60,61] Data for cannabis use disorder have been negative for mirtazapine, bupropion, nabilone and dronabinol.[47,48] In a study of adolescent cannabis users without psychosis, one trial suggested the benefit of oral N-acetylcysteine when combined with contingency management.[61] No trials are available regarding this agent in persons with schizophrenia and coexisting cannabis use disorder. Equally disappointing has been the lack of efficacy of specific psychosocial interventions despite well-designed studies.[60,62] Despite negative findings, research on treatments for cannabis use disorder should be a priority.

Treatment—Psychosocial

A variety of psychosocial interventions have been trialed in persons with psychosis and coexisting substance use disorders, including contingency management (CM), cognitive behavioural therapy (CBT)/relapse prevention, motivational interviewing (MI) and combination CBT and MI. Brief interventions (founded on MI principles, but more advice driven) have been used, as have family interventions and the use of assertive community treatment (ACT). All have demonstrated some efficacy (Grade: Low to Moderate)[63] and should be used if available.

Recommendation 33

Do not exclude adults and young people with psychosis and coexisting substance use from contingency management (CM) programs because of their psychosis.

[NICE Guidelines (Strong)]

When treating patients with psychosis and coexisting substance use disorders, the focus should be on retention in treatment, gradual change in substance use behaviour over time (decreased use initially aiming for abstinence), improved physical and mental health and improved function as the primary treatment targets.[30,31] Stage of change should be evaluated for each substance of use, as stage of change may differ between substances (e.g., a person may be precontemplative in regard to changing cigarette smoking but in the preparatory stage of change regarding cannabis use). Try to best match an intervention to current stage of change. Persons in precontemplation and contemplation stages may benefit more from brief psychoeducation and motivational approaches, whereas persons in preparatory and action stages may benefit more from active intervention and relapse prevention planning.[31]

If a person is referred to a residential/inpatient treatment program or a structured day treatment for substance use disorders, coordinated follow-up care for his or her substance use disorder is required after completion of treatment. The optimal duration of treatment is uncertain, but patients staying in treatment longer typically have better overall outcomes.[31,64]

Substance Use Treatment Services

Recommendation 34

Health care professionals in substance use services should be competent in the following:

Recognizing the signs and symptoms of psychosis
Undertaking a mental health needs and risk assessment sufficient to determine how and when to refer to mental health services

[NICE Guidelines (Strong)]

Recommendation 35

Adults and young people with psychosis and coexisting substance use disorders attending substance use treatment services should be offered a comprehensive, multidisciplinary mental health assessment in addition to an assessment of their substance use.

[NICE Guidelines (Strong)]

Recommendation 36

Collaboration between substance use treatment services and psychosis treatment services should occur, involving the following:

- Joint meetings
- Advice, consultation and training for treatment of substance use disorders
- Development of treatment protocols for persons with schizophrenia and coexisting substance use disorders

[Modified from NICE Guidelines (Strong)]

Inpatient Mental Health Services

Persons with schizophrenia and coexisting substance use disorders have increased rates of hospitalization. When they present to inpatient units, the setting should be conducive to recovery from both disorders for best outcomes.

Recommendation 37

All inpatient mental health services should have policies and procedures for promoting a therapeutic environment free from cigarettes, drugs and alcohol.

[Modified from NICE Guidelines (Strong)]

Recommendation 38

When carrying out a comprehensive assessment for all adults and young people admitted to inpatient mental health services, ensure that they are assessed for current substance use and evidence of withdrawal symptoms at the point of admission.

[NICE Guidelines (Strong)]

Recommendation 39

Drug testing should only be considered in inpatient services as part of the assessment and treatment planning for adults and young people with psychosis and coexisting substance use disorders.

[Modified from NICE Guidelines (Strong)]

Recommendation 40

For people in inpatient settings who do not want to stop smoking, offer nicotine replacement therapy to help them to reduce or temporarily stop smoking.

[NICE Guidelines (Strong)]

Although detoxification alone from either drugs or alcohol does not change treatment outcomes,[65] detoxification can be an important part of the coordinated treatment plan for adults and young people with schizophrenia and coexisting substance use disorders.

Recommendation 41

Ensure that planned detoxification from either drugs or alcohol is undertaken only in the following circumstances:

- With the involvement and advice of substance use treatment services
- In an inpatient setting
- As part of an overall coordinated treatment plan

[Modified from NICE Guidelines (Strong)]

Recommendation 42

Do not discharge adults and young people with psychosis and coexisting substance use disorders from an inpatient mental health service solely because of their substance use.

[Modified from NICE Guidelines (Strong)]

Recommendation 43

When adults and young people with psychosis and coexisting substance use disorders are discharged from an inpatient mental health service, ensure they have all of the following:

- An identified care coordinator
- A care plan that includes consideration of needs associated with both their psychosis and their substance use disorders
- Information about the risks of overdose if they start reusing substances, especially opioids and/or benzodiazepines that have been reduced or discontinued during the inpatient stay

[Modified from NICE Guidelines (Strong)]

Conclusion

Adults and young people with schizophrenia and coexisting substance use disorders commonly present for treatment in clinical practice. Despite this, limited treatment data are available that demonstrate preferential treatment practices regarding the use of specific pharmacotherapies or psychosocial interventions for people with schizophrenia and coexisting substance use disorders. Best practices involve integrated psychosis and substance use treatments, emphasizing inclusion in treatment, ongoing evaluation of substance use patterns, and coordinated care attempting to match treatment needs to severity of both disorders and stage of change. Although treatment of people with schizophrenia and coexisting substance use disorders can have its challenges, outcome data demonstrate that treatment is beneficial, and there being significant optimism for potentially greater improvements when substance use is stopped.

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Supplementary Material

Supplementary material is available for this article online.

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