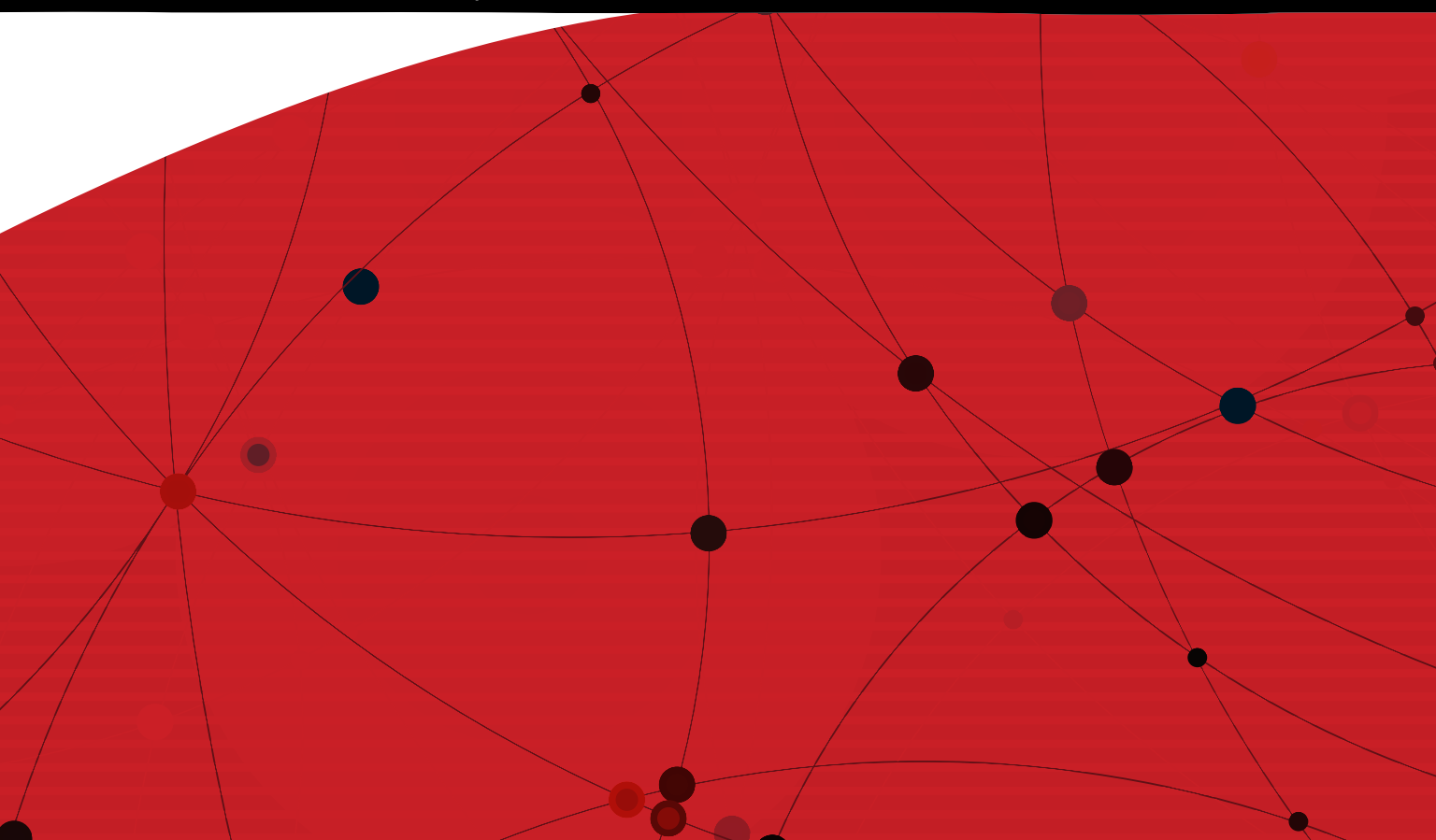
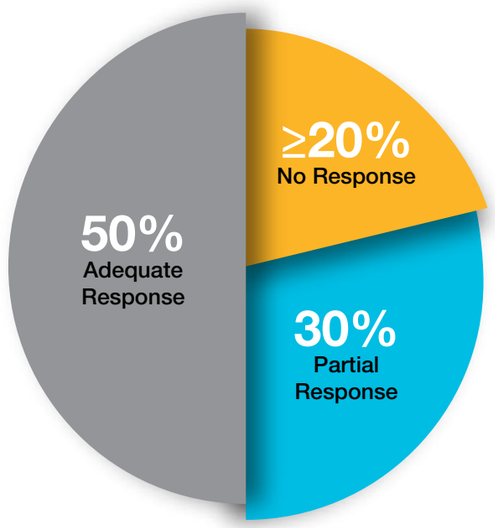
Treatment-resistant schizophrenia in Canada

Prevalence, impact, and treatment recommendations



Treatment-resistant schizophrenia (TRS): it's more common than you may think

At least 50% of patients have a sub-optimal response despite adequate pharmacotherapy.[1]



- Despite adequate pharmacotherapy, at least 20% of multiple-episode patients have no positive-symptom response to antipsychotics, and a further 30% respond only partially.[1]

*The CPA Guidelines define treatment resistance as a failed trial of **two** antipsychotics.[1]**

* An adequate trial of an antipsychotic prior to being deemed treatment-resistant is considered to be 4 to 8 weeks' duration on the maximum tolerated dosage within the recommended range.

The devastating impact of schizophrenia

Schizophrenia profoundly affects virtually every aspect of a person's life—self-care, relationships, employment, school, housing, and social life.[2]

Only 10–30% of individuals with schizophrenia are employed at any given time, and few are able to maintain employment.[3]

60–70% of people with schizophrenia do not marry and most have limited social contacts.[2]

50–85% of people with schizophrenia will develop a co-occurring substance use disorder.[3]

40–50% of patients with schizophrenia attempt suicide, and approximately 10% will die from suicide.[2]

In 1996, the total cost of schizophrenia in Canada was an estimated **$2.35 billion**.[2]

"Given the clinical picture of schizophrenia, preventing or increasing the time period between full or partial psychotic relapses is one of the primary goals of treatment." – Ziedonis D, Yanos PT, and Silverstein SM[3]

Recommended Canadian guidelines for treating schizophrenia*

"Clozapine remains the treatment of choice for partial or total non-response to treatment. Clozapine should be considered as soon as treatment non-response has been demonstrated, even in the first or second year of the disorder." – Canadian Psychiatric Association Clinical Practice Guidelines[1]

STEP 1

- **Before treatment, clarify diagnosis.**
- **Do a physical examination.**
- **Investigate to obtain baseline values if unavailable.**
- **Treatment: Administer either an SGA† (except clozapine) OR an oral FGA‡ previously effective and tolerated.**
- **Assess over 4 to 8 weeks.**

Effective and tolerated → **Continue with oral therapy or switch to long-acting injectable depot (if available) to improve medication adherence.**

Ineffective/partial response **OR** intolerable/side effects

STEP 2

- **Try augmentation OR another SGA† (except clozapine).**
- **Assess over 4 to 8 weeks.**

Effective and tolerated → **Continue with oral therapy or switch to long-acting injectable depot (if available) to improve medication adherence.**

Ineffective/partial response **OR** intolerable/side effects

STEP 3

- **Try a third SGA† (assess over 4 to 8 weeks) OR consider optimization OR change to clozapine.**
- **Assess over 4 to 6 months.**

Effective and tolerated → **Continue with treatment.**

Clozapine, drug optimization, or a third SGA† may be considered in patients who have failed on two antipsychotics.[1]

Adapted from the Canadian Psychiatric Association Clinical Practice Guidelines for the Treatment of Schizophrenia.[1]

Note: Tailor all treatment approaches to the individual patient. Consider assessment, pharmacotherapy, and psychosocial interventions at ALL stages of treatment.

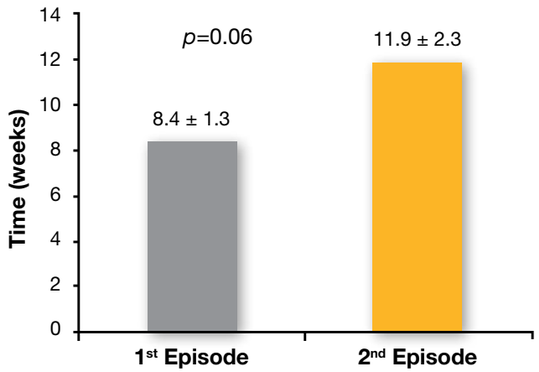
Please see Canadian clinical practice guidelines for detailed treatment recommendations.

* Stabilization and Stable Phase.
† SGA=second-generation antipsychotic. Second-generation antipsychotics refer to clozapine, olanzapine, quetiapine, and risperidone.
‡ FGA=first-generation antipsychotic.

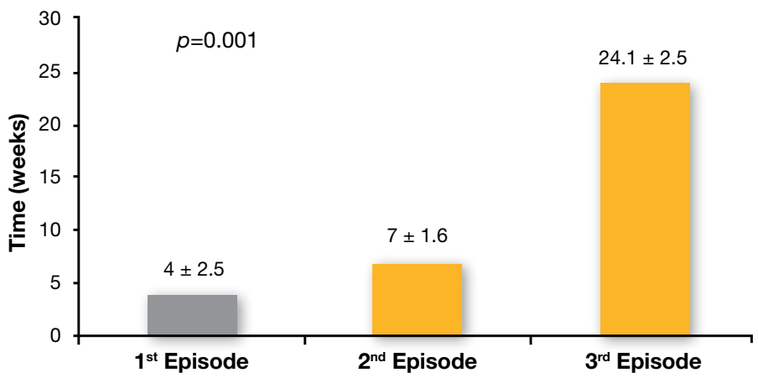
The long-term impact of psychosis

The number of episodes of psychotic relapse is associated with increased time to remission.[4]*

Median ± SE time in weeks to remission among patients with TWO episodes of relapse



Median ± SE time in weeks to remission among patients with THREE episodes of relapse

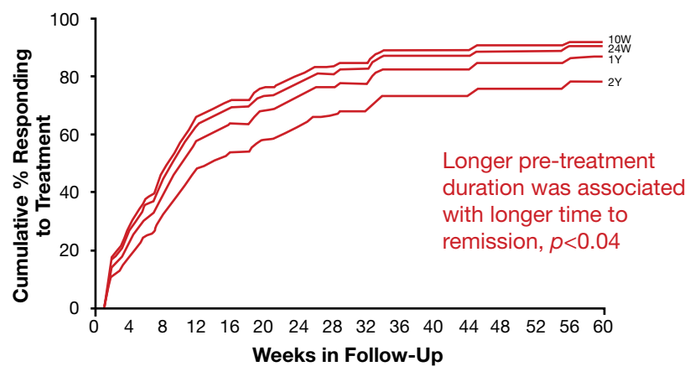


Adapted from Lieberman JA *et al.*[4]

* Patients admitted to hospital with their first episode of psychosis were given baseline assessments, and then received controlled treatment within a standardized protocol to a point of remission. Patients were followed for up to 5 years during which time the clinical and biological assessments were repeated at specific time intervals, including performing MRIs at 18-month intervals. If patients relapsed, they were re-treated with the same regimen to which they responded during their first (or prior) episode, and in the context of standardized protocol.

The duration of untreated psychosis has also been linked to poorer longer-term outcomes.[1,4]*

Cumulative percentage of first-episode patients responding to treatment by duration of illness prior to study entry



Adapted from Lieberman JA *et al.*[4]
10W=10 weeks; 24W=24 weeks; 1Y=1 year; 2Y=2 years.

Psychotic relapse is associated with:

- A need for increased doses of medication[6]
- A longer time to recovery[6]
- A lower level of function[6]
- Increased residual dysfunction and deterioration[7]

"Relapses can occur and are very detrimental to the successful management of this disorder. With each relapse, there is a longer period of time to recover." – *Bostrom AC, Boyd MA*[5]

Treatment-resistant schizophrenia in Canada

- **More than 50% of schizophrenia patients** are resistant to treatment.[1]
- Schizophrenia profoundly **affects virtually every aspect of a person's life**, from relationships to employment.[1]
- **Clozapine is the treatment of choice** for partial or total non-response to treatment according to Canadian clinical practice guidelines.[1]
- **Psychotic relapse is associated with** a need for increased doses of medication, a longer time to recovery/remission, and a lower level of function.[4,6]

References: 1. Canadian Psychiatric Association (CPA). Clinical Practice Guidelines–Treatment of schizophrenia. *Can J Psychiatry.* 2005; 50(13): 1S–56S. https://ww1.cpa-apc.org/Publications/Clinical_Guidelines/schizophrenia/november2005/cjp-cpg-suppl1-05_full_spread.pdf. Accessed November 7, 2016. **2.** Health Canada. A Report on Mental Illnesses in Canada: Chapter 3 Schizophrenia. Health Canada Web site. http://www.phac-aspc.gc.ca/publicat/miic-mmac/chap_3-eng.php. Accessed November 7, 2016. **3.** Ziedonis D, Yanos PT, Silverstein SM. Relapse prevention for schizophrenia. In: Witkiewitz DA, Marlatt GA, eds. *Therapist's guide to evidence-based relapse prevention.* San Diego, CA: Elsevier; 2007:117–140. **4.** Lieberman JA, Alvir JM, Koreen A, *et al.* Psychobiologic correlates of treatment response in schizophrenia. *Neuropsychopharmacology*. 1996; 14(3 Suppl): 13S–21S. **5.** Bostrom AC, Boyd MA. Schizophrenia: Management of thought disorders. In: Boyd MA, ed. *Psychiatric nursing: Contemporary practice.* 4th ed. Hong Kong, China: Wolters Kluwer/Lippincott Williams & Wilkins; 2008: 276–324. **6.** Siegel SJ, Ralph LN. *Demystifying schizophrenia for the General Practitioner.* Sudbury, MA: Jones and Bartlett; 2011. **7.** Varcarolis EM. *Essentials of psychiatric mental health nursing: A communication approach to evidence-based care.* 2nd ed. New York, NY: Elsevier; 2014.

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