Children's Mental Health Research
Quarterly
Children's Health Policy Centre

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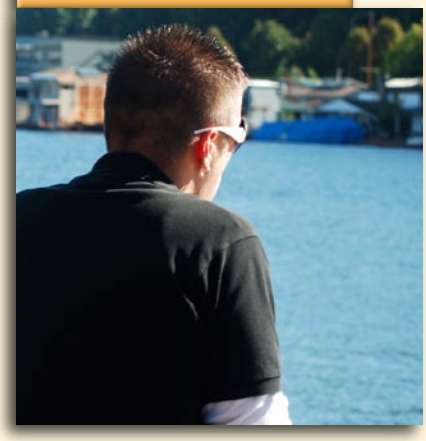

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About the Children's Health Policy Centre

As an interdisciplinary research group in the Faculty of Health Sciences at Simon Fraser University, we aim to connect research and policy to improve children's social and emotional well-being, or *children's mental health*. We advocate the following public health strategy for children's mental health: addressing the determinants of health; preventing disorders in children at risk; promoting effective treatments for children with disorders; and monitoring outcomes for all children. To learn more about our work, please see www.childhealthpolicy.sfu.ca

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This Issue

About the Quarterly

The *Quarterly* is a resource for policy-makers, practitioners, families and community members. Its goal is to communicate new research to inform policy and practice in children's mental health. The publication is funded by the British Columbia Ministry of Children and Family Development, and topics are chosen in consultation with policy-makers in the Ministry's Child and Youth Mental Health Branch.

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How to Cite the *Quarterly*

We encourage you to share the *Quarterly* with others and we welcome its use as a reference (for example, in preparing educational materials for parents or community groups). Please cite this issue as follows:

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The ABCs of psychosis

- *Do you ever think that people are out to get you?*
- *Do you hear voices when no one is there or see things that shouldn't be there?*
- *Do you have unusual abilities or powers?*
- *Do you sometimes believe things on TV or online are personally directed at you?*

These are just a few of the questions practitioners ask to help them understand the distressing experiences of a young person with psychosis.

Psychotic symptoms are essentially signals that the brain is not functioning properly.

The hallmark symptoms

Adolescents with psychosis have difficulty with thinking, behaving and communicating — and with understanding reality. These challenges can seriously impair their development and functioning. Table 1 describes the hallmark symptoms of psychosis.

Psychotic symptoms are often classified as either "positive" or "negative." *Positive symptoms* include delusions and hallucinations. In contrast, *negative symptoms* are characterized by a loss or reduction in typical functioning[1] and include flat affect, limited speech and diminished energy.[2] Negative symptoms are thought to have a stronger effect on cognitive and other areas of functioning than positive symptoms.[3]

Table 1: Psychotic symptoms

Symptom	Definition[1]	Example
Delusions	Strongly held false beliefs involving a misinterpretation of sensory information or experiences often based on a given theme.	Sanjit believes the creators of a new and extremely popular video game have included hidden messages in the game that only he can decipher.
Hallucinations	Perceptions occurring in any of the five senses without external stimuli. Auditory hallucinations are the most frequent.	Jenny alone hears a voice warning that her biology teacher is trying to harm her.
Disorganized Behaviours	Behaviours preventing effective functioning, including difficulties engaging in goal-directed actions, incoherent speech and agitation.	Quon abruptly starts rambling on about food safety while his mother is preparing to leave for work. This, and his poor hygiene, cause Quon's mother to be increasingly worried about his well-being.

The differing reasons for psychosis

Psychotic symptoms are essentially signals that the brain is not functioning properly. Such symptoms can occur in many different conditions, including schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, bipolar disorder and major depression with psychotic features. Psychosis can also be caused by substance use (including intoxication or withdrawal from alcohol, street drugs or prescription medications) and medical conditions (such as infection, epilepsy, head injury, cancer or autoimmune disorders).[1] Collectively, these conditions are referred to as *psychotic disorders*. Because most of the high-quality research on psychotic disorders focuses on *schizophrenia*, here we mainly focus on this condition. (Additional information on depression and bipolar disorder can be found in previous issues of the *Quarterly*.)

Up to 80% of individuals will experience a remission of psychotic symptoms within their first year of treatment with antipsychotic medication.

More than a numbers game

Although limited information exists on the number of children affected by psychosis across all diagnostic categories, high-quality epidemiological data on schizophrenia *have* been collected. These data show that while schizophrenia does affect young people, it rarely begins in childhood.

Among children age 9 to 13, for example, the estimated prevalence is only 0.1%, or 1 in 1,000.[4] This suggests that only 300 children in this age range in British Columbia (or 2,100 in Canada) would meet diagnostic criteria for schizophrenia.[5] However, the disorder becomes increasingly prevalent in later adolescence, eventually reaching an estimated prevalence of 1%, or 1 in 100, for the population as a whole.[1] Furthermore, among individuals who are eventually diagnosed with schizophrenia, nearly one-third will experience their first psychotic episode by age 19.[6]

Gender differences in incidence and prevalence of schizophrenia are quite pronounced. Males have a 30% to 40% higher lifetime risk of developing the condition than females.[7] As well, the peak age of onset for schizophrenia among males is 18 to 23 years, compared with 25 to 35 years for females.[8]

A typical course

Schizophrenia usually includes periods of illness mixed with periods of remission.[9] It typically begins with a "prodromal" stage during which a youth's functioning noticeably declines.[2] Characteristic symptoms include social withdrawal, poor self-care, suspiciousness, apathy, sleep disturbances and mood changes (including irritability and low mood).[3] This prodromal stage can last from weeks to years.[10] It is usually followed by an acute phase, marked by delusions and hallucinations, typically lasting from one to six months.[10] Most adolescents then experience several months of significant negative symptoms without acute psychotic symptoms.[10] The cycle often then begins again with similar declines in functioning followed by the re-emergence of positive symptoms, particularly if adolescents do not receive early diagnosis and treatment.[9]

Although most adolescents with schizophrenia continue to experience the disorder as adults, outcomes vary a great deal.[11] A better short-term course is associated with better long-term outcomes.[12] As well, up to 80% of individuals will experience a remission of psychotic symptoms within their first year of treatment with antipsychotic medication.[13]

> *"When a youth is suspected of having a psychosis, a careful evaluation by an experienced practitioner is essential."*

What causes schizophrenia?

In some cases, the cause of psychosis can be clearly identified and treated, for example, when it is due to substance use or a medical condition. However, the cause of psychotic disorders such as schizophrenia is considerably more complicated, involving genetic as well as environmental factors.

Evidence of the importance of genetics comes, in part, from studies finding that adopted monozygotic twins (who share most genetic material while being raised in different environments) are four times more likely to both be diagnosed with schizophrenia than adopted dizygotic twins (who share somewhat less genetic material).[8] Although the genes involved have yet to be conclusively identified, current research suggests that the development of schizophrenia is likely due to complex genetic interactions (including gene-environment interactions), rather than to any single gene.[8] Nonetheless, it is important to recognize that most children and youth with genetic vulnerability for schizophrenia will not develop the disorder. For example, a study of women with schizophrenia found that only 6.7% of their children developed the disorder.[14]

Schizophrenia is also increasingly being recognized as a neuro-developmental disorder, in part because many individuals with schizophrenia have a history of abnormal fetal development and birth complications.[7] As well, disruptions in brain development are often found among individuals who eventually develop schizophrenia. Expressions of these challenges can

include delayed achievement of developmental milestones, reduced cognitive functioning, limited social competence and challenges in motor skills.[7]

Although environmental factors do not cause schizophrenia per se, they can play a role in its development, likely through influencing gene expression. For example, some studies have found that individuals born in urban areas have 2 to 4 times the risk of developing schizophrenia compared to those born in rural areas.[7] These differences exist despite the incidence of schizophrenia being very similar across regions and cultures.[15] As well, the risk of schizophrenia is 2 to 25 times higher among individuals who have used marijuana.[7] Because of study design limitations, it cannot be concluded that marijuana use caused schizophrenia. Rather, it is possible that marijuana use resulted in schizophrenia presenting earlier in young people who eventually would have developed the disorder anyway. Other variables, such as parenting practices, are now clearly known to *not* cause schizophrenia.[16]

> *"In Canada, the direct health care and non–health care costs of schizophrenia have been estimated at $2 billion annually."*

The importance of accurate diagnosis

Identifying children and adolescents with psychosis is a fundamental precursor to providing appropriate treatment. Unfortunately, many barriers can hamper a timely and accurate diagnosis. For example, there is often a significant delay (averaging nine months)[17] between psychotic symptoms starting and an adolescent seeking treatment. A frequent barrier to seeking assistance is the stigma associated with psychosis specifically and mental disorders more generally. As well, many of the actual symptoms of psychosis, such as suspiciousness, can militate against seeking help. Help seeking is often finally precipitated by a crisis, such as suicidal or violent behaviour.[8]

Once a young person is referred for assessment, the practitioner first needs to determine whether symptoms are due to psychosis or another condition, such as a delirium. If symptoms are caused by a psychosis, the practitioner then needs to establish which disorder is causal. For example, a practitioner may have to sort out whether an adolescent's symptoms are due to schizophrenia or drug use. This process can be arduous; some studies have found that as many as 55% of individuals first presenting with psychotic symptoms receive different diagnoses within two to six years of their initial evaluation.[18] Nonetheless, providing an accurate diagnosis is critical. If a psychosis is due to an underlying medical condition, it will often resolve once the underlying condition is treated. If the psychosis is due to schizophrenia, appropriate early treatment can improve outcomes.

Given these challenges, when a youth is suspected of having a psychosis, a careful evaluation by an experienced practitioner is essential. A qualified child and adolescent psychiatrist working with an interdisciplinary mental health team can provide the type of comprehensive assessment needed.

The evaluation process requires considerable time and effort. Clinical interviews with youth and family members are essential. To help in this process, there are many structured interviews designed for gathering information about psychotic symptoms in children and adolescents. Practitioners should be sensitive to the possibility of adolescents and their families underreporting the duration and severity of symptoms due to stigma, stress and fear.[17] A medical evaluation and a review of developmental, medical and school records are also needed. Currently, no definitive blood or brain imaging tests have been established as a reliable diagnostic tool. When such tests are performed, they are usually done to rule out other treatable conditions, such as infections.

Additional challenges that accompany psychosis

Adolescents with psychotic disorders often have additional mental health concerns or concurrent problems. Those with schizophrenia frequently experience conduct disorder and depression.[11] As well, rates of suicidal behaviour have been found to range from 11% to 26% during first episodes of psychosis.[3] Suicide attempts are especially prevalent among youth using street drugs.[3] Problems with cognition,[19] language,[2] motor skills and social issues[10] also commonly co-occur with schizophrenia.

> *"We have enough evidence to know that we can help youth with psychotic disorders."*

When schizophrenia begins in adolescence rather than adulthood, it can be associated with greater functional impairment, including less independence, poorer educational achievement and increased unemployment.[19] However, given that a shorter time period between the onset of symptoms and receiving treatment is associated with a more positive outcome, there is much potential to help youth with psychosis.[17]

The financial costs

As well as causing personal burdens, schizophrenia is associated with significant financial costs. For example, adolescents and their families frequently incur medication expenses. In 2007, Canadians spent $629 million on antipsychotic drugs.[20]

Schizophrenia has also been identified as one of the world's top 10 causes of disability-adjusted life-years.[13] Adding to this, lifetime disability costs are far greater when schizophrenia begins in adolescence rather than adulthood. In Canada, the direct health care and non–health care costs of schizophrenia have been estimated at $2 billion annually (in 2004 CDN$).[21] When lost productivity costs are included, the total cost reached nearly $7 billion in 2004.

What we can do to assist

There are effective treatments for youth with psychosis. Medications can lessen psychotic symptoms and improve general functioning. (Our Review article presents information on the efficacy and side effects of medications commonly used to treat adolescent psychosis.) However, adherence to medication regimens can be poor due to unpleasant side effects, denial of the disorder[17] and a desire to not be different from peers.[8] Practitioners can help to minimize medication side effects by using the lowest possible doses to control symptoms and by using adjunctive medications to address side effects. Regular monitoring is also essential.

In comprehensive treatment plans, psychosocial interventions are also frequently included. All young people and their families should be provided with educational information about these additional treatment options.[10] As well, youth with schizophrenia typically require intensive community supports such as day programming, specialized education programs and vocational training.[10]

Regarding psychosocial therapies per se, preliminary evaluations offer encouraging results. Family therapy has been shown to be effective among adults (using randomized controlled trials) and among youth (using less rigorous evaluations).[9] However, there is still an absence of high-quality research on the effectiveness of cognitive-behavioural therapy (CBT) for teens experiencing psychosis. Given CBT's demonstrated effectiveness with adults,[9] evaluations with adolescents are warranted and needed. Despite these limitations, we have enough evidence to know that we can help youth with psychotic disorders.

What we tried to bring you — but could not

Many practitioners consider psychosocial interventions to be a vital component in treating psychosis. For example, a well-respected practice parameter stresses using a "comprehensive multimodal approach" to most effectively reduce symptoms and relapse rates among adolescents with schizophrenia.[10] However, such recommendations come without high-quality evaluations supporting the use of psychosocial interventions. Our five-year search of four databases uncovered only one psychosocial treatment for adolescent psychosis evaluated using randomized controlled trials (RCTs) (see our Feature article). We focus on RCTs because this research design helps to ensure that any improvements are due to the actual treatment rather than other factors. (See the In Commentary section of our first issue for further information about our research methodology.) In an effort to provide information on a broader array of psychosocial treatments, we searched two systematic reviews — including one that was not restricted to newer journal publications.[9,13] Despite our efforts, we did not locate any additional RCTs on psychosocial treatments for adolescents with psychosis. Rigorous evaluations of these treatments are greatly needed. Investing in such research will help to ensure that vulnerable youth are offered the best possible treatment choices.

Antipsychotics: Prescribing for success

With careful management, medications can dramatically improve functioning and reduce suffering for youth with psychosis.

Medications are widely accepted as an essential treatment for psychosis in young people despite somewhat limited research on their effectiveness. Two recent systematic reviews[22, 23] and one recent practice parameter[10] uncovered only two English-language, randomized placebo-controlled trials of antipsychotics with individuals age 18 and younger. Both of the older antipsychotics evaluated — haloperidol and loxapine — were effective for young people with schizophrenia.[24, 25]

Since these evaluations occurred, many new antipsychotics have been developed, including risperidone and olanzapine. Most practitioners prescribe these newer medications when treating youth with psychosis.[26] Because of this, there is a critical need for information on the effectiveness and side effects of these commonly prescribed antipsychotics. Consequently, we sought to identify and summarize the newest high-quality research available on the benefits and risks of medications used to treat psychosis in young people.

Our systematic method for selecting research

We used systematic methods adapted from the *Cochrane Collaboration*.[27] We limited our search to randomized controlled trials (RCTs) published in peer-reviewed scientific journals.

To identify studies, we first applied the following search strategy:

Sources	• Medline, PsycINFO, CINAHL and CENTRAL
Search Terms	• Schizophrenia, disorders with psychotic features *or* psychosis *and* prevention, treatment *or* intervention
Limits	• English-language articles published in 2004 through January 2009* • Child participants aged 0–18 years

* We limited our search to five years given that our previous report *Early Psychosis: A Review of the Treatment Literature*[9] included publications prior to 2004.

As well, we hand-searched previously published systematic reviews and all accepted RCTs for additional relevant publications.

Next, we applied the following criteria to ensure we included only the highest-quality pertinent studies:

- Mean age of sample 18 years or less
- Interventions aimed at preventing or treating psychosis
- Clear descriptions of participant characteristics, settings and interventions
- Random assignment of participants to intervention and control/comparison groups at study outset
- Double blinding (for medication trials only)
- Attrition rates below 20% or use of intention-to-treat analysis
- Levels of statistical significance reported for all psychosis outcomes at final measurement period

Two different team members assessed each retrieved study to ensure accuracy.

Finding the highest-quality evaluations

Of the 11 evaluations retrieved for assessment, seven medication trials met our criteria. (The two psychosocial intervention trials that met our criteria are highlighted in our Feature article.) Table 2 presents the details of these studies. The medications evaluated included aripiprazole, clozapine (brand name *Clozaril*), haloperidol (formerly sold in Canada under the brand name *Haldol*), molindone, olanzapine (brand name *Zyprexa*) and risperidone (brand name *Risperdal*).

All but two of the medications reviewed are for sale in Canada. Aripiprazole is classified as an investigational drug and is only available through Health Canada's *Special Access Programme (SAP)*. (The *SAP* considers practitioners' requests for aripiprazole only after other treatments have been considered and ruled out — for reasons such an ineffectiveness and unsuitability). Molindone is not available in Canada.

Three evaluations were placebo controlled[28–30] while four directly compared two or more medications without a placebo.[18, 26, 31, 32] One study was a prevention trial that included young people who had never had a psychotic disorder but were at high risk for psychosis.[28] Among the six treatment studies, two were limited to youth with schizophrenia[29, 30] and two were limited to young people with treatment-resistant schizophrenia[32] and/or treatment-resistant schizoaffective disorder.[31] (*Treatment resistant* was defined as previous failures to respond to two antipsychotic medications.) The remaining two studies included young people with a range of psychotic disorders including schizophreniform disorder,[18, 26] delusion disorder, and

> *"Among medications for sale in Canada, clozapine, haloperidol, olanzapine and risperidone have solid evidence supporting their effectiveness in treating psychosis in young people."*

Table 2: Medications assessed

Medication *(brand name)**	Mean Daily Dose (milligrams)**	Number of Participants	Medication Duration†	Participant Age (years)	Participant Gender
Placebo-controlled trials — Prevention					
Olanzapine[28] *(Zyprexa)*	5–15‡	Medication: 31 Placebo: 29	52 weeks	Mean: 18 Range: 12–36	65% male
Placebo-controlled trials — Treatment					
Aripiprazole[29]	10 or 29	Medication: 202 Placebo: 100	6 weeks	Mean: 16 Range: 13–17	57% male
Olanzapine[30]	11	Medication: 72 Placebo: 35	6 weeks	Mean: 16 Range: 13–17	70% male
Medication comparison trials — Treatment					
Clozapine[31] *(Clozaril)* **Olanzapine**	403 26	18 21	12 weeks	Mean: 16 Range: 10–18	54% male
Clozapine[32] **Olanzapine**	327 18	12 13	8 weeks	Mean: 12 Range: 7–16	60% male
Haloperidol[18] **Olanzapine** **Risperidone** *(Risperdal)*	5 12 4	15 16 20	8 weeks	Mean: 15 Range: 8–19	60% male
Molindone[26] **Olanzapine** **Risperidone**	60 11 3	41 36 42	8 weeks	Mean: NR Range: 8–19	65% male

NR Not reported
* Where applicable, brand names are provided for drugs currently sold in Canada.
** Different medications have different standard dosages. Therefore, a medication with a higher mean daily dose than another medication cannot be assumed to be a stronger dose.
† During RCT phase of study.
‡ Authors only reported medication dose range.

depression and bipolar disorder with psychotic features.[18] Although most studies included only American participants,[18, 26, 31, 32] children and youth from Canada,[33] Russia,[30] Africa, South America, Asia, Europe and the Caribbean[29] participated in three studies.

Funding research: Who's paying the bills?

In five of the studies, at least one author received research funding from a drug company.[18, 26, 28–30] Only one study was conducted by researchers with no financial relationship to pharmaceutical firms.[31] The authors in the remaining study did not disclose whether there was drug company funding.[32]

We can treat psychosis but can we prevent it?

In the placebo-controlled evaluations, olanzapine was not effective in preventing the *onset* of psychosis among children and youth at high risk for developing the condition.[28] Olanzapine was, however, effective in *reducing* positive symptoms, general symptoms and psychosis severity among schizophrenic youth.[30] Similarly, aripiprazole was effective in reducing positive symptoms, negative symptoms and psychosis severity and in improving remission rates, global functioning and quality of life among youth with schizophrenia.[29]

In evaluations directly comparing medications, clozapine was superior to olanzapine among treatment-resistant children and youth with schizophrenia for both overall response rate and negative symptoms in one trial[31] and for negative symptoms and rapidity of symptom improvement in another trial.[32]

In separate trials comparing olanzapine and risperidone to haloperidol[18] and to molindone[26] among children and youth with a variety of psychotic disorders, no significant differences were found between the medications on any symptom outcome measure. In one trial, however, children and youth treated with olanzapine had a significantly shorter medication response time (1.6 weeks) than children and youth treated with either risperidone (2.3 weeks) or haloperidol (2.4 weeks).[18] All four medications produced significant reductions in psychotic symptoms from baseline to treatment end, with effect sizes ranging from 0.5 to 1.8[18] and average symptom declines ranging from 21% to 47%.[26] Table 3 presents findings from all the medication comparison trials.

Table 3: Medication outcomes from comparison evaluations

Clozapine[31] significantly better than **Olanzapine** on:	
• response rate* (66% versus 33%)	• negative symptoms
Clozapine[32] significantly better than **Olanzapine** on:	
• rapidity of symptom improvement	• negative symptoms
Olanzapine[18] significantly better than **Haloperidol** and **Risperidone** on:	
• rapidity of symptom improvement	
Olanzapine, Risperidone and **Molidone**[26] were not significantly different on any outcome measure	

* Response rate defined as ≥ 30% decrease in symptoms *and* psychosis improvement rated as much/very much improved.

Recognizing the limitations

Despite restricting our review to the highest-quality studies, the evaluations still had limitations. Most studies had very small sample sizes, which limited the likelihood of identifying small to moderate effects. As a result, some clinically significant benefits of the medications may have been underestimated. As well, four of the medications — clozapine, haloperidol,

risperidone and molindone — were evaluated without a placebo control. As a result, improvements due to factors other than the medications themselves cannot be ruled out.[34] However, the fact that each medication was compared to olanzapine, which *was* proven effective in placebo-controlled RCTs, increases confidence in the positive findings.

Risks that accompany benefits

Side effects and *adverse events* were reported for all the medications evaluated, despite their use being limited to 12 weeks or less in most studies. Side effects generally constituted symptoms that were serious but manageable. In contrast, adverse events generally constituted symptoms that posed significant threats to the young person's health and often necessitated stopping the medication.

Regarding side effects, all medications produced neurological (or extrapyramidal) symptoms, including involuntary movements and restlessness. In one study, the majority of participants required adjunctive medications (low-dose anticholinergics) to control these symptoms (67% on haloperidol, 56% on olanzapine and 53% on risperidone).[18] Weight gain was another common side effect for all the medications except molindone. Average gains ranged from 3.5 kilograms (for haloperidol) to 7.1 kilograms (for olanzapine) after only eight weeks of medication use.[26]

Many additional side effects were reported. Among medications for general sale in Canada — clozapine, haloperidol, olanzapine and risperidone — all produced sweats/chills, constipation and dry mouth. Olanzapine was further associated with elevated blood sugar levels, which puts young people at risk of future diabetes.[31] Clozapine was associated with increased blood lipid levels, which puts young people at risk of future cardiovascular disease.[31, 32] As well, clozapine produced increased salivation.[31]

Regarding adverse events, olanzapine was associated with abnormalities in both liver and heart functioning[30, 32] as well as significantly reduced counts of neutrophils (one of the white blood cells essential for fighting infections).[31, 32] Similarly, clozapine was linked to abnormalities in heart functioning[32] and significantly reduced neutrophil counts,[32] seizures[32] and upper bowel obstruction.[31] Although not found in the current studies, agranulocytosis, a potentially fatal condition, can be associated with clozapine use. In this rare condition, white blood cell counts drop dramatically, leaving individuals extremely vulnerable to infections.[10] The potential for agranulocytosis necessitates regular blood tests and close monitoring for anyone using this medication.

> *"For the best possible long-term outcomes, medications are best prescribed by practitioners working in collaboration with youth and their families as partners in the process."*

Practice applications

Among medications for general sale in Canada, clozapine, haloperidol, olanzapine and risperidone have solid evidence supporting their effectiveness in treating psychosis in young people. Deciding which medication to prescribe requires practitioners to carefully consider many factors, including effectiveness, side effect profile and cost. For example, clozapine — although highly effective — is typically reserved for youth who have not responded to at least two other antipsychotic medications because of its side effect profile.[10] When price is a consideration, older antipsychotics have the benefit of costing less[35] while having similar effectiveness profiles.[18, 26]

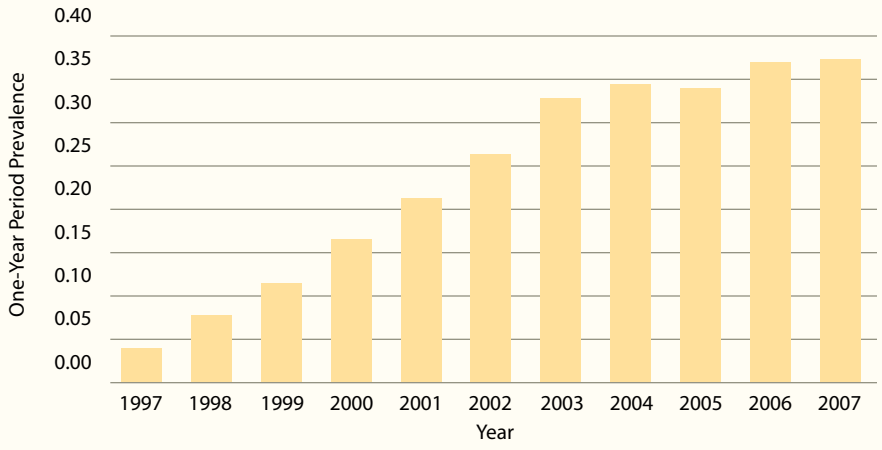
Once an appropriate antipsychotic is prescribed, practitioners can take steps to maximize benefits and minimize risks. As with any treatment, evaluation of effectiveness and side effects should be ongoing. Youth should initially be monitored at least weekly.[10] Such monitoring often includes physical examinations such as measuring weight and assessing for neurological problems. As well, regular laboratory tests such as heart and liver functioning along with white blood cell counts can help monitor and manage side effects.[10]

With careful management, medications can dramatically improve functioning and reduce suffering for youth with psychosis. For the best possible long-term outcomes, medications are best prescribed by practitioners working in collaboration with youth and their families as partners in the process.

Use of antipsychotics surges dramatically

On July 2, many people were shocked to hear a Canadian Broadcasting Corporation news anchor announce a striking increase in antipsychotic prescriptions to B.C. children. The CBC reported on data released by the Therapeutics Initiative (TI), which conducts independent medication reviews. The TI's examination of health databases (PharmaNet and the Medical Services Plan) revealed a tenfold increase over the past decade in prescriptions for risperidone, quetiapine, olanzapine and clozapine among children ages 14 and younger.[51] This dramatic rise is particularly alarming given the age of the children and the very limited research on the effectiveness and safety of these medications. To ensure that *only* children who require such medications receive them, prescriptions should be considered only after a comprehensive evaluation by a qualified practitioner.

Figure 1: Trends in antipsychotic use among B.C. children age 14 and younger



One-year period prevalence refers to the percentage of children in BC who were dispensed risperidone, quetiapine, olanzapine and clozapine. Source: Therapeutics Initiative (2009).

Feature

Skills beyond pills: Boosting brain power

Youth with psychosis typically experience cognitive difficulties, including impairments in attention, memory, planning and flexible thinking.[6] *Cognitive Remediation Therapy* (*CRT*), which teaches information processing strategies through guided mental exercises,[19] was specifically developed to address these types of difficulties. Here we present two randomized controlled trials of *CRT*, the only psychosocial treatment that met the rigorous acceptance criteria described in our Review article.

Both evaluations took place in Europe. The Norwegian study included adolescents with a variety of psychotic disorders (for which 77% were being treated with antipsychotic medications).[36] All youth — regardless of treatment assignment — participated in a psycho-educational program, which included parent seminars, problem-solving sessions and milieu therapy. In contrast, the UK study was limited to youth with schizophrenia on a stable medication for at least one month.[19] Participants also had to have difficulties with cognitive and social functioning. Interventions and participant characteristics are described in Table 4.

Youth receiving *CRT* showed significantly better visual information processing skills.

Table 4: *Cognitive Remediation Therapy (CRT)* — Program and study descriptions

Location	Participant Number	Intervention Description and Length	Participant Age (years)	Participant Gender
Norway[36,37]	*CRT* = 14 Control = 12	Problem-solving, attention, memory and social perception skills taught by schoolteachers and therapist for 30 hours (plus 15-minute work sessions) over 12 weeks	Mean: 15 Range: 12–18	54% male
United Kingdom[19]	*CRT* = 21 Standard care = 19	Memory, planning and problem-solving tasks demonstrated by therapist and then practised overtly and covertly by youth for 40 hours over 12 weeks	Mean: 18 Range: 14–22	65% male

Youth who received *CRT* improved more on a test of cognitive flexibility than youth who received standard care.

Brain training: Is it worth the effort?

The Norwegian study found only one significant difference between *CRT* and control group participants at 12-month follow-up (for details, see Table 5). Youth receiving *CRT* showed significantly better visual information processing skills when intellectual functioning was controlled for. Interestingly, this improvement was not present at three-month follow-up.

The UK evaluation also found only one significant improvement. At three-month follow-up, youth who received *CRT* improved more on a test of cognitive flexibility (effect size 0.6) than youth who received standard care. Although there were no significant differences between treatments on any non-cognitive outcome measures, *CRT* was found to have a moderating effect on psychiatric outcomes. Improvements in cognitive planning were associated with decreases in psychiatric symptoms only among youth who received *CRT*.

Teaching cognitive skills — What's involved

Ueland and Rund[37] provided the following description of the goals and training components included in their *CRT* program:

Module Goals	Tasks
Cognitive Differentiation: Improving cognitive skills to enhance social interactions and problem-solving abilities	Card sorting Matching synonyms and antonyms Word association
Attention: Bettering selective attention, sustained attention and visual scanning abilities	Identifying items in cartoon drawings Identifying target letters within array Mazes
Memory: Strengthening verbal and visual memory	Object memorization Sentence repetition
Social Perception: Improving social knowledge by enhancing attention to relevant social information	Describing, interpreting and discussing the social meaning of slides portraying actors in social activities

Table 5: Evaluations of *Cognitive Remediation Therapy (CRT)*

Evaluation Period	Outcomes Favouring *CRT*	Non-significant Outcomes	
3-month follow-up[19]	Cognitive flexibility	*Cognitive* Memory Planning	*Functional* Psychiatric symptoms Self-esteem Social functioning and relationship quality
12-month follow-up[37]	Visual information processing	*Cognitive* Attention Cognitive flexibility Executive functioning Verbal and visual memory	*Functional* Global functioning Psychiatric symptoms

Detecting the differences: The power in numbers

These two recent evaluations provide evidence that *CRT* can address two common problems experienced by youth with psychosis — improving both cognitive flexibility and visual information processing. Given that these gains were found between three and twelve months after the training programs ended, there is good evidence that *CRT* can produce long-lasting benefits. *CRT* also may produce improvements not identified in these evaluations. Because both studies had very small sample sizes, the power to detect benefits from *CRT* was very limited. This means that even greater gains might have been found if the studies had more participants. Accordingly, although only two improvements were found, larger evaluations of *CRT* are well warranted. It would be particularly helpful to assess the impact of *CRT* on functioning in daily living to ensure that any benefits produced are clinically meaningful as well as statistically significant.

> *"There is good evidence that CRT can produce long-lasting benefits."*

Adhering to the manual: How much does it matter?

To the Editors:

Your recent article on *Multisystemic Therapy* (*MST*) highlighted both the very successful outcomes achieved by this treatment in the United States and the less promising findings among youth from other countries, including Canada. It is important to recognize that in some trials where *MST* has failed to reduce behavioural problems, concerns with poor treatment fidelity have been raised. Such results suggest that how well the treatment has been implemented can have as dramatic effects on outcomes as where it is implemented.

Bob Pushak
Port Moody, BC

Treatment fidelity, defined as the degree to which the intervention was delivered as intended, *is* recognized as a variable that can influence clinical outcomes. Nonetheless, it is infrequently assessed in therapeutic outcome research. A recent review of 342 studies found only 27% evaluated whether the intervention was delivered as specified.[38] When treatment fidelity is not monitored, alternative explanations for the success or failure of the intervention cannot be ruled out. For example, an intervention with significant benefits could be due to a practitioner adding a novel treatment component. Alternatively, a lack of success could be due to omission of a key element of the intervention.

Consistently assessing treatment fidelity

A strength of many *MST* evaluations is the use of a treatment fidelity measure, namely the Therapist Adherence Measure-Revised (TAM-R).[39] This 26-item scale can be completed by therapists, parents and/or youth to assess therapists' adherence to *MST* principles during treatment sessions.[40] Although studies measuring the relationship between *MST* treatment fidelity and clinical outcomes have been inconsistent, many have found a positive association, as shown in Table 6.

In contrast, some studies have found no relationship between treatment fidelity and clinical outcomes. For example, treatment fidelity scores were unrelated to *any* recidivism outcome measure in a Canadian *MST* evaluation.[46] As well, improvements have still been reported for youth

Table 6: *MST* studies with positive relationships between treatment fidelity and outcomes

Country	Outcome
Norway	Treatment sites with the lowest fidelity scores had the least favourable outcomes while those with the highest scores had the best outcomes.* [41]
Sweden	Although *MST* was not more successful than usual treatment services, high treatment fidelity was associated with fewer arrests and better social competence. [42]
United States	Improvement in official rearrest rates achieved among youth who received *MST* delivered with high fidelity.** [43]
United States	Substantially better outcomes associated with high treatment adherence ratings among youth engaged in criminal activity with and without co-occurring substance abuse. [40]
United States	High parent and adolescent treatment adherence ratings predicted low rearrest rates. High therapist treatment adherence ratings predicted low criminal offence and incarceration rates. [44]
Multiple nations	Among 16,764 youth, average therapist adherence at international sites was significantly lower than at American sites. International sites had poorer results on arrest rates and youth engagement in school or work.* [45]

* Study authors did not report whether tests of statistical significance between fidelity and outcome measures were performed.
** A statistical examination of the relationship was not conducted because of the limited availability of treatment fidelity data.

receiving *MST* delivered with poor treatment fidelity, including reductions in externalizing behaviours and criminal activity among American youth.[47] Even among studies finding an overall positive relationship between fidelity and clinical gains, some unexpected process level outcomes have been found.[40] For example, in a study of American adolescents, youth-rated family-therapist conflict (reflecting poor adherence to the *MST* treatment model) was associated with *less* delinquent peer affiliation while caregiver-rated therapist-directed sessions (reflecting high *MST* adherence) was associated with *more* delinquent behaviour.[48]

Concerns have also been raised regarding *MST*'s treatment fidelity measure. The *MST* Cochrane review authors noted that the TAM-R assesses constructs that are not unique to *MST,* such as engagement, treatment participation and therapeutic alliance.[49] As well, correlations between TAM-R ratings from youth, parents and therapists have been quite low in some studies.[40]

Applauding the effort

Despite the acknowledged concerns, attempts by researchers to understand the relationship between *MST* treatment fidelity and outcomes should be recognized and encouraged. Researchers also need to continue to explore additional explanations when programs produce inconsistent outcomes. Other important variables that need ongoing evaluation include participant characteristics, comparison services offered, and differing law and policies across regions and nations.[50] With efforts to better understand factors influencing treatment outcomes, we can help to consistently deliver effective interventions to children and families.

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BC government staff can access original articles from BC's Health and Human Services Library.

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