CHILDREN'S MENTAL HEALTH RESEARCH

Quarterly

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Helping children with depression

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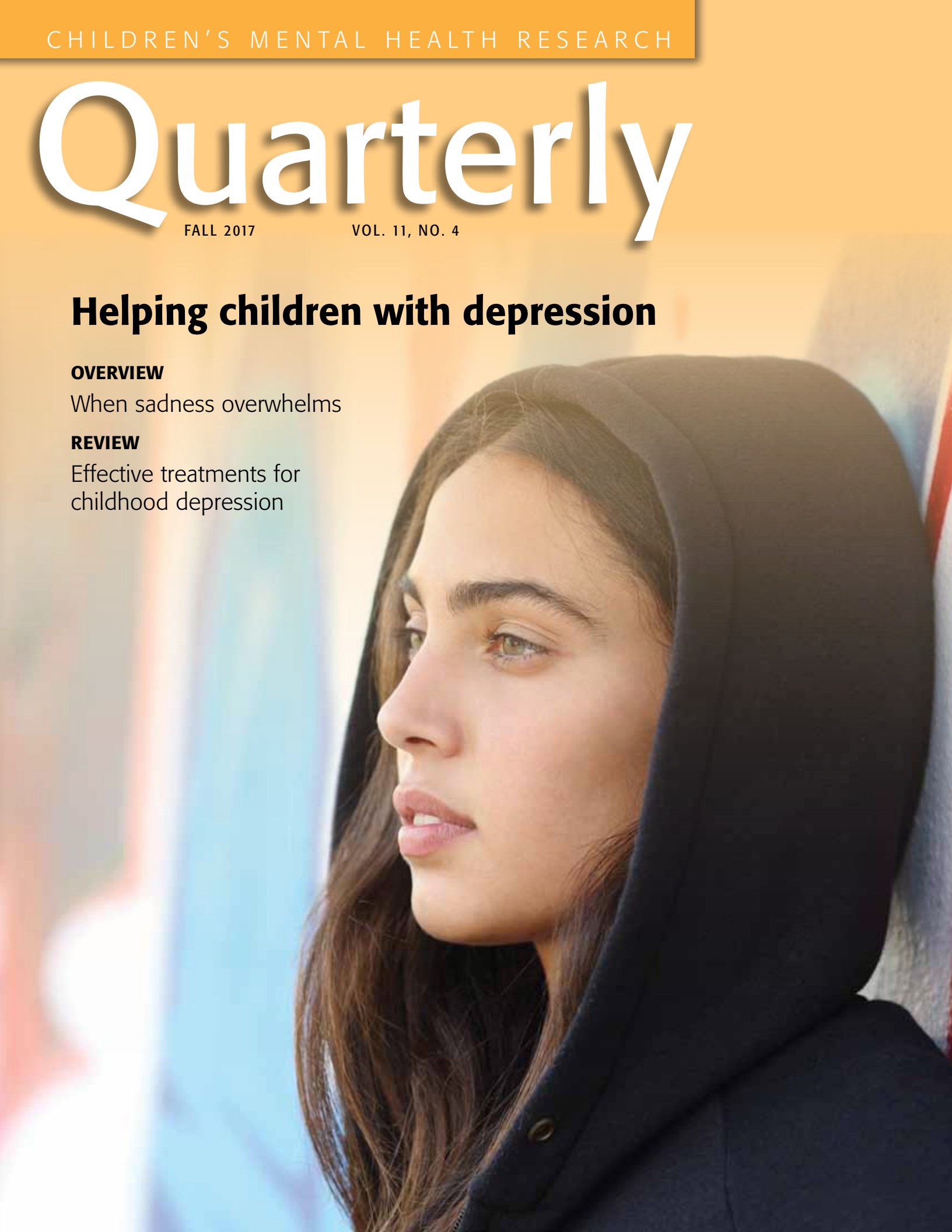

Fall

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Children's Health Policy Centre

About the Children's Health Policy Centre

We are an interdisciplinary research group in the Faculty of Health Sciences at Simon Fraser University. We focus on improving social and emotional well-being for all children, and on the public policies needed to reach these goals. To learn more about our work, please see childhealthpolicy.ca.

About the *Quarterly*

We summarize the best available research evidence on a variety of children's mental health topics, using systematic review and synthesis methods adapted from the *Cochrane Collaboration* and *Evidence-Based Mental Health*. We aim to connect research and policy to improve children's mental health. The BC Ministry of Children and Family Development funds the *Quarterly.*

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This Issue

NEXT ISSUE

Preventing childhood substance misuse

Many young people experiment with substances at some point during their adolescence. We examine ways to prevent these experiences from leading to problematic substance use.

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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OVERVIEW

When sadness overwhelms

Every child experiences bouts of sadness from time to time. For most children, these bouts are transient and do not interfere with development and well-being. Yet for some young people, their low mood becomes prolonged and impedes their ability to thrive. In these situations, a thorough clinical assessment can help families and health practitioners figure out what steps to take next.

For depression, as with many mental disorders, the most effective way to help children is to prevent this condition from ever occurring.

Determining if a diagnosis is warranted

When a practitioner conducts a mental health assessment, often as part of a multidisciplinary team, they typically begin by interviewing the child and the caregiver. The practitioner will commonly ask questions about the onset, frequency, severity and impact of symptoms — which may affect mood, activities, sleep, eating and energy levels. If a child is experiencing multiple depressive symptoms that impair their functioning, the practitioner must also ascertain that the problems are not due to another mental disorder, such as anxiety, or due to adverse circumstances, such as parenting problems or even child maltreatment. (Whenever there are any questions or concerns about possible child maltreatment, the appropriate child protection agency must be contacted.) Table 1 describes the full criteria for diagnosing depression (known as major depressive disorder), as set out in the *Diagnostic and Statistical Manual of Mental Disorders*.[1]

According to updated global burden-of-disease data, major depressive disorder is among the top five leading causes of years-lived-with-disability worldwide.

Table 1: Diagnostic Criteria for Major Depressive Disorder[1]

Major depressive disorder occurs when a child experiences at least five of the symptoms listed below during the same two-week period. These symptoms must include either a depressed or irritable mood or loss of interests or pleasures. Beyond causing distress, symptoms must also result in impaired functioning at home, at school or in the community.

- Depressed or irritable mood most of the day, nearly every day
- Greatly reduced interests or pleasures affecting almost all activities, nearly every day
- Significant changes in weight or appetite
- Sleep disturbances most nights
- Significant changes in activity levels most days
- Tiredness or loss of energy most of the time
- Feelings of worthlessness or excessive guilt nearly every day
- Reduced ability to concentrate most days
- Recurrent thoughts of death or suicide

What puts children at risk for depression?

Although researchers have yet to determine the causes of depression, they have been able to identify a number of important risk factors. We present the factors that have been established using strong research methodology — namely, surveys following large groups of children who were representative of the populations they were drawn from. While such studies cannot prove causation, they can nevertheless identify factors that clearly precede depression in children and that may be amenable to interventions.

We identified four such surveys. One included more than 100,000 American youth and found that being female was a risk factor for depression.[2] In fact, girls were approximately three times more likely than boys to develop depression.[2] A second survey, of more than 2,700 American youth, identified several other risk factors for depression.[3] These included parents having depression or antisocial behaviour and children having frequent negative moods, impulsivity or behaviour problems at age 11.[3] While these five factors increased the likelihood of being diagnosed with depression by age 17, the strongest predictor was nevertheless a sixth factor: a history of child maltreatment. In fact, children who experienced physical abuse had a tenfold increase in their odds of later being diagnosed with depression compared to children without this history.[3]

Adverse childhood experiences were found to be risk factors for depression, including parental depression and child maltreatment.

A third survey, in New Zealand, followed 945 children from age three to 32.[4] The risk factors identified by the researchers included a family history of depression and child behaviour problems between ages five and 11.[4]

A fourth survey, of 1,715 Canadian children, confirmed many of the same risk factors.[5] When children were between ages four and eight, having anxiety and depressive symptoms predicted later depression, but only for boys, while having a depressed caregiver or losing a biological parent predicted later depression, but only for girls.[5] In contrast, when children were between ages 10 and 14, having anxiety and depressive symptoms increased the likelihood for both boys and girls going on to experience depression in their later teen years. Yet some other risk factors for these older children did vary by gender. Low self-esteem predicted later depression for adolescent boys, while behaviour problems predicted later depression for girls. Age, however, was a consistent factor overall, with both boys and girls showing more depressive symptoms as they became older.

Interplay between genes and environment

Across these four surveys, adverse childhood experiences were found to be risk factors for depression, including parental depression and child maltreatment. Ideally, no child should be exposed to these kinds of adversities. Still, not all children who have these experiences go on to develop depression. To help identify which children are particularly vulnerable, and to help inform interventions, researchers have examined the interplay between genetics and adverse experiences. We report on two studies that have investigated this interplay and its impact on the development of depression.

One study on gene-environment interplay included nearly 500 American children, roughly half of whom had experienced maltreatment. This included neglect (79%), emotional abuse (67%), physical abuse (32%) and/or sexual abuse (8%), with most children having been exposed to multiple types of maltreatment.[6] The researchers demonstrated that depressive symptoms were more likely following child maltreatment when specific interactions between gene systems associated with cortisol regulation and stress sensitivity occurred. They concluded that the impact of a chronic stressor such as child maltreatment was indeed moderated by genetic variation.[6]

The importance of gene-environment interplay was similarly shown in the survey mentioned previously that followed children from New Zealand.[7] Researchers examined stressful life events and genetic profiles in a subsample of 847 participants. They found that child maltreatment — as well as financial, housing, health or relationship concerns in early adulthood — predicted depression diagnoses at age 25, but only among individuals with specific genetic profiles affecting stress sensitivity.[7] These researchers concluded that negative life events can influence gene expression, contributing to mental health symptoms later in life.

Research continues on gene-environment interactions and on the implications for helping children — and the adults they will become. This research does not tell the whole story for a condition like depression that has multiple causes. But these studies nevertheless highlight the importance of understanding individual differences in genetic vulnerability. Even more importantly, however, they underscore the importance of intervening early to prevent harmful events such as child maltreatment that can play a role in depression.[6, 8]

Intervening to reduce risk

For depression, as with many mental disorders, the most effective way to help children is to prevent this condition from ever occurring. Even though the causes of depression have yet to be fully determined, we know enough about modifiable risk factors to take action now. We can prevent many cases of child maltreatment. Our Spring 2009 issue identified programs that can effectively reduce this important risk factor, such as nurse home visitation. (This program is now known as *Nurse-Family Partnership*.) We can also implement effective depression prevention programs in childhood, including for children whose parents are depressed, as outlined in our Summer 2017 issue.

It is crucial not only to prevent depression in childhood, but also to treat depression effectively when it usually first occurs – in childhood.

Beyond the fundamental issue of ensuring positive childhood experiences, depressive disorders have collective importance for another reason. According to updated global burden-of-disease data, major depressive disorder is among the top five leading causes of years-lived-with-disability worldwide.[9] To reduce this burden for individuals and for societies, it is crucial not only to prevent depression in childhood, but also to treat depression effectively when it usually first occurs — in childhood. Our Summer 2017 issue covered the prevention options. The Review article that follows identifies the treatment options.

Even though the causes of depression have yet to be fully determined, we know enough about modifiable risk factors to take action now.

REVIEW

Effective treatments for childhood depression

Children and adolescents who develop depression need timely and effective treatments. To ensure good care for these young people, practitioners and policy-makers in turn need credible information on treatments that work. To meet these needs, this review set out to identify the most effective treatments for childhood depression.

All four CBT evaluations showed benefits for children with depression, including substantially lowered rates of diagnoses and symptoms.

We conducted a 20-year search for randomized controlled trials (RCTs) evaluating childhood depression treatments. Quality assessment was built into our inclusion criteria to ensure we reported on the best available evidence. (For more information, please see our Methods.) We retrieved and assessed 99 RCTs, 14 of which met our inclusion criteria. The 14 trials comprised four RCTs evaluating cognitive-behavioural therapy (CBT), nine evaluating medications, and one evaluating CBT and the medication fluoxetine — both independently and combined. (Because we covered this latter RCT in our Spring 2008 issue, we provide only the main highlights in the sidebar on page 11.)

The ABCs of the CBT trials

All four CBT programs — *Individual CBT*, *SPARX*, and two separate trials of *Coping with Depression* — provided participating children with core CBT components. These components were education on the CBT model, encouragement to engage in pleasant or fun activities, and instruction and practice in challenging inaccurate thinking (i.e., cognitive restructuring). All four programs also taught children techniques for improving relationships, ranging from interpersonal skills to social problem-solving techniques to conflict resolution strategies. Still, the programs varied: in format, with individual (*Individual CBT*), group (*Coping with Depression*) and self-delivery (*SPARX*) options; and in the number of sessions or modules (which ranged from seven to 16).

All four RCTs compared CBT to another intervention. *Individual CBT* was compared to a brief supportive intervention in the United Kingdom. This comparison condition involved children providing information about their mental health symptoms, their school and family life, and their engagement in social activities.[11]

What about interpersonal psychotherapy?

Some readers may be surprised that no RCTs assessing interpersonal therapy (IPT) were included in our review, particularly given that IPT was identified as reducing depressive symptoms in children and youth in our 2014 report *Child and Youth Mental Disorders: Prevalence and Evidence-Based Interventions*.[10] Although we did assess six RCTs of IPT for our current review, none met inclusion criteria due to methods concerns — mainly a lack of follow-up. This suggests that although there is evidence supporting IPT, this evidence is not as robust as for CBT. When practitioners choose to use IPT, they should therefore pay particularly close attention to ensuring that child outcomes are positive.

SPARX, a self-delivered computer program, was compared to typical treatment services available to youth in New Zealand. While most comparison youth received counselling at clinics or in schools (the type of counselling was not reported), 13% were put on waitlists and received no treatment.[12] A very small number (2%) were also prescribed medication (the type was not reported).[12] As well, this RCT was specifically designed to assess whether *SPARX* was "not inferior" to usual treatment (rather than assessing whether it was superior).

Coping with Depression I, meanwhile, was compared to life skills training in the United States. This comparison program focused on preparing youth for adulthood, including activities such as completing job applications and renting an apartment, and also provided tutoring.[13] In contrast, *Coping with Depression II* was compared to typical treatment services available at a health maintenance organization in the US. These services included outpatient mental health specialty care visits, inpatient services and medications. (These services were also available to youth randomized to *Coping with Depression II*; in other words, intervention children received the CBT program plus usual services.)[14] Table 2 gives more information on these four CBT programs and their evaluations.

All children with depression should have ready access to CBT – through publicly provided children's mental health services.

Table 2: Cognitive-Behavioural Therapy (CBT) Evaluations

Intervention Comparison	**Delivery format**	**Sample size**	**Child ages** (Country)
Individual CBT[15]	9 individual CBT sessions delivered in community settings over 6 months	31	8 –17 years (United Kingdom)
Brief supportive intervention	9 individual sessions reviewing well-being + social activities delivered in community settings over 6 months	30	
SPARX[12]	7 computerized CBT modules individually completed over 4–7 weeks	94	12 –19 years (New Zealand)
Treatment as usual	Youth could access regularly available treatment services at community clinics + schools	93	
Coping with Depression I[13]	16 group CBT sessions delivered in community settings over 8 weeks + 2 optional parent information sessions	45	13 –17 years (United States)
Life skills training	16 group sessions focused on life skills + tutoring delivered in community settings over 8 weeks	48	
Coping with Depression II[14]	16 group CBT sessions delivered in community settings over 8 weeks + 3 parent information sessions	41	13 –18 years (United States)
Treatment as usual	Youth could access regularly available treatment services at community clinics + hospitals	47	

Keeping CBT research relevant

Researchers for these four RCTs also paid careful attention to who was included in the studies. In particular, because *SPARX* was self-administered, youth were excluded if they were at high risk for self-harm or suicide, or if their depression was assessed as being too severe for a self-help resource.[12]

The three other CBT RCTs, meanwhile, tested effectiveness in populations typically seen in clinical practice. In addition to all young people meeting criteria for depression (or dysthymia for *Coping with Depression II*), most participants had concurrent mental disorders. In *Individual CBT*, 65% of young people also met criteria for oppositional defiant, conduct or anxiety disorders.[15] In *Coping with Depression I*, which recruited from juvenile justice settings, all youth met diagnostic criteria for both depression and conduct

disorder.[13] As well, 72% had one or more substance use disorders and 40% had a history of attempting suicide.[13] In *Coping with Depression II*, participating young people had an average of 1.9 diagnoses, and all had a parent with a mood disorder.[14]

Medication trials: What's being prescribed?

A drug by any other name

The medications listed in this article are sold in Canada under various brand names, summarized in the table below.

Antidepressant Medications [25]	
Generic name	**Brand name**
Amitriptyline	Elavil
Clomipramine	Anafranil
Desipramine	Not applicable
Duloxetine	Cymbalta
Escitalopram	Cipralex
Fluoxetine	Prozac

The nine medication RCTs that met our inclusion criteria evaluated six different drugs. Four medications — amitriptyline, clomipramine, desipramine and escitalopram — were each evaluated in a single RCT. In contrast, fluoxetine was evaluated in five separate RCTs, and duloxetine was evaluated in two separate RCTs (with one evaluating two different doses of this medication). All medications were compared to a placebo. As well, all medications were provided orally, except clomipramine, which was provided intravenously in a single dosage.

Seven RCTs were conducted exclusively in the US. The remaining two RCTs were conducted in multiple countries (including Canada in one case). Participants in one fluoxetine evaluation (fluoxetine V) stood out because beyond having depression, they also all met diagnostic criteria for a current substance use disorder as well as current or past conduct disorder.[16] So all adolescents in this study also received CBT to address their substance use issues, regardless of whether they received fluoxetine or placebo.[16] Table 3 gives more information on all nine medication RCTs.

Table 3: Medication Evaluations

Medication	Dosage + duration	Sample size*	Child ages (Country)
Amitriptyline [17]	300 mg maximum daily dose taken over 10 weeks	27	12–18 years (US)
Clomipramine [18]	200 mg single intravenous dose taken over 3 hours	16	14–18 years (US)
Desipramine [19]	300 mg maximum daily dose taken over 6 weeks	45	13–17 years (US)
Escitalopram [20]	20 mg maximum daily dose taken over 8 weeks	268	6–17 years (US)
Duloxetine I [21]	120 mg maximum daily dose taken over 10 weeks	337	7–17 years (9 countries)
Fluoxetine I [21]	40 mg maximum daily dose taken over 10 weeks		
Duloxetine II [22]	30 or 60 mg fixed daily dose taken over 10 weeks	463	7–17 years (4 countries)
Fluoxetine II [22]	20 mg fixed daily dose taken over 10 weeks		
Fluoxetine III [23]	20 mg fixed daily dose taken over 8 weeks	96	7–17 years (US)
Fluoxetine IV [24]	20 mg fixed daily dose taken over 9 weeks	219	8–17 years (US)
Fluoxetine V [16]	20 mg fixed daily dose taken over 16 weeks	126	13–19 years (US)

* Sample size includes children receiving both medication(s) and placebo.

How well did the CBT programs work?

Individual CBT and *Coping with Depression I* and *II* all assessed depression diagnoses at final follow-up, one to two years after the interventions ended. According to this outcome indicator, most children participating in CBT no longer had depression — despite 100% meeting criteria for this diagnosis (or dysthymia for *Coping with Depression II*) at study outset. After-treatment diagnosis rates ranged from only 10.5% for *Coping with*

Depression II to 36.6% for *Coping with Depression I*.[13–14, 26] However, these differences in diagnosis rates were not statistically significant in the three studies.[13–14, 26] (The *SPARX* RCT did not assess diagnoses.)

Beyond diagnoses, these three CBT programs also substantially reduced depression symptoms at final follow-up — by child, parent and clinician ratings. Children participating in *Individual CBT* and *Coping with Depression I* and *II* experienced symptom reductions of greater than 50% on at least one measure.[13–14, 26] *Coping with Depression II* had particularly varied rates of symptom reductions because parent-rated symptoms were relatively low compared to child-rated symptoms at baseline. Still, similar to the diagnostic findings, these three studies found no significant difference between CBT and the comparison interventions.[13–14, 26]

Meanwhile, teens participating in *SPARX* experienced slightly greater symptom reductions than teens receiving treatment as usual, when assessed at three-month follow-up. Since this was a "non-inferiority trial," rather than assessing whether *SPARX* was superior to treatment as usual, it assessed and confirmed that *SPARX* was as beneficial as typical treatments offered in the community.[12] Table 4 summarizes the findings from the four CBT studies, including diagnosis and symptom reductions at final follow-up.

Table 4: Cognitive-Behavioural Therapy (CBT) Outcomes at Final Follow-Up*

Intervention Comparison	Follow-up	Diagnostic rates	Symptom reductions
Individual CBT[26]	2 years	25.9%	49.4 – 53.9%
Brief supportive intervention		14.8%	56.6 – 60.6%
SPARX[12]	3 months	Not assessed	32.7%
Treatment as usual			30.2%
Coping with Depression I[13]	1 year	36.6%	40.4 – 60.6%
Life skills training		37.0%	51.3 – 70.3%
Coping With Depression II[14]	2 years	10.5%	12.5 – 65.8%
Treatment as usual		7.7%	14.0 – 61.4%

* None of the differences between intervention and comparison groups were statistically significant.

How well did the medications work?

For the six medications, effects were assessed for the duration of the nine RCTs, which ranged from six days (for intravenous clomipramine) to 16 weeks (for oral fluoxetine V), but long-term follow-up was not conducted for any medications.[16–24] Diagnostic outcomes were only assessed for amitriptyline and desipramine.[17, 19] Neither medication significantly outperformed the placebo on this important outcome indicator. Three of the six medications — amitriptyline, desipramine and duloxetine — also failed to outperform placebo on any symptom measures.[17, 19, 21–22]

In comparison, clomipramine, escitalopram and fluoxetine resulted in significant symptom reductions compared to placebo on at least one measure.[16, 18, 19, 23–24] The clomipramine RCT found reductions on two of three symptom measures, while the escitalopram RCT found reductions on one of three symptom measures.[18, 20]

If medication is being considered as part of a child's treatment plan, fluoxetine should be the first choice.

Meanwhile, results varied across the five fluoxetine trials. In two RCTs (fluoxetine I and II), the medication failed to outperform placebo on either of the two symptom measures.[21–22] However, the three other RCTs (fluoxetine III through V) did show significant benefits on one to four symptom measures.[16, 23–24] Two of the successful fluoxetine RCTs also assessed the clinical importance of the symptom reductions. In fluoxetine IV, effect sizes were medium for two outcomes (Cohen's $d = 0.51$ and

0.54) and small for one (Cohen's d = 0.31), while in fluoxetine V, the effect size was large for one outcome (Hedges' g = 0.78).[16, 24] Table 5 summarizes the findings from all the medication evaluations.

Table 5: Medication Outcomes at Post-Test

Medication	Favouring medication	No significant difference over placebo
Amitriptyline[17]	None	Diagnosis + symptoms (4 of 4)
Clomipramine[18]	↓ Symptoms (2 of 3)	Symptoms (1 of 3)
Desipramine[19]	None	Diagnosis + symptoms (4 of 4)
Escitalopram[20]	↓ Symptoms (1 of 3)	Symptoms (2 of 3)
Duloxetine I[21]	None	Symptoms (2 of 2)
Fluoxetine I[21]	None	Symptoms (2 of 2)
Duloxetine II[22]	None	Symptoms (2 of 2)
Fluoxetine II[22]	None	Symptoms (2 of 2)
Fluoxetine III[23]	↓ Symptoms (2 of 4)	Symptoms (2 of 4)
Fluoxetine IV[24]	↓ Symptoms (4 of 5)	Symptoms (1 of 5)
Fluoxetine V[16]	↓ Symptoms (1 of 2)	Symptoms (1 of 2)

Side effects can be substantial

All six medications led to side effects for children, including the three medications that reduced depressive symptoms (clomipramine, escitalopram and fluoxetine). With clomipramine, 25% experienced dizziness, 25% experienced sedation and 13% experienced nausea.[18] (The authors did not report whether these rates significantly differed from placebo.)[18]

With escitalopram, 23% experienced headaches and 11% experienced abdominal pain (although rates for both side effects were similar for placebo).[20] For escitalopram, two serious adverse events were also reported (pneumonia and an accidental injury), and 2% of children discontinued the study due to side effects.[20]

With fluoxetine, reporting of side effects varied across the five RCTs. With fluoxetine I, 5% of children experienced side effects serious enough to require hospitalization, including gastritis and lymphadenitis.[21] As well, one child discontinued the study after a suicide attempt.[21] With fluoxetine II, 5% of children also experienced side effects serious enough to require hospitalization, including aggression, somnolence, destructive behaviour and intentional overdose.[22] With fluoxetine III, 8% of children discontinued the study due to side effects, which included manic symptoms and severe rash.[23] With fluoxetine IV, 5% of children discontinued the study due to side effects, which included manic symptoms, rash and agitation.[24] As well, in this trial, significantly more children on fluoxetine reported headaches compared to those on placebo.[24] Finally, with fluoxetine V, 6% of adolescents were evaluated in an emergency room or were hospitalized due to increased suicidality during the study.[16]

Making sense of the findings

All four CBT evaluations showed benefits for children with depression, including substantially lowered rates of diagnoses and symptoms. In fact, rates of depression diagnoses dropped by 74% for *Individual CBT* and by 63% for *Coping with Depression I*. Still, paradoxically, these differences were not statistically significant — probably because comparison children also had large diagnostic reductions. One possible explanation for this result is that the comparison interventions likely offered some therapeutic benefit. In fact, two of the four comparison conditions comprised usual treatment services in the community. So some comparison children may also have received CBT, boosting their outcomes.

Another explanation is that many children failed to complete the CBT programs. For example, with *Individual CBT*, only 50% of participants completed all the sessions and only 50% attended the sessions on cognitive restructuring, a core component of CBT.[11] Similarly, with *Coping with Depression I*, children attended only eight of 16 sessions on average.[13] Compliance was also a concern with *Coping with Depression II*; youth attended only 10 of 16 sessions, on average, and completed homework for only 35% of sessions they attended, on average.[14] Finally, with *SPARX*, 40% of youth did not complete all seven program modules and 38% failed to complete most or all of the homework.[12] On balance, therefore, children may not have received adequate "doses" of CBT in these trials — a situation that may mirror typical clinical practice.

Two of the five fluoxetine RCTs also did not find benefits for this medication. Compared to the three trials with positive findings, these two used the same or higher doses, for similar time periods, and in children of similar ages.[16, 21–24] However, three of five fluoxetine studies did result in youth experiencing significant symptom improvement.

Recapping the results

This 20-year review of childhood depression treatments found that three CBT programs — *Individual CBT*, *SPARX* and *Coping with Depression* — reduced diagnoses and symptoms from three to 24 months after the programs ended. (Similarly, our previous review showed that a 15-session CBT program reduced depression symptoms for the majority of adolescents.[27] Please see the sidebar for more information on this earlier review.) Still, the three CBT programs did not show statistically significant benefits over the comparison interventions — perhaps because the comparison interventions were also likely quite robust, and perhaps because many children did not complete their full course of CBT (which is common with childhood mental health treatments in general).[28] Nevertheless, among the psychosocial treatments, CBT still has the strongest evidence supporting its use.

Revisiting a noteworthy study

We devoted an article in our Spring 2008 issue to the Treatment for Adolescents with Depression Study. This randomized controlled trial examined whether *combining* CBT and fluoxetine would provide better outcomes than either treatment alone. The authors found that combining CBT and fluoxetine was significantly more effective than CBT alone, but not fluoxetine alone, in reducing depression diagnoses after 12 weeks of treatment.[29–30] However, after 36 weeks of treatment, no significant differences in depression symptoms were reported among the three treatments — fluoxetine alone, CBT alone, or the two combined — according to either child or clinician ratings.[31] (Diagnoses were not assessed at 36 weeks.)

This review also found that the medication fluoxetine led to significant improvements for young people in three of five RCTs. (These outcomes build on our previous review of a fluoxetine study, also highlighted in the sidebar, showing that depression symptoms improved for the majority of adolescents on the medication.) Our current review also found evidence supporting the use of the medications clomipramine and escitalopram, according to one RCT each. Notably, fluoxetine, clomipramine and escitalopram were all associated with side effects. Meanwhile, we found no evidence supporting the use of the medications amitriptyline, desipramine or duloxetine for childhood depression.

Implications for practice and policy

Our findings suggest the following six implications for practitioners and policy-makers:

- *Make CBT available to all children with depression.* Strong evidence still supports CBT for treating childhood depression. It is the best among the psychosocial interventions, and it comes with no side effects. Consequently, all children with depression should have ready access to CBT — through publicly provided children's mental health services, to ensure that families do not have to incur the costs for essential treatments. To facilitate this, children's mental health services need to train and support practitioners to provide CBT. Such training and support initially occurred in BC through the first *Child and Youth Mental Health Plan* (2003–08).[32] These efforts need to be supported and maintained.

- *Practise in ways that encourage children to complete the treatment.* Young people often stop before completing a full course of CBT, according to the studies we reviewed. So practitioners must find ways to engage and retain young people. Strategies can include offering flexible appointment times, finding innovative ways to teach CBT skills, and ensuring that materials are adapted to the individual's learning needs and cultural setting. (Please see the final sidebar for more information on ways to encourage young people's participation.)
- *Consider self-directed CBT for lower-risk youth.* For adolescents with milder depression who are not at risk for suicide, computer-based, self-administered CBT programs such as *SPARX* can be effective. These programs can also reach greater numbers of young people than more traditional individual- or group-delivered approaches. However, careful monitoring is warranted when using this approach. As with other forms of CBT, self-administered programs are best provided through publicly funded children's mental health services so cost is not a deterrent. Public provision can also ensure appropriate oversight (e.g., monitoring to ensure that young people do not require more intensive, practitioner-delivered interventions).
- *Use the most effective medications.* Of the current medication choices, the evidence is most robust for fluoxetine in treating childhood depression. Therefore, if medication is being considered as part of a child's treatment plan, fluoxetine should be the first choice.
- *If medication is prescribed, monitor outcomes and side effects frequently and comprehensively.* Young people who are prescribed fluoxetine are at risk for experiencing side effects. Although rare, serious events such as suicidal thoughts can occur. As a result, anyone prescribed this medication needs regular monitoring for both benefits and side effects.
- *When medication is prescribed, also offer children CBT.* Many children and adolescents experience great benefit from taking an antidepressant. Still, the available evidence on fluoxetine is almost exclusively based on short-term use. CBT should therefore also be provided because it has more enduring benefits, equipping children and youth to cope long after medications are finished.

All young people with depression need timely access to effective treatments, including psychosocial interventions such as CBT and medications such as fluoxetine. These treatments can reduce distress and disability in the short term. They can also reduce future distress and disability, particularly if enduring treatments such as CBT are offered — giving children coping skills for life.

Keep them coming back

Young people commonly drop out of treatment early,[28] so practitioners need strategies to address this issue. Fortunately, several approaches can help when using cognitive-behavioural therapy (CBT) for depression. *First,* let young people know why it is worth their time to keep coming back. Practitioners can do this by educating children and youth about the benefits of CBT, including its success rates. *Second,* give young people and their parents or caregivers an overview of what CBT entails and why. Educate them about the CBT model and the need to apply their new skills on a daily basis for maximum benefit. Caregivers, in particular, can offer crucial day-to-day supports to help young people stick with the program. *Third,* give children choices. For example, young people can select the ordering of core CBT components, including whether they want to begin with increasing activities that bring them pleasure or challenging inaccurate thinking. *Fourth,* make CBT culturally relevant. For example, children can be encouraged to identify and engage in traditional cultural practices that bring them satisfaction. In this way, CBT can be made applicable to any culture. *Fifth,* track young people's symptoms using a rating scale at every session, giving concrete feedback on how the hard work is paying off. *Finally,* ask for feedback after every session, including what went well and what was challenging. Taken together, these strategies can help to ensure that when young people walk out the door, they will be certain to return.

For more information on our research methods, please contact

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METHODS

We use systematic review (SR) methods adapted from the *Cochrane Collaboration* and *Evidence-Based Mental Health*. We build quality assessment into our inclusion criteria to ensure that we report on the best available evidence, requiring that intervention studies use randomized controlled trial (RCT) methods and also meet additional quality indicators (as outlined in Table 7, below). This review involved a 20-year search for RCTs evaluating treatments for childhood depression. Table 6 outlines our database search strategy.

Table 6: Search Strategy

Sources	• Campbell, Cochrane, CINAHL, ERIC, Medline and PsycINFO
Search Terms	• Depression or depressive or major depressive disorder (MDD) or dysthymia *and* treatment or intervention or therapy
Limits	• Peer-reviewed articles published in English between 1997 and 2017* • Children aged 18 years or younger • Systematic review, meta-analysis or RCT methods used

* A newly published article outside the search dates was also retrieved and assessed.

To identify additional RCTs, we also hand-searched reference lists from previous Children's Health Policy Centre publications. Using this approach, we identified 99 RCTs in total. Two team members then independently assessed each RCT, applying the inclusion criteria outlined in Table 7.

Table 7: Inclusion Criteria for RCTs

- Clear descriptions were provided of participant characteristics, settings and interventions
- Interventions were evaluated in a high-income country (according to World Bank standards), for comparability with Canadian policy and practice settings
- Interventions aimed to treat childhood depression
- At study outset, most participants had a depression diagnosis
- Reliability and validity of all primary outcome measures or instruments was documented
- Levels of statistical significance were reported for primary outcome measures
- Studies were excluded where authors indicated lack of statistical power for assessing primary outcomes

Psychosocial Treatment Studies

- Participants were randomly assigned to intervention and comparison groups at study outset
- Follow-up was three months or more (from the end of the intervention)
- Attrition rates were 20% or less at follow-up and/or intention-to-treat analysis was used
- Child outcome indicators included depression diagnoses and symptoms, assessed at follow-up using two or more informant sources (e.g., child, parent, teacher, clinician, observation)
- At least one outcome rater was blinded to participants' group assignment

Medication Studies

- Participants were randomly assigned to intervention and placebo groups at study outset
- Attrition rates were 20% or less at post-test and/or intention-to-treat analysis was used
- Child outcome indicators included depression diagnoses and symptoms, assessed at post-test using two or more informant sources (e.g., child, parent, teacher, clinician, observation)
- Double-blinding procedures were used

Fourteen RCTs met all the inclusion criteria. Data from these studies were then extracted, summarized and verified by two or more team members. Throughout our process, any differences between team members were resolved by consensus.

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

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The *Children's Mental Health Research Quarterly* Subject Index provides a detailed listing of specific topics covered in past issues, including links to information on specific programs.

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