

CHILDREN'S MENTAL HEALTH RESEARCH

Quarterly

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Helping children cope with trauma

OVERVIEW

Addressing avoidable
adversities

REVIEW

Intervening after
serious trauma



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*.

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.

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We present findings from studies on the prevalence of childhood trauma and discuss what protects children. We also address the fundamental importance of preventing adversities in childhood.



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Treating posttraumatic stress disorder in children

At any given time, approximately 700 BC children meet diagnostic criteria for posttraumatic stress disorder. We review the latest research evidence on effective treatments for this condition.



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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Resources for COVID-19

The Children's Health Policy Centre recently completed two reports focused on helping children through the coronavirus pandemic. *COVID-19 and the Impact on Children's Mental Health* describes the potential consequences of the pandemic on children's well-being and suggests public policy responses that can prevent additional adversities for young people. *Supporting Children — By Supporting Practitioners and Families During COVID-19 and Beyond* highlights effective virtual and self-delivered interventions to ease anxiety that may be particularly helpful while physical distancing is still required. Both reports may be downloaded for free from our publications page.

Addressing avoidable adversities

Experiencing a significant injury. Witnessing the death of a loved one. Being sexually assaulted. These are just a few of the serious traumas children may experience, which are also commonly referred to as adverse childhood experiences or ACEs. Traumatic experiences recognized by the *Diagnostic and Statistical Manual of Mental Disorders (DSM)* include exposure to actual or threatened death and exposure to serious injury or sexual violence.¹ In addition to being traumatized by being a direct victim, a young person can be traumatized by learning that a family member or friend has experienced such adversities, or by witnessing such events.¹

To support children who have experienced such extreme adversities, it is important to understand the prevalence of the problem and how to better protect children. We identified two studies providing prevalence data, based on large, representative samples of young people.

How common are serious childhood traumas?

The first study involved interviews with 2,000 Welsh and English youth at age 18.² Based on *DSM* definitions, 31.1% reported experiencing at least one trauma during their lifetime. The most frequent trauma was learning details about a traumatic event affecting someone close to them, without directly witnessing it (27.9%). Being assaulted or threatened with assault, including maltreatment by adults, was also common (21.5%). As well, many youth described experiencing significant accidents or illnesses (19.0%). The median age when these traumas occurred was 15 years.²

This study also examined the links between serious adversities and mental disorders.² Seven specific mental disorders were assessed, and the odds for experiencing each of them were significantly increased as a result of trauma:

- substance use disorder (other than alcohol or cannabis) — 3.5 times higher odds
- conduct disorder — 2.3 times higher odds
- cannabis use disorder — 2.3 times higher odds
- generalized anxiety disorder — 2.2 times higher odds
- depression — 2.2 times higher odds
- attention-deficit/hyperactivity disorder — 1.9 times higher odds
- alcohol use disorder — 1.5 times higher odds²

Youth who experienced serious trauma also had 3.5 times higher odds of engaging in self-harm, nearly five times higher odds of attempting suicide, and more than 1.5 times higher odds of committing a violent offence, compared with youth who did not have such experiences.²

The second study involved interviews with nearly 6,500 American youth aged 13 to 17 years.³ Also based on *DSM* definitions, 61.8% reported being exposed to at least one potentially traumatic event during their lifetime. Experiencing the unexpected death of a loved one was the most frequent trauma (28.2%), followed



Parents play a vital role in protecting children from experiencing preventable traumas.

All traumatic exposures assessed were associated with up to double the risk for developing a substance use disorder.

by experiencing disasters (14.8%) and witnessing death or injury (11.7%). Adding to this burden, 14.1% of youth reported experiencing two traumatic events, and 18.6% reported being exposed to three or more.³

This study also examined links between trauma and mental disorders.⁴ All traumatic exposures assessed were associated with up to double the risk for developing a substance use disorder, and exposure to interpersonal violence more than doubled the risk for developing conduct disorder (in girls).⁴

What more than 100,000 young people can teach us

Research has also emerged on factors that help young people cope with adversity. A meta-analysis that combined findings from more than 100 studies identified various factors that buffered the negative effects of experiencing or witnessing violence at home or in the community, including family, peer and school supports.⁵ Family support included having a warm and accepting parent as well as a cohesive family. Peer support involved receiving emotional and social encouragement and being satisfied with one's friendships. School support included having teachers and other school staff help children and make them feel valued and safe.⁵

Preventing childhood adversities wherever possible is crucial.

Preventing serious childhood adversities

While this issue focuses on helping children who have experienced trauma, preventing childhood adversities wherever possible is crucial. The United Nations' Convention on the Rights of the Child states that all children are entitled to protection from violence and injury, including all forms of child maltreatment.⁶ Canada has been a signatory to this convention since 1991. Policy-makers and practitioners can play important roles by keeping prevention in the spotlight.⁷


Practitioners also have a role to play in delivering programs proven to prevent child maltreatment, highlighted in a [previous issue](#). Among them, [Nurse-Family Partnership](#) has shown particularly strong outcomes for children and families in the US.⁸ This program, currently being [evaluated in BC](#), is [available](#) as an enhanced public health service for first-time mothers and their children who meet eligibility criteria. Investing in such efforts can help to ensure that fewer children experience serious adversities. (The sidebar below discusses Indigenous communities and the continuing intergenerational effects of colonialism, a profound form of childhood adversity.)

Overcoming adversities arising from colonialism

Indigenous communities in Canada have long displayed strength and resilience in the face of multiple adversities associated with colonialism and its legacies. These legacies have included the forced removal of children into residential schools, the multi-generational aftermath of these policies, continuing overrepresentation of Indigenous children in the child protection and youth justice systems, and ongoing exposure to individual and systemic racism.⁹⁻¹⁰

To redress these legacies, in 2015 the Truth and Reconciliation Commission (TRC) issued 94 [calls to action](#).¹⁰ In particular, these calls to action address the deep social and health disparities Indigenous children and families experience in Canada — which are preventable forms of serious adversity. Reducing these adversities is essential to enable all Indigenous children to flourish.

All Canadians can support this flourishing by engaging in reconciliation. For example, we can express support for the TRC's calls to action and call on federal and provincial or territorial governments to enact them. In BC, the First Nations Health Authority provides valuable [resources on promoting wellness](#) for Indigenous young people.¹¹

Yet even with strong investments in prevention, some children will still experience serious adversities.⁶ When these occur, adults can take steps to help minimize negative consequences. These steps include helping parents to provide high levels of support and encouraging supports from peers and schools. With such supports, many children will not require interventions from mental health practitioners. However, some children may need assistance to strengthen their coping skills and to encourage their healthy development. In the [Review article](#) that follows, we assess four interventions designed to help children flourish even when they are faced with difficult circumstances. 

Intervening after serious trauma

Many children who have experienced trauma display considerable resilience, maintaining a positive developmental trajectory. Some children, however, will need support to ensure that traumatic experiences do not lead to additional concerns, including the development of mental health conditions such as substance use disorders, depression, conduct disorder or posttraumatic stress disorder.

To determine which interventions can effectively prevent the development of mental disorders for children after serious adverse experiences, we conducted a

systematic review. We built quality assessment into our inclusion criteria, requiring studies to use randomized controlled trial (RCT) evaluation methods. We searched for RCTs published in the past 11 years, since we last reviewed this topic. We also examined previous *Quarterly* issues to identify studies that met our current inclusion criteria. Because of our focus on the *prevention* of mental disorders, we included only those studies where most children did not have a disorder at the outset. We also required studies to report on at least one mental health outcome. (The Methods section gives more details on our search strategy and inclusion criteria.)

After retrieving and evaluating 119 studies, we accepted four RCTs evaluating three psychosocial interventions: It's My Turn Now,¹² Fostering Healthy Futures (two studies)¹³⁻¹⁴ and Multisystemic Therapy for Child Abuse and Neglect (MST).¹⁵ All three interventions were delivered to children who had been maltreated. We also accepted one RCT evaluating the medication propranolol for children who had sustained physical injuries, mainly due to motor vehicle accidents.¹⁶ Although no evaluations of critical incident debriefing met our inclusion criteria, we provide more information about this intervention in a sidebar at the end of this article.

Helping children who were maltreated

It's My Turn Now focused on Dutch children aged six to 12 who had witnessed physical or psychological intimate partner violence (IPV).¹² All children were living with the non-offending parent (approximately 95% were mothers). Children participated in nine group sessions that focused on helping them “process” their IPV experiences. The sessions taught children to recognize their emotions and to cope with feelings and problems without using violence. Non-offending mothers and fathers participated in nine group sessions to help them strengthen their parenting skills and enhance their own emotional well-being. Comparison children participated in nine group sessions providing social support without the therapeutic elements of It's My Turn Now.¹²

Both evaluations of Fostering Healthy Futures included American children aged nine to 11 living in foster care due to maltreatment.¹³⁻¹⁴ The program aimed to improve children's mental health and quality of life. Children participated in 30 group sessions that taught skills such as recognizing emotions, solving problems



Even one child being exposed to serious avoidable adversities is one too many.

Many children who have experienced trauma display considerable resilience, maintaining a positive developmental trajectory.

and managing anger. Children also received 30 one-on-one mentoring sessions to provide support and positive recreational opportunities, and to teach them to apply techniques from the skills group by completing weekly activities. Control children had access to typical social services interventions, such as psychotherapy.¹⁷ (Children in the Fostering Healthy Futures program could also access these services.)

Multisystemic Therapy for Child Abuse and Neglect, meanwhile, focused on American children aged 10 to 17 who had been physically abused and whose families were involved with child protective services.¹⁵ (Children were still living with their families.) MST aimed to improve functioning for both children and parents and to decrease further abuse by parents. Families participated in daily to weekly therapy sessions for up to 12 months, depending on need. Interventions were tailored to each family's circumstances and typically included creating plans to address situations where family members felt unsafe, fostering positive relationships between the family and child protective services, and helping parents take responsibility for their abusive behaviour. Cognitive-behavioural and behavioural therapy strategies were also used as needed, teaching families ways to address anger, solve problems and communicate better. Comparison families received standard community treatments, including therapy for children and assistance for caregivers to address their own mental health issues.¹⁵

All three psychosocial programs resulted in at least one positive mental health outcome for children.

Helping children who were injured

The propranolol evaluation focused on American children aged 10 to 18 who had attended an emergency department as a result of physical injuries, mainly due to motor vehicle accidents.¹⁶ Children also had to score in the “at risk” range on a PTSD screening measure. The study aimed to determine whether propranolol could prevent PTSD, given that this medication has been found to block the memory-enhancing effects of emotional arousal. Intervention children began the medication within 12 hours of their hospital visit and took it twice daily for 10 days. Control children received a placebo, also for 10 days.¹⁶ Table 1 provides more details about the five studies.

Table 1: Interventions for Children Who Experienced Serious Adversities			
Intervention	Approach	Sample size	Ages (years) (countries)
Psychosocial interventions for children who experienced maltreatment			
It's My Turn Now ¹²	Weekly child skills group + weekly parent skills group delivered in community settings for 9 weeks; aimed to help children who had witnessed intimate partner violence cope with their experiences	164	6 – 12 (Netherlands)
Fostering Healthy Futures ¹³	Weekly child skills group + weekly individual child mentoring delivered in community settings for 9 months; aimed to improve mental health and quality of life for children in foster care due to maltreatment	156	9 – 11 (United States)
Fostering Healthy Futures ¹⁴	As above	426	9 – 11 (United States)
Multisystemic Therapy ¹⁵	Daily to weekly abuse- + skills-focused sessions delivered to families in homes + community settings for 8 months (on average); aimed to increase functioning + reduce further abuse for children living with a parent who had abused them	90	10 – 17 (United States)
Medications for children who experienced physical injuries			
Propranolol ¹⁶	Twice daily oral solution of propranolol for 10 days; aimed to prevent posttraumatic stress disorder for children presenting in an emergency department due to injury	29	10 – 18 (United States)

Which psychosocial interventions were effective?

All three psychosocial programs resulted in at least one positive mental health outcome for children, including reducing disorder symptoms and/or mental health service use. Parents in the It's My Turn Now program rated their children as having significantly fewer PTSD symptoms six months after the intervention ended.¹² But no differences were found for child-rated PTSD or depressive symptoms, or for parent- or teacher-rated emotional or behaviour problems.¹²

In the first Fostering Healthy Futures study, intervention children reported fewer dissociative symptoms six months after the program ended.¹³ (Dissociation is one symptom of PTSD.) As well as being statistically significant, these improvements made a meaningful difference in the children's lives — exemplified by a medium effect size (Cohen's d [d] = 0.39). Intervention children also had fewer emotional problems based on a composite measure including child, caregiver and teacher reports, also with a medium effect size (d = 0.51).¹³ As well, intervention children were significantly less likely to report accessing additional mental health services in the prior six months, although this was not confirmed by caregiver report. There were no significant differences in children's use of psychiatric medications by caregiver report, or in child-reported posttraumatic stress symptoms.¹³

The Fostering Healthy Futures replication trial also led to several positive child outcomes six months after the program ended.¹⁴ Intervention children reported significantly fewer PTSD and dissociative symptoms, both with small effect sizes (d = 0.20 and d = 0.29, respectively). Intervention children also had fewer emotional problems based on a composite measure including child, caregiver and teacher reports, also with a small effect size (d = 0.25). As well, intervention children had significantly lower odds of using other mental health services (odds ratio = 0.62). However, the program made no difference in child psychiatric medication use.¹⁴

Multisystemic Therapy also resulted in several positive child outcomes approximately four months after the program ended.¹⁵ MST children experienced fewer PTSD symptoms — according to both child and parent report — with medium effect sizes (d = 0.68 and d = 0.55, respectively). MST children also reported fewer dissociative symptoms, with a large effect size (d = 0.73), and had significantly fewer emotional problems, based on parent report, also with a large effect size (d = 0.71). As well, MST children had fewer overall mental

Even after children have experienced a serious adversity such as maltreatment, it is possible to prevent mental health symptoms from developing.



Family support can buffer the negative effects of trauma on children.

health symptoms (including emotional, behaviour, attention and thought problems) based on parent report ($d = 0.85$). However, MST made no difference in parent-reported behaviour problems, or in child-reported depressive and anxiety symptoms or anger.¹⁵

The propranolol study attempted to assess whether the medication reduced PTSD diagnoses.¹⁶ But because only one child met criteria for this disorder approximately one month after medication and placebo were discontinued, researchers instead assessed whether the medication made a difference in a combined measure of PTSD diagnoses and subthreshold diagnoses. Propranolol made no difference on this outcome.¹⁶ Table 2 provides details on all study outcomes.

Table 2: Intervention Outcomes for Children Who Experienced Serious Adversities		
Intervention	Follow-up	Outcomes*
Psychosocial interventions for maltreatment		
It's My Turn Now ¹²	6 months	↓ Posttraumatic stress symptoms (1 of 2 measures) ₪ Emotional problems (2 measures) ₪ Depressive symptoms ₪ Behaviour problems (2 measures)
Fostering Healthy Futures ¹³	6 months	₪ Posttraumatic stress symptoms ↓ Dissociative symptoms ↓ Emotional problems ↓ Mental health service use (1 of 2 measures) ₪ Psychiatric medication use
Fostering Healthy Futures ¹⁴	6 months	↓ Posttraumatic stress symptoms ↓ Dissociative symptoms ↓ Emotional problems ↓ Mental health service use ₪ Psychiatric medication use
Multisystemic Therapy ¹⁵	4 months**	↓ Posttraumatic stress symptoms (2 of 2 measures) ↓ Dissociation symptoms ↓ Emotional problems ↓ Overall mental health problems ₪ Behaviour problems ₪ Depressive symptoms ₪ Anxiety symptoms ₪ Anger
Medications for injury		
Propranolol ¹⁶	1 month	₪ Combined posttraumatic stress disorder diagnoses + subthreshold diagnoses
* Unless otherwise specified, there was a single measure for each outcome. ↓ Statistically significant improvements for intervention relative to comparison/control group. ₪ No significant difference between intervention and comparison/control group. ** Follow-up was at least four months but was as long as 14 months for some children.		

Implications for practice and policy

All three psychosocial interventions designed for children with a history of maltreatment produced at least one beneficial outcome. However, the medication propranolol made no difference for children who had sustained injuries. Our review suggests four implications for practice and policy.

- **Intervene before mental health symptoms develop.** Even after children have experienced a serious adversity such as maltreatment, it is possible to prevent mental health symptoms from developing — and adding further to their distress and burdens. Fostering Healthy Futures prevented emotional problems and reduced the need for future mental health interventions for children in foster care. MST reduced mental health concerns for children involved with protective services but still living with their parents. And

It's My Turn Now helped children who had been exposed to IPV. Helping parents develop new skills to support their children was a component of these latter two programs.

- **Consider other effective interventions for preventing behaviour problems and substance use.** None of the programs we reviewed showed evidence of success in preventing common difficulties associated with childhood trauma, such as problematic behaviour or substance use. But both these challenges can be prevented by using other proven psychosocial interventions, including parent training programs to prevent behaviour problems and Preventure to prevent problematic substance use.^{18–19}
- **Implement prevention programs before maltreatment occurs.** The ideal approach is to prevent exposure to avoidable serious adverse experiences such as child maltreatment. Prevention also recognizes children's rights — to safety and to having their basic needs met. Yet the most recent Canadian data identified more than 236,000 child maltreatment investigations based on data from 2008, with approximately 36% of these cases being substantiated.²⁰ As highlighted in our Summer 2018 issue, practitioners can play an important role in prevention by delivering effective parenting programs, including programs that can reduce child injuries.²¹
- **Enact policies to reduce socio-economic disparities.** The link between a major form of trauma — child maltreatment — and socio-economic disadvantage is well established.^{22–23} So successful prevention also likely involves addressing this larger societal issue. Other countries have made progress. For example, Denmark, Finland, Iceland and Norway have successfully reduced socio-economic disparities through long-standing social programs that redistribute income.^{24–25} Canada can follow suit by enacting similar programs, as the federal government and some provinces and territories have done in recent years.^{26–27}

When traumatic events have occurred, there are still many ways to help children.

Even one child being exposed to serious avoidable adversities is one too many. This is particularly true given that there are effective approaches that can reduce children's exposure to these adversities. Yet when traumatic events have occurred, there are still many ways to help children. Foremost is to ensure the child's ongoing safety and stability — and to ensure that their basic needs are met. Beyond this, policy-makers can make sure that effective preventive programs, such as those we have reviewed here, are available. The objective would be to ensure that secondary mental health problems do not add to children's difficulties. As well, larger-scale policy approaches such as reducing socio-economic disparities can help to ensure that all children have what they need to be resilient and to flourish. 🖐️

What about critical incident debriefing?

Critical incident debriefing (or simply *debriefing*) typically involves a single-session intervention where participants describe their experiences very soon after witnessing or being a victim of a traumatic event and then discuss strategies for coping.²⁸ While debriefing was initially designed for adults, its use with children has increased.²⁸ We found two randomized controlled trials (RCTs) on debriefing after traffic accidents. (These RCTs did not meet the criteria for our systematic review because one used inappropriate statistical analyses and the other had insufficient statistical power).^{29–30} In a British study, children received the intervention approximately one month after their accident.²⁹ In a Swiss study, children and parents received the intervention approximately 10 days after the accident.³⁰

In the British study, nearly eight months after the debriefing, both intervention and control children showed many improvements. The only significant difference between the groups was that debriefing children

experienced fewer emotional and behavioural problems, leading researchers to conclude the intervention was not successful.²⁹ Similarly, the Swiss study found that children in both the intervention and control groups improved over time, with no differences between the groups at six-month follow-up.³⁰ A systematic review of child debriefing, which included less rigorous studies, also concluded that the evidence was too limited to endorse this form of intervention.²⁸

Importantly, cautions about debriefing have also emerged from adult studies, with some studies finding adverse events, such as increased long-term distress.³¹ Some authors have speculated that single-session debriefing does not provide enough time for participants to emotionally process the traumatic event.³¹ Given almost no evidence of benefits, coupled with the potential for harm, debriefing should not be used with children unless better studies emerge showing positive results.

We use systematic review 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 research evidence — requiring that intervention studies use randomized controlled trial (RCT) evaluation methods and meet additional quality indicators. For this review, we searched for RCTs on effective interventions for preventing mental health problems among children exposed to trauma. Table 3 outlines our database search strategy.

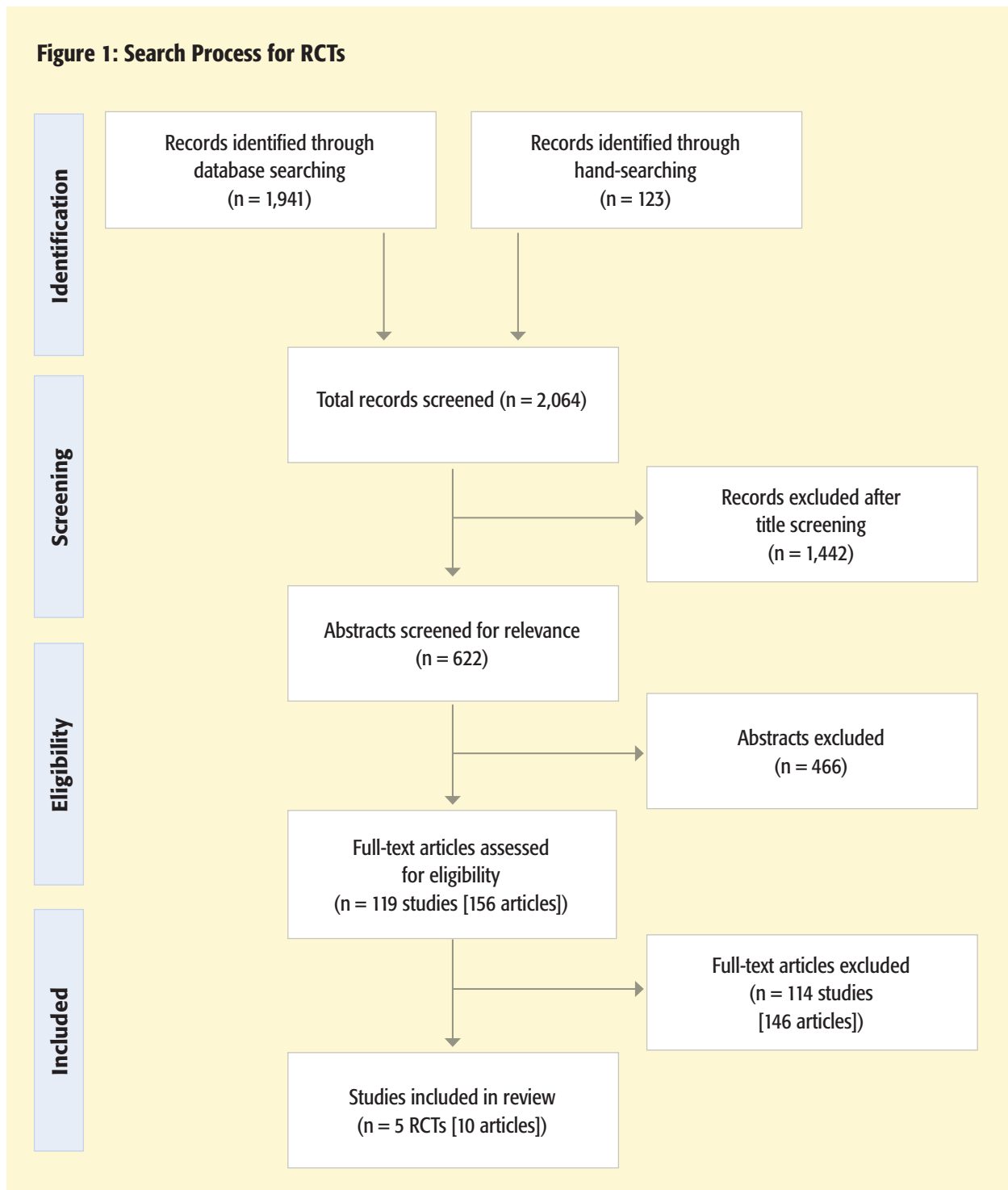
Table 3: Search Strategy	
Sources	• CINAHL, ERIC, Medline and PsycINFO
Search Terms	• Post-traumatic stress disorders, post-traumatic stress, trauma <i>and</i> intervention or treatment
Limits	• Peer-reviewed articles published in English between 2009 and 2020 • Pertaining to children aged 18 years or younger • RCT methods used

To identify additional RCTs, we also hand-searched the Web of Science database and reference lists from relevant published systematic reviews. Using this approach, we identified 119 studies. Two team members then independently assessed each study, applying the inclusion criteria outlined in Table 4.

Table 4: Inclusion Criteria for RCTs	
	<ul style="list-style-type: none"> • Studies provided clear descriptions of participant characteristics, settings and interventions • Interventions were evaluated in settings comparable to Canada • All participants were exposed to a traumatic event but most did not have a mental disorder at study outset • Attrition rates were 20% or less at final assessment and/or intention-to-treat analysis was used • Child outcome indicators included mental health measures, assessed using two or more informant sources • Reliability and validity were documented for all primary outcome measures • Statistical significance was reported for primary outcome measures • Studies were excluded when authors stated there was insufficient statistical power or we found inappropriate analysis*
Psychosocial Intervention Studies	<ul style="list-style-type: none"> • Participants were randomly assigned to intervention and comparison groups (i.e., active control or treatment-as-usual) at study outset • Follow-up was three months or more (from the end of the intervention)
Medication Studies	<ul style="list-style-type: none"> • Participants were randomly assigned to intervention and placebo control groups at study outset • Double-blinding procedures were used
* We defined inappropriate analysis as not controlling for multiple comparisons or variables that might influence outcomes.	

Five RCTs met all the inclusion criteria. Figure 1 depicts our search process, adapted from Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Data from these studies were then extracted, summarized and verified by two or more team members. Throughout our process, any differences among team members were resolved by consensus. 🤝

For more information on our research methods, please contact
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Figure 1: Search Process for RCTs

RESEARCH TERMS EXPLAINED

Practitioners and policy-makers need good evidence about whether a given intervention works to help children. **Randomized controlled trials** (RCTs) are the gold standard for assessing whether an intervention is effective. In RCTs, children, youth or families are randomly assigned to the intervention group or to a comparison or control group. By randomizing participants — that is, by giving every young person an equal likelihood of being assigned to a given group — researchers can help ensure the only difference between the groups is the intervention. This process provides confidence that benefits are due to the intervention rather than to chance or other factors.

The highest standard for assessing medication effectiveness and safety involves RCTs in which control youth receive a placebo and youth and assessors are unaware of who is in the intervention and who is in the control groups, known as a **double-blinded** study. This approach is typical for medication studies; it helps to ensure that beliefs about the potential effectiveness of the intervention do not influence outcomes.

Then, to determine whether the intervention actually provides benefits, researchers analyze relevant outcomes. If an outcome is found to be **statistically significant**, it helps provide certainty the intervention was effective rather than results appearing that way due to chance. In the studies we reviewed, researchers used the typical convention of having at least 95% confidence that the observed results reflected the program's real impact.

As well, several studies included in this issue also calculated **effect sizes**, which described the degree of clinically meaningful difference the intervention made in young people's lives. The studies reported on **Cohen's *d***, which can range from 0 to 2. Standard interpretations are 0.2 = small effect; 0.5 = medium effect; and 0.8 = large effect. **Odds ratio** indicates the probability of an event occurring, with values above 1 indicating an increased probability and values below indicating a decreased probability. 🖐



If an outcome is found to be statistically significant, it helps provide certainty the intervention was effective rather than results appearing that way due to chance.

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BC government staff can access original articles from [BC's Health and Human Services Library](#). Articles marked with an asterisk (*) include randomized controlled trial data that was featured in our Review article.

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