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# Canadian surveillance study of complex regional pain syndrome in children

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**Abstract**

This study describes the minimum incidence of pediatric complex regional pain syndrome (CRPS), clinical features, and treatments recommended by pediatricians and pain clinics in Canada. Participants in the Canadian Paediatric Surveillance Program reported new cases of CRPS aged 2 to 18 years monthly and completed a detailed case reporting questionnaire from September 2017 to August 2019. Descriptive analysis was completed, and the annual incidence of CRPS by sex and age groupings was estimated. A total of 198 cases were reported to the Canadian Paediatric Surveillance Program, and 168 (84.8%) met the case definition. The minimum Canadian incidence of CRPS is estimated at 1.14/100,000 (95% confidence interval 0.93-1.35/100,000) children per year. Incidence was highest among girls 12 years and older (3.10, 95% confidence interval 2.76-3.44/100,000). The mean age of CRPS diagnosis was 12.2 years (SD = 2.4), with the mean time from symptom onset to diagnosis of 5.6 months (SD = 9.9) and no known inciting event for 19.6% of cases. Most cases had lower limb involvement (79.8%). Nonsteroidal anti-inflammatory drugs (82.7%) and acetaminophen (66.0%) were prescribed more commonly than antiepileptic drugs (52.3%) and antidepressants (32.0%). Referrals most commonly included physical therapy (83.3%) and multidisciplinary pain clinics (72.6%); a small number of patients withdrew from treatment because of pain exacerbation (5.3%). Pain education was recommended for only 65.6% of cases. Treatment variability highlights the need for empiric data to support treatment of pediatric CRPS and development of treatment consensus guidelines.

**Keywords:** Complex regional pain syndrome, Incidence, Population surveillance, Pediatrics, Pain management

## 1. Introduction

Complex regional pain syndrome (CRPS) is a severe pain condition characterized by pain intensity out of proportion to the inciting trauma or stimulus and associated with a wide variety of autonomic, trophic, and motor changes.[16] Pain with CRPS is often not responsive to common analgesic medications or opioids.[6,8] As with other chronic pain syndromes, complex biopsychosocial factors can have an impact on how children recover from CRPS, placing them at risk of poor long-term physical and psychological health outcomes.[6,22,29,35] Children with CRPS are particularly vulnerable because of stressful life events and display more somatic symptoms than children with other pain conditions.[22] A delay in diagnosis and access to appropriate treatment can further affect recovery. A shorter time to diagnosis is associated with more favorable outcomes in children.[26] Prompt referral to physiotherapy and initiation of multidisciplinary treatment relies on a high index of suspicion.[21]

The International Association for the Study of Pain adopted the Budapest Criteria for diagnosis of CRPS and use has been adopted internationally; however, this has not been validated in pediatric populations.[13,16] Some case series report the complex diagnostic and interventional histories of children with CRPS.[3,4,9,26,37] However, little is known about the epidemiology

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of pediatric CRPS. A Scottish surveillance study described 26 children and reported an estimated annual pediatric CRPS incidence of 1.2 per 100,000 using the Budapest Criteria; the youngest case reported was age 5.5 years.[2] Previous population-based studies include 14 cases in total, and they reported an incidence of 1.58 to 5.2 per 100,000 children.[27,32] Cases were primarily Anglo-American in the American population–based study where only 3 pediatric cases were identified.[32] In other studies, ethnicity was not specified.[2,27] In adults, CRPS has incidence rates ranging from 2.7 to 16.8 new cases per 100,000 annually.[27,32]

The primary objective of this surveillance study was to determine the minimum incidence of CRPS in Canadian children and youth. Secondary outcomes include describing pathways of referral, clinical presentation, diagnostic interventions, and treatments used by Canadian pediatricians, pediatric subspecialists, and pain specialists.

## 2. Methods

The Canadian Paediatric Surveillance Program (CPSP), established in 1996, is a joint project of the Public Health Agency of Canada and the Canadian Paediatric Society. The CPSP contributes to the improvement of the health of children and youth in Canada by national surveillance and research into low frequency childhood disorders associated with high disability, morbidity, and economic costs to society. Approximately 2800 Canadian pediatricians and pediatric subspecialists participate in active monthly surveillance capturing all settings participating in CPSP, including primary care, subspecialty care, and inpatient care.[7] During the study period, multidisciplinary pediatric pain clinics at tertiary care hospitals across Canada were included in the surveillance and site champions were identified to optimize reporting. Through the established methodology of the CPSP, participating pediatricians and pain clinics received a monthly email from September 2017 to August 2019 asking them to notify the program if they encounter new cases of CRPS or if they have nothing to report. Participants who identified cases were asked to complete a detailed case report form.[7] During the 2-year surveillance study, the CPSP reported an average monthly response rate of 81% and case report form response rate of 89%.[7]

In accordance with CPSP protocols, this study was approved by the University of Saskatchewan (REB 17-169) and IWK Health Centre (REB #1022863) Research Ethics Boards and by the institutional review boards at collaborating centers in accordance with site-specific protocols. In accordance with CPSP procedures, case reports are deidentified at the clinic level with a minimum aggregate reporting of 5 when fewer cases are reported.

### 2.1. Case definition

Canadian Paediatric Surveillance Program participants were instructed to report any new patient presenting between the ages of 2 and 18 years (up to the 18th birthday) with a new diagnosis of CRPS, meeting the Budapest Criteria.[16] The *case definition* was met if at least 3 of 4 symptom categories (ie, sensory, vasomotor, sudomotor or edema, and motor or trophic) and at least 2 of 4 sign categories (ie, sensory, vasomotor, sudomotor or edema, and motor or trophic) were present.[16] The sensitivity and specificity of the Budapest Criteria have been reported as 0.99 and 0.79, respectively, in an adult patient population.[14] However, a recent review demonstrates variability with sensitivity is 0.45 to 0.99 and specificity is 0.68 to 0.85 in adult populations.[25] Specificity may be lower in pediatric CRPS.[11]

### 2.2. Case report form

The case report form includes minimal nonnominal patient information, such as the month and year of birth and sex of the child to enable identification of duplicate cases by the CPSP. Demographic information, clinical presentation, pain impact, health utilization and treatments since symptom onset, adverse outcomes, medical history, and follow-up plan are included in the case report form. To assess the distribution of symptoms and signs, at the item and category level, each CRPS symptom and sign was included with 3 response options (yes, no, or unknown). The case report form and study protocol are available at https://www.cpsp.cps.ca/surveillance/concluded-studies.

### 2.3. Data analysis

Analyses were conducted with IBM SPSS (Statistical Package for the Social Sciences) Statistics Version 27.0.[17] The number of cases meeting the case definition was calculated from clinical decision rules. Cases meeting the case definition were defined as *confirmed cases* and those that remained were defined as *nonconfirmed cases*. Descriptive analyses were conducted on demographic, clinical presentation, and treatment data. We further examined the distribution of symptoms and signs at category levels among the cases reported that did not meet the case definition.

By examining the total number of people at risk in the study population during the 2-year surveillance study and the number of new cases during this time, we calculated the crude incidence rate (per 100,000 person-years) and 95th confidence interval (CI) for all cases and by sex and age groups. Cases with a date of diagnosis outside the 2-year surveillance period or a past history of CRPS were excluded from the incidence calculation. The denominator was defined as the total number of people at risk (children and youth aged 2–18 years) according to the population estimation on July 1 from Statistics Canada.[34]

## 3. Results

During the study period, 236 cases were reported to the CPSP and 198 case report forms were returned for analysis (see **Fig. 1** for the study population). Of these, 84.8% (168/198) met the case definition.[14] We assessed the distribution of case reporting over the 24-month reporting period; 97 case report forms were returned for year 1 of the study and 101 forms for year 2 of the study.

Most confirmed cases were females (83.3%), with a mean age at diagnosis of 12.2 years. A single site was affected in 89.3%, most frequently in a lower limb (79.8%). Musculoskeletal trauma or injury was an inciting event for most cases (65.5%), with 19.6% of cases reporting no known inciting event. Further characteristics of the study population are reported in **Table 1**.

The most common symptoms in each symptom category of the Budapest Criteria were skin color changes (86.2%), allodynia (83.9%), decreased range of motion (83.3%), and edema (77.4%). The most common signs in each sign category were decreased range of motion (86.3%), allodynia with light touch (81.5%), skin color changes (66.7%), and edema (50.6%). The presence or absence of each sign and symptom in the Budapest Criteria is reported for confirmed and total cases in **Table 2**.

Sixty-one percent of confirmed cases had visited the emergency department since the onset of symptoms (60.7%). The most common special investigation patients received for CRPS was plain radiographs (83.3%). Most confirmed cases (79.7%) reported 3 or more specialist referrals. Treatment focused on pain education (65.6%), psychological strategies (62.4%), desensitization (59.5%), and fitness or exercise (54.1%). Additional health utilization and treatments since the onset of symptoms are reported for confirmed and total cases in **Table 3**.

Among the 30 nonconfirmed cases, 73.3% were females compared with 83.3% in the 168 confirmed cases, which was not statistically different. Of the nonconfirmed reported cases, 14 had 2 or more signs of CRPS but did not meet the symptom criteria. The values of mean and median of age or time from onset to CRPS diagnosis were not statistically different between these nonconfirmed cases compared with the confirmed cases.

### *3.1. Incidence*

After exclusion of 7 cases with a history of CRPS and 4 cases with diagnosis outside the 2-year surveillance period, 157 cases remained for calculation of the estimated minimum incidence rate. According to the 2017 Statistics Canada census, the Canadian population between 2 and 18 years of age was 6,786,484 people.[34] The minimum CRPS incidence was 1.14 (0.93-1.35) per 100,000 Canadian children aged 2 to 18 years. The incidence for all ages by sex and age groups is reported in **Table 4**.

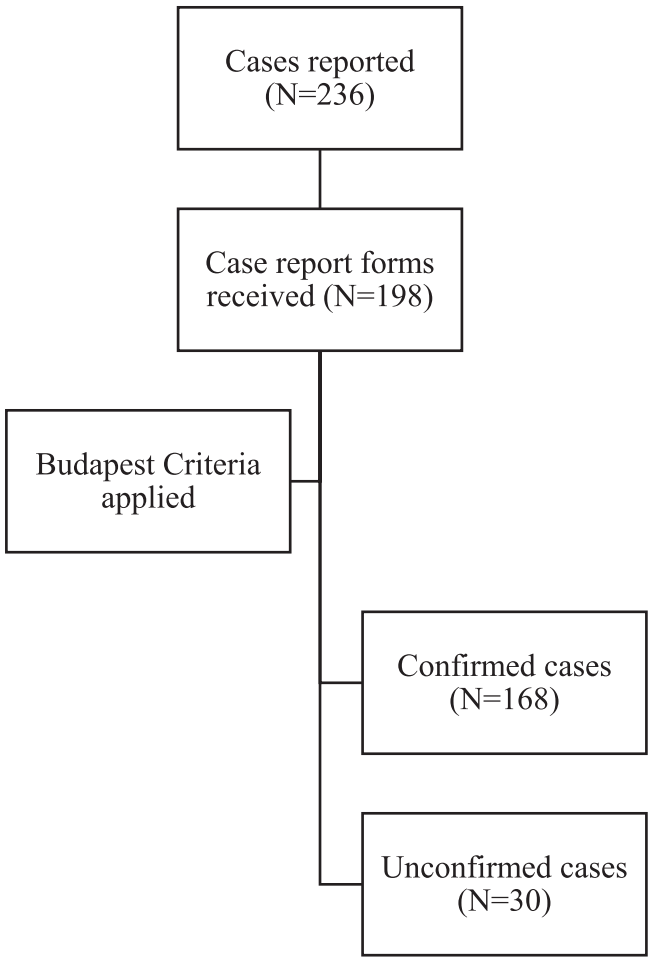


**Figure 1.** Study population.

## 4. Discussion

We report a minimum CRPS incidence of 1.14 per 100,000 (95% CI 0.93-1.35/100,000) Canadian children aged 2 to 18 years, with rising incidence after age 12 years. Incidence was highest among girls 12 years and older (3.10, 95% CI 2.76-3.44/100,000). These findings are consistent with the Scottish surveillance study.[2] The current study may represent a more diverse study population than has been previously reported, with 15.5% of confirmed cases of non-White or mixed ethnicity. As would be expected, CRPS symptoms were typically associated with moderate-to-severe pain. Age at diagnosis, median time to diagnosis, female predominance, and lower limb predominance are similar to previously published case series.[2,26] Reports of movement disorders (dystonia, 8% and tremor, 8%) and multisite involvement (9%) were less common than previous reports. Among previously published case series, movement disorders were reported in 25% to 38% of cases.[1,2,26] In the Scottish surveillance study, 38% of cases had secondary site involvement.[2]

A milestone paper by Wilder et al.[37] described clinical characteristics of 70 children with CRPS; the average time from the initial injury to the diagnosis was 1 year, suggesting CRPS was underrecognized in pediatric patients. In a more recent retrospective review of children with CRPS, children with favorable outcomes had significantly shorter time to diagnosis and lower mean symptom duration of 8.5 months compared with patients who had unfavorable outcomes.[26] The mean time to diagnosis in the current study was approximately 6 months, but some children experienced delayed diagnosis. Given that pediatric patients with delayed diagnosis may be more likely to have poor outcomes,[33] professional education and clinical treatment pathways are recommended. Given the frequency that diagnosis is made by pediatricians, pediatric subspecialists, and orthopedic surgeons, it is reasonable to ensure that pediatric CRPS is included in professional education for these professions, as well as primary care practitioners.

A small number of cases met the Budapest Criteria for clinical diagnosis during the study period but were excluded from the incidence calculation because of personal history of CRPS. Two recent retrospective chart reviews reported complex diagnostic and interventional histories of children with CRPS, with poor outcomes and rates of recurrence ranging from 10% to 55%.[4,9,26] Longitudinal studies are required to improve the understanding of pediatric CRPS including risk of relapse, persistence, spread to secondary sites, and chronic pain in adulthood. Because algorithms to identify patients with CRPS demonstrate low sensitivity and limit the utility of administrative data for studying CRPS, pediatric registry data and multicenter trials may be most promising.[18]

Complex regional pain syndrome is commonly linked with high health utilization and functional disability, including impact on school attendance and achievement.[4,9] We have captured some data on health utilization that reveals the significant burden of CRPS including health visits, special investigations, medication use, and specialist referrals, most commonly to physical therapists and multidisciplinary pain clinics typically comprised of a nurse, physical therapist, physician, and psychologist. Functional impact since symptom onset was common in all domains; 24.9% missed more than 2 weeks of school, and 6% enrolled in online school because of pain.

Complex regional pain syndrome treatment recommendations typically include physical therapy and intensive cognitive behavioral therapy with pharmacotherapy and referral to

**Table 1**

**Characteristics of the study population.**

| | Confirmed cases (n = 168) | Total (n = 198) |
|---|---|---|
| | n (%) | n (%) |
| Social characteristics | | |
| Sex | | |
| Male | 28 (16.7) | 36 (18.2) |
| Female | 140 (83.3) | 162 (81.8) |
| Location of residence | | |
| British Columbia | 23 (13.7) | 29 (14.6) |
| Quebec | 33 (19.6) | 35 (17.8) |
| Ontario | 85 (50.6) | 98 (49.5) |
| Prairie provinces (AB, SK, and MB) | 22 (13.1) | 28 (14.1) |
| Atlantic provinces (NB, NS, PE, and NL) | 5 (3.0) | 8 (4.0) |
| Ethnicity | | |
| White | 126 (75.0) | 151 (76.3) |
| Non-White | 26 (15.5) | 28 (14.1) |
| Unknown | 16 (9.5) | 19 (9.6) |
| Clinical features | | |
| Age at diagnosis, y | | |
| Mean (SD) | 12.2 (2.4) | 12.8 (2.5) |
| Median (min-max) | 12.9 (7.0-18.0) | 12.9 (7.0-19) |
| Onset to diagnosis, mo | | |
| Mean (SD) | 5.6 (9.9) | 5.6 (10.0) |
| Median (IQR) | 2.0 (4.0) | 2.0 (4.0) |
| Diagnosing professional | | |
| General pediatrician | 22 (13.1) | 27 (13.6) |
| Pain clinic team members | 55 (32.7) | 63 (31.8) |
| Pediatric rheumatologist | 23 (13.7) | 28 (14.1) |
| Orthopedic surgeon | 20 (11.9) | 25 (12.6) |
| General or pediatric emergency physician | 13 (7.7) | 14 (7.1) |
| Others | 35 (20.8) | 41 (20.7) |
| Localization at diagnosis (more than one possible) | | |
| Right | 74 (44.0) | 86 (43.4) |
| Left | 78 (46.4) | 87 (43.9) |
| Bilateral | 13 (7.7) | 18 (9.0) |
| Upper limb | 36 (21.4) | 43 (21.7) |
| Lower limb | 134 (79.8) | 153 (77.2) |
| Others or unknown | <5 | <5 |
| Number of sites affected | | |
| Single site | 150 (89.3) | 171 (86.3) |
| Multiple sites | 15 (8.9) | 22 (11.1) |
| Others or unknown | <5 | 7 (3.5) |
| Inciting or triggering event | | |
| None | 33 (19.6) | 40 (20.2) |
| Trauma or injury | 110 (65.5) | 128 (64.6) |
| Operation or surgery | 12 (7.1) | 14 (7.1) |
| Others | 6 (3.6) | 8 (4.0) |
| Unknown | 7 (4.2) | 8 (4.0) |
| Family history | | |
| CRPS affecting the first degree relative | <5 | <5 |
| Pain intensity | | |
| Mild | 6 (3.6) | 12 (6.1) |
| Moderate | 52 (31.0) | 59 (29.8) |
| Severe | 97 (57.7) | 109 (55.1) |
| Missing | 13 (7.7) | 18 (9.1) |
| Functional impact of symptoms | | |
| Impact on the following (yes) | | |
| Physical activity | 157 (93.5) | 182 (91.9) |
| Sleep | 91 (54.2) | 103 (52.0) |
| School achievement | 54 (32.1) | 61 (30.8) |
| Social activities | 91 (54.2) | 104 (52.5) |
| Family function | 68 (40.5) | 77 (38.9) |
| Mood | 84 (50.0) | 98 (49.5) |
| High level sport | 53 (31.5) | 64 (32.3) |
| Enrolled in home or cyber or online school as a result of pain | 10 (6.0) | 11 (5.6) |

(*continued on next page*)

Table 1 (*continued*)

| | Confirmed cases (n = 168) | Total (n = 198) |
|---|---|---|
| | n (%) | n (%) |
| Amount of school missed (choose one) | | |
| None | 47 (28.0) | 53 (26.8) |
| <2 wk | 43 (25.6) | 47 (23.7) |
| 2-4 wk | 16 (9.5) | 20 (10.1) |
| 1-3 mo | 14 (8.3) | 16 (8.1) |
| >3 mo | 12 (7.1) | 15 (7.6) |
| Unknown or missing | 36 (21.4) | 47 (23.6) |
| Personal history (more than one possible) | | |
| Conversion disorder | <5 | <5 |
| Prematurity | <5 | <5 |
| Rheumatologic condition or arthritis | 5 (3.0) | 5 (2.5) |
| CRPS | 7 (4.1) | 8 (4.0) |
| Hypermobility | 9 (5.3) | |
| ADHD | 13 (7.7) | 15 (7.6) |
| Learning disability (modified class) | 18 (10.7) | 20 (10.1) |
| Migraine headache | 20 (11.9) | 24 (12.1) |
| Mood or anxiety disorder | 42 (25.0) | 51 (25.8) |
| Personal history (others) | | |
| Neurologic disorder | 9 (5.3) | 10 (5.1) |
| Orthopedic disorder | 6 (3.5) | 7 (3.5) |
| Other mental health disorders | 5 (3.0) | 6 (3.0) |
| Other medical disorders | 11 (6.5) | 13 (6.5) |
| Other pain disorders | 20 (11.9) | 21 (10.6) |
| Adverse outcomes | | |
| Withdrawal from treatment because of exacerbated pain | 9 (5.3) | 9 (4.6) |
| Accidental overdose of pain medications | 0 (0.0) | 0 (0.0) |
| Suicide attempt | <5 | 5 (2.5) |
| Prescription misuse (eg, diversion and early renewal) | 0 (0.0) | 0 (0.0) |
| Use of street drugs (eg, cannabis and gabapentin) | 0 (0.0) | 0 (0.0) |

ADHD, attention deficit hyperactivity disorder; CRPS, complex regional pain syndrome; IQR, interquartile range.

specialist care. Mirror therapy or graded motor imagery, as a component of physical therapy, has also been recommended.[12,19,20,33,38] It is reassuring that therapy referrals in this study most commonly included physical therapy (83.3%) and multidisciplinary pain clinics (72.6%). A small number of patients withdrew from physical treatments because of pain exacerbation (5.3%). Pain education was recommended for only 65.6% of cases. To date, there are no specific pharmacological treatments recommended for pediatric CRPS and no large scale clinical trials have been conducted.[36] Although efficacy data are limited for pediatric CRPS, standard treatments for both nociceptive and neuropathic pain (eg, tricyclic antidepressants and gabapentinoids) are commonly used to support engagement in physical therapy and target functional goals.[5,12,16,23,30] In this study, topical treatments were more common than opioids, perhaps representing a change in prescribing patterns. Topical prescribing has not been reported in past studies.[2,26] Analgesic use was similar in the Scottish surveillance study, but in that study, more than 60% of patients received pain-modulating agents.[2] Previous adult research has reported limited effect from common analgesics such as acetaminophen and ibuprofen.[6,8] In this study, analgesics (eg, acetaminophen or nonsteroidal anti-inflammatory agents) were more commonly prescribed than antiepileptic drugs or antidepressants, and graded motor imagery was not used commonly, which raises concerns as to whether clinicians are relying on ineffective treatments for children.

At the present time, there may be children who would benefit from similar multimodal treatment approaches, even if they are not formally classified as CRPS. Although the Budapest Criteria are used clinically, validation in pediatric CRPS populations is required.[25] Children may present with fewer signs and symptoms than adults and diagnosis of pediatric CRPS solely on Budapest Criteria may be inadequate.[11] Some studies suggest CRPS may be milder in children, and the diagnostic threshold should be lowered.[24] In this study, a subgroup of children, reported as cases of CRPS by healthcare providers, did not fulfill the Budapest Criteria (n = 30). Of these, 14 children had 2 or more signs, but symptoms in 3 or more categories were not confirmed. Difficulty expressing children's symptoms may have contributed to missing data along with inconsistent assessment and documentation practices. Further research is needed to determine if modification of diagnostic criteria for children and youth may be warranted (eg, 2 symptoms and 2 signs) or if a diagnostic screening tool might support clinical decision-making.[25] Some ambiguities related to the Budapest Criteria (eg, spreading) have been clarified recently, and categorization of cases as CRPS unspecified may be considered when no better explanation of features is available.[13] Diagnostic tools that support symptom reporting (child self-report and parent-proxy report) and further clarification of CRPS taxonomy (eg, recurrence, relapse, and remission) would be helpful. Systematically asking patient about symptoms at each encounter is recommended.[13] To support standardized assessment of signs and symptoms at diagnosis and follow-up visits, modification of a checklist, such as the CRPS Severity Score,[15] may prove helpful for pediatricians.

### 4.1. Limitations

The pediatric incidence rate reported may be lower than the true incidence. Furthermore, some children may experience a relapsing and remitting course and, at the time of evaluation, may

**Table 2**

**Reports of symptoms and signs.**

| | Confirmed cases (n = 168) | | | Total (n = 198) | | |
|---|---|---|---|---|---|---|
| | Present, n (%) | Absent, n (%) | Unknown/missing, n (%) | Present, n (%) | Absent, n (%) | Unknown/missing, n (%) |
| Symptom | | | | | | |
| Sensory | 167 (99.4) | | | 182 (91.9) | | |
| Hyperesthesia | 118 (70.2) | 21 (12.5) | 29 (17.3) | 139 (70.2) | 24 (12.1) | 35 (17.7) |
| Allodynia | 141 (83.9) | 14 (8.3) | 13 (7.7) | 160 (80.8) | 19 (9.6) | 19 (9.6) |
| Vasomotor | 158 (94.0) | | | 168 (84.8) | | |
| Temperature asymmetry | 114 (67.9) | 36 (21.4) | 18 (10.7) | 122 (61.6) | 47 (23.8) | 29 (14.6) |
| Skin color changes | 144 (86.2) | 18 (10.7) | 6 (3.6) | 155 (78.3) | 29 (14.6) | 14 (7.1) |
| Skin color asymmetry | 128 (76.2) | 31 (18.5) | 9 (5.4) | 139 (70.2) | 42 (21.2) | 17 (8.6) |
| Sudomotor or edema | 142 (84.5) | | | 143 (72.2) | | |
| Edema | 130 (77.4) | 33 (19.6) | 5 (3.0) | 137 (69.2) | 47 (23.7) | 14 (7.1) |
| Sweating changes | 19 (11.3) | 111 (66.1) | 38 (22.6) | 21 (10.6) | 125 (63.1) | 52 (26.2) |
| Sweating asymmetry | 15 (8.9) | 113 (67.3) | 40 (23.8) | 16 (8.1) | 127 (64.1) | 55 (27.8) |
| Motor or trophic | 151 (89.9) | | | 179 (90.4) | | |
| Decreased range of motion | 140 (83.3) | 17 (10.1) | 11 (6.5) | 158 (79.8) | 24 (12.1) | 16 (8.1) |
| Weakness | 122 (72.6) | 26 (15.5) | 20 (11.9) | 139 (70.2) | 31 (15.7) | 28 (14.1) |
| Tremor | 18 (10.7) | 126 (75.0) | 23 (14.3) | 19 (9.6) | 140 (70.7) | 39 (19.7) |
| Dystonia | 17 (10.1) | 132 (78.6) | 18 (11.3) | 18 (9.1) | 146 (73.7) | 34 (17.2) |
| Trophic change—hair, skin, or nails | 32 (19.0) | 106 (63.1) | 30 (17.9) | 35 (17.7) | 120 (60.6) | 43 (21.7) |
| Sign | | | | | | |
| Sensory | 168 (100.0) | | | 182 (91.9) | | |
| Hyperesthesia | 98 (58.3) | 23 (13.7) | 47 (28.0) | 108 (54.5) | 31 (15.7) | 59 (29.8) |
| Allodynia with light touch | 137 (81.5) | 27 (16.1) | <5 | 150 (75.8) | 34 (17.2) | 14 (7.0) |
| Allodynia with temperature | 40 (23.8) | 34 (20.2) | 94 (56.0) | 42 (21.2) | 40 (20.2) | 118 (58.6) |
| Allodynia with deep somatic pressure | 101 (60.1) | 22 (13.1) | 45 (26.8) | 108 (54.5) | 28 (14.1) | 62 (31.4) |
| Allodynia with joint movement | 135 (80.4) | 19 (11.3) | 14 (8.3) | 148 (74.7) | 25 (12.6) | 25 (12.6) |
| Vasomotor | 140 (83.3) | | | 145 (73.2) | | |
| Temperature asymmetry | 76 (45.2) | 65 (38.7) | 27 (16.1) | 82 (41.4) | 79 (39.9) | 37 (18.7) |
| Skin color changes | 112 (66.7) | 51 (30.4) | 5 (3.0) | 117 (59.1) | 69 (34.9) | 12 (6.0) |
| Skin color asymmetry | 100 (59.5) | 61 (36.3) | 7 (4.2) | 106 (53.5) | 78 (39.4) | 14 (7.1) |
| Sudomotor or edema | 96 (57.1) | | | 92 (46.5) | | |
| Edema | 85 (50.6) | 78 (46.4) | 5 (3.0) | 86 (43.4) | 98 (49.5) | 14 (7.1) |
| Sweating changes | 12 (7.1) | 135 (80.4) | 21 (12.5) | 12 (6.0) | 155 (78.3) | 31 (15.7) |
| Sweating asymmetry | 12 (7.1) | 135 (80.4) | 21 (12.5) | 13 (6.6) | 154 (77.8) | 31 (15.6) |
| Motor or trophic | 163 (97.0) | | | 176 (88.9) | | |
| Decreased range of motion | 145 (86.3) | 20 (11.9) | <5 | 158 (79.9) | 29 (14.6) | 11 (5.5) |
| Weakness | 127 (75.6) | 24 (14.3) | 17 (10.1) | 139 (70.2) | 33 (16.7) | 26 (13.1) |
| Tremor | 14 (8.3) | 138 (82.1) | 16 (9.5) | 14 (7.1) | 157 (79.3) | 27 (13.6) |
| Dystonia | 13 (7.7) | 138 (82.1) | 17 (10.1) | 14 (7.1) | 156 (78.8) | 28 (13.1) |
| Trophic change—hair, skin, or nails | 33 (19.6) | 121 (72.0) | 14 (8.3) | 34 (17.2) | 140 (70.7) | 24 (12.1) |

not have met diagnostic criteria.[13] As this is a clinical surveillance program, we relied on clinician reports of symptoms and signs. Two studies reported good agreement (51%-96% agreement) between physician examination and objective measures.[28,31] The usual limits of retrospective chart review apply; when responses were reported as "unknown," it is not known if these items were not assessed or not recorded in the medical chart; some of these cases may have fulfilled criteria, but we excluded cases from the incidence calculation when symptoms and signs criteria were absent or unknown. Canadian Paediatric Surveillance Program strives to optimize the response rate by sending regular reminders to participants. Owing to the voluntary nature of the surveillance program, cases may have been missed. Furthermore, other professions who diagnose CRPS would not be captured unless they referred to a pediatrician or pediatric pain clinic (eg, physical therapists, family physicians, and nonpediatric specialists such as orthopedic surgeons), as well as regions of Canada without access to pediatric specialist care or pediatric pain clinics. Clinical characteristics such as disease severity, time to diagnosis, treatments, and medication use may differ among these patients. We asked clinicians to categorize pain subjectively because the variable use of pain intensity scales was expected. We are also unable to determine if some cases had discrete peripheral nerve damage to suggest CRPS type II. Electrodiagnostic testing was uncommon, and the number of cases with results available did not meet our threshold for minimum aggregate reporting. Although CRPS type II was typically classed as neuropathic pain previously,[10] a recent consensus article states it should not be.[13] The clinical relevance of this subgrouping remains unclear.[13] Finally, a change in Quebec legislation midway through the study limited case reporting by primary pediatricians and subspecialist practicing outside of tertiary care.[7] Because collaborating sites in academic centers had project-specific ethics approval, this change did not affect reporting from collaborating pediatric pain clinics in Quebec.

## 5. Conclusions

We report a minimum CRPS incidence rate of 1.14 per 100,000 person-years in Canadian children aged 2 to 18 years, with rising

**Table 3**

**Health utilization and treatments since onset of symptoms.**

| | Confirmed cases (N = 168) | Total (N = 198) |
|---|---|---|
| Health visits (more than one possible) | | |
| Psychiatric admission | 0 (0) | <5 |
| Pediatric or hospital admission | 19 (11.3) | 23 (11.6) |
| Transfer to tertiary care | 39 (23.2) | 46 (23.2) |
| Emergency department | 102 (60.7) | 117 (59.1) |
| Blood work received | | |
| Complete blood count | | |
| Yes or ordered | 57 (33.9) | 67 (34.0) |
| Unknown | 26 (15.5) | 31 (15.7) |
| No | 85 (50.6) | 99 (50.3) |
| CRP | | |
| Yes or ordered | 53 (31.5) | 61 (31.0) |
| Unknown | 29 (17.3) | 34 (17.2) |
| No | 86 (51.2) | 102 (51.8) |
| ESR | | |
| Yes or ordered | 38 (22.6) | 46 (23.4) |
| Unknown | 30 (17.9) | 35 (17.8) |
| No | 100 (59.5) | 116 (58.9) |
| Special investigations patients received for this problem (more than one possible)* | | |
| CT of the brain | <5 | <5 |
| MRI of the brain | 12 (7.1) | 13 (6.6) |
| CT of the limb | 13 (7.7) | 17 (8.6) |
| Nerve conduction studies | 15 (8.9) | 18 (9.1) |
| Bone scan | 35 (20.8) | 36 (18.2) |
| Ultrasound | 35 (20.8) | 42 (21.2) |
| MRI of the limb | 86 (51.2) | 98 (48.5) |
| Radiographs | 140 (83.3) | 163 (82.3) |
| Number of specialist referrals for this problem | | |
| 1 | 13 (7.7) | 16 (8.1) |
| 2 | 21 (12.5) | 27 (13.6) |
| 3 | 43 (25.6) | 49 (24.7) |
| 4 | 49 (29.2) | 55 (27.8) |
| 5 | 22 (13.1) | 29 (14.6) |
| ≥6 | 20 (11.9) | 22 (11.1) |
| Specialist referrals for this problem (more than one possible)* | | |
| Psychiatry | <5 | <5 |
| Counselor (social work or school counselor) | <5 | 5 (2.5) |
| Others or unspecified | <5 | < 5 |
| Intensive pain rehab program | <5 | < 5 |
| Sports medicine or general practitioner with specialization | 7 (4.2) | 7 (3.5) |
| Surgical specialist (plastic surgeon, surgeon, neurosurgeon, or neurovascular) | 10 (5.9) | 12 (6.0) |
| Interventional anaesthesiologist or anesthesiologist | <5 | <5 |
| Internal medicine subspecialist (rheumatologist, neurologist, dermatologist, or bone specialist) | <5 | <5 |
| Physiatry or rehabilitation medicine | 21 (12.5) | 22 (11.1) |
| Occupational therapist | 21 (13.2) | 26 (13.1) |
| Pediatric neurology | 22 (13.1) | 30 (15.2) |
| Orthopedics | 27 (16.1) | 31 (15.7) |
| Pediatric rheumatology | 42 (25.3) | 53 (26.8) |
| General pediatrician | 54 (32.1) | 66 (33.3) |
| Psychologist | 59 (35.7) | 66 (33.3) |
| Pediatric orthopedics | 60 (36.3) | 68 (34.3) |
| Multidisciplinary pain clinic, transition clinic, or somatic rehabilitation clinic | 122 (72.6) | 137 (69.2) |
| Physical therapist | 140 (83.3) | 165 (83.3) |
| Pain medications and adjuvants (more than one possible)* | | |
| SNRIs | 5 (2.9) | 6 (3.0) |
| Sodium channel agents | 5 (2.9) | 6 (3.0) |
| Bisphosphonates | 5 (2.9) | 5 (2.5) |
| Medical cannabis | 5 (2.9) | 6 (3.0) |
| Ketamine infusion | 6 (3.6) | 6 (3.0) |
| Regional block | 8 (4.7) | 9 (4.5) |
| SSRIs | 9 (5.3) | 9 (4.5) |
| Tramadol | 14 (7.7) | 15 (7.6) |

(*continued on next page*)

Table 3 (*continued*)

| | Confirmed cases (N = 168) | Total (N = 198) |
|---|---|---|
| Other opioids | 20 (11.9) | 25 (12.6) |
| Compounded topical | 20 (11.9) | 30 (15.1) |
| Tricyclic antidepressants | 35 (20.8) | 41 (21.2) |
| Topicals | 39 (22.2) | 46 (23.2) |
| Gabapentinoids | 88 (52.3) | 96 (48.4) |
| Acetaminophen | 111 (66.0) | 133 (67.1) |
| Nonsteroidal anti-inflammatories | 139 (82.7) | 164 (82.8) |
| Complementary medicine seen or advised for this problem (more than one possible)* | | |
| Naturopath or reflexologist | 5 (2.9) | 5 (2.5) |
| Acupuncture | 12 (7.1) | 12 (6.1) |
| Massage therapist | 13 (7.7) | 15 (7.6) |
| Chiropractor | 23 (13.7) | 26 (13.1) |
| Exercise therapist | 28 (17.8) | 30 (15.1) |
| Treatments initiated for this problem (more than one possible)* | | |
| Botox injections | <5 | <5 |
| Yoga | <5 | <5 |
| TENS | 25 (14.8) | 28 (14.1) |
| Pool hydrotherapy | 34 (20.3) | 37 (18.7) |
| Bracing or AFO or boot; cast | 57 (33.9) | 58 (29.2) |
| Orthotic or shoe inserts | 15 (8.9) | 18 (9.0) |
| Graded motor imagery | 65 (28.7) | 71 (35.8) |
| Psychological strategies | 88 (62.4) | 99 (50.0) |
| Fitness exercise | 91 (54.1) | 107 (54.0) |
| Desensitization | 100 (59.5) | 109 (55.0) |
| Pain education | 110 (65.6) | 125 (63.1) |
| Nutritional supplements initiated for this problem (more than one possible)* | | |
| Vitamin C | 37 (22.0) | 40 (20.2) |
| Omega 3 | 7 (4.2) | 9 (4.5) |
| Magnesium | 11 (6.5) | 12 (6.0) |
| Others | 5 (2.9) | 5 (2.5) |

* Affirmative responses included "yes" and "ordered."

AFO, ankle foot orthosis; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; CT, computed tomography; MRI, magnetic resonance imaging; SNRI, serotonin–norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitors; TENS, transcutaneous electrical nerve stimulation.

incidence after age 12 years. Most cases were female, had lower limb involvement, single site involvement, and trauma or injury as an inciting event. This 2-year surveillance study provides foundational data to describe pathways of referral for children with CRPS, their clinical presentation, and the diagnostic interventions and treatments used by Canadian pediatricians and pain specialists. Variability in reporting may represent geographic variation in referral patterns or underrecognition of CRPS. Asking systematically about CRPS symptoms may improve pediatric diagnostic yield with the Budapest Criteria. Treatment variability exists highlighting the need for empiric data to inform treatment of pediatric CRPS. Further research is needed to determine if modification of diagnostic criteria or a screening tool would improve identification of pediatric CRPS. Longitudinal studies are required to better understand the natural history of pediatric CRPS.

**Table 4**

**Incidence rate (per 100,000 person-years) of complex regional pain syndrome by sex and age groups (N = 157).**

| | Incidence | Lower 95% CI | Upper 95% CI |
|---|---|---|---|
| All ages | | | |
| All | 1.14 | 0.93 | 1.35 |
| Males | 0.39 | 0.26 | 0.51 |
| Females | 1.93 | 1.65 | 2.19 |
| <12 years old | | | |
| All | 0.73 | 0.56 | 0.89 |
| Males | 0.20 | 0.14 | 0.28 |
| Females | 1.28 | 1.06 | 1.5 |
| ≥12 years old | | | |
| All | 1.88 | 1.61 | 2.15 |
| Males | 0.73 | 0.56 | 0.89 |
| Females | 3.10 | 2.76 | 3.44 |

CI, confidence interval.

## Conflict of interest statement

K. Baerg reports royalties from Brush Education and serves on the Board of Directors, Saskatchewan Pain Society Inc., outside the submitted work. S. M. Tupper serves as the Chair, Board of Directors, Saskatchewan Pain Society Inc., outside the submitted work. L. M. Chu reports he is a paid employee in the Department of Pediatrics, related to the submitted work. N. Cooke has nothing to disclose. B. D. Dick has nothing to disclose. M.-J. Doré-Bergeron has nothing to disclose. S. Findlay serves as Co-Chair, Ontario Chronic Pain Network, outside the submitted work. P. M. Ingelmo has nothing to disclose. C. Lamontagne has nothing to disclose. G. Mesaroli reports funding from RESTRACOMP Clinician Scientist Training Program and Frederick Banting and Charles Best Canada Graduate Scholarship (CGS-M) from the Canadian Institutes of Health Research (CIHR), outside the submitted work. T. F. Oberlander has nothing to disclose. R. Poolacherla has nothing to disclose. A. O. Spencer has nothing to disclose. J. Stinson has nothing to disclose. G. A. Finley serves on the Executive Board, Canadian Pain Society, outside the submitted work.

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