Pain among children and adults living with arthrogryposis multiplex congenita: A scoping review

Alexa Cirillo | Jessica Collins | Bonita Sawatzky | Reggie Hamdy | Noémi Dahan-Oliel

Shriners Hospital for Children-Canada, Montreal, Canada
School of Physical and Occupational Therapy, Faculty of Medicine, McGill University, Montreal, Canada
University of British Columbia, Department of Orthopedics, Vancouver, Canada
Department of Orthopedics, Faculty of Medicine, McGill University, Montreal, Canada

Correspondence
Noémi Dahan-Oliel, Clinical Research Department, Shriners Hospital for Children-Canada, 1003 Décarie Boulevard, Montreal, QC H4A 0A9, Canada.
Email: ndahan@shrinenet.org

Abstract
Clinical interventions and research have mostly focused on the orthopedic and genetic outcomes of individuals with arthrogryposis multiplex congenita (AMC), and although pain has gained recognition as an important issue experienced by individuals with AMC, it has received little attention within the AMC literature. The aims of this scoping review were to describe the pain experiences of children and adults with AMC, to identify pain assessment tools and management techniques, and document the impact of pain on participation in everyday activities among children and adults with AMC. A search of the literature was conducted in four search engines and identified a total of 89 articles. Once study eligibility was reviewed, 21 studies met the selection criteria and were included in this review. Pain appears to be more commonly experienced in adults with AMC compared with children with AMC, with individuals having undergone multiple corrective procedures self-reporting pain more often. In adult populations, musculoskeletal chronic pain is a significant problem, resulting in restrictions in activities of daily living, mobility, and participation. Researchers and clinicians must agree on the use of validated measures appropriate for evaluating pain in AMC and the use of appropriate pain management techniques to relieve pain. Pediatric studies should focus on determining how commonly pain is experienced in infants, children, and adolescents with AMC. Pain in adults with AMC should be acknowledged to offer proper client-centered interventions throughout the lifespan.

KEYWORDS
adult, arthrogryposis multiplex congenita, child, pain, participation

INTRODUCTION
Arthrogryposis multiplex congenita (AMC) is a term used to describe multiple joint contractures that can affect the upper limbs, lower limbs, jaw, and/or spine (Hall, 2014). Typically, contractures in AMC are non-progressive but are severe enough to limit independence in mobility and daily life activities, especially in the areas of upper extremity function, transfers, mobility, and physical activity (Amor, Spaeth, Chafey, & Gogola, 2011; Dillon, Bjornson, Jaffe, Hall, & Song, 2009; Ho & Karol, 2008; Spencer, Bowen, Caputo, Green, & Lawrence, 2010). Individuals with AMC may also have impairments in other systems, including gastro-intestinal, genito-urinary and central nervous systems (Bernstein, 2002), abnormally slender and fragile long bones, and oral anomalies, such as, limited jaw mobility and muscle weakness, and periodontal disease (Alves, Zhao, Patel, & Bolognese, 2007; Brei, 2007; Mielenik-Blaszczak & Borowska, 2002; Steinberg, Nelson, Feinberg, &
Calhoun, 1996). Treatment typically involves early intensive and continuous rehabilitation including bracing, splinting, range of motion exercises, and surgeries, which may improve contractures, provide the potential for functional ambulation and promote daily activities (Bernstein, 2002; Sells, Jaffe, & Hall, 1996; Södergård, Hakamies-Blomqvist, Sainio, Ryöppö, & Vuorinen, 1997).

Youth and adults living with AMC, their caregivers, and clinicians have identified “gaining more knowledge on reasons for pain in AMC and its management” as a main research priority, during a knowledge exchange day held in December 2016 at the Shriners Hospitals for Children, Montreal, Canada (Dahan-Ojie et al., 2018). Pain was also reported by youth as an intrinsic factor to living with AMC that limited walking endurance (Elfassy et al., 2019). Due to AMC’s multiple different etiologies, pain experienced in AMC is speculated to be nociceptive (both musculoskeletal and visceral) and/or neuropathic (Jones, Miller, Street, & Sawatzky, 2018; Nouraei, Sawatzky, MacGillivray, & Hall, 2017). Individuals with AMC may also present with neuropathic pain due to a potential neuropathic component in AMC affecting the brain, spinal cord, and peripheral nerves (Behm & Kearns, 2001). Children and adults with AMC will often require multiple corrective surgeries over the lifespan (Eamsobhana, Kaewponsawan, & Vanitcharoenkul, 2014; Sawatzky, Jones, Miller, & Nouraei, 2019). As chronic postsurgical pain is a common adverse consequence of undergoing multiple corrective procedures, individuals with AMC are at considerable risk of developing chronic postsurgical pain (Bruce & Quinlan, 2011; Searle & Simpson, 2009). Individuals with AMC can develop arthritic symptoms of pain due to secondary degeneration of abnormal joints (Fisher & Fisher, 2014). Stiffness due to reduced joint mobility may also be responsible for pain in AMC.

The Internal Association for the Study of Pain defines pain as an “unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” (Loeser & Treede, 2008). The World Health Organization further elaborates on this definition, defining pain as a “multidimensional phenomenon with sensory, physiological, cognitive, affective, behavioral, and spiritual components” (2012). Chronic pain, which is pain that recurs and persists beyond normal periods of healing (Melzack & Casey, 1968) has been reported to have major impacts on the daily functioning of children and adults with musculoskeletal conditions. Children and adolescents with osteogenesis imperfecta (OI) experience complex and mild pain, leading to lower levels of quality of life (QoL) (Tsimicas et al., 2018). Pain in OI has been further identified as a long-term symptom that persists into adulthood, causing significant restrictions in ADLs throughout the lifespan (Nghiem et al., 2018). In children with spina bifida, pain was often reported, yet remained frequently unmanaged, leading to poorer QoL (Clancy, McGrath, & Oddson, 2005; Oddson, Clancy, & McGrath, 2006). Because of pain, children with cerebral palsy also experienced decreased participation in school, daily activities, and family life (Houlihan, O’Donnell, Conway, & Stevenson, 2004).

As pain may likely develop in individuals with AMC, pain can also negatively impact the QoL of these individuals. Therefore, adequate pain assessment and management by health-care professionals and AMC caregivers is crucial to minimize the negative impacts of pain on both children and adults living with AMC. However, until improved knowledge of pain experiences of individuals with AMC is obtained, health-care professionals will be unable to identify appropriate pain assessment tools and provide effective pain management for this population. Thus, this scoping review was conducted to explore what is known about pain among children and adults with AMC. Specific aims include describing the pain experiences of children and adults with AMC, to identify pain assessment tools and management techniques, and document the impact of pain on participation among children and adults with AMC.

2 | MATERIALS AND METHODS

Scoping reviews are designed to collect, evaluate, and present a comprehensive map of existing evidence on a chosen research topic (Thomas, Lubarsky, Durning, & Young, 2017). A scoping review was thus chosen as our methodological approach using the methodological framework for scoping reviews (Arksey & O’Malley, 2005; Levac, Colquhoun, & O’Brien, 2010).

2.1 | Search strategy and selection criteria

A search of the electronic databases Medline (1996 to 2018), CINAHL (1990 to 2018), PsycINFO (1987 to 2018), and the Cochrane Library was conducted in December 2018. The search included a combination of terms, related to AMC: “arthrogryposis,” “amyoplasia,” “multiple congenital contractures” and pain: “pain,” “pain management,” “pain management techniques,” “pain measurement,” “pain evaluation,” and “pain assessment.” The search was developed for Medline and was then adapted for the other search engines. Pain keyword terms did not differentiate between types of pain such as “chronic pain,” “acute pain,” or “bodily pain” because the main objective of the scoping review was to explore the general pain experiences of children and adults with AMC. Additional relevant articles were identified through Google Scholar and hand-searching of reference lists from included studies. Authors were contacted when full-text articles were not available through the McGill University Library and its online interlibrary loan system (ILL). Results from the searches were exported into EndNote and duplicates were removed. Two independent reviewers (A.C. and J.C.) applied the selection criteria for titles and abstracts, and then full-texts according to the inclusion criteria. No restrictions were placed on: (a) study design, (b) date of publication, (c) sample size, or (d) country origin of publication. Refer to Table 1 for the selection criteria. The Rayyan software (Ouzzani, Hammady, Fedorowicz, & Elmagarmid, 2016) was used for screening of articles. If agreement was not reached between the two reviewers, conflicts were resolved through discussion with a third reviewer (N.D.-O.), until consensus was achieved.
2.2 | Data extraction and synthesis

A data extraction form was created to identify study characteristics and key findings of included studies. Two reviewers independently piloted the data extraction form on seven studies at random to ensure consistency in data extraction. Data extraction samples were compared between two reviewers (A.C. and J.C.) and any discrepancies were resolved by discussion with a third reviewer (N.D.-O.). Data from included studies was then extracted by a single reviewer (A.C.) and the completed data extraction form was then reviewed by another team member (J.C.). Levels of evidence were reported as indicated in the study; however, if studies did not provide a level of evidence, a reviewer (A.C.) assigned the level of evidence using the Levels of Evidence for Primary Research guidelines by the Center for Evidence-based Medicine (Wright, Swiontkowski, & Heckman, 2003). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flowchart was used to verify that all aspects of the scoping review were considered (Moher, Liberati, Tetzlaff, Altman, & Prisma Group, 2009).

### TABLE 1 Selection criteria

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population: age</td>
<td>Any age</td>
</tr>
<tr>
<td>Population: diagnosis</td>
<td>Any type of AMC</td>
</tr>
<tr>
<td>Study design</td>
<td>Any study design</td>
</tr>
<tr>
<td>Language</td>
<td>English or French or provide English/French translation</td>
</tr>
<tr>
<td>Pain</td>
<td>Describes pain; assesses pain using specific tool, including the use of validated or nonvalidated tools or outcome measures, interviews, and questionnaires; discusses pain management. Does not describe pain, or measure pain, or provide pain management information</td>
</tr>
<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Studies that did not provide English or French translation</td>
</tr>
<tr>
<td></td>
<td>Does not describe pain, measure pain, or provide pain management techniques</td>
</tr>
</tbody>
</table>

3 | RESULTS

3.1 | Search strategy and study selection

The search yielded 89 articles. After duplicates were removed, a total of 79 abstracts were reviewed for study eligibility. Forty-two articles were excluded at screening of titles and abstracts. Remaining full-text articles were assessed for eligibility, resulting in the exclusion of 16 articles. A total of 21 studies were included in the scoping review. Refer to Figure 1 for PRISMA flowchart.

3.2 | Study characteristics and levels of evidence

Included studies were published between 1999 and 2018 across 12 different countries, with seven studies published in the United States. Six studies were published in journals relating to pediatric orthopedics and one article was published in an online newsletter for an AMC support group. Most studies were case reports/case series with a low level of evidence (level IV), followed by prospective (n = 5), cross-sectional (n = 3), and retrospective studies (n = 3) (level II). There were two expert opinion/review papers and one mixed-methods study. The main limitations of the included studies included small sample sizes, lack of standardized assessment tools, and low follow-up rates in prospective cohort studies.

3.3 | Sample characteristics

Total number of participants from the 21 studies represented 654 participants (range: 1–177 participants) from infancy to older adulthood. Mean and age range were not calculated as age of participants was not provided in four studies. Nine studies included pediatric populations (Azbell & Dannemiller, 2015; Behn & Kearns, 2001; Canavese & Sussman, 2009; Cassis & Capdevila, 2000; Chotigavanichaya,
Ariyawatkul, Eamsohmana, & Kaewpornsawan, 2015; Matar, Beirne, & Garg, 2016; Savenkov, Pajard, Agranovich, & Zabolotskiy, 2017; Segev, Ezra, Yaniv, Wientroub, & Hemo, 2008; Spencer et al., 2010), and nine studies included only adult populations (Dai et al., 2018; Dalton, Magill, & Mulhall, 2015; de Andrade, Hotta, Mazzetto, de Felicio, & Bataglione, 2000; Fisher & Fisher, 2014; Hartley, Baker, & Whittaker, 2013; Jones et al., 2018; Nouraei et al., 2017; Riemer & Steen, 2013; Sneddon, 1999). Two studies included both pediatric and adult populations (Kimber, Tajsharghi, Kroksmark, Oldfors, & Tulinius, 2012; Sneddon, 1999). Two studies included both pediatric and adult populations (Kimber, Tajsharghi, Kroksmark, Oldfors, & Tulinius, 2012; Nicomedez, Li, & Leong, 2003), and one study did not specify age of participants (Yau, Chow, Li, & Leong, 2002). Fourteen of the 21 studies reported participants having AMC; the remaining seven studies reported nongenetic arthrogryposis, distal arthrogryposis, amyoplasia congenita, classic AMC, and nonsyndromic arthrogryposis. Refer to Table 2 for full list of study and sample characteristics.

3.4 | Pain assessment tools

Nine of the 21 studies used one or more tools or outcome measures to assess pain (Azbell & Dannemiller, 2015; Behm & Kearns, 2001; Chotigavanichaya et al., 2015; Dalton et al., 2015; Jones et al., 2018; Nicomedez et al., 2003; Nouraei et al., 2017; Segev et al., 2008; Spencer et al., 2010). Twelve tools were used to assess pain in AMC, including one the Oswetry Disability Index (ODI), which was validated for use in adults with AMC by Jones et al. (2018). Six out of the 12 tools were designed to measure pain, such as the Modified Neonatal or Infant Pain Scale (Behm & Kearns, 2001), the Face, Legs, Activity, Cry and Consolability scale (FLACC) (Azbell & Dannemiller, 2015), and the Brief Pain Inventory (BPI) (Jones et al., 2018). The remaining six tools were primarily developed to measure another construct but included item(s) on pain, such as the Pediatric Outcomes Data Collection Instrument (PODCI) used in the study by Spencer and colleagues (Spencer et al., 2010). Two studies assessed some components of pain within a larger study using an online questionnaire (Hartley et al., 2013; Sneddon, 1999). Three studies assessed pain as a dichotomous variable (e.g., presence or absence of pain after surgery) (Cassisi & Capdevila, 2000; Matar et al., 2016; Riemer & Steen, 2013). Presence of pain was also assessed using informal semi-structured interviews conducted by physicians and psychologists in adults with AMC (Dai et al., 2018). Five studies assessed pain as a clinical finding but did not specify the pain assessment method used (Cavanese; de Andrade et al., 2000; Fisher & Fisher, 2014; Kimber et al., 2012; Sevenkov). Refer to Table 3 for a description of the pain assessment tools used in the included studies.

3.5 | Pain description in children with AMC

Two studies described factors that produced significant pain in an infant with AMC such as slight movements, including small flexion and extension of the wrist (Behm & Kearns, 2001), being placed on the stomach, and the application and removal of splints (Azbell & Dannemiller, 2015). Kimber et al. (2012) reported that generalized muscle pain was less commonly reported in younger individuals with AMC compared with older individuals, and when pain was experienced in children, it was mostly attributed to the result of repeated surgical interventions, specifically in the feet. Two studies reported that pain was not a significant problem presenting in children with AMC (Canavese & Sussman, 2009; Spencer et al., 2010). In 30 patients aged 5 to 18 years, PODCI normative scores were normal in the pain and comfort domain (Spencer et al., 2010). In children with AMC presenting with unilateral hip dislocation, pain was reported as not being an issue since dislocation was present at birth (Canavese & Sussman, 2009).

3.6 | Pain description in adults with AMC

Of the 11 studies that reported pain in adults with AMC, a few provided a detailed description on such aspects as location and severity of pain. High incidence of self-reported pain was found in two studies as reported by 75% (n = 137) of participants as pain being a significant problem, (Nouraei et al., 2017), and 91% (n = 39) of participants complaining of regular pain (Dai et al., 2018). In another study, 85% of participants (82/96) reported having experienced pain in the last month, and 63 of these (83%) stated that their pain was related to AMC (Hartley et al., 2013). A follow-up study on 15 individuals with AMC (age not specified) reported no pain or occasional hip pain at a mean follow-up of 20 years (Yau et al., 2002) and a case-report of a 98-year old woman with amyoplasia reported musculoskeletal pain decreasing during aging with sporadic complaints of intense lower back pain (Riemer & Steen, 2013). Single studies reported on pain duration, pain severity, and pain frequency (Fisher & Fisher, 2014; Hartley et al., 2013; Jones et al., 2018). Hartley et al. (2013) reported 15 individuals experienced pain all the time, while 29 had pain on most days.

Pain locations mentioned in the included studies included the hips, knees, ankle/ft, hands/arms, jaw, neck, back, and spine. Four studies identified that pain was most predominantly located in the lower extremities (e.g., primarily knee and ankles) and the trunk (spine area), and less often in the upper limbs (e.g., shoulder, elbows, and hands) (Dai et al., 2018; Jones et al., 2018; Nouraei et al., 2017; Sneddon, 1999). In a study investigating the clinical findings of 39 patients with AMC, pain in hands was also rarely reported (Kimber et al., 2012). Pain onset, referring to age at which individuals with AMC first developed pain, was mentioned in three studies (Dai et al., 2018; Riemer & Steen, 2013; Sneddon, 1999) and was reported as being present since childhood (Dai et al., 2018) and adolescence (Riemer & Steen, 2013; Sneddon, 1999).

In addition, four studies identified factors associated with increased pain in 86 adults with AMC (Dai et al., 2018; Fisher & Fisher, 2014; Kimber et al., 2012; Sneddon, 1999), including undergoing multiple orthopedic procedures (Kimber et al., 2012) and previous surgeries (Sneddon, 1999). Pain was also more frequent in patients with more severe joint contractures (Kimber et al., 2012). Weight bearing (Fisher & Fisher, 2014), exercising (Dai et al., 2018), activities requiring exertion (Kimber et al., 2012), as well as nighttime (Fisher & Fisher, 2014) were factors cited that increased pain among adults.
<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Study purpose</th>
<th>Sample size, age</th>
<th>Type of AMC</th>
<th>Measure used for pain</th>
<th>Frequency and timing of pain measurement</th>
<th>Pain experience (description of pain scores/results on the pain measure)</th>
<th>Pain management/main intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azbell &amp; Dannemiller, 2015</td>
<td>Single case study</td>
<td>To document limitations of body structures and function, activity, and participation for an infant with AMC; to report frequency and timing of PT/OT; to evaluate the child’s outcome with respect to participation, activity, and impairments of body structures and functions</td>
<td>N = 1, range: 11 days–9 months</td>
<td>Amyoplasia</td>
<td>FLACC pain scale</td>
<td>Conducted during passive ROM and 5 mins after passive ROM at: 11 days, 3 months and 9 months of age</td>
<td>At 11 days of age: severe pain/discomfort (score = 10) during passive ROM, decreased to mild/discomfort pain (score = 1) 4–5 min after ROM. At 9 months of age: mild pain/discomfort (score = 1) during passive ROM, no pain (score = 0) 4–5 min after ROM</td>
<td>Home exercise program for remediation and compensation, alternating OT/PT (stretching, splints activity modification)</td>
</tr>
<tr>
<td>Behm &amp; Kearns, 2001</td>
<td>Single case study</td>
<td>To report case of neonate with amyoplasia congenita who was successfully and safely treated with GBP to relieve pain; to assess potential efficacy of GBP</td>
<td>N = 1, 3 weeks</td>
<td>Amyoplasia congenita</td>
<td>Modified infant pain scale</td>
<td>Periodically over the 200 hr hospitalization period</td>
<td>At Day 2 of life, with acetaminophen only, resulted in no pain (score = 0.6) with PT. At Day 5 of life and at time of discharge, with GBP 10 mg/kg, resulted in no pain (score = 0) pain score, calmer mood, and able to tolerate increased PT. Infant could be swaddled, undergo diaper change, and play with mother with no pain</td>
<td>GBP treatment, gradually increased before discharged</td>
</tr>
<tr>
<td>Canavese &amp; Sussman, 2009</td>
<td>Review paper/expert opinion</td>
<td>To provide overview of current strategies of hip management in neuromuscular disorders (Duchenne muscular dystrophy, spinal muscular dystrophy, Charcot–Marie–Tooth disease and AMC)</td>
<td>N = not specified, children (not specified)</td>
<td>Neuromuscular disorders (including AMC)</td>
<td>Presence of pain Not specified</td>
<td>Hip pain is not usually an issue since unilateral hip dislocation is usually present at birth, minimal or no pain and the long-term functional results were comparable among patients with hip contractures and hip subluxation or dislocation</td>
<td>No intervention directly or indirectly aimed at reducing pain</td>
<td></td>
</tr>
</tbody>
</table>

(Continues)
<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Study purpose</th>
<th>Sample size, age</th>
<th>Type of AMC</th>
<th>Measure used for pain</th>
<th>Frequency and timing of pain measurement</th>
<th>Pain experience (description of pain scores/results on the pain measure)</th>
<th>Pain management/main intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cassis &amp; Capdevila, 2000</td>
<td>Retrospective chart review</td>
<td>To review results of 101 talectomies in 56 patients with arthrogrypotic clubfeet; to evaluate long-term results of talectomy in arthrogrypotic severe rigid clubfeet</td>
<td>N = 56, range: 10 months-9.6 years</td>
<td>AMC</td>
<td>Results were classified by positioning, function/pain, and satisfaction. For function/pain, results were “good” if patients were able to wear shoes and were satisfied.</td>
<td>Once, post op</td>
<td>65 good results; 36 poor results; results were compared according to age (good results for 63% &lt; 4 years, and 66% &gt; 4 years), having an Achilles tendon tenotomy (good results with tenotomy 81%, and 60% for those who did not), cast for &gt; 8 weeks (good results for 69% for cast &gt; 8 weeks, 36% &lt; 8 weeks)</td>
<td>Surgeries for clubfeet: talectomy, salvage procedure talectomy, Achilles tendon tenotomy</td>
</tr>
<tr>
<td>Chotigavanichaya et al., 2015</td>
<td>Retrospective chart review</td>
<td>To evaluate results of primary talectomy in infants and toddlers; to evaluate functional results of talectomy in clubfeet</td>
<td>N = 10, 0.5 days-3</td>
<td>Classic and distal AMC</td>
<td>VRS</td>
<td>Once, at last follow up</td>
<td>VRS at last F/U; 0 all patients had plantigrade foot without pain. No baseline score provided</td>
<td></td>
</tr>
<tr>
<td>Dai et al., 2018</td>
<td>Retrospective chart review</td>
<td>To understand the disability of adults with AMC; to describes disability patterns of a cohort of adults with AMC by genotype</td>
<td>N = 43, range 20–46</td>
<td>AMC</td>
<td>Presence of pain at data collection</td>
<td>Overall, 39 participants complained of pain (91%); pain was chronic (sometimes since childhood); Overall, pain was identified as a less visible disorder that could severely restrict participation</td>
<td>No intervention directly or indirectly aimed at reducing pain</td>
<td></td>
</tr>
</tbody>
</table>

(Continues)
<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Study purpose</th>
<th>Sample size, age</th>
<th>Type of AMC</th>
<th>Measure used for pain</th>
<th>Frequency and timing of pain measurement</th>
<th>Pain experience (description of pain scores/results on the pain measure)</th>
<th>Pain management/main intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalton et al., 2015</td>
<td>Single case study</td>
<td>To present case of patient with AMC who underwent bilateral THR; to discuss considerations for perioperative period and outcomes; to understand limitations and risks associated with THR in AMC</td>
<td>N = 1, 56 years</td>
<td>AMC</td>
<td>HHS</td>
<td>Twice, pre and post-op</td>
<td>Patient pain-free post-op (no specific pain score provided)</td>
<td>Bilateral THR</td>
</tr>
<tr>
<td>de Andrade et al., 2000</td>
<td>Single case study</td>
<td>To describe case of AMC and concomitant bruxism with limited mouth opening and pain in TMJ; to describe use of splint and PT to improve muscular and joint conditions and to reduce pain</td>
<td>N = 1, adult (not specified)</td>
<td>AMC</td>
<td>Not specified</td>
<td>Not specified</td>
<td>No descriptor of pain</td>
<td>Myorelaxing interocclusal splint; PT following splint (e.g., active stretching and reflex relaxation); later on, increased thickness of splint on right side (dental and PT specific to areas)</td>
</tr>
<tr>
<td>Fisher &amp; Fisher, 2014</td>
<td>Single case study</td>
<td>To discuss the intraoperative difficulties and techniques of one patient who underwent bilateral total hip and total knee arthroplasties, and the potential indications for joint arthroplasty in this challenging group of patients</td>
<td>N = 1, 38 years</td>
<td>AMC</td>
<td>Presence of pain</td>
<td>Not specified</td>
<td>Right hip pain resolved after procedure. Patient pleased with relief of pain suffered prior to hip and knee reconstruction</td>
<td>Bilateral total hip and knee arthroplasty</td>
</tr>
<tr>
<td>Hartley et al., 2013</td>
<td>Cross-sectional study</td>
<td>To explore views and opinions of adults with AMC about their lives</td>
<td>N = 96, range 18–38</td>
<td>AMC</td>
<td>Authors developed questionnaire which included: frequency, intensity, location and</td>
<td>Once, at data collection</td>
<td>82/95 experienced pain over the last month; 68/95 stated pain was related to their AMC; 15/95 had pain all the time; 29/95 had pain on most days; 48/95 pain</td>
<td>No intervention directly or indirectly aimed at reducing pain</td>
</tr>
</tbody>
</table>

(Continues)
<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>Study purpose</th>
<th>Sample size, age</th>
<th>Type of AMC</th>
<th>Measure used for pain</th>
<th>Frequency and timing of pain measurement</th>
<th>Pain experience (description of pain scores/results on the pain measure)</th>
<th>Pain management/main intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jones et al., 2018</td>
<td>Cross-sectional study</td>
<td>To validate the ODI as a pain and disability outcome measure in the AMC population. To investigate the nature, location, frequency, intensity and impact of pain and disability in AMC</td>
<td>N = 50, range 21–85</td>
<td>AMC</td>
<td>ODI, SF-36, SF-MPQ-2, Short form BPI, EQ-5D</td>
<td>Once, at data collection</td>
<td>SF-36: Inverse association between frequency of continuous pain and severity; not seen in with neuropathic, intermittent or affective pain. ODI: 70.5% identified their pain related impairments as ≤40% (minimal and moderate disability categories). BPI: ≤5/40 (severe pain). EQ-5D: mobility and self-care most impaired, with less severe/disabling score for pain and anxiety/depression.</td>
<td>No intervention directly or indirectly aimed at reducing pain</td>
</tr>
<tr>
<td>Kimber et al., 2012</td>
<td>Cross sectional study</td>
<td>To describe clinical and molecular genetic findings in individuals with DA, to evaluate genotype–phenotype correlation; to classify individuals with DA into different DA syndromes</td>
<td>N = 39, range: 9 months –65 years</td>
<td>Distal arthrogryposis</td>
<td>Presence of pain</td>
<td>Once, at data collection</td>
<td>Pain more frequent in patients with more severe joint contractures and in patients who underwent multiple orthopedic surgeries; muscle fatigue and pain on exertion reported</td>
<td>No intervention directly or indirectly aimed at reducing pain</td>
</tr>
<tr>
<td>Study</td>
<td>Study design</td>
<td>Study purpose</td>
<td>Sample size, age</td>
<td>Type of AMC</td>
<td>Measure used for pain</td>
<td>Frequency and timing of pain measurement</td>
<td>Pain experience (description of pain scores/results on the pain measure)</td>
<td>Pain management/main intervention</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>------------------</td>
<td>-------------</td>
<td>-----------------------</td>
<td>------------------------------------------</td>
<td>----------------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Matar et al., 2016</td>
<td>Retrospective</td>
<td>To evaluate effectiveness of Ponseti method in treating clubfoot in arthrogryposis; to present experiences in treating clubfeet using Ponseti method</td>
<td>N = 10, 2–20 weeks</td>
<td>AMC</td>
<td>Presence of pain</td>
<td>Once, post-op</td>
<td>Satisfactory outcome (i.e., plantigrade, braceable, pain-free foot) achieved in 7/10 patients</td>
<td>Ponseti method; tenotomy of Achilles tendon undertaken if necessary</td>
</tr>
<tr>
<td>Nicomedez et al., 2003</td>
<td>Prospective</td>
<td>To determine clinical presentation, functional outcome and pain patterns of five patients with AMC who underwent tibiocalcaneal fusion after previous takedown; to determine long-term effects of tibiocalcaneal fusion on midtarsal joints and knee joints of affected limb</td>
<td>N = 5, range: 10–31 years</td>
<td>AMC</td>
<td>AOFAS</td>
<td>Once, post-op</td>
<td>AOFAS increased from poor to fair post-op score results four out of five patients noted significant improvement in character of pain after surgery</td>
<td>Tibiocalcaneal arthrodesis fusion</td>
</tr>
<tr>
<td>Nouraei et al., 2017</td>
<td>Cross-sectional</td>
<td>To identify and examine long-term outcomes of adults with AMC (emphasis on impact of disability and treatment on education, employment, and home life)</td>
<td>N = 177, range 19–84 years</td>
<td>AMC</td>
<td>SF-36</td>
<td>Once, at data collection</td>
<td>Pain was a significant problem in 75%. Of those 75%, 88% experienced joint pain, 49% experienced muscle pain mostly in knees and ankles, 63% chronic back pain</td>
<td>No intervention directly or indirectly aimed at reducing pain</td>
</tr>
<tr>
<td>Riemer &amp; Steen, 2013</td>
<td>Single case study</td>
<td>To present case of 93-year old woman with amyoplasia including development of physical limitations and coping strategies; to describe how amyoplasia develops into older age</td>
<td>N = 1, 93 years</td>
<td>Amyoplasia</td>
<td>Pain present, or not present</td>
<td>Periodically throughout life time</td>
<td>Musculoskeletal pain decreased during aging; participant reported bilateral hip pain during adolescence; and LBP due to lumbar stenosis at 73 years. Over the last two decades, she reported sporadic</td>
<td>No intervention directly or indirectly aimed at reducing pain</td>
</tr>
<tr>
<td>Study</td>
<td>Study design</td>
<td>Study purpose</td>
<td>Sample size, age</td>
<td>Type of AMC</td>
<td>Pain experience (description of pain scores/results on the pain measurement)</td>
<td>Frequency and timing of pain measurement</td>
<td>Measure used for pain</td>
<td>Pain management/main intervention</td>
</tr>
<tr>
<td>------------------------------</td>
<td>----------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>------------------</td>
<td>-------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------</td>
<td>----------------------------------------</td>
<td>----------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Savenkov et al., 2017</td>
<td>Review paper/expert opinion</td>
<td>To discuss information presented at 2nd International Symposium on Arthrogryposis; to discuss difficulties in anesthetic treatment and postoperative pain management in individuals with AMC</td>
<td>N = not specified, children age not specified</td>
<td>AMC</td>
<td>Pain controlled for 14 days, which allows for aggressive passive range of motion of joints and allows for decrease in the amount of narcotic that is needed post-operatively</td>
<td>Twice, pre and post-op</td>
<td>Axillary, supraclavicular and infracavicular blocks (UE); paravertebral, lumbar, paraspinal, iliac, iliac, sciatic, femoral nerve, and sciatic nerve block (LE)</td>
<td>Axillary, supraclavicular and infracavicular blocks (UE); paravertebral, lumbar, paraspinal, iliac, iliac, sciatic, femoral nerve, and sciatic nerve block (LE)</td>
</tr>
<tr>
<td>Segev et al., 2008</td>
<td>Prospective longitudinal study (1 follow-up)</td>
<td>To report treatment outcomes of V:osteotomy and Ilizarov technique for residual idiopathic or neurogenic clubfeet; to report 9-year experience in treatment of residual idiopathic or neurogenic clubfeet</td>
<td>N = 10 range 8-18</td>
<td>Distal</td>
<td>No change in pain results, at both baseline and post-op</td>
<td>Twice, pre and post-op</td>
<td>Modified clubfoot grading system</td>
<td>No intervention directly aimed at reducing pain</td>
</tr>
<tr>
<td>Sneddon, 1999</td>
<td>Cross-sectional study</td>
<td>To determine what happens to individuals with AMC during the aging process; to report the presence of pain and whether these symptoms developed over time; to report on the frequency and timing of pain measurement</td>
<td>N = 100, range 18-63</td>
<td>AMC</td>
<td>32% named pain, ache, or stiffness as most noticeable symptom from aging; 20% reported pain in hips; 11% had developed pain in one or both knees; 11% had ankle or foot problems; 8% had aches or pain in arms or hands; 5% reported new pain or numbness in hands; 3%</td>
<td>Once, at data collection</td>
<td>Presence of pain - based on author created online questionnaire</td>
<td>Once, at data collection</td>
</tr>
<tr>
<td>Study</td>
<td>Study design</td>
<td>Study purpose</td>
<td>Sample size, age</td>
<td>Type of AMC</td>
<td>Measure used for pain</td>
<td>Frequency and timing of pain measurement</td>
<td>Pain experience (description of pain scores/results on the pain measure)</td>
<td>Pain management/main intervention</td>
</tr>
<tr>
<td>---------------------------</td>
<td>-------------------------------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>-----------------</td>
<td>------------------------------------------------------------------------------</td>
<td>----------------------</td>
<td>------------------------------------------</td>
<td>---------------------------------------------------------------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Spencer et al., 2010</td>
<td>Cross-sectional study</td>
<td>To document the BMD and compare results with normative values; to compare BMD with functional ability on the PODCI, WeeFIM and fracture risk</td>
<td>N = 30, range: 5–18 years</td>
<td>Amyoplasia or nonsyndromic arthrogryposis with predominantly LE involvement</td>
<td>PODCI</td>
<td>Once, at data collection</td>
<td>PODCI normative scores were normal in pain/comfort</td>
<td>No intervention directly or indirectly aimed at reducing pain</td>
</tr>
<tr>
<td>Yau et al., 2002</td>
<td>Cross-sectional study on retrospective cohort</td>
<td>To report results of hip problems in patients with arthrogryposis after mean follow-up of 20 years</td>
<td>N = 15, no age specified</td>
<td>AMC</td>
<td>Modified hospital of special surgery score</td>
<td>Once, at data collection</td>
<td>Mean pain score: 9 (score of 10 = no pain)</td>
<td>Surgeries for hip dislocations and subluxations and contractures (types of surgeries not specify)</td>
</tr>
</tbody>
</table>

Abbreviations: AFO, ankle foot orthosis; BMD, bone mineral density; DA, distal arthrogryposis; GBP, gabapentin; KFO, knee foot orthosis; LBP, low back pain; LE, lower extremity; OT, occupational therapy; PT, physical therapy; ROM, range of motion; THR, total hip replacement; TMJ, temporomandibular joint; UE, upper extremity.
<table>
<thead>
<tr>
<th>Pain assessment tool</th>
<th>Purpose</th>
<th>Administration</th>
<th># Pain items</th>
<th># Total items</th>
<th>Domains</th>
<th>Scoring and interpretation</th>
<th>Used in</th>
</tr>
</thead>
</table>
| **Face, legs, activity, cry and consolability pain scale (FLACC pain scale)** | Assess pain in children between the ages of 2 months and 7 years, or individuals who are unable to communicate pain/have cognitive impairment | Clinician observed and completed | 5 | 5 | 1. Face  
2. Legs  
3. Activity  
4. Cry  
5. Consolability | 0–10 (relaxed/comfortable)  
To severe discomfort/pain | Azbell & Dannemiller, 2015 |
| **Modified neonatal or infant pain scale** | Behavioral scale; utilizes body language to determine if the infant is in pain | Clinician observed and completed | 8 | 8 | 1. Sleep  
2. Facial expression  
3. Quality of cry  
4. Spontaneous motor activity  
5. Sucking  
6. Consolable  
7. Sociability  
8. Overall tone | 0–1 (each item scored on 0, 0.5, 1 and then average of all items)  
(high score indicate more pain) | Behm & Kearns, 2001 |
| **Verbal rating scale (VRS)** | Assess pain while utilizing adjectives to allow respondent to describe different levels of pain in children/adolescent/adults | Self-report | 1 (or more, if used for multiple activities and/or different timeframes) | 1 (or more) | 1. Pain | 0–4 (no pain to severe pain) | Chotigavanichaya et al., 2015 |
| **Harris hip score (HHS)** | To evaluate various hip disabilities and methods of treatment in an adult population | Clinician observed and completed | 1 | 13 | 1. Pain  
2. Function  
3. Absence of deformity  
4. Range of motion | 0–100 (higher scores representing less dysfunction and better outcomes) | Dalton et al., 2015 |
| **Oswetry disability index (ODI)** | Low-back disability questionnaire; to measure and quantify permanent functional disability for low-back pain in adults | Self-report | 1 items to pain  
9 items impact of pain on function | 10 | 1. Pain  
2. Personal care  
3. Lifting  
4. Walking  
5. Sitting  
6. Standing  
7. Sleeping  
8. Sex life  
9. Social life  
10. Traveling | 0–100 (higher score indicate higher impact on function) | Jones et al., 2018 |
| **Medical outcomes study short-form 36 (SF-36)** | Measure of health status among adults | Self-report | 2 | 36 | 1. Vitality  
2. Physical functioning  
3. Bodily pain  
4. General health perceptions  
5. Physical role functioning  
6. Emotional role functioning  
7. Social role functioning  
8. Mental health | 0–100 (higher the score less disability) | Jones et al., 2018 & Nouraei et al., 2017 |
<table>
<thead>
<tr>
<th>Pain assessment tool</th>
<th>Purpose</th>
<th>Administration</th>
<th># Pain Items</th>
<th># Total Items</th>
<th>Domains</th>
<th>Scoring and interpretation</th>
<th>Used in</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short form brief pain inventory (short form BPI)</td>
<td>To evaluate severity and impact of pain in adults. Used in wide range of chronic cancer-related and non-malignant pain conditions, such as arthritis and low-back pain</td>
<td>Self-report</td>
<td>15</td>
<td>15</td>
<td>1. Pain severity 2. Pain interference</td>
<td>Severity scored from 0–40; interference scored from 0–70 (higher score more pain)</td>
<td>Jones et al., 2018</td>
</tr>
<tr>
<td>EuroQol five dimensions questionnaire (EQ-5D)</td>
<td>Evaluate health-related quality of life in adults that can be used in a wide range of health conditions and treatments.</td>
<td>Self-report</td>
<td>1</td>
<td>5</td>
<td>1. Mobility 2. Self-care 3. Usual activities 4. Pain/discomfort 5. Anxiety/depression</td>
<td>5–25 (higher number, more impact on function) 0–100 (higher number more impact on health)</td>
<td>Jones et al., 2018</td>
</tr>
<tr>
<td>Short form McGill pain questionnaire (SF-MPQ-2)</td>
<td>To assess multiple types of acute and chronic pain, in adults</td>
<td>Self-report</td>
<td>13</td>
<td>13</td>
<td>1. Pain descriptor 2. Pain intensity</td>
<td>0–40 (higher scores, more pain)</td>
<td>Jones et al., 2018</td>
</tr>
<tr>
<td>American orthopedic foot and ankle society score (AOFAS)</td>
<td>To evaluate symptoms and functional status of ankle and foot in children and adults with ankle/ft trauma or surgery</td>
<td>Self-report and clinician observed and completed</td>
<td>1</td>
<td>9</td>
<td>1. Pain, 2. Function 3. Alignment</td>
<td>0–100 (better score better ankle/ft function)</td>
<td>Nicomedez et al., 2003</td>
</tr>
<tr>
<td>Pediatric outcomes data collection instrument (PODCI)</td>
<td>To assess changes following pediatric orthopedic interventions for broad range of diagnoses, with a focus on function and quality of life in children and adolescents.</td>
<td>Self or parent (proxy) report</td>
<td>2</td>
<td>108 child 86 parent</td>
<td>1. Upper extremity and physical function 2. Transfers and basic mobility 3. Sports and physical functioning 4. Pain/comfort 5. Happiness 6. Global functioning</td>
<td>0–100 (better score better health)</td>
<td>Spencer et al., 2010</td>
</tr>
</tbody>
</table>
Two studies compared pain experiences among different groups (Dai et al., 2018; Yau et al., 2002). Pain prevalence and location did not differ between amyoplasia and other types of AMC (distal arthrogryposis, multiple pterygium syndrome, dominant Larsen syndrome and, neurogenic AMC without clinical, or molecular diagnosis) (Dai et al., 2018). Yau et al. (2002) found that long-term results for pain were comparable in 15 patients with AMC presenting with hip contractures and subluxation. Refer to Table 2 for a description of pain in adults and children.

3.7 | Pain management techniques

A total 11 studies reported on interventions either directly or indirectly aimed at reducing pain. Pain management techniques included surgeries, pharmacological interventions, and rehabilitation. Surgeries reported in this scoping review aimed at increasing function as well as directly or indirectly reducing pain. Pharmacological interventions included over-the-counter and prescribed medications, administered orally or as nerve blocks. Rehabilitation consisted of occupational therapy, physical therapy, splinting, orthotics, and casting.

In eight pediatric studies surgical interventions (n = 5), pharmacological interventions (n = 2) and rehabilitation interventions (n = 1) were reported to directly or indirectly reduce pain. The primary outcome of the surgical interventions was to correct deformities and improve function (Cassis & Capdevila, 2000; Chotigavanichaya et al., 2015; Matar et al., 2016; Nicomedez et al., 2003; Segev et al., 2008). Tibiocalcanal arthrodesis fusion surgery was found to improve pain symptoms, overall pain patterns and provide pain relief in four out of five individuals with AMC at mean follow-up of 5 years (Nicomedez et al., 2003). Rehabilitation intervention found to have decreased FLACC pain scores during passive stretching of an infant’s joints (Azbell & Dannemiller, 2015). Pharmacological interventions included the use of gabapentin (GBP) therapy in an infant (Behm & Kearns, 2001) and the use of peripheral nerve blocks for children undergoing orthopedic surgeries (Savenkov et al., 2017). GBP was proven to be a safe and effective treatment for pain relief, decreasing one neonatal’s pain scores 22 hr following initiation of GBP therapy; decreased production of severe pain was also found to increase an infant’s ability to tolerate extensive physical therapy (Behm & Kearns, 2001). To modulate intraoperative pain and provide initial postoperative pain relief, peripheral nerve blocks including axillary, supraclavicular, and infraclavicular blocks were recommended for use during upper-extremity surgery in children with AMC. Paravertebral, lumbar epidural, iliofascial, femoral nerve, and sciatic nerve blocks to modulate were also recommended to provide similar functions during lower-extremity surgery (Savenkov et al., 2017).

In three studies on adults, surgery (n = 2) and rehabilitation (n = 1) were used for pain management and relief. Bilateral total hip replacements were performed in an adult with AMC experiencing osteoarthritis pain to address deteriorating function and provide pain-relief and were determined to be safe and effective for pain relief (Dalton et al., 2015). However, in a 38-year old with nongenetic arthrogryposis, physiotherapy provided limited improvements in pain or function (Fisher & Fisher, 2014). Physiotherapy exercises and splints were also prescribed for myofascial pain reduction in the temporomandibular joints in an adult patient (de Andrade et al., 2000).

Six studies reported on pain that was not directly linked to a specific intervention, these studies were cross-sectional, retrospective chart reviews, or single case studies (Canavese & Sussman, 2009; Dai et al., 2018; Hartley et al., 2013; Nouraei et al., 2017; Riemer & Steen, 2013; Sneddon, 1999). One study reported 13 adults with AMC (Hartley et al., 2013) commonly requested physiotherapy for pain relief. Alternative interventions were reported by Sneddon (1999) techniques included hydrotherapy, massage, acupuncture and heat therapy (e.g., hot tubs and hot baths). Nouraei et al. (2017) reported that almost half of 177 participants required pain medications during their lifespan, with 46% of participants regularly taking pain medications. Pain or anti-inflammatory medications included both over the counter pain relief medications and prescription analgesia, and was also reported by Hartley et al. (2013) and (Sneddon, 1999). Riemer and Steen (2013) described the case of a 93-year old woman who reported no regular use of pain medications throughout her life; however, painkillers such as paracetamole, ibuprofene, nonsteroidal anti-inflammatory drugs, and codeine were used sporadically during shorter periods of time. Medicine patches were also used for pain relief (Sneddon, 1999). Authors did not elaborate on the meaning of character of pain (e.g., type of pain, pain intensity, pain description). Finally, no studies discussed the use of psychological interventions for pain management in children or adults. Refer to Table 2 for a description of pain management techniques used.

3.8 | Impact of pain on participation

In children and adults with AMC, activity limitations were found to be mainly correlated to pain and muscle fatigue (Kimber et al., 2012), and pain was reported to impair an infant’s ability to participate in daily routines and play (Azbell & Dannemiller, 2015). Four studies reported that AMC-related pain caused restrictions in participation, impacting work, education, career goals, lifestyle, and independence in adults living with AMC (Dai et al., 2018; Hartley et al., 2013; Nouraei et al., 2017; Sneddon, 1999). Tasks most frequently reported as affected by pain included walking, standing, self-care, using stairs and sitting (Jones et al., 2018). Four studies reported that AMC-related pain led to restrictions on physical function in adults with AMC, ranging from decreased mobility, decreased ability to walk long distances, to decreased time spent outdoors (Hartley et al., 2013; Nicomedez et al., 2003; Nouraei et al., 2017; Sneddon, 1999). One study measuring the degree of pain-related disability in adults with AMC identified pain-related impairment as 40% or less according to the ODI, placing adults living with AMC into minimal and moderate disability categories (Jones et al., 2018). According to EQ-5D scores, mobility and self-care activities were most limited, with less severe and/or disabling scores for pain, anxiety and depression (Jones et al., 2018). Although pain was frequently self-reported in Nouraei et al. (2017) study, the QoL reported by study participants using the SF-36 questionnaire was better for the pain domain; in comparison with the US population
4.1 Pain experience in children with AMC

The studies reporting on pain in children had small sample sizes and rarely used validated pain tools, providing insufficient knowledge on how children with AMC experience pain and its impact on everyday life. Although the findings of this scoping review suggest that musculoskeletal pain is more frequently reported by adults with AMC and thus less commonly experienced by children with AMC, future research in the pediatric population should determine the prevalence of pain in children with AMC using validated pain tools. Considering that pain was also found to restrict participation in daily activities, clinicians and researchers should focus on assessing the multidimensional pain experiences and the effect of pain on levels of QoL, function, and participation in children with AMC. In the studies on infants with AMC, clinician-reported pain tools, such as the modified NIPS and FLACC pain scales, were used to measure pain (Azbell & Dannemiller, 2015; Behm & Kearns, 2001). Self-report tools to assess pain were also used among older children and adolescents, such as with the AOFAS (Nicomzedez et al., 2003) and the PODCI (Spencer et al., 2010). Future studies should focus on incorporating both observational and self-report measures of pain when appropriate, to adequately understand how pain is experienced in infants, children, and adolescents with AMC. Children may receive inadequate pain management because of difficulties of perception, identification, and verbalization of pain, or as result of underutilization of tools to assess pain. Thus, health-care professionals should seek to understand the child’s own complaints of pain, considering the pain characteristics and intensity as well as the psychological and social aspects involved (de Freitas, de Castro, Castro, & Heineck, 2014). For a multidimensional assessment of pain in children with AMC, we recommend the use of the Adolescent Pediatric Pain Tool (APPT). The APPT has been shown to provide a deeper understanding of pain experiences and can be used to examine the effectiveness of pain management interventions (Fernandes, De Campos, Batalha, Perdigão, & Jacob, 2014; Jacob, Mack, Savedra, Van Cleve, & Wilkie, 2014). Future research should validate the use of the APPT with children and adolescents with AMC.

4.2 Pain experience in adults with AMC

Pain seems to be commonly experienced by adults with AMC, with high incidence of self-reported pain in several studies (Dai et al., 2018; Hartley et al., 2013; Kimberly et al., 2012; Nouraei et al., 2017). Very few studies assessing or measuring pain in adults with AMC examined the sensory-discriminative characteristics of pain, such as pain frequency, pain severity, pain duration, quality of pain. Thus, knowledge on these aspects of pain remains unclear. However, in studies assessing pain location, pain was found to be more frequently located in the lower extremity, trunk and spine (Dai et al., 2018; Jones et al., 2018; Nouraei et al., 2017). Despite many studies suggesting that pain is a common symptom experienced by adults with AMC, there are no standardized approaches to measuring pain in this population, with most measures or pain tools used not validated for use in AMC. Only one existing disability measure used in adult orthopedics has been validated for use in adults with AMC (Jones et al., 2018). Although the ODI demonstrated construct and content validity in adults with AMC, it focuses on the low-back and lower-extremity pain-related disability experienced. Thus, certain aspects of pain may not be addressed by the ODI, warranting future research using consensus-based methods to verify whether domains not addressed by the ODI are missing (Jones et al., 2018). Other tools used in the studies included in this scoping review were often disease-specific, thus need to be validated for use in AMC to ensure they can characterize the degree of chronic pain and the effectiveness of pain management in AMC (Jones et al., 2018; Nouraei et al., 2017).

4.3 Pain management techniques

Overall, children and adults rely on both pharmacological and nonpharmacological approaches to relieve and manage their pain. Few researchers have investigated the specific approaches that children, adolescents and adults living with AMC use to relieve pain. In infants with AMC, two studies reported that analgesic therapy and the use of pain management techniques allowed for infants to better tolerate aggressive postoperative passive range of motion exercises and physical therapy, and infants were better prepared for discharge (Behm & Kearns, 2001; Savenkov et al., 2017). Our findings seem to suggest that pain medications and analgesia, whether prescribed or over the counter pain medications, were most commonly used for pain relief and management in children and adults with AMC. Understanding the type of pain experienced and the etiology of the underlying diagnosis will help toward a more effective and appropriate pain management approach. For example, Amyoplasia, the most common form of AMC, is considered to be caused from a failure of the anterior horn cells in...
the spinal cord to not develop properly (Hall, Aldinger & Tanaka, 2014). Pain in Amyoplasia may therefore not only be musculoskeletal or nociceptive, but may also be neuropathic. Jones et al. (2018) indicated that part of the pain experience was neuropathic based on the McGill Pain Questionnaire.

Nonpharmacological approaches such as surgeries, rehabilitation programs, and alternative therapies (e.g., heat and massage therapy) were also used for pain relief and management. Yet, little is known with regards to their effectiveness in the context of procedural and acute postoperative pain experienced in pediatric populations and recurrent and persistent chronic pain experience in adult populations. Prospective intervention studies should be conducted to establish effectiveness of such treatment approaches. Current research has shown that including psychological therapies in multidisciplinary approaches to the management of chronic pain can reduce pain-related disability, improve pain-coping resources and increase self-management of pain (Eccleston et al., 2014; Roditi & Robinson, 2011). However, psychological approaches to pain management were not discussed in any of the 21 included studies, despite psychosocial and psychological impacts of pain mentioned by adults with AMC in one study included in this review (Dai et al., 2018). Thus, understanding the different types of pain will help guide the selection of pain approaches and the need for evaluation.

4.4 | Impact of pain on participation

Although seven studies included in this scoping review have acknowledged the impact of pain experiences on the daily lives of children and adults with AMC, the impact of pain experiences on both individual and societal dimensions of health (i.e., disability or QoL) is yet to be analyzed using appropriate pain tools (Jones et al., 2018; Nouraei et al., 2017). The ODI determined pain-related impairment as 40% or less, placing adults with AMC experiencing pain as minimal and moderate disability categories, while the results from the EQ-5D found less severe disabling scores for pain, anxiety, and depression in comparison with disabling scores for mobility and self-care activities. This result may be explained by the fact that individuals with AMC must adapt to significant physical joint limitations and pain early on. Thus, due to this adaptive nature and having endured multiple challenges throughout the lifespan, individuals with AMC may perceive pain as something that can be easily managed and overcome (Nouraei et al., 2017; Staheli, Hall, Jaffe, & Paholke, 1998). Moreover, there are only two questions specifically relating to pain on the SF-36: “how much bodily pain have you experienced in the past 4 weeks?” and “how much did pain interfere with your normal work?” Therefore, the specific way in which questions on pain are formulated may have also affected this result. Although restrictions on function and participation experienced by individuals with AMC may result from a composite of factors including physical limitation, mental health, social barriers, and subjective pain, it is important for clinicians and researchers further examine pain-related disability in both children and adults with AMC, using appropriate measures and tools.

4.5 | Strengths and limitations

This scoping review includes a wide range of study designs and methodologies as well as empirical studies and gray literature, thus providing a detailed overview of the state of knowledge of pain research in AMC. Conversely, limitations of the scoping review include lack of reporting of the intraclass correlation coefficient at the screening stage to determine agreement between reviewers. Even though the data extraction form was piloted by two reviewers, overall data extraction was conducted by one reviewer, which may lead to bias in data extraction. For the purposes of this scoping review, studies using any type of study design (e.g., case reports, retrospective, and observational designs) were included, therefore generalizability of results may be limited and should be interpreted with caution. Moreover, many of the designs included lower levels of evidence, further limiting the generalizability of the findings to children and adults with AMC.

4.6 | Future research

As clinical decisions on pain management require accurate assessments of pain (Fernandes et al., 2014), future research should focus on the development and validation of proper pain assessment tools for children and adults with AMC. A focus on validating tools that examine all dimensions of the pain experience, including sensory-discriminative (i.e., duration, location, intensity, and quality of pain), motivational-affective (i.e., emotional associations of pain); and cognitive-evaluative (i.e., meanings associated to pain and its impact) (Melzack & Casey, 1968) is needed for individuals with AMC. Although psychological therapies for pain were not explored in any of the studies, this area should be addressed in future studies. In addition, determining whether the pain experienced is acute (i.e., sudden onset, severe, and generally disappears over a short period) or chronic (i.e., persists beyond normal periods of healing) (Melzack & Casey, 1968) is crucial for proper pain management.

Future studies should also aim to identify the preferences of patients with AMC in terms of non-pharmacological approaches. The high incidence of self-reported pain in adults with AMC, indicated by the results of our scoping review, highlights the need for better knowledge on preferences in pain treatment approaches and effectiveness of these approaches, in order for health-care professionals to address pain and pain-related loss of function in these individuals with AMC. Studies are needed to develop and examine the effectiveness of surgical, nonsurgical, and pharmacological interventions in the management of pain in both children and adults with AMC.

5 | Conclusion

Limited attention has been given to the pain experiences of adults, and most notably, children with AMC. Although chronic musculoskeletal pain is common in adults living with AMC, many different tools are being used to measure and assess pain in both children and adults living with AMC and methods for assessing pain in AMC remain
inconsistent. Appropriate pain assessment tools and specialized pain treatments for individuals with AMC are lacking. Future studies are required to further quantify and qualify pain among children and adults with AMC. Guidelines to evaluate and manage pain in this population are needed to standardize practice among health-care professionals.

ACKNOWLEDGMENTS
We are grateful for the assistance provided by of Jill Boruff, librarian at McGill University for assistance with the search strategy, and for the methodological advice provided by Dr. Andre Bussières, Assistant Professor at McGill University’s School of Physical and Occupational Therapy. This project was funded by a Microgrant (#2030) funded by the Rare Disease Foundation and the BC Children’s Hospital Foundation.

CONFLICTS OF INTEREST
The authors have no conflicts of interest to declare.

ORCID
Alexa Cirillo https://orcid.org/0000-0002-6330-623X
Jessica Collins https://orcid.org/0000-0002-0186-8309
Bonita Sawatzky https://orcid.org/0000-0002-8901-2301
Reggie Hamdy https://orcid.org/0000-0002-0664-2843
Noémi Dahan-Oliel https://orcid.org/0000-0001-8567-7173

REFERENCES


