Psychological and Physical Interventions for the Management of Cancer-Related Pain in Pediatric and Young Adult Patients: An Integrative Review

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Purpose/Objectives: To identify and appraise current evidence related to the effectiveness of psychological and physical (nonpharmacologic) pain management modalities for children and young adults with cancer.

Data Sources: Electronic searches in MEDLINE®, EMBASE, CINAHL®, PsycINFO, and Web of Science™ (from database inception to June 2013) for clinical trials.

Data Synthesis: A total of 32 unique studies were identified. Substantial heterogeneity existed across identified studies, precluding meta-analysis. Therefore, a narrative review of included studies is presented. Studies featured psychological and/or physical pain interventions for children and young adults (N = 1,171) aged 1–21 years with a variety of cancer diagnoses. Interventions included aromatherapy, art therapy, distraction, hypnosis, physical activity, physical positioning, touch therapy, and multimodal cognitive-behavior therapy. Twenty-two studies (69%) reported success in preventing or reducing pain intensity. The level of evidence and methodologic quality of studies were generally low.

Conclusions: Current nonpharmacologic pain interventions for pediatric and young adult patients with cancer are diverse. Several modalities significantly decreased pain intensity, suggesting that these strategies may be effective methods of pain treatment, particularly in the case of painful medical procedures. Future well-designed, multicenter, randomized, controlled trials are needed to further discern treatment effects on pain and other health outcomes in this population and to compare the relative effectiveness of different modalities.

Implications for Nursing: Nurses play a key role in pain assessment and management in pediatric and young adult patients with cancer. The studies included in this review constitute the beginnings of an evidence base that supports the need to implement psychological and physical interventions to improve pain outcomes in pediatric and young adult patients with cancer.

Key Words: cancer; pediatric; pain management; psychological; physical; nonpharmacologic

ONF, 42(6), E339–E357. doi: 10.1188/15.ONF.E339-E357

Pain is one of the most distressing symptoms for children and young adults with cancer (Hedén, Pöder, von Essen, & Ljungman, 2013; Olson & Amari, 2015). Studies show that 49%–62% of children and young adults with cancer experience pain, often prolonged, during the course of their treatment (Baggott et al., 2010; Varni, Burwinkle, & Katz, 2004). Pain negatively affects a young person's quality of life (Bhat et al., 2005; Sung et al., 2009; Varni et al., 2004), impedes cancer recovery (Shepherd, Woodgate, & Sawatzky, 2010), results in patient and family distress (Hedén et al., 2013; Miller, Jacob, & Hockenberry, 2011; Walker, Gedaly-Duff, Miaskowski, & Nail, 2010), and is associated with long-term morbidity (Chordas et al., 2013; Lu et al., 2011). Pain related to cancer also represents a significant cost burden to the healthcare system and families (Abernethy, Samsa, & Matchar, 2003), with pain being the most common reason adult patients with cancer use emergency health services (Barbera, Taylor, & Dudgeon, 2010; Kuo, Saokaew, & Stenehjem, 2013; Tsai, Liu, Tang, Chen, & Chen, 2009; Walker et al., 2010). Despite this knowledge, the management of pain in pediatric and young adult patients with cancer has not kept pace with advancements in treatment protocols (Woodgate, 2008). Several reasons have been proposed to explain why this pain is undermanaged, including (a) misconceptions about analgesic use and pain expression, (b) concern about undesirable diagnostic tests in the case of pain, (c) concern about opioid addiction, and (d) patient temperament and reported quality of life (Ameringer, 2010; Fortier et al., 2012; Fortier, Wahi, Bruce, Maurer, & Stevenson, 2014).

The causes of pain in pediatric and young adult patients with cancer are diverse, likely also contributing to difficulties in its management. Cancer pain may result from the disease itself or from the many associated in-

vasive diagnostic and treatment procedures, and it can be either acute or chronic in nature. The quality of pain resulting from the disease can vary depending on the type of cancer and source of the pain (Collins, Stevens, & Berde, 2008). Major sources of treatment-related pain include mucositis (Green et al., 2010), postoperative pain, infection-related pain such as that associated with typhlitis (Gray et al., 2010), graft-versus-host-disease (Oberg et al., 2013), and phantom limb pain related to limb amputation (Burgoyne et al., 2012). Pain also is a side effect of pediatric chemotherapy protocols that include platinum compounds (e.g., cisplatin [Platinol®]) and vinca alkaloids (e.g., vincristine [Oncovin®]) (Gilchrist, 2012; Vondracek et al., 2009). Causes of cancer-related procedural pain include lumbar puncture (LP), bone marrow aspiration (BMA), and venipuncture, as well as central venous catheter insertion and removal, and insertion of a needle into a subcutaneously implanted venous access port (Collins et al., 2008; Hockenberry et al., 2011; Wint, Eshelman, Steele, & Guzzetta, 2002).

Psychological and physical therapies are increasingly used by patients and families to manage cancer care in this unique population (Adams et al., 2013). Nonpharmacologic therapies include a variety of different techniques classified as psychological (e.g., distraction, relaxation, hypnosis, guided imagery, psychotherapy) or physical (e.g., massage, therapeutic touch, yoga). Evidence has shown prevalence rates for the use of these therapies in pediatric patients with cancer to be from 6%–91% (Bishop et al., 2010). Because of the acceptability of these therapies and the scope of cancer pain, a need exists to carefully examine nonpharmacologic intervention effectiveness in the context of pain, including when it is used in combination with pharmacologic modalities (Collins et al., 2008).

Although only a limited number of reviews look into the effectiveness of psychological and physical interventions for the treatment of pain in pediatric and young adult patients with cancer (Landier & Tse, 2010; Rheingans, 2007; Thrane, 2013), a comprehensive, systematically conducted, integrative review of the literature has not previously been conducted. The three available reviews have focused solely on the mitigation of procedural pain, used highly limited search criteria, and used study identification and abstraction procedures that may increase susceptibility to bias. In addition, research studies conducted in the field of nonpharmacologic pain interventions often use single-arm or nonrandomized study designs. These study design choices are likely caused by perceived difficulty in developing reasonable intervention controls, the stage of development, and evaluation of relative novel interventions (i.e., preliminary intervention testing), as well as other issues, including cost and recruitment feasibility (Eccles, Grimshaw, Campbell, & Ramsay, 2003). Because of this variation in study design, a need exists to broadly identify and appraise research conducted using various research methods. A broad identification and appraisal of the state of the science in this area is needed to inform clinical practice decisions and future research questions. However, this broad approach has not been strategically employed by published literature reviews.

Therefore, this study sought to systematically review and appraise the scientific literature on the effectiveness of psychological and physical interventions, across the breadth of research designs, for the management of pediatric cancer-related pain. Specifically, this review (a) describes identified research, (b) summarizes pain-related findings in terms of effectiveness (including an attempt to do so by age of the patient), (c) appraises the methodologic quality of each study, and (d) recommends future direction related to nonpharmacologic pain management research for pediatric and young adult patients with cancer.

Methods

Data Sources

To conduct this review, MEDLINE®, EMBASE, CINAHL®, PsycINFO, and Web of Science™ databases were searched from the date the database was established until June 17, 2013. Database queries were developed in consultation with a reference and information services librarian who was familiar with the field.

Study Selection

Studies were eligible for inclusion if they met the following criteria: (a) research published in an English-language, peer-reviewed journal, (b) clinical study of any design, (c) patient population of children and young adults (aged 1–21 years) diagnosed with cancer, (d) any dimension of pain (i.e., sensory, affective, or evaluative) examined as a primary or secondary outcome, (e) examination of the effectiveness of a pain intervention that was not solely pharmacologic in nature, and (f) pain measured using self-report (i.e., child or young adult as the source), proxy report (i.e., healthcare professional or caregiver as the source), or behavior or physiological indices of pain. In addition, despite the number of available validated pain assessment measures for infants, children, and young adults, these measures are unfortunately not always used in routine clinical (Stevens et al., 2012) and research practices (McGrath et al., 2008). In an effort to capture all of the research related to cancer pain management in children, the authors of the current review included studies that assessed pain outcomes using non-validated measures. Because non-validated measures negatively

affect the interpretability of a study, the authors noted this information and included it as a methodologic limitation of the corresponding study. Non-validated pain assessment measures were (a) those without evidence of reliability and validity based on current systematic reviews or (b) validated measures used in an age group where psychometric properties had not been established (e.g., use of a numeric rating scale in children younger than age 8 years).

Two authors reviewed the titles and full abstracts of studies identified through the search. There was excellent agreement (greater than 90%) between reviewers, and a third author arbitrated discrepancies. Full-text articles of potentially relevant abstracts were obtained, read, and assessed.

Abstraction of Data

Data abstraction from identified studies was conducted using a systematic approach. One author independently abstracted data related to study characteristics and design, as appropriate. All data were categorized according to a standardized table created by the authors. A second author then reviewed the data extraction and categorization for accuracy. Abstracted data were also categorized by participant age in an effort to describe any potential impact of child age on intervention effectiveness.

Quality Assessment

The U.S. Preventive Services Task Force ([USPSTF], 2008) has presented a hierarchy of evidence to assess the benefits and harms of various clinical interventions. This schema was used to categorize the studies in the current review because it provides a means to assess studies across a wide breadth of designs. According to the schema, level I evidence describes randomized, controlled trials (RCTs), systematic reviews, or meta-analyses of homogeneous RCTs; level II–1 evidence describes controlled trials not employing randomization; level II–2 evidence describes well-designed cohort or case-control studies; level II–3 evidence describes multiple time series or uncontrolled trials; and level III evidence describes descriptive studies or case reports and the opinions of respected clinical experts. Because of the subjective nature of pain (Schiavenato & Craig, 2010), for the purpose of this study, children and young adults were considered clinical experts, and qualitative interview-based studies with these patients were graded as level III evidence. The authors included only primary data sources in this review. Therefore, systematic reviews and meta-analyses on the topic are not presented. The criteria provided by the USPSTF (2008) to guide internal and external validity assessment was used to rate identified studies. The authors did not assess the internal validity of studies classified as levels II and III because the USPSTF does not provide criteria for doing so.

Data Synthesis

The authors' original intent was to use meta-analysis methods to conduct a quantitative synthesis of data across identified RCTs. However, because of a high level of heterogeneity in study design, study population, outcomes assessed, and pain measurement tools used, the authors were not able to collate results. Therefore, a narrative review of the literature detailing quantitative and qualitative findings related to the identified pain management interventions is presented.

Results

Study Characteristics

Figure 1 shows the study identification process according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA) guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009). A total of 1,171 children and young adults participated across the 32 studies identified by the authors. The number of participants in each study ranged from 8–124 ($\bar{X}$ = 37, SD = 24). Participants ranged in age from 1–21 years

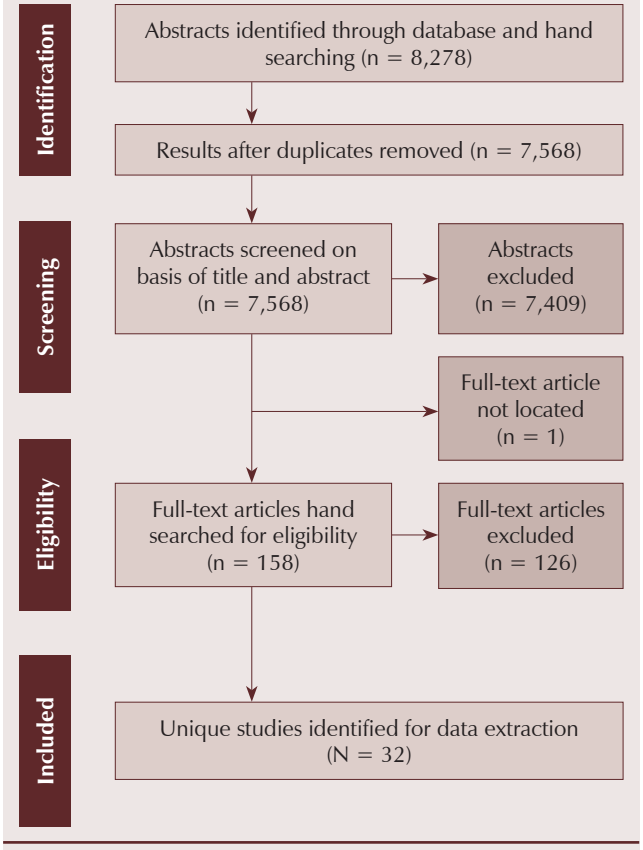

Figure 1. Flowchart of the Study Identification, Screening, and Inclusion Process

and had a variety of cancer diagnoses. Twenty-five studies were conducted within oncology programs at pediatric tertiary care centers, one study was conducted both at a pediatric tertiary care center and a community hospital, and six studies did not specify the study setting. Fifteen studies (47%) included pharmacologic pain management in at least one of the treatment arms. Of note, eight studies (25%) did not report the use of a validated pain assessment tool. Details of study characteristics are presented in Table 1.

Regarding the association between person rating pain and outcome, the following results were found: (a) of studies reporting youth self-reported pain, 13 of 30 studies showed a decrease in pain; (b) of studies reporting parents' rating of their child's pain, 5 of 9 studies showed a decrease in pain; (c) of studies reporting nurses' ratings of youth pain, 2 of 5 studies showed a decrease in pain; (d) of studies reporting third-party observers' ratings of youth pain, 3 of 5 studies showed a decrease in pain; and (e) when physiological proxy was used (e.g., heart rate), 3 of 5 studies showed a decrease in pain.

Psychological and Physical Pain Interventions

Aromatherapy: A single study has evaluated the impact of aromatherapy on pain during stem cell transplantation (Ndao et al., 2012). Pain prevalence did not significantly decrease over time as a result of aromatherapy and no difference was noted in pain between the intervention group and a sham control.

Art therapy: One study examined the impact of creative art therapy on quality of life in children and young adults during cancer treatment. Pain was assessed as a subscale of a validated health-related quality-of-life (HRQOL) measure by parent and youth report (Madden, Mowry, Gao, Cullen, & Foreman, 2010). An improvement on the parent-reported pain item compared to the control group was demonstrated, and no difference for youth-rated pain was observed.

Distraction: Six studies examined the impact of distraction on pain in children with cancer, with generally positive results. Virtual reality distraction, where a child is immersed in a virtual world through the use of visual and auditory stimuli, was compared to non-virtual reality distraction and standard medical treatment in a study of patients undergoing subcutaneous port access (Gershon, Zimand, Pickering, Rothbaum, & Hodges, 2004). Less nurse-reported pain, behavioral indicators of pain, and heart rate were observed in the distraction groups compared to control, with no difference in youth or parent pain reports. Active distraction (i.e., bubble blowing) compared to attention control (i.e., heated pillow) during subcutaneous port access has been investigated in a sample of younger children (Hedén, von Essen, & Ljungman, 2009) with no observed between-group difference in pain. A study of musical distraction on pain during LP in school-age children with cancer showed reduced child-reported pain, heart rate, and respiratory rate in the musical distraction group compared to control (Nguyen, Nilsson, Hellström, & Bengtson, 2010). An additional study of the effectiveness of youth-selected distraction (e.g., book) during subcutaneous access or venipuncture showed no between-group difference in youth-rated pain compared to control (Windich-Biermeier, Sjoberg, Dale, Eshelman, & Guzzetta, 2007). However, participants in the distraction group rated the procedure more positively than those in the control group. The effect of virtual reality compared to standard care in decreasing LP-related pain has also been investigated with no differences noted (Wint et al., 2002). However, youth in the distraction group qualitatively reported use of the system to be a positive experience. Finally, the impact of virtual reality distraction on procedural pain in patients undergoing subcutaneous access showed observer-rated pain and heart rate to be lower in the virtual reality group compared to standard care (Wolitzky, Fivush, Zimand, Hodges, & Rothbaum, 2005).

Hypnosis: Nine identified studies examined the effect of hypnosis on pain in children and young adults with cancer. First, the effectiveness of direct versus indirect hypnosis on LP-related pain in children and young adults was compared (Hawkins, Liossi, Ewart, Hatira, & Kosmidis, 1998). Direct hypnosis refers to suggestions provided by a hypnotist that are immediately related to anesthesia. In contrast, indirect hypnosis evokes thoughts of colors, aromas, and/or temperatures that can be discussed as a proxy for anesthesia (Liossi & Hatira, 1999). The Hawkins et al. (1998) study found no difference in pain between indirect and direct hypnosis groups. In addition, no between-groups differences were observed in a study comparing hypnosis to quiet play during BMA; however, pain decreased in both groups when compared to a baseline BMA (Katz, Kellerman, & Ellenberg, 1987). A study of the effect of hypnosis, distraction, and standard care on pain related to BMA showed observer-rated pain for older children (i.e., 7–10 years) to be less in the hypnosis and distraction groups compared to control (Kuttner, Bowman, & Teasdale, 1988). In a comparison of direct hypnosis, cognitive behavioral therapies (CBTs) (i.e., relaxation training, deep-breathing, and positive reframing), and lidocaine injection during BMA, pain change scores from baseline were significantly greater than control in the hypnosis and CBT groups (Liossi & Hatira, 1999). A second study comparing direct hypnosis, indirect hypnosis, play, and education alone on youth-reported LP-related pain showed both hypnosis groups to report decreased pain compared to baseline (Liossi & Hatira, 2003). Direct hypnosis also was compared to play and

Table 1. Characteristics of Identified Nonpharmacologic Pain Management Studies

Study	Sample	Pain Source	Intervention Groups	Instrument	Findings
Aromatherapy					
Ndao et al., 2012 United States	37 patients aged 5–21 years (10 female, 27 male) with unspecified cancers	Unspecified pain related to stem cell transplantation therapy	Bergamot essential oil aromatherapy versus placebo fluid administered using an aromatherapy diffuser during stem cell transplantation (typically one hour in duration)	Pain was rated by youth on a 10 cm VAS.	No difference was noted in pain between groups at any time point following transplantation.
Art therapy					
Madden et al., 2010 United States	18 patients aged 2–13 years (4 female, 14 male) in the RCT and 32 patients aged 3–21 years (14 female, 18 male) in the qualitative study	Unspecified pain related to cancer and/or treatment	Creative arts therapy (including dance or movement, music, and art) versus nurse's attention (reading, talking) or watching TV for one hour per week for six sessions	In the RCT phase, parents and youth rated pain on the pain and hurt subscales of the PedsQL™; in the qualitative study, interviews with care providers were conducted.	Less parent-rated pain and hurt ($p = 0.03$) between groups in the RCT phase. Qualitative analysis of the interview study was not available.
Distraction					
Gershon et al., 2004 United States	59 patients aged 7–19 years (29 female, 30 male) with leukemia, lymphoma, or solid tumor	Subcutaneous port access	Virtual reality distraction using a head-mounted display with stereo earphones transmits the image plus EMLA application versus non-virtual reality distraction on a computer monitor plus EMLA application versus EMLA application for procedure	Pain was rated by youth, parent, and nurse using a 10 cm VAS; pain was rated by the researcher using CHEOPS; and pulse rate was measured using a pulse-oxygen monitor.	No difference in youth- or parent-rated pain between groups. Less nurse-rated pain was noted in the distraction groups compared to control ($p < 0.05$). No difference was noted between groups on overall CHEOPS scores. Less muscle tension was recorded in the distraction groups compared to control ($p < 0.05$). Lower pulse rate was noted in the virtual reality distraction group compared to control ($p < 0.05$).
Hedén et al., 2009 Sweden	28 patients aged 2–7 years (11 female, 17 male) with leukemia, central nervous system tumor, or solid tumor	Subcutaneous port access	Bubble blowing plus EMLA application and education versus heated pillow plus EMLA application and education	Pain was rated by parent and nurse using a 10 cm VAS.	No difference was noted in pain from initial access or between groups.
Nguyen et al., 2010 Vietnam	40 patients aged 7–12 years (15 female, 25 male) with leukemia	Lumbar puncture	Listening to youth-selected music via earphones versus earphones without music during procedure	Pain was rated by youth using an 11-point numeric rating scale; heart rate, blood pressure, and oxygen saturation were measured electronically; respiratory rate was measured manually; open-ended interviews were conducted about the process.	Less between-group pain was noted during ($p < 0.001$) and after ($p < 0.003$) the procedure in the distraction group. Lower heart rate ($p = 0.012$) was recorded during procedure and lower respiratory rate during ($p = 0.09$) and after ($p = 0.03$) procedure for the distraction group. Open-ended interviews with the distraction group revealed a perceived positive experience, including less pain and fear.

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CHEOPS—Children's Hospital of Eastern Ontario Pain Scale; EMLA—eutectic mixture of local anaesthetics; RCT—randomized, controlled trial; VAS—visual analog scale

Table 1. Characteristics of Identified Nonpharmacologic Pain Management Studies *(Continued)*

Study	Sample	Pain Source	Intervention Groups	Instrument	Findings
Distraction *(Continued)*					
Windich-Biermeier et al., 2007 United States	50 patients aged 5–18 years (23 female, 27 male) with leukemia, lymphoma, solid tumor, or histiocytosis	Subcutaneous port access or venipuncture	Youth-selected distraction (i.e., book, video game, virtual reality glasses, bubbles, or music table) plus EMLA application and education versus EMLA application and education during the procedure	Youth rated pain with a color analog scale; an investigator-developed tool rated the acceptability of the intervention.	No difference in pain between groups. Most parents ($p = 0.007$) and youth ($p = 0.05$) in the distraction group reported procedure as "better" or "much better" than previous procedures.
Wint et al., 2002 United States	30 patients aged 10–19 years (14 female, 16 male) with leukemia or lymphoma	Lumbar puncture	Virtual reality distraction using head-mounted display plus conscious sedation, EMLA application, and education versus conscious sedation, EMLA application, and education	Youth rated pain using a 10 cm VAS (when the patient met the minimal level of recovery from sedation). Participants also were questioned about the procedure using an investigator-developed tool.	No difference in youth-reported pain between groups. Findings from the qualitative component showed a perceived positive experience for the distraction group, including less pain.
Wolitzky et al., 2005 United States	20 patients aged 7–14 years (8 female, 12 male) with unspecified cancers	Subcutaneous port access	Virtual reality distraction using head-mounted display versus no listed treatment during procedure	Pain was rated by youth, parent, and nurse on a 10 cm VAS; the researcher used CHEOPS during the procedure; heart rate was measured using a pulse-oxygen meter.	No difference in youth-reported pain (measured as part of distress data) was noted between groups. The distraction group had a lower heart rate ($p < 0.05$) and CHEOPS scores ($p < 0.01$) during the procedure compared to control.
Hypnosis					
Hawkins et al., 1998 Greece	30 youth aged 6–16 years (18 female, 12 male) with leukemia or lymphoma	Direct hypnosis versus indirect hypnosis (baseline procedure conducted)	Age-appropriate direct hypnotic suggestions for analgesia versus indirect hypnotic suggestion for analgesia for procedure (baseline procedure conducted)	Youth rated pain using a six-point FACES scale; nurses rated pain using a checklist of distress behaviors.	No difference was noted in pain between groups on youth or nurse report. Pain reduction over time was related to hypnotizability of youth ($p < 0.001$).
Katz et al., 1987 United States	36 patients aged 6–11 years (12 female, 24 male) with leukemia	Direct hypnosis, indirect hypnosis, and relaxation versus quiet, still play during three procedures (baseline procedure conducted)	Direct and indirect hypnotic suggestions for analgesia and relaxation versus quiet, still play during three procedures (baseline procedure conducted)	Youth rated pain from 0–100 on a thermometer graphic scale.	No difference was noted in pain between groups on youth report. Pain related to procedure decreased in both groups compared to baseline ($p < 0.05$). Subgroup analysis showed females report higher pain than males on procedure ($p < 0.05$).

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Table 1. Characteristics of Identified Nonpharmacologic Pain Management Studies *(Continued)*

Study	Sample	Pain Source	Intervention Groups	Instrument	Findings
Hypnosis *(Continued)*					
Kuttner et al., 1988 Canada	48 patients aged 3–10 years (18 female, 30 male) with leukemia	Direct and indirect hypnosis versus distraction versus education and anesthetic during bone marrow aspiration	Direct and indirect hypnotic suggestions for analgesia and procedural success versus age-appropriate distraction before and during procedure versus education and anesthetic during each of the two bone marrow aspirations	Pain was rated by the observer using a five-point Likert-type scale; pain was rated by youth using a five-point FACES scale developed by the research team.	Pain was lower among patients aged 7–10 years in the hypnosis and distraction groups ($p < 0.05$) according to observer. No difference in pain for patients aged 3–6 years or using any youth rating. All children reported the second procedure as less painful than the first ($p = 0.01$).
Liossi et al., 2006 Greece	45 patients ages 6–16 years (22 female, 23 male) with leukemia or lymphoma	Lumbar puncture	Direct hypnosis, self-hypnosis, EMLA, and education versus non-medical play, EMLA, and education versus EMLA and education for four lumbar punctures (self-hypnosis used on second and third procedure)	Youth rated pain using the Wong-Baker FACES scale.	Pain related to procedure was less in the hypnosis group compared to control groups ($p < 0.001$). Pain related to procedure decreased in all groups compared to baseline ($p < 0.001$). A correlation was noted between hypnotizability and decreased pain ($p < 0.05$).
Liossi et al., 2009 Greece	45 patients ages 7–16 years (25 female, 20 male) with unspecified cancer	Venipuncture	Self-hypnosis, EMLA, and education versus non-medical play, EMLA, and education versus EMLA and education for three venipunctures (self-hypnosis used on second and third procedure)	Youth reported pain on a 10 cm VAS.	Pain was less in the hypnosis group compared to the control groups ($p < 0.001$) at baseline and on both follow-up procedures.
Liossi & Hatira, 1999 Greece	30 patients aged 5–15 years (13 female, 17 male) with leukemia	Bone marrow aspiration	Direct hypnosis versus relaxation, deep breathing, and positive reframing versus lidocaine injection before procedure (baseline procedure conducted)	Youth rated pain on a six-point FACES scale.	Pain related to procedure was less in the hypnosis ($p = 0.005$) and behavior intervention ($p = 0.008$) groups compared to baseline. Difference was noted in baseline and post-procedure pain when hypnosis ($p = 0.001$) and behavior intervention were compared to control ($p = 0.002$). No difference in pre- and post-procedure pain was noted between hypnosis and behavior intervention ($p = 0.2$).
Liossi & Hatira, 2003 Greece	80 patients aged 6–16 years (gender ratio unspecified) with leukemia or lymphoma	Lumbar puncture	Direct hypnosis, self-hypnosis, and education versus indirect hypnosis, self-hypnosis, and education versus non-medical play and education versus education alone	Youth rated pain using the Wong-Baker FACES scale.	Pain related to procedure was less in both hypnosis groups compared to baseline ($p < 0.001$), but relationship was not maintained until the last procedure. No change in pain was noted in the control group over time. Less pain was noted over time in the hypnosis groups compared to control groups ($p < 0.001$). A correlation was noted between hypnotizability and decreased pain ($p < 0.01$).

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Table 1. Characteristics of Identified Nonpharmacologic Pain Management Studies *(Continued)*

Study	Sample	Pain Source	Intervention Groups	Instrument	Findings
Hypnosis *(Continued)*					
Wall & Womack, 1989 United States	20 patients aged 5–18 years (gender ratio unspecified) with unspecified cancer	Bone marrow aspirate or lumbar puncture	Indirect hypnosis versus distraction (baseline procedure conducted)	Youth rated pain using a 10 cm VAS (all patients) and the McGill Pain Questionnaire (for those younger than age 12); the observer rated pain using a 10 cm VAS; heart rate and temperature were assessed using unspecified methods.	A decrease was noted in youth-rated ($p < 0.02$) and observer-rated ($p < 0.009$) pain from baseline procedure to follow-up procedures in both treatment groups. No significant difference was noted in pain reduction between groups.
Zeltzer & LeBaron, 1982 United States	23 patients aged 6–17 years (6 female, 17 male) with leukemia, lymphoma, or a central nervous system tumor	Bone marrow aspiration or lumbar puncture	Indirect hypnosis versus deep breathing, distraction, and procedure practice session	Youth rated pain on a five-point Likert-type scale.	In the bone marrow aspirate cohort, pain related to the procedure decreased in both groups compared to baseline ($p < 0.01$). Hypnosis was more effective than other treatments ($p < 0.001$). In the lumbar puncture cohort, pain related to procedure decreased in the hypnosis group compared to baseline ($p < 0.001$).
Physical activity					
Speyer et al., 2010 France	31 patients aged 9–18 years (13 female, 18 male) with leukemia, lymphoma, or solid tumor	Unspecified pain related to cancer and/or treatment	Youth-selected physical activity (e.g., basketball, dance) personalized to health condition for three sessions of 30 minutes per week during hospitalization versus no physical activity	Youth and parents rated pain on the bodily pain subscale of the Child Health Questionnaire.	No difference was noted in youth-rated bodily pain between groups. Parent-rated bodily pain was less ($p = 0.0004$) between periods.
Physical positioning					
Marec-Bérard et al., 2009 France	124 patients aged 2–17 years (49 female, 75 male) with unspecified cancers	Lumbar puncture	Positioning pillow to ensure maximum lumbar flexion and paravertebral muscle relaxation plus EMLA and mild sedation versus no pillow during a single lumbar puncture plus EMLA and mild sedation	Youth rated pain on a VAS (length unspecified) for patients older than age 6 years.	No difference was noted in pain between groups.
Touch therapy					
Ackerman et al., 2012 United States	23 patients aged 5–18 years (7 female, 8 male) with leukemia, lymphoma, congenital immune deficiency, or solid tumor	Unspecified pain related to stem cell transplantation therapy	Trained practitioner-performed massages and acupressure treatments during hospitalization (average was 1.6 sessions per week and length was 10–30 minutes); parents were trained in massage and acupressure and could perform on child ad hoc (study did not use comparator group)	Open-ended interviews with parents about the process, detailed handwritten notes by massage practitioners about the massage session, and interviews with two massage practitioners	Parents reported that massage provided varying degrees of relief from pain for most participants. Parents reported increased caregiver competence and closeness with their child.

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Table 1. Characteristics of Identified Nonpharmacologic Pain Management Studies *(Continued)*

Study	Sample	Pain Source	Intervention Groups	Instrument	Findings
Touch therapy *(Continued)*					
Post-White et al., 2008 United States	25 patients aged 1–18 years (10 female, 15 male) with leukemia, lymphoma, solid tumor, or central nervous system tumor	Unspecified pain related to cancer and/or treatment	Trained practitioner-performed massages versus quiet time (play, rest, or watch a movie with parent) for four sessions per week for about 30 minutes each	Youth reported pain using a 10 cm VAS (14–18 years) or Wong-Baker FACES scale (ages 3–13 years); parents reported pain using the Pain Assessment Tool for children 1–2 years; heart and respiratory rate auscultated; blood pressure assessed electronically; qualitative structured interview with patients and parents related to process	No difference was noted between groups on pain, respiratory rate, or blood pressure. Heart rate was lower in response to massage compared to quiet time ($p = 0.02$). No difference was noted between groups on pain, respiratory rate, or blood pressure. Interview data revealed a perceived improvement in pain for patients in the massage group.
Weekes et al., 1993 United States	20 patients age 11–19 years (10 female, 10 male) with solid tumor or renal failure (comparison group)	Bone marrow aspiration, lumbar puncture, shunt placement, or venipuncture	Hand-holding (either mother or nurse) during a single procedure	Qualitative semistructured interview with patients related to the process	Findings from interviews showed that both cancer and renal failure groups perceived hand-holding as a positive experience and thought it diminished pain. Both groups preferred holding hands with mother instead of nurse.
Wong et al., 2013 United States	9 patients aged 3–18 years (5 female, 4 male) with unspecified cancers	Unspecified pain related to cancer and/or treatment	Healing touch by a trained practitioner versus reading or play activity with a volunteer for 30 minutes once per day during all inpatient and outpatient visits for about a year	Youth, parents, and nurses rated pain using the Wong-Baker FACES scale.	Pain after healing touch was less than pre-therapy on youth, parent, and nurse reports ($p < 0.001$ for all). No difference over time in control group by any report. Between-group pain scores decreased by a greater amount in the healing touch group on youth ($p = 0.0023$) and parent ($p = 0.019$) reports.
Multimodal cognitive-behavior therapy					
Bisignano & Bush, 2006 United States	30 patients aged 7–18 years (15 female, 15 male) with leukemia, lymphoma, solid tumor, or hematologic disorders	Central venous catheter insertion	Interactive CDs focused on education, preparation, modeling, deep breathing, and imagery plus EMLA versus EMLA and education prior to a single procedure	Youth rated pain from 0–100 on a thermometer graphic scale.	No difference was noted in pain between groups.
Broome et al., 1992 United States	14 patients aged 3–15 years (3 female, 11 male) with leukemia	Lumbar puncture	Guided imagery, coached relaxation, and distraction taught prior to procedure and practiced nightly at home with parents for two procedures (baseline procedure conducted; study did not use comparator group)	Youth reported pain using the Wong-Baker FACES scale.	Pain related to procedure decreased compared to baseline ($p < 0.008$).

(Continued on the next page)

CHEOPS—Children's Hospital of Eastern Ontario Pain Scale; EMLA—eutectic mixture of local anaesthetics; RCT—randomized, controlled trial; VAS—visual analog scale

Table 1. Characteristics of Identified Nonpharmacologic Pain Management Studies *(Continued)*

Study	Sample	Pain Source	Intervention Groups	Instrument	Findings
Multimodal cognitive-behavior therapy *(Continued)*					
Broome et al., 1998 United States	28 patients aged 4–18 years (11 female, 17 male) with unspecified cancer	Lumbar puncture	Guided imagery, coached relaxation, and distraction taught prior to procedure and practiced nightly at home with parents for procedure (baseline procedure conducted)	Youth rated pain using the Oucher scale.	Improvement in pain scores was noted during a five-month period ($p < 0.01$). Parent reports of technique practice effectiveness correlated with pain at five months ($p < 0.05$).
Jay et al., 1987 United States	56 patients ages 3–13 years (20 female, 36 male) with leukemia	Bone marrow aspiration	Filmed modeling, breathing exercises, positive incentive, imagery, distraction, and rehearsal versus oral diazepam versus attention control (cartoon watching for 30 minutes pre-procedure)	Youth rated pain from 0–100 on a thermometer graphic scale.	Pain was less in the behavior intervention period ($p < 0.01$) compared to the other periods.
Jay et al., 1991 United States	83 patients aged 3–12 years (38 female, 45 male) with leukemia or lymphoma	Bone marrow aspiration or lumbar puncture	Filmed modeling of procedure, rehearsal, deep breathing, imagery, distraction, and positive incentive versus same plus diazepam before procedure (baseline procedure conducted)	Youth rated pain on a five-point FACES scale.	Pain decreased over time ($p < 0.01$) in both groups. No effect of group
Jay et al., 1995 United States	18 patients ages 3–12 years (9 female, 9 male) with leukemia	Bone marrow aspiration	Filmed modeling, positive coping skill teaching, imagery, distraction, and rehearsal versus general anesthesia each during procedure	Youth rated pain on a five-point FACES scale.	No difference in pain between groups.
Manne et al., 1990 United States	23 patients ages 3–9 years (12 female, 11 male) with leukemia, lymphoma, solid tumor, or congenital immune disorders	Venipuncture	Parent-led distraction, deep breathing, and positive reinforcement versus parent use of techniques they previously found helpful for each of three procedures (baseline procedure conducted)	Youth rated pain using the FACES scale, and parents rated pain using a VAS (length unspecified).	No difference was noted between groups on youth-rated pain scores over time. Decrease in parent-rated pain from baseline procedure to follow-up procedures was noted in the intervention group only ($p = 0.005$).
Månsson et al., 1993 Sweden	30 patients aged 4–17 years (11 female, 19 male) with leukemia or lymphoma	Lumbar puncture	Procedure practice with a doll and education on procedure once plus topical anesthetic and benzodiazepine versus procedure practice with a doll and education on procedure three times plus topical anesthetic and benzodiazepine versus topical anesthetic and benzodiazepine	Youth rated pain using a 10 cm VAS. A qualitative interview with patients after the procedure also was conducted.	No difference between groups on pain scores over time.
Pederson, 1996 United States	8 patients aged 6–14 years (3 female, 5 male) with leukemia	Lumbar puncture	Filmed modeling, deep breathing, relaxation, and distraction plus lidocaine injection versus lidocaine injection during procedure (baseline procedure conducted)	Youth rated pain using a 10 cm VAS.	No difference between groups on pain scores or on pre- and post-procedure pain.

CHEOPS—Children's Hospital of Eastern Ontario Pain Scale; EMLA—eutectic mixture of local anaesthetics; RCT—randomized, controlled trial; VAS—visual analog scale

education alone during LP with the addition of topical anesthetic (i.e., eutectic mixture of local anesthetics) at the procedure site for all patients (Liossi, White, & Hatira, 2006). Youth-reported pain was less in the hypnosis group compared to control. Self-directed hypnosis was then compared to play and a no-treatment control with respect to effectiveness in decreasing venipuncture-related pain (Liossi, White, & Hatira, 2009). Participants in the hypnosis group reported less pain than those in the control groups.

An additional study of the effectiveness of indirect hypnosis versus distraction at decreasing procedural pain did not demonstrate between-group differences but did show decreased youth- and observer-rated ($p < 0.009$) pain from baseline procedure across groups (Wall & Womack, 1989). A study by Zeltzer and LeBaron (1982) compared indirect hypnosis to deep breathing, distraction, and procedural practice in children and young adults undergoing BMA or LP. Results showed hypnosis to be more effective than the comparator, particularly in the case of LP.

Physical activity: To date, one study has examined the effectiveness of three 30-minute sessions of physical activity per week, with pain assessed as the bodily pain subscale of a HRQOL measure (Speyer, Herbinet, Vuillemin, Briançon, & Chastagner, 2010). Results showed the intervention decreased parent-rated bodily pain compared to control, with no differences in youth-reported pain being observed.

Physical positioning: The impact of physical positioning on pain has been examined in a single study, where a positioning pillow intended to facilitate appropriate youth positioning during LP was trialed (Marec-Bérard et al., 2009). Results showed procedural pain was not affected by pillow use.

Touch therapy: Four studies have evaluated the effect of healing touch, massage, or acupressure on pain in children and young adults with cancer and have demonstrated mixed results. A study of massage and acupressure on pain during the course of cancer treatment showed parents to qualitatively report that their child experienced pain relief as a result of the therapy (Ackerman et al., 2012). The effectiveness of massage compared to quiet play on pain related to cancer and its treatment has also been examined (Post-White et al., 2008). Results showed no difference in observer- or youth-reported pain; however, heart rate was lower following massage compared to play, and qualitative interviews with children indicated that the massage intervention lessened pain. Another interview-based study with patients undergoing various painful procedures showed that holding hands with either their mother or nurse was perceived as lessening pain (Weekes, Kagan, James, & Seboni, 1993). In Wong et al. (2013), the effect of touch by a trained practitioner on pain during the course of cancer therapy has been compared to attention control in a study of patients aged 3–18 years. Children and young adults in the intervention group had one 30-minute healing touch session each day while receiving inpatient cancer therapy and at each outpatient clinic visit. The authors reported that pain in the intervention group decreased after each 30-minute session compared to immediately prior according to youth, parent, and nurse reports. This trend was not observed in the attention control group. Pain also decreased more in the healing touch group compared with control.

Multimodal cognitive-behavior therapies: Nine studies examined the effectiveness of CBT on pain related to skin-breaking procedures (i.e, BMA, LP, venipuncture, or central venous catheter insertion). A study of procedural preparation, relaxation, and distraction group compared to standard care found no differences in pain reports between groups (Bisignano & Bush, 2006). The influence of guided imagery, relaxation, and distraction on youth-rated procedural pain also has been examined (Broome, Lillis, McGahee, & Bates, 1992). Results showed that CBT instruction resulted in lower pain reports compared to a baseline procedure. An additional study by the same researcher examined the impact of guided imagery, relaxation, and distraction taught to children and young adults, and practiced with parents, on pain (Broome, Rehwaldt, & Fogg, 1998). Procedural pain following CBT instruction was compared to baseline procedures, and patients showed an improvement in pain scores over time.

A study by Jay, Elliott, Katz, and Siegel (1987) compared CBT, minimal pharmacologic sedation, and an attention control treatment, and demonstrated CBT to be more effective in decreasing youth-rated pain than the other treatments. The effect of modeling, relaxation, distraction, and procedural rehearsal has been compared to the same training plus pharmacologic sedation (Jay, Elliott, Woody, & Siegel, 1991). Results demonstrated reduced pain in both groups compared to a baseline procedure; however, a between-group reduction in pain was not observed. Procedural preparation, coping-skill teaching, relaxation, and distraction were compared to general anesthesia on procedural pain, and no difference in between-group pain was observed (Jay, Elliott, Fitzgibbons, Woody, & Siegel, 1995).

Additional research has examined the impact of distraction, deep-breathing exercises, and positive reinforcement compared to parent-initiated intervention on pain related to serial procedures (Manne et al., 1990). Results indicated a difference in parent-rated pain over time in the intervention group only. In addition, two CBT treatment arms (practice plus education prior to only the first of three procedures and the same prior to each of three procedures) were compared to standard care in a study showing no between-group difference

in youth-rated pain (Månsson, Björkhem, & Wiebe, 1993). A study investigating the impact of preparation, relaxation, and distraction with lidocaine to lidocaine alone demonstrated no difference in between-group procedural pain (Pederson, 1996).

Impact of Child Age on Pain Outcome

The participant age ranges in identified studies were wide ($\bar{X}$ = 10.5 years, SD = 3.1) and often spanned several development stages (e.g., toddler to young adult). It was, therefore, not possible to provide any narrative comment on which, if any, nonpharmacologic strategies are effective at managing pain in children or young adults of different ages. Only a minority of studies (n = 6) conducted any analyses to elucidate whether or not pain outcomes were age-dependent (Gershon et al., 2004; Jay et al., 1987; Kuttner et al., 1988; Manne et al., 1990; Pederson, 1996; Wolitzky et al., 2005). Of these studies, two showed child age as having an effect on pain management outcomes. Specifically, Kuttner et al. (1988) showed that observer-rated pain was less in children aged 7–10 years compared to those aged 3–6 years during hypnosis and distraction ($p < 0.05$). Gershon et al. (2004) showed that pulse rates in younger children (12.7 years or younger) during virtual reality and non-virtual reality distraction were significantly higher during subcutaneous port accesses than older children, even after controlling for age as a covariate ($p < 0.05$).

Methodologic Quality of Studies

Twenty-five studies (78%) presented evidence that was graded as level I. However, the internal validity of these studies was either fair or poor, and the external validity was generally poor (n = 19 studies, 76%) according to the framework established by the USPSTF (2008). Internal validity was negatively affected by small samples and the omission of details on participant, observer, and analyst blinding, among other flaws. In addition, despite conducting hypothesis-testing statistical data analyses, only two studies reported a priori sample size calculations (Marec-Bérard et al., 2009; Nguyen et al., 2010). Limitations to external validity included high rates of participation refusal, single-center studies, and a lack of reporting on participant demographics. A critique of the quality of each study is presented in Table 2.

Discussion

This review has described and critically appraised the current scientific knowledge related to psychological and physical pain management for children and young adults with cancer. In total, 32 studies of differing design were identified, which investigated the effect of nonpharmacological interventions on cancer-related pain in pediatric and young adult patients. Of these studies, 25 used designs graded as level I evidence; however, methodologic limitations that compromised internal and external validity were common. Still, the main finding of this review, that 69% of identified studies reported a decrease in pain (18 statistically significant decreases and 4 anecdotal qualitative reports) because of a psychological or physical intervention, suggests the beginning of an evidence base for the use of these modalities in pediatric and young adult cancer pain.

Although outcomes varied greatly across study and pain management intervention, certain intervention types more frequently resulted in decreases in pain. In particular, seven studies examining the impact of hypnosis on procedural pain showed a positive impact. Touch-based therapy and youth distraction also were effective in decreasing pain. Of note, the majority of identified studies (n = 27, 84%) have attempted to examine the impact of psychological or physical pain interventions on pediatric and young adult patients for pain caused by invasive procedures. Only five studies examined interventions for pain related to the disease (e.g., tumor-related pain) or treatment (e.g., surgery-related pain). These few studies were exclusively published from 2010 onwards, and additional investigation in this area will be important in examining the use of nonpharmacologic pain management techniques for use beyond painful procedures.

Previous research also has indicated that specific characteristics of pediatric and young adult patients may predict pain outcomes. Specifically, girls with cancer have been shown to report higher pain intensity than boys when diagnosis, physical status, and cause of pain are taken into account (Hechter et al., 2009). In addition, age is an important predictor of pain reports with children and young adults' understanding of pain progressing from a simple understanding of global pain severity toward an appreciation of the multidimensional nature of pain by older childhood (Craig, Grunau, & Branson, 1998). Diagnosis also can predict child pain, with certain cancers known to be particularly painful (Collins et al., 2008). The small samples included in studies identified in this review mean that identification of the participant-level characteristics that may predict intervention effectiveness was not possible. Future research into this area is needed.

Methodologic Critique of Studies

The results of the identified studies should be interpreted with caution given the level of evidence and the methodologic quality issues of each. Major methodologic concerns included small sample sizes without computations suggesting adequate statistical power,

Table 2. Design and Methodologic Rigor for Nonpharmacologic Pain Management Studies

Study	Level of Evidence	Design	Internal Validity	External Validity	Limitations
Aromatherapy					
Ndao et al., 2012	I	RCT (parallel group)	Fair	Poor	Small sample size; comparable groups not assembled (baseline pain differed across groups); pain data dichotomized (loss of variability); only generalizable to patients undergoing stem cell transplantation
Art therapy					
Madden et al., 2010	I and III	RCT (parallel group) and uncontrolled trial with baseline measures plus qualitative analysis of open-ended interviews	Poor and NA	Poor	Small sample size; retrospective quality-of-life assessment; high rate of outcome measure omission by patients; pain not assessed using a symptom-specific validated and reliable instrument; recruitment information not provided
Distraction					
Gershon et al., 2004	I	RCT (parallel group)	Fair	Poor	Small sample size; observer not blinded (risk of detection bias)
Hedén et al., 2009	I	RCT (parallel group)	Fair	Poor	Small sample size; baseline differences between groups; recruitment information not provided
Nguyen et al., 2010	I and III	RCT (parallel group) and qualitative analysis of qualitative analysis of open-ended interviews	Fair and NA	Poor	Sample size reported as adequate to detect a Cohen's effect size of 0.5; pain assessment measure not validated for children younger than age 8 years; participants not blinded to treatment (risk of performance bias); standard of medical care not generalizable (topical anesthetics or sedation not used during procedure)
Windich-Biermeier et al., 2007	I	RCT (parallel group)	Poor	Fair	Small sample size; no baseline outcome measurements; participants not blinded to treatment (risk of performance bias); excellent recruitment rate (100%)
Wint et al., 2002	I and III	RCT (parallel group) and qualitative analysis of open-ended interviews	Poor and NA	Poor	Small sample size; no baseline outcome measurements; participants not blinded to treatment (risk of performance bias); recruitment information not provided
Wolitzky et al., 2005	I	RCT (parallel group)	Fair	Poor	Small sample size; pain and anxiety data collapsed by researchers and analyzed as distress; observer not blinded (risk of detection bias); comparable groups not assembled; high attrition rate
Hypnosis					
Hawkins et al., 1998	I	RCT (parallel group)	Poor	Poor	Small sample size; validity and reliability of measurement tool unknown; demographic and recruitment information not provided
Katz et al., 1987	I	RCT (parallel group)	Fair	Poor	Small sample size; intervention fidelity unknown; demographic and recruitment information not provided
Kuttner et al., 1988	I	RCT (parallel group)	Poor	Poor	Small sample size; intervention fidelity unknown; observer not blinded (risk of detection bias); demographic and recruitment information not provided
Liossi et al., 2006	I	RCT (parallel group)	Fair	Poor	Demographic information not provided
Liossi et al., 2009	I	RCT (parallel group)	Fair	Fair	Small sample size; limited demographic information provided

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NA—not applicable; RCT—randomized, controlled trial

Table 2. Design and Methodologic Rigor for Nonpharmacologic Pain Management Studies *(Continued)*

Study	Level of Evidence	Design	Internal Validity	External Validity	Limitations
Hypnosis *(Continued)*					
Liossi & Hatira, 1999	I	RCT (parallel group)	Fair	Poor	Small sample size; intervention fidelity unknown; outcome rater not blinded (risk of detection bias); recruitment information not provided
Liossi & Hatira, 2003	I	RCT (parallel group)	Fair	Fair	Small sample size; intervention fidelity unknown; outcome rater not blinded (risk of detection bias)
Wall & Womack, 1989	II–3	Uncontrolled trial with baseline measures	NA	Poor	Small sample size; treatment fidelity unknown; potential confounding variables not accounted for in analysis
Zeltzer & LeBaron, 1982	I	RCT (parallel group)	Poor	Poor	Small sample size; validity of pain assessment measure unknown; baseline procedures was recorded for 39% of participants because pain and anxiety were so extreme during pre-intervention; observer not blinded (risk of detection bias); recruitment information not provided
Physical activity					
Speyer et al., 2010	I	RCT (crossover)	Fair	Poor	Possible confounding variables during hospital stay not accounted for; a number of families refused to participate; no analysis of possible sequence effects; treatment fidelity unknown
Physical positioning					
Marec-Bérard et al., 2009	I	RCT (parallel group)	Fair	Fair	Observer not blinded (risk of detection bias)
Touch therapy					
Ackerman et al., 2012	III	Qualitative analysis of open-ended interviews	NA	Poor	Small sample size; nonvalidated pain assessment measure; interviews were not conducted with patients; intervention fidelity unknown; interviews conducted retrospectively (risk of recall bias)
Post-White et al., 2008	I and III	RCT (crossover) and qualitative analysis of qualitative analysis of open-ended interviews	Fair and NA	Poor	Small sample size; interviews conducted retrospectively (risk of recall bias); high proportion (50%) of families refused to participate; no analysis of possible sequence effects
Weekes et al., 1993	III	Descriptive study with a comparison group	NA	Poor	Small sample size; observer not blinded (risk of detection bias); comparable groups not assembled (ethnicity differed across groups); data on many possible confounding factors not collected
Wong et al., 2013	I	RCT (parallel group)	Poor	Poor	Small sample size; intervention fidelity unknown; confounding potential of attention in intervention group; comparable groups not assembled; high attrition rate
Multimodal cognitive-behavior therapy					
Bisignano & Bush, 2006	I	RCT (parallel group)	Fair	Poor	Small sample size; high proportion (70%) of families refused to participate; painful procedure not standardized
Broome et al., 1992	II–3	Uncontrolled trial with baseline measures	NA	Poor	Small sample size; intervention fidelity unknown; demographic and recruitment information not provided
Broome et al., 1998	II–3	Uncontrolled trial with baseline measures	NA	Poor	Small sample size; intervention fidelity unknown; high proportion (64%) of families refused to participate

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NA—not applicable; RCT—randomized, controlled trial

Table 2. Design and Methodologic Rigor for Nonpharmacologic Pain Management Studies *(Continued)*

Study	Level of Evidence	Design	Internal Validity	External Validity	Limitations
Multimodal cognitive-behavior therapy *(Continued)*					
Jay et al., 1987	I	RCT (crossover)	Poor	Fair	Small sample size; observers not blinded (risk of detection bias); intervention fidelity unknown; pain not assessed before intervention (risk of confounding)
Jay et al., 1991	I	RCT (crossover)	Fair	Fair	Observers not blinded (risk of detection bias); intervention fidelity unknown; pain not assessed before intervention (risk of confounding); validity and reliability of pain measure unknown
Jay et al., 1995	I	RCT (crossover)	Fair	Poor	Small sample size; observers not blinded (risk of detection bias); intervention fidelity unknown; pain not assessed before intervention (risk of confounding); recruitment information not provided
Manne et al., 1990	II–1	Nonrandomized controlled trial	NA	Fair	Small sample size; observer not blinded (risk of detection bias); unknown whether comparable groups were assembled
Mansson, 1993	II–1	Nonrandomized controlled trial	NA	Poor	Small sample size; measures translated to Swedish without cross-cultural validity testing; non-equivalent control group (did not receive the same number of procedures as treatment groups); demographic and recruitment information not provided
Pederson, 1996	I	RCT (parallel group)	Fair	Poor	Small sample size; a number of families refused to participate

NA—not applicable; RCT—randomized, controlled trial

bias stemming from a lack of blinding in observer-rated pain reporting, unclear information surrounding the randomization procedures, high proportion of participation refusal or lack of information on recruitment rates (suggesting a possible selection bias), and lack of clear detail on intervention integrity (particularly in studies on CBT and hypnosis).

Because psychological and physical pain management interventions often are complex and are likely to incorporate several core components, careful examination and reporting of treatment fidelity is necessary to interpret results. Gearing et al. (2011) recommended that four key intervention elements be reported to allow for interpretation of fidelity: design, training, monitoring delivery, and monitoring receipt. Unfortunately, no study included in the current review adequately presented information related to the fidelity with which interventions were delivered, limiting the interpretability of the results. Researchers investigating psychological and physical pain management therapies should make clear how treatment fidelity was implemented and assessed.

An additional methodologic concern arose related to the mode of pain assessment in studies. Pain is generally appreciated as a subjective phenomenon. As such, consensus in the field is that pain measurement by self-report, as opposed to observation, proxy report (i.e., by parent or clinician), or physiological sign measurement, should be conducted whenever possible (von Baeyer, 2007). The empirical literature also overwhelmingly endorses the feasibility and validity of child self-report in children possessing the requisite cognitive development and acquisition of social communication skills (Huguet, Stinson, & McGrath, 2010; Stanford, Chambers, & Craig, 2005; Stinson, Kavanagh, Yamada, Gill, & Stevens, 2006; von Baeyer, 2006). The identified studies often used proxy-reported pain or both youth- and proxy-reported pain as intervention outcomes. In addition, the studies that used both youth and proxy report did not provide detail, including a priori rationale, regarding how discrepancies in outcomes reporting were addressed. Studies did not consistently use valid and reliable pain assessment measures, diminishing the interpretability of their results.

Despite the risk of adverse events (e.g., anxiety, severe symptoms) being relatively low in psychological or physical studies, particularly in the context of brief interventions to reduce procedural pain, there remains an obligation of researchers to adequately assess and report these events. Without adverse event assessments, the true harm/benefit ratios of nonpharmacologic interventions cannot be ascertained (McGrath et al.,

Knowledge Translation

To maximize quality of life for pediatric and young adult patients with cancer, all appropriate pain management modalities should be incorporated into practice.

Nonpharmacologic techniques are a simple and economical way to improve holistic cancer care delivered to pediatric and young adult patients.

Investigations into the safety and effectiveness of nonpharmacologic pain management will be important to improving pain outcomes and, ultimately, quality of life.

2008). None of the identified studies described assessing adverse events. Given the importance of reporting adverse events and the priority to involve children with cancer more actively in research (Reeve et al., 2013), future studies should include the recording and public reporting of these events in their designs.

Implications for Practice and Research

Several patient-, family-, and institution-level benefits have been associated with incorporating nonpharmacologic interventions into the treatment of pain in pediatric and young adult patients with cancer. These benefits specifically include (a) strong patient and family support (Adams et al., 2013; Bishop et al., 2010); (b) potential effectiveness of the interventions in managing pain, as demonstrated in other painful conditions of childhood (Palermo, Eccleston, Lewandowski, Williams, & Morley, 2010; van der Veek, Derkx, Benninga, Boer, & de Haan, 2013); and (c) a potentially attractive cost-benefit ratio (Kemper, Vohra, & Walls, 2008). However, the current article has demonstrated that there continues to be a paucity of well-designed, rigorous studies of adequate power investigating the impact of these therapies on pain. Reasons for this include the relative lack of research funding for the approaches compared to pharmacologic studies (Tabbers, Boluyt, Berger, & Benninga, 2011), challenges in blinding participants and interventionists (Eccleston, Palermo, Fisher, & Law, 2012), as well as difficulty in implementing appropriate control groups in RCTs (Danaher & Seeley, 2009). These barriers will require careful navigation to facilitate future research in this area.

The authors' findings suggest several important areas for design improvements in future research, which can strengthen the knowledge base in this area and inform the clinical care of children with cancer. Studies should include larger samples, particularly recruited from multiple sites, to improve the generalizability of results. The method of pain assessment (i.e., by youth report, proxy report, or physiological monitoring) should also be considered and, if multiple means of measurement are made, clear rationale for the interpretation of results should be provided. Improved methods of monitoring treatment fidelity also are needed. The development of guides to improve treatment fidelity in psychological research (Gearing et al., 2011) will be useful in this regard. In addition, according to this review, the effectiveness of psychological and physical interventions for the management of cancer pain in pediatric and young adult patients not related to invasive procedures has not been widely investigated. Studies that are designed with the active collaboration of researchers and interdisciplinary clinicians also are required to improve the use, acceptability, and safety of developed interventions. Finally, the majority of studies conducted to date have used small samples of participants who varied greatly in terms of age (e.g., toddlers to young adults). However, the inherent developmental differences across the range of child ages indicates that responses to certain pain management treatments may differ (Craig, Lilley, & Gilbert, 1996). Research should focus on elucidating the particular strategies that work optimally for different age groups of children and young adults with cancer.

Limitations

The USPSTF (2008) guideline was used to evaluate the methodologic quality and validity of study results. This guideline was used because it provides a method to rate the quality of studies across a spectrum of research designs. However, the guideline does not provide specific direction to grading all study designs, thereby precluding the authors from rating the internal validity of level II and III evidence. In addition, the results of this review may be susceptible to bias as the current authors were not blinded to study researchers, journal, or publication year. The current authors also did not include studies published in languages other than English. Finally, because this review was intentionally broad with respect to the details of included studies, the current authors were unable to conduct any quantitative syntheses of data or to draw any meaningful conclusions related to how the effectiveness of interventions differs by child age. As more studies of sound methodologic quality are conducted within the realm of nonpharmacologic cancer pain management for children, the results should be synthesized as appropriate to provide an overall understanding of intervention effectiveness.

Conclusion

The majority of identified studies showed a decrease in pain resulting from the use of psychological or physical intervention in pediatric and young adult patients

with cancer. The combination of small samples and low methodologic quality means that the results should be carefully interpreted. In addition, very limited research has been conducted into the nonpharmacologic management of pediatric and young adult oncology pain because of causes other than painful medical procedures.

Despite the limitations of the identified studies, important clinical implications related to these therapies should be considered. In particular, because of the necessity to maximize HRQOL of children and young adults with cancer, including by minimizing pain, attention should be given to incorporating all pain management modalities into practice. Psychological and physical techniques represent simple and economic means to improve holistic cancer care delivered to children and young adults, particularly when used as adjuncts to pharmacologic approaches or incorporated in multimodal treatment plans. Investigations into the safety and effectiveness of psychological and physical pain management, as well as means to translate these interventions into practice, will be important in improving pain outcomes and, ultimately, quality of life for pediatric and young adult patients with cancer.

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