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Psychological interventions for vaccine injections in children and adolescents: Systematic review of randomized and quasi-randomized controlled trials

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Psychological Interventions for Vaccine Injections in Children and Adolescents

Systematic Review of Randomized and Quasi-Randomized Controlled Trials

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Background: This systematic review evaluated the effectiveness of psychological interventions for reducing vaccination pain and related outcomes in children and adolescents.

Design/Methods: Database searches identified relevant randomized and quasi-randomized controlled trials. Data were extracted and pooled using established methods. Pain, fear, and distress were considered critically important outcomes.

Results: Twenty-two studies were included; 2 included adolescents. Findings showed no benefit of false suggestion (n = 240) for pain (standardized mean difference [SMD] −0.21 [−0.47, 0.05]) or distress (SMD −0.28 [−0.59, 0.11]), or for use of repeated reassurance (n = 82) for pain (SMD −0.18 [−0.92, 0.56]), fear (SMD −0.18 [−0.71, 0.36]), or distress (SMD 0.10 [−0.33, 0.54]). Verbal distraction (n = 46) showed reduced distress (SMD −1.22 [−1.87, −0.58]), but not reduced pain (SMD −0.27 [−1.02, 0.47]). Similarly, video distraction (n = 328) showed reduced distress (SMD −0.58 [−0.82, −0.34]), but not reduced pain (SMD −0.88 [−1.78, 0.02]) or fear (SMD 0.08 [−0.25, 0.41]). Music distraction demonstrated reduced pain when used with children (n = 417) (SMD −0.45 [−0.71, −0.18]), but not with adolescents (n = 118) (SMD −0.04 [−0.42, 0.34]). Breathing with a toy (n = 368) showed benefit for pain (SMD −0.49 [−0.85, −0.13]), but not fear (SMD −0.60 [−1.22, 0.02]); whereas breathing without a toy (n = 136) showed no benefit for pain (SMD −0.27 [−0.61, 0.07]) or fear (SMD −0.36 [−0.86, 0.15]). There was no benefit for a breathing intervention (cough) in children and adolescents (n = 136) for pain (SMD −0.17 [−0.41, 0.07]).

Conclusions: Psychological interventions with some evidence of benefit in children include: verbal distraction, video distraction, music distraction, and breathing with a toy.

Key Words: pain management, randomized controlled trial, systematic review, vaccination, psychological, children, adolescents

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Vaccine injections are unique in that they are regularly experienced by children who are healthy as well as those who have chronic illness, making them the most common painful medical procedure performed worldwide.[1] Multipronged approaches to pain management include pharmacological, psychological, procedural, and physical strategies, all of which have been studied to reduce the pain and distress associated with vaccine injections.[2–4] Of these approaches, psychological interventions hold considerable appeal to families given that they capitalize on strategies that children and parents already engage in naturally to some extent (eg, distraction), and, due to their non-pharmacological nature, are generally met with higher acceptance by parents. Many psychological interventions are simple and require minimal or no training, are able to be implemented directly by children, parents, and immunizers, and are applicable across a wide age range. Furthermore, they generally capitalize on available resources, making them easy to implement across different clinical settings.[5]

In a previous knowledge synthesis on this topic, support was found for several different psychological interventions for vaccination pain, including breathing exercises,

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child-led or nurse-led distraction, and combined cognitive-behavioral interventions (ie, strategies aimed at modifying emotions, behaviors, and cognitions).[3] These interventions were subsequently incorporated into a clinical practice guideline for childhood vaccination pain management.[6] Since the original guideline was developed, additional research in the area has been published. Furthermore, the previous systematic review and meta-analysis grouped together infants and children, and omitted adolescents; this led to a gap in knowledge synthesis and recommendations for each pediatric population who present unique developmental considerations.[3] Given recent evidence suggesting possible differences in treatment efficacy based on intervention characteristics,[5] alternative approaches to examining the literature are warranted, in particular, the type of distracter used. Our previous synthesis examined the literature according to the individual directing the intervention.[3] The current systematic review and meta-analysis was therefore undertaken to provide the evidence base for an update and expansion of the original guideline in the specific area of psychological interventions for children and adolescents undergoing vaccine injections and evaluated the data according to the type of distractor used.

This review reports the results for trials that evaluated the effect of any of the following psychological interventions for the management of vaccination pain and related outcomes: (1) false suggestion, (2) repeated reassurance, (3) verbal distraction, (4) video distraction, (5) music distraction, (6) breathing with toy, (7) breathing without toy, and (8) breathing intervention (cough). Separate papers explore the effectiveness of psychological interventions in young children (0 to 3 y)[7] and adults,[8] as well as pharmacological, physical, procedural, and process approaches for infants, children, adolescents, and adults.

METHODS

This systematic review was conducted as part of the Canadian multidisciplinary Help ELiminate Pain in Kids and Adults (HELPinKids&Adults) team, which was assembled with the goal of developing an evidenced-based clinical practice guideline, and undertaking knowledge translation activities, for reducing vaccination pain. As such, an identical methodological approach was applied across reviewed areas (psychological, pharmacological, physical, procedural, and process) for reducing vaccination injection pain. A separate manuscript describes this methodological approach in greater detail.[9]

In brief, systematic review and meta-analytic methodologies were informed by GRADE (Grading of Recommendations, Assessment, Development and Evaluation)[10] and the Cochrane Collaboration.[11] The search was developed in consultation with an experienced librarian and included the following databases: EMBASE, Medline, PsycINFO, and CINAHL. Search results were screened for eligibility.[9] Peer-reviewed publications (full or short report) and published academic theses/dissertations were included. Through a voting process, the HELPinKids&Adults team identified clinical questions (ie, psychological interventions) to be examined, as well as critical and important outcomes to be included in each review. Specifically, candidate questions were identified based on prior clinical practice guidelines,[3] clinical experience, and knowledge of existing research. Clinical questions were retained if considered important by at least two-thirds of the HELPinKids&Adults team, and were modified as appropriate after preliminary review and discussion of the research evidence by the HELPinKids&Adults team.[9] Two of the included clinical questions pertained to individuals across the lifespan (ie, use of false suggestion or repeated reassurance); however, evidence was only available from children.

This review focused on studies of psychological interventions including children (aged above 3 to 12 y) and adolescents (aged above 12 to 17 y) undergoing vaccination in any setting using randomized or quasi-randomized study designs. Only simple psychological interventions were sought for inclusion (ie, those involving distraction, and/or interactions between children and parent/nurse/immunizer). More complex psychological interventions, such as hypnosis, were not included, as they typically require special training to be implemented. Psychological interventions related to treating high needle fear are discussed in another review in this series.[12] Pain and fear were typically prioritized as critically important outcomes, respectively, defined as self-report of pain or self-report of fear during vaccination. The overall effectiveness of an intervention was determined according to the effects on critically important outcomes. Distress was also accepted as a critically important outcome if children below 7 years were included in the evidence base, due to the possibility that self-report was unreliable.[13–15] Distress was defined as observer ratings of an individual's behavioral response during vaccination (ie, pain, fear, distress). When available, other important outcomes included procedure outcomes (eg, procedure success, duration), parent fear, use of the intervention, compliance, memory, preference, and satisfaction.

As per the standard approach across reviewed content areas,[9] outcomes that were assessed at multiple time-points during the vaccination procedure were analyzed as follows: (1) the preprocedure phase, which occurred post-intervention but before vaccine injection(s); (2) the acute phase (within the first minute of needle puncture and vaccine injection); and (3) the recovery phase (1 to 5 min after vaccine injection(s)). Phases were combined when outcomes were not assessed separately for each phase (eg, acute + recovery). Delayed onset of pain (ie, pain occurring hours to days after injection) was not considered. Data from multiple observers assessing the same outcome (eg, parent-rated child distress, clinician-rated child distress, observational behavior coding) was combined into a single point estimate and associated variance before inclusion in the meta-analysis using established methods.[16]

Attempts were made to contact study authors when data necessary for pooling were not included in published papers (ie, means, SDs). An emphasis was placed on including data from all possible studies. As such, when means and SDs were not available, they were estimated from medians, ranges, SEs, 95% confidence intervals (CIs), or graphs. This was done only as needed, on a very restricted predefined basis, and followed established methods.[17]

Data was pooled using RevMan (version 5.2, Cochrane Collaboration, Copenhagen, Denmark), and effects of interventions were expressed as a standardized mean difference (SMD) with accompanying 95% CI or relative risk and CI, as appropriate. Separate analyses were conducted for children (above 3 to 12 y old) and adolescents (above 12 to 17 y old) when possible. A random effects model was used for all analyses. Statistical heterogeneity was assessed using I^2 and χ^2 tests. Additional post hoc analyses were carried out to examine the effects of study methodology and/or heterogeneity. Risk of bias was

assessed for critical outcomes for all included studies using the Cochrane risk of bias tool (https://bmg.cochrane.org/assessing-risk-bias-included-studies).

Evidence profiles and summary of findings tables were created using the GRADE profiler software (version 3.6.1). When analyses demonstrated a consistent benefit of the intervention across critically important outcomes, it was said to have "benefit across all measured outcomes." Findings were described as "mixed" when results were inconsistent across critically important outcomes, and were described as having "no evidence of a benefit" when any statistical evidence of benefit was lacking.

RESULTS

Database searches returned a total of 114,251 citations, including 32,155 duplicates. An additional 138 citations were identified from manual searches. The remaining 82,234 citations were reviewed for eligibility by 2 members of the HELPinKids&Adults (Help ELiminate Pain in Kids and Adults) Team: Taddio, A., McMurtry C.M., Chambers C.T., Pillai Riddell R., Shah V., Noel M., MacDonald N.E., Rogers J., Bucci L., Mousmanis P., Halperin S.A., Bowles S., Halpert C., Ipp M., Rieder M., Robson K., Asmundson G.J.G., Antony M., Alexander D., Appleton M., Dubey V., Hanrahan A., Lockett D., Scott J., Votta Bleeker E.). Twenty-two studies investigating psychological interventions in children and/or adolescents were identified and included in the review.[18–39] In 1 case, there were multiple publications emanating from the same study, including a dissertation and published manuscript of the same data.[37] Most studies used a between-subjects (parallel) design (n = 20), with 2 studies using a within-subjects (cross-over) design.[23,38] Data were provided for 2 or more treatment groups from all trials. Three trials examined multiple psychological interventions, with different treatment groups included in their respective clinical questions.[27,29,33] Twenty studies included children only (above 3 to 12 y old), 1 study included adolescents only (above 12 to 17 y old), and 1 study included both children and adolescents. Two studies were excluded due to the: (1) study design not being randomized or quasi-randomized (n = 1)[40]; and (2) intervention was not psychological (n = 1).[41] See Figure 1 for a flowchart depicting study identification, screening, and inclusion. Table 1 outlines the clinical questions and critically important and important outcomes. Table 2 describes characteristics of included trials for each clinical question examining psychological interventions in children and/or adolescents.

Quality of Studies and Risk of Bias

Assessment of risk of bias for all included trials for critically important outcomes are reported in Table 3. All trials had high overall risk of bias, primarily due to lack of blinding of: participants, clinicians administering the intervention, and/or individual providing the ratings of critically important outcomes of pain, fear, and/or distress.

Overall Quality of Evidence and Treatment Effects

For all clinical questions, results for critically important outcomes only are described below, and are summarized

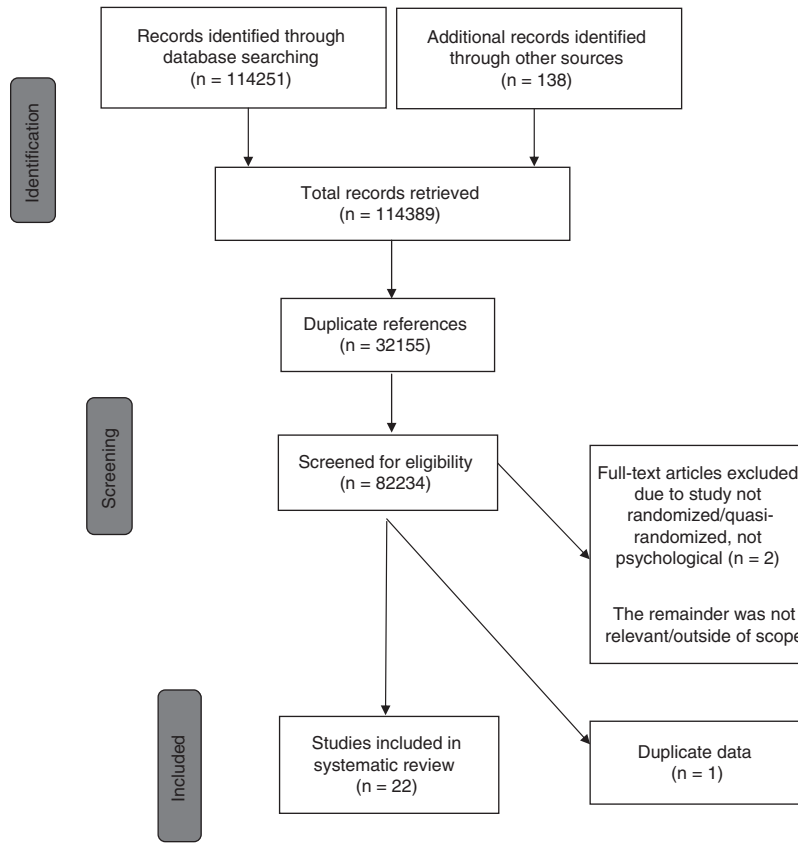

FIGURE 1. Flowchart of study identification, screening, and inclusion.

TABLE 1. Clinical Questions and Outcomes

Clinical Questions	Critical Outcomes*	Important Outcomes
Psychological interventions		
Should false suggestion be used during vaccine injections in individuals of all ages?	Pain, distress, fear	Procedure outcomes, parent fear, compliance, memory, preference, satisfaction
Should repeated reassurance be used during vaccine injections in individuals of all ages?	Pain, distress, fear	Procedure outcomes, parent fear, use of intervention, compliance, memory, preference, satisfaction
Should verbal distraction be used during vaccine injections in children >3-12 y?	Pain, fear	Distress, procedure outcomes, parent fear, use of intervention, use of intervention, compliance, memory, preference, satisfaction
Should video distraction be used during vaccine injections in children >3-12 y?	Pain, fear	Distress, procedure outcomes, parent fear, use of intervention, compliance, memory, preference, satisfaction
Should music distraction be used during vaccine injections in children >3-12 y?	Pain, fear	Distress, procedure outcomes, parent fear, use of intervention, compliance, memory, preference, satisfaction
Should music distraction be used during vaccine injections in adolescents >12-17 y?	Pain, fear	Distress, procedure outcomes, parent fear, use of intervention, compliance, memory, preference, satisfaction
Should breathing with a toy (blowing bubbles, pinwheel) be used during vaccine injections in children >3-12 y?	Pain, fear	Distress, procedure outcomes, parent fear, use of intervention, compliance, memory, preference, satisfaction
Should breathing without a toy (blowing, deep breathing) be used during vaccine injections in children >3-12 y?	Pain, fear	Distress, procedure outcomes, parent fear, use of intervention, compliance, memory, preference, satisfaction
Should breathing interventions (cough) be used during vaccine injections in children >3-17 y?	Pain, fear	Distress, procedure outcomes, parent fear, use of intervention, compliance, memory, preference, satisfaction

*Distress was considered when data were only available from young children (below 7 y old) with whom self-report is less reliable.

in Table 4. More detailed GRADE Evidence Profiles and Summary of Findings tables (Tables, Supplemental Digital Content 1 to 9, http://links.lww.com/CJP/A183, http://links.lww.com/CJP/A184, http://links.lww.com/CJP/A185, http://links.lww.com/CJP/A186, http://links.lww.com/CJP/A187, http://links.lww.com/CJP/A188, http://links.lww.com/CJP/A189, http://links.lww.com/CJP/A190, http://links.lww.com/CJP/A191,) and accompanying Forest plots (Figures, Supplemental Digital Content 1 to 9, http://links.lww.com/CJP/A192, http://links.lww.com/CJP/A193, http://links.lww.com/CJP/A194, http://links.lww.com/CJP/A195, http://links.lww.com/CJP/A196, http://links.lww.com/CJP/A197, http://links.lww.com/CJP/A198, http://links.lww.com/CJP/A199, http://links.lww.com/CJP/A200), for all critically important and important outcomes are provided as Supplemental Digital Content.

Should False Suggestion be Used During Vaccine Injections in Individuals of All Ages?

Two trials including 240 children aged 4 to 7 years investigated the impact of false suggestion.[26,27] In both trials, children were told by the immunizer or researcher that something was being done to help make the injection easier or less painful. Depending on the treatment group, this was accompanied by a potentially pain reducing intervention (ie, music distraction or vapocoolant) or a placebo (ie, wearing headphones with no music or aerosol spray). There was low quality of evidence for the critically important outcome of pain, largely due to inconsistent blinding of immunizer and outcome assessor, as well as selective outcome reporting (Table, Supplemental Digital Content 1, http://links.lww.com/CJP/A183). Both trials found no benefit of suggestion for the critically important outcome of pain: SMD −0.21 (−0.47, 0.05). Findings were consistent with and without the data from false suggestion with placebo intervention groups. No trials examined the critically important outcome of fear. Given the young age of participants, distress was also examined for the 1 trial containing these data,[26] which showed no benefit of suggestions for preprocedural distress: SMD −0.28 (−0.91, 0.34) (Table, Supplemental Digital Content 1, http://links.lww.com/CJP/A183 and Figure, Supplemental Digital Content 10, http://links.lww.com/CJP/A192). No other important outcomes were assessed.

Should Repeated Reassurance be Used During Vaccine Injections in Individuals of All Ages?

Two trials including 82 children aged 3 to 7 years investigated repeated reassurance by parents during vaccination.[29,33] Parents were trained before the procedure through oral instruction, modeling, and practice; during the vaccination, parents were repeatedly prompted to engage in reassurance. For example, saying reassuring statements such as "You're ok" or "It's almost over." There was low quality of evidence for the critically important outcome of pain, and very low quality of evidence for the critically important outcome of fear, largely due to inconsistent blinding of participants, immunizers, and outcome assessors, and contamination of treatment effects in the control group (ie, parents engaging in reassurance) (Table, Supplemental Digital Content 2, http://links.lww.com/CJP/A184). One trial[29] found no benefit for the critically important outcome of pain (SMD −0.18 [−0.92, 0.56]), whereas the other trial[33] found no benefit for the critically important outcome of preprocedural fear (SMD −0.18 [−0.71, 0.36]). Given the young age of participants, distress was also examined (preprocedure, acute, and recovery distress combined) and showed no benefit of repeated reassurance in both trials: SMD 0.10 (−0.33, 0.54) (Table, Supplemental Digital Content 2, http://links.lww.com/CJP/A184 and Figure, Supplemental Digital Content 11, http://links.lww.com/CJP/A193). Other assessed important outcomes included parent fear and parent use of intervention.

TABLE 2. Characteristics of the Trials Included in the Systematic Review

First Author Year, Country	Injection Details	Population Enrolled, Design, Setting	Intervention	Critical Outcomes
Should false suggestion be used during vaccine injections in individuals of all ages?				
Eland 1981 (1,2),[26] USA	DPT 0.5 mL, IM; 25 G, 5/8-inch needle; vastus lateralis	N = 40; children 4-5 y; between-groups design; single center, pediatric clinic	Refrigerant topical anesthetic spray (Frigiderm) plus cognitive information: child told by the nurse "I'm going to spray something on your leg before your shot that will not hurt, will make your leg feel cool, and the spray will make this shot hurt less than other shots you've had" (n = 10) or Refrigerant topical anesthetic spray (Frigiderm) plus no cognitive information: child told the nurse was "going to spray something on their leg before their shot" (n = 10) or Aerosol air spray plus cognitive information (n = 10) or Aerosol air spray plus no cognitive information; spray applied 3-5 s on the leg before vaccination (n = 10)	Pain: Adapted Eland's Color Assessment Tool
Fowler-Kerry (1,3),[27] Canada	DPT; no injection details	N = 200; children 4-7 y; between-groups design; multicenter, community health clinic	Suggestion: child told that the experimenter was going to help them when they had their injection. They wore headphones but no music was played (n = 40) or No treatment: 2 control groups combined: (1) child wore headphones (n = 40); (2) child did not wear headphones (n = 40) (n = 80 total) or Suggestion plus music distraction: child told that the experimenter was going to help them when they had their injection. Child wore headphones and listened to music immediately before and during the injection (n = 40) or Music distraction only: child wore headphones and listened to music immediately before and during the injection (n = 40)	Pain: VAS
Should repeated reassurance be used during vaccine injections in individuals of all ages?				
Gonzalez 1993 (2),[29] USA	Vaccine NR; no injection details	N = 42; children 3-7 y; between-groups design; single center, hospital primary care clinic	Reassurance: before the immunization, parents received oral instructions and audiocassette modeling on how to reassure, time to practice, and were reminded to engage in reassurance every 10 s throughout the procedure by a researcher (n = 14) or Distraction: before the immunization, parents received oral instructions and audiocassette modeling on how to distract, time to practice, and were reminded to engage in distraction every 10 s throughout the procedure by a researcher (n = 14)*	Pain: Oucher

(*Continued*)

TABLE 2. (*continued*)

First Author Year, Country	Injection Details	Population Enrolled, Design, Setting	Intervention	Critical Outcomes
			or Control: before the immunization, parents listened to a lecture and an audiocassette on transportation to the hospital and discussed transportation with a researcher (n = 14)	
Manimala 2000 (2),[33] USA	Vaccine NR; no injection details	N = 82; children 4-6 y; between-groups design; single center, county health department	Reassurance: before the immunization, 10 min of training including rationale, examples of reassurance and when to use it during the procedure; researchers acted as role models then parent and child also role played procedure (n = 27) or Distraction: before the immunization, 10 min of training including rationale, example techniques (eg, drawing, puzzles, talking about other things), asked to coach child to use a party blower throughout procedure; researchers acted as role models then parent and child also role played procedure (n = 28)* or Control: 10 min discussion with research on child's medical history and how parent typically interacted with child during medical procedures (n = 27)	Fear: Faces Scale
Should verbal distraction be used during vaccine injections in children >3-12 y?				
Gonzalez 1993 (1),[29] USA	Vaccine NR; no injection details	N = 28; children 3-7 y; between-groups design; single center, hospital (primary care clinic)	Reassurance: before the immunization, parents received oral instructions and audiocassette modeling on how to reassure, time to practice, and were reminded to engage in reassurance every 10 s throughout the procedure by a researcher (n = 14)* or Distraction: before the immunization, parents received oral instructions and audiocassette modeling on how to distract, time to practice, and were reminded to engage in distraction every 10 s throughout the procedure by a researcher (n = 14) or Control: before the immunization, parents listened to a lecture and an audiocassette on transportation to the hospital and discussed transportation with a researcher (n = 14)	Pain: Oucher
O'Laughlin 1995 (1),[36] USA	Vaccine NR; no injection details	N = 36; children 4-5 y; between-groups design; single center, private pediatric practice	Mothers present for injection, no training; assisted nurse by holding the child when necessary (n = 11) or Mother absent for injection (n = 9)* or Mother present for injection, instructed to watch only (n = 9)* or	NA (this study was not included in the meta-analysis for critical outcomes)

(*Continued*)

TABLE 2. (*continued*)

First Author Year, Country	Injection Details	Population Enrolled, Design, Setting	Intervention	Critical Outcomes
			Parent present for injection, instructed to coach child in using distraction: counting, rhyme, or poem recitation, singing, or looking at an object (n = 7)	
Should video distraction be used during vaccine injections in children >3-12 y?				
Cassidy 2002,[21] Canada	DPTP 1 mL IM; 25 G, 1.5-cm needle; 90-degree angle; mid-deltoid	N = 59; children 5 y; between-groups design; 2 centers, urban pediatric setting	Video distraction: child watched age-appropriate musical cartoon on TV screen (n = 31) or Control: child watched blank TV screen (n = 28)	Pain: Faces Pain Scale
Cohen 1997 (1,2),[22] USA	DPT and MMR; no injection details	N = 92; children 4-6 y; between-groups design; single center, rural health center	Video distraction with immunizer training: nurses received 15-min training involving role-playing of coaching behaviors. They were instructed to prompt the child to select a movie to view and taught to use questions, comments and direct commands during the movie (n = 31) or Video distraction plus parent and immunizer training: nurses received 15-min training involving role-playing of coaching behaviors. They were instructed to prompt the child to select a movie to view and taught to use questions, comments and direct commands during the movie. Parents were also provided with brief rationale for intervention followed by modeling and role-playing the coaching behaviors (n = 32) or Typical care: nurses instructed to interact according to her own routine (n = 29)	Fear: Faces Scale
Cohen 1999 (1),[23] USA	Hepatitis B; no injection details	N = 34; children 8-11 y; cross-over design; single center, school health clinic	Lidocine-prilocaine cream 2 g 1 h before the procedure (n = 34)* or Movie distraction plus nurse coaching: nurse received a 15-min training program in distraction then encouraged child while they were distracted by a video before, during, and after the injection (n = 34) or Typical care: nurse instructed to interact according to her own routine (n = 34)	Pain: VAS Fear: VAS
Cohen 2015 (1),[25] USA	DPTP, MMR, varicella; no injection details	N = 90; children 4-6.5 y; between-groups design; single center, pediatric clinic	Distraction: parents provided with laptop installed with parent-led computer game to use in waiting room. A portable DVD player with a selection of movies was provided for use during the procedure (n = 30) or	Pain: FPS-R

(*Continued*)

TABLE 2. (*continued*)

First Author Year, Country	Injection Details	Population Enrolled, Design, Setting	Intervention	Critical Outcomes
			Education: parents provided with laptop installed with an interactive training computer program to use in waiting room. A narrator explained the impact (positive and negative) of different parent behaviors (eg, distraction, criticism, reassurance). Typically the child watched. A portable DVD player with a selection of movies was provided for use during the procedure (n = 30)* or Control (no intervention) (n = 30)	
Luthy 2013 (2),[32] USA	Vaccine NR; no injection details	N = 68; children 2-12 y; between-groups design; single center, pediatric office	Distraction (DVD before, during and after the procedure) (n = 27) or Vapocoolant spray for 3-7 s before the procedure (n = 18)* or Control (no intervention) (n = 22)	NA (this study was not included in the meta-analysis for critical outcomes)
Should music distraction be used during vaccine injections in children >3-12 y?				
Fowler-Kerry 1987 (2,4),[27] Canada	DPT; no injection details	N = 200; children 4-7 y; between-groups design; 3 centers, community health clinic	Music distraction only: child wore headphones and listened to music immediately before and during the injection (n = 40) or No treatment: 2 control groups combined: (1) child wore headphones (n = 40); (2) child did not wear headphones (n = 40) (n = 80 total) or Music distraction plus suggestion: child told that the experimenter was going to help them when they had their injection. Child wore headphones and listened to music immediately before and during the injection (n = 40) or Suggestion: child told that the experimenter was going to help them when they had their injection. They wore headphones but no music was played (n = 40)	Pain: VAS
Megel 1998,[34] USA	Vaccine NR; IM or SC; vastus lateralis	N = 99; children 3-6 y; between-groups design; single center, general pediatric clinic	Music distraction: 9 musical compositions and 9 verbal lullabies were available. Children were allowed to choose the lullaby they wished to hear and listened via headphones. Accompanied by parent (n = 50) or Control: given immunization as usual with parent present (n = 49)	Pain: Oucher
Noguchi 2006 (1,2),[35] USA	At least one of DTaP, IPV, MMR, Hepatitis A, Hepatitis B, or PPD; IM; upper arm or thigh	N = 62; children 4-6 y; between-groups design; multicenter, medical clinic	Music distraction: children listened to musical story using headphones and pointed to accompanying photos (n = 21) or	Pain: Faces Pain Scale

(*Continued*)

TABLE 2. (*continued*)

First Author Year, Country	Injection Details	Population Enrolled, Design, Setting	Intervention	Critical Outcomes
			Spoken distraction: children listened to a spoken story using headphones and pointed to accompanying photographs (n = 21) or Standard care (n = 20)	
Yinger 2012,[39] USA	At least one of DPT, IPV, MMR, varicella, or influenza; no injection details	N = 56; children 4-6 y; between-groups design; 3 centers, family medicine practice or pediatric practice at hospital	Music therapy: single session music therapy intervention, including live music and cognitive-behavioral techniques as procedural support. Information about the procedure provided to children via song and story; and also taught deep breathing. Music used to distract before and after procedure. Child took deep breaths and focused on the music therapist during procedure (n = 29) or Standard care (n = 27)	NA (this study was not included in the meta-analysis for critical outcomes)
Should music distraction be used during vaccine injections in adolescents >12-17 y?				
Kristjansdottir 2011 (1,2),[31] Iceland	Vaccine NR; no injection details	N = 118; children 13-15 y; between-groups design; single center, school-based health clinic	Music distraction (with headphones): adolescents were told the purpose of listening to music and were asked to concentrate on and "disappear into" the music. They were given a choice of CD and volume setting. Adolescents listened to music through headphones (n = 38) or Music distraction (without headphones): adolescents were told the purpose of listening to music and were asked to concentrate on and "disappear into" the music. They were given a choice of CD and volume setting. Adolescents did not wear headphones (n = 41) or Standard care: described as nurses maintaining normal modes of caring by comforting and guiding adolescents verbally (n = 39)	Pain: VAS
Should breathing with a toy (blowing bubbles, pinwheel) be used during vaccine injections in children >3-12 y?				
Beran 2013,[18] Canada	Influenza vaccine 0.5 mL IM; 25 G, 1-inch needle; deltoid muscle	N = 57; children 4-9 y; between-groups design; single center, pediatric hospital clinic	Robot condition: included a humanoid robot who talked to the child before, during, and after the immunization procedure. The robot asks the child to blow on dusty toy during the immunization (n = 28) or Control: child seated with their parent, and in front of the nurse with several toy objects on a table. The nurse administered the vaccine using current immunization guidelines (includes minimal distraction) (n = 29)	Pain: FPS-R
Blount 1992,[19] USA	Vaccine NR; no injection details	N = 60; children 3-7 y; between-groups design;	Coping Skills Training: parent coached and rehearsed with research	Pain: Faces Scale (this study was

(*Continued*)

TABLE 2. (*continued*)

First Author Year, Country	Injection Details	Population Enrolled, Design, Setting	Intervention	Critical Outcomes
		single center, local health department	assistant and child during mock needle before immunization procedure. Parent taught to distract the child preprocedure and then directed the child to blow on party blower before and during procedure. Included high (n = 15) and low (n = 15) distressed children (n = 30 total) or Control: child and parent waited until called for their immunization. Included high (n = 15) and low (n = 15) distressed children (n = 30 total)	not included in the meta-analysis as data was not available)
Bowen 1999 (1,2),[20] USA	Vaccine NR; no injection details	N = 80; children 3-6 y; between-groups design; single center, county flu clinic	Party blower: nurse provided party blower to child and instructed them to blow as hard as they could (n = 29) or Pinwheel: nurse provided pinwheel to child and instructed them to blow as hard as they could (n = 30) or Standard care (n = 21)	Fear: Faces Scale
Krauss 1997,[30] USA	DPT and MMR; IM or SC	N = 50; children 4-7 y; between-groups design; single center, local health department	Treatment group: before immunization, the child and parent watched a brief videotape of a child using a party blower during immunization. The video encouraged parents to engage their child in the use of the technique during the procedure (n = 25) or Control: standard immunization procedures (n = 25)	NA (this study was not included in the meta-analysis for critical outcomes)
Manimala 2000 (1),[33] USA	Vaccine NR; no injection details	N = 55; children 4-6 y; between-groups design; single center, county health department	Reassurance: before the immunization, 10 min of training including rationale, examples of reassurance and when to use it during the procedures; researchers acted as role models then parent and child also role played the procedure (n = 27)* or Distraction: before immunization, 10 min of training including rationale, example techniques (eg, drawing, puzzles, talking about other things), asked to coach child to use a party blower throughout procedure; researchers acted as role models then parent and child also role played procedure (n = 28) or Control: 10 min discussion with research on child's medical history and how parent typically interacted with child during medical procedures (n = 27)	Fear: Faces Scale
Sparks 2001 (2) (same as	DTP (n = 22) or DTaP (n = 83) ± oral polio	N = 105; children 4-6 y; between-groups design;	Stroking before and during injection with instruction to "keep thinking	Pain: Oucher

(*Continued*)

TABLE 2. (*continued*)

First Author Year, Country	Injection Details	Population Enrolled, Design, Setting	Intervention	Critical Outcomes
Sparks 1998 thesis),[37] USA	(preinjection) 0.5 mL IM; 22 G, 25-mm needle; vastus lateralis muscle, right or left leg	multicenter, school clinics and walk-in public health clinic	about how nice that feels" by immunizer (n = 35)* or Bubble blowing: child blew bubbles just before and during immunization (n = 35) or Control (n = 35)	
Should breathing without a toy (blowing, deep breathing) be used during vaccine injections in children >3-12 y?				
Cohen 2002a,[24] USA	DPT and MMR; no injection details	N = 61; children 3-6 y; between-groups design; single center, rural health department	Coping skills: before immunization, child watched a 7-min video of a researcher and child providing instructions/modeling deep breathing and other coping skills (eg, positive self-statements). Child then given time to practice skills (n = 31) or Control: before immunization, child watched a 7-min video where researcher explained that people cope with immunizations in various ways. Did not provide specific suggestions. Showed child sitting quietly and getting immunization (n = 30)	Pain: Faces Scale Fear: Faces Scale
French 1994,[28] USA	DPT; no injection details	N = 75; children 4-7 y; between-groups design; multicenter, public health immunization clinics	Blowing plus teaching: child was told what to expect and that it was OK to cry. Child then practiced blowing out air before the immunization and was coached to blow by investigator during immunization (n = 39) or Control plus teaching: child was told what to expect and that it was OK to cry (n = 36)	Pain: VAS
Should a breathing intervention (cough) be used during vaccine injections in children >3-17 y?				
Wallace 2010,[38] USA	DTaP or IPV (children); Tdap or meningococcal conjugate (adolescents); no injection details	N = 68; children 4-5 y and adolescents 11-13 y; cross-over design; single center, outpatient pediatric clinic in a large public hospital	"Cough trick": child was told to cough twice; the injection was delivered with the second cough (n = 68) or Treatment as usual: nurses were not instructed regarding what strategies to use, and the procedures varied to some extent (n = 68)	Pain: VAS

Studies were identified using the following notation: "First Author" "Year of Publication" "Country" (eg, Taddio 2014, Canada). If studies contributed to multiple analyses, then "(#)" was added to enable their discernment (eg, Taddio 2014 [1]). If the same author published more than 1 study in the same year, then a lower case letter was added after the first article in the same year by the same author (eg, Taddio 2014a [1]).

See cited papers for details.

*Data not included in the analysis.

Route: DTap, tetanus toxoid-reduced diphtheria toxoid-acellular pertussis; IM, intramuscular; SC, subcutaneous. Outcomes: FPS-R, Faces Pain Scale-Revised; VAS, visual analog scale. Vaccines: DPT, diphtheria, pertussis, tetanus; DPTP, diphtheria, pertussis, tetanus, polio; DTaP, diphtheria, tetanus, acellular pertussis; IPV, inactivated polio vaccine; MMR, measles, mumps, and rubella; NA, not applicable; NR, not reported; PPD, purified protein derivative (tuberculosis skin test).

Should Verbal Distraction be Used During Vaccine Injections in Children >3 to 12 Years?

Two trials including 46 children aged 3 to 7 years investigated the impact of verbal distraction.[29,36] Verbal distraction involved an adult attracting the child's attention away from the needle by using their voice only; no additional physical, visual, or auditory distracter is used. In both trials, verbal distraction was provided by mothers who received instruction (written or oral) about how to engage in distraction with their child during the vaccine injection (eg, talking, counting, singing, reciting a poem/rhyme). There was low quality of evidence for outcome data pertaining to all assessed outcomes, largely due to lack of blinding of immunizers and/or outcome assessors (Table, Supplemental Digital Content 3, http://links.lww.com/CJP/A185). Only 1 trial[29] examined the critically important outcome of pain and found no benefit of verbal distraction: SMD −0.27 (−1.02,

TABLE 3. Assessment of Risk of Bias of Included Trials for Critical Outcomes

References	Adequate Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data Addressed	Free of Selective Reporting	Free of Other Bias	Overall Risk
Should false suggestion be used during vaccine injections in individuals of all ages?								
Eland 1981 (1,2)[26]	Unclear	Unclear	No	No	Yes	Yes	No	High
Fowler-Kerry 1987 (1,3)[27]	Unclear	Unclear	No	No	Yes	Unclear	Unclear	High
Should repeated reassurance be used during vaccine injections in individuals of all ages?								
Gonzalez 1993 (2)[29]	Unclear	Unclear	No	No	Yes	Yes	No	High
Manimala 2000 (2)[33]	No	No	No	No	Yes	Yes	No	High
Should verbal distraction be used during vaccine injections in children >3-12 y?								
Gonzalez 1993 (1)[29]	Unclear	Unclear	No	No	Yes	Yes	No	High
O'Laughlin 1995 (1)[36]	No	Unclear	No	No	Unclear	Yes	No	High
Should video distraction be used during vaccine injections in children >3-12 y?								
Cassidy 2002[21]	Yes	Unclear	No	No	Unclear	Yes	No	High
Cohen 1997 (1,2)[22]	No	Unclear	No	No	Unclear	No	No	High
Cohen 1999 (1)[23]	Unclear	Unclear	No	No	Yes	Unclear	No	High
Cohen 2015 (1)[25]	Yes	Yes	No	No	Yes	Yes	Yes	High
Luthy 2013 (2)[32]	Yes	Yes	No	No	Yes	Yes	No	High
Should music distraction be used during vaccine injections in children >3-12 y?								
Fowler-Kerry 1987 (2,4)[27]	Unclear	Unclear	No	No	Yes	Unclear	Unclear	High
Megel 1998[34]	Yes	Unclear	No	Yes	Yes	Yes	No	High
Noguchi 2006 (1,2)[35]	Yes	Unclear	No	No	No	Unclear	No	High
Yinger 2012[39]	Unclear	Unclear	No	No	Yes	No	No	High
Should music distraction be used during vaccine injections in adolescents >12-17 y?								
Kristjansdottir 2011 (1,2)[31]	Yes	Unclear	No	No	Unclear	Unclear	Unclear	High
Should breathing with a toy (blowing bubbles, pinwheel) be used during vaccine injections in children >3-12 y?								
Beran 2013[18]	Yes	Unclear	No	No	No	No	No	High
Blount 1992[19]	Unclear	Unclear	No	No	Yes	No	No	High
Bowen 1999 (1,2)[20]	No	No	No	No	Yes	No	No	High
Krauss 1997[30]	Yes	No	No	No	Yes	Unclear	Unclear	High
Manimala 2000 (1)[33]	No	No	No	No	Yes	Yes	No	High
Sparks 2001 (2)[37]	No	No	No	No	Yes	No	Unclear	High
Should breathing without a toy (blowing, deep breathing) be used during vaccine injections in children >3-12 y?								
Cohen 2002a[24]	No	No	No	No	Unclear	Yes	Unclear	High
French 1994[28]	No	No	No	No	Yes	Yes	Unclear	High
Should breathing interventions (cough) be used during vaccine injections in children >3-17 y?								
Wallace 2010[38]	Unclear	Unclear	No	No	No	No	No	High

0.47). No trials examined the critically important outcome of fear. Given the young age of participants, distress was also examined, which contained data from both trials (preprocedure, acute, and recovery distress combined) and showed a significant benefit of verbal distraction: SMD −1.22 (−1.87, −0.58) (Table, Supplemental Digital Content 3, http://links.lww.com/CJP/A185 and Figure, Supplemental Digital Content 12, http://links.lww.com/CJP/A194). Other assessed important outcomes included parents' use of the intervention.

Should Video Distraction be Used During Vaccine Injections in Children >3 to 12 Years?

Five trials including 328 children aged 2 to 12 years investigated the impact of video distraction.[21–23,25,32] In these studies, interventions generally involved having the child watch an age-appropriate movie on a television screen or portable DVD player. In 3 trials, children were able to choose from a selection of movies and received additional distraction coaching while watching the movie from a nurse and/or parent.[22,23,25] There was very low quality of evidence for outcome data pertaining to critically important outcomes of pain and fear, largely due to lack of blinding of immunizers and/or outcome assessors, inclusion of cross-over and quasi-randomized trials, and possible contamination of treatment effects in control groups (eg, engaging in distraction) (Table, Supplemental Digital Content 4, http://links.lww.com/CJP/A186). Four trials[21–23,25] found no benefit for the critically important outcome of pain: SMD −0.88 (−1.78, 0.02). Only 1 trial[23] examined the critically important outcome of fear and also found no benefit of video distraction: SMD 0.08 (−0.25, 0.41). The important outcome of distress was also considered given the younger age of children (below 7 y old) providing self-report in 3 of 4 trials, the reliance on data from a single cross-over study for self-reported fear, as well as the inclusion of 1 trial that did not examine critically important outcomes of pain or fear.[32] All 5 trials examined distress during at least 1 phase of treatment, with evidence of benefit of video distraction during the preprocedure (SMD −0.65 [−1.18, −0.12]), acute (SMD −0.96 [−1.85, −0.08]), and preprocedure + acute + recovery (SMD −0.58 [−0.82, −0.34]) phases (Table, Supplemental

TABLE 4. Summary of Results for Critically Important Outcomes

Clinical Questions	Critical Outcomes*	Benefit of Intervention†	Quality of Evidence‡
Psychological interventions			
Should false suggestion be used during vaccine injections in individuals of all ages?	Pain, distress, fear	No	Low
Should repeated reassurance be used during vaccine injections in individuals of all ages?	Pain, distress, fear	No	Very low
Should verbal distraction be used during vaccine injections in children >3-12 y?	Pain, fear	Mixed§	Low
Should video distraction be used during vaccine injections in children >3-12 y?	Pain, fear	Mixed§	Very low
Should music distraction be used during vaccine injections in children >3-12 y?	Pain, fear	Yes	Low
Should music distraction be used during vaccine injections in adolescents >12-17 y?	Pain, fear	No	Low
Should breathing with a toy (blowing bubbles, pinwheel) be used during vaccine injections in children >3-12 y?	Pain, fear	Mixed	Very low
Should breathing without a toy (blowing, deep breathing) be used during vaccine injections in children >3-12 y?	Pain, fear	No	Very low
Should breathing interventions (cough) be used during vaccine injections in children >3-17 y?	Pain, fear	No	Low

*Includes results for the critical outcomes that were evaluated in included studies only.

†The results for the effect of the intervention have been summarized across all evaluated critical outcomes, and are expressed using the following notation: Yes, benefit was observed across all evaluated critical outcomes; Mixed, benefit was observed for 1 or more but not all evaluated critical outcomes; No, no evidence of benefit was observed for any of the evaluated critical outcomes.

‡Reflects the lowest quality of evidence rating across all evaluated critical outcomes, whereby rankings range from high to moderate to low to very low.

§Reflects inclusion of important outcome of distress in evaluating the effect of the intervention.

Digital Content 4, http://links.lww.com/CJP/A186 and Figure, Supplemental Digital Content 13, http://links.lww.com/CJP/A195). Other assessed important outcomes included parent fear, immunizer fear, parent and child preferences, and use of intervention by children, parents, and/or immunizers.

Should Music Distraction be Used During Vaccine Injections in Children >3 to 12 Years?

Four trials including 417 children aged 3 to 7 years investigated the impact of music distraction in children.[27,34,35,39] In 3 of these studies, children listened to music using headphones[27,34,35]; in 1 study, children engaged in live music with a music therapist.[39] There was low quality of evidence for outcome data pertaining to the critically important outcome of pain and important outcome of distress, largely due to inconsistent blinding of participants, immunizers, and outcome assessors (Table, Supplemental Digital Content 5, http://links.lww.com/CJP/A187). Three trials that could be pooled for the critically important outcome of pain[27,34,35] found a benefit of music distraction: SMD −0.45 (−0.71, −0.18) (Table, Supplemental Digital Content 5, http://links.lww.com/CJP/A187 and Figure, Supplemental Digital Content 14, http://links.lww.com/CJP/A196). No trials examined the critically important outcome of fear.

Given the young age of participants, the important outcome of distress was also considered and was assessed in 2 trials at various phases of the procedure. There was a beneficial effect on preprocedure distress (SMD −0.48 [−0.86, −0.10]) and acute distress (SMD −0.49 [−0.87, −0.11]). Whereas, there was no benefit on distress during the acute plus recovery phases combined (SMD −0.27 [−0.65, 0.10]), or during the recovery phase only (SMD −0.09 [−0.46, 0.29]) (Table, Supplemental Digital Content 5, http://links.lww.com/CJP/A187 and Figure, Supplemental Digital Content 14, http://links.lww.com/CJP/A196). Other assessed important outcomes included procedure duration, parent preferences, and child use of intervention.

Should Music Distraction be Used During Vaccine Injections in Adolescents >12 to 17 Years?

One trial including 118 adolescents aged 13 to 15 years investigated the impact of music distraction in adolescents.[31] In this trial, adolescents listened to music of their choice from an available selection. Half of adolescents who received the intervention wore headphones, whereas the other half did not. There was low quality of evidence due to lack of blinding of participants, who reported no benefit of the intervention for the critical outcome of pain: SMD −0.04 (−0.42, 0.34) (Table, Supplemental Digital Content 6, http://links.lww.com/CJP/A188 and Figure, Supplemental Digital Content 15, http://links.lww.com/CJP/A197). No data were available for the critically important outcome of fear or other important outcomes.

Should Breathing With a Toy (Blowing Bubbles, Pinwheel) be Used During Vaccine Injections in Children >3 to 12 Years?

Six trials including 368 children aged 3 to 9 years investigated the impact of breathing with a toy in children.[18,19,20,30,33,37] In all studies, children were directed to blow on a toy (ie, party blower, pinwheel, bubbles, small toy). One study provided instruction from a robot to blow on a dusty toy,[18] and in 3 trials, children were supported with additional rehearsal or coaching from parents,

researchers, or immunizers.[19,30,33] There was very low quality of evidence for outcome data pertaining to critically important outcomes of pain and fear, largely due to lack of blinding of immunizers, participants, and/or outcome assessors, inclusion of quasi-randomized trials, and possible contamination of treatment effects in control groups (Table, Supplemental Digital Content 7, http://links.lww.com/CJP/A189).

Two trials[18,37] found a benefit of breathing with a toy for the critically important outcome of pain: SMD −0.49 (−0.85, −0.13), whereas 2 different trials[20,33] found no benefit of breathing with a toy for the critically important outcome of fear preprocedure (SMD −0.53 [−1.07, 0.01]) or acute fear (SMD −0.60 [−1.22, 0.02]).

Given the young age of participants, the important outcome of distress was also considered. Two trials[18,20] found a benefit of breathing with a toy for acute distress: SMD −0.80 (−1.17, −0.42); and 4 trials[18,19,30,33] found a benefit for preprocedure + acute + recovery phases combined: SMD −0.55 (−0.82, −0.28) (Table, Supplemental Digital Content 7, http://links.lww.com/CJP/A189 and Figure, Supplemental Digital Content 16, http://links.lww.com/CJP/A198). Other assessed important outcomes included parent fear, child and parent use of intervention, and child and parent preferences.

Should Breathing Without a Toy (Blowing, Deep Breathing) be Used During Vaccine Injections in Children >3 to 12 Years?

Two trials including 136 children aged 3 to 7 years investigated the impact of breathing without a toy in children.[24,28] In 1 study, children were taught deep breathing, in addition to coping skills[24]; in the other study, were instructed to blow out air during the injection.[28] In both trials, children were given time to practice the skills before the injection. There was very low quality of evidence for outcome data pertaining to critically important outcomes of pain and fear, largely due to lack of blinding of participants and outcome assessors, inclusion of quasi-randomized trials, and selective outcome reporting (Table, Supplemental Digital Content 8, http://links.lww.com/CJP/A190). Both trials found no benefit of breathing without a toy for the critically important outcome of pain: SMD −0.27 (−0.61, 0.07). One trial[24] examined the critically important outcome of fear and found no benefit of the intervention: SMD −0.36 (−0.86, 0.15). Given the young age of participants, the important outcome of distress was also considered. Distress was examined in both trials, although the phase of procedure was unclear. No benefit of breathing without a toy was observed: SMD −0.27 (−0.61, 0.07) (Table, Supplemental Digital Content 8, http://links.lww.com/CJP/A190 and Figure, Supplemental Digital Content 17, http://links.lww.com/CJP/A199). No other important outcomes were assessed.

Should a Breathing Intervention (Cough) be Used During Vaccine Injections in Children >3 to 17 Years?

One trial including 136 children (aged 4 to 5 y) and adolescents (aged 11 to 13 y) investigated the impact of a breathing intervention (cough).[38] Children and adolescents were asked to cough once before and once at the time of the injection. There was low quality of evidence for outcome data pertaining to the critically important outcome of pain, largely due to lack of blinding of participants and inclusion of a cross-over trial (Table, Supplemental Digital Content 9, http://links.lww.com/CJP/A191). No benefit was found for the critically important outcome of pain: SMD −0.17 (−0.41, 0.07). No data were available for the critically important outcome of fear (Table, Supplemental Digital Content 9, http://links.lww.com/CJP/A191 and Figure, Supplemental Digital Content 18, http://links.lww.com/CJP/A200). Other assessed important outcomes included distress and child satisfaction.

DISCUSSION

This systematic review was conducted to investigate the effectiveness of various psychological interventions used by children, adolescents, their parents, and/or immunizers to reduce adverse effects from vaccine injections including pain and pain-related outcomes. Only simple psychological interventions were considered, such as those including distraction and/or interactions between children and parents, nurses, and/or immunizers. There was some evidence to support the following interventions in children: verbal distraction, video distraction, music distraction, and breathing with a toy. Available evidence was insufficient to support the following interventions with children: false suggestion, repeated reassurance, and breathing without a toy. There was insufficient evidence to support use of breathing intervention (cough) with children or adolescents, or use of music distraction with adolescents.

The only psychological intervention with consistent evidence supporting its use across pain and pain-related outcomes was music distraction in children younger than 12 years old. Benefit was shown in studies that used age-appropriate recorded music delivered to children using headphones, as well as more involved live music distraction interventions provided by a music therapist. Behavioral distraction (ie, requiring children to do something distracting) is a generally effective coping strategy in young children,[42] and in most of the included trials, children received additional support to engage fully with the music. The positive benefit of music in children is promising, as it can rely on minimal resources and no training to be implemented effectively by parents or immunizers. In general, music seems to be an effective pain management strategy for children, with supportive evidence from other types of medical procedures.[43]

The results were mixed regarding the benefit of verbal distraction in children. Child ratings of pain indicated no benefit from the intervention, whereas observer ratings of the child's distress were reduced. In both trials, mothers received instruction on how to verbally distract their child by counting, singing, or talking about topics other than the vaccine injection. This pattern of findings, including benefit for reducing observed child distress but not self-reported pain, has been noted in studies examining parent-led distraction for other types of needle procedures.[44] Although providing instruction to parents was shown to increase their use of distraction with their child during vaccine injections, equivocal findings with regards to self-reported pain may be explained due to the mix of parent behaviors observed in both the distraction intervention and the control group.[29] More specifically, some mothers in the distraction intervention group also engaged in behaviors that have been shown to increase children's pain (ie, reassurance),[45] and some mothers in the control group naturally engaged in distraction.[29] Although not examined in the included trial, increased doses of verbal distraction from parents have been associated with greater reduction of pain and distress

in children undergoing other needle procedures regardless of training in verbal distraction.[46] Furthermore, not all parents are effective distraction coaches. In particular, highly distressed parents seem less able to successfully distract their child.[47,48] None of the included studies examined nurse-led verbal distraction; however, other nurse-led psychological interventions have previously been shown to be effective for vaccine injections,[3] and may pose a reasonable alternative when parents are highly distressed. Relatively minor resources are needed to instruct parents in use of verbal distraction (eg, providing a pamphlet).[36] Furthermore, parents are typically present at vaccine injections with young children, making this a very feasible intervention to implement.

The results were also mixed for video distraction with demonstrated benefit of reduced distress across all procedure phases (pre, acute, and recovery), but not reduced pain or fear. Given that distraction is most effective when it is interesting, enjoyable, and engaging, the child's ability to choose and interact with the video distracter may be critical.[49] The reviewed video distraction interventions generally relied on older technology (ie, DVD players and televisions). This may pose some impediment to clinical settings when required resources are limited or unavailable for families to use. Readily available smartphones and smart devices offer a feasible and promising alternative, and are already being used by some in clinical practice to manage pediatric procedural pain.[50] In support of this hypothesis, a recent nonrandomized study reported reduced distress in children aged 2 to 5 when iPads were used to distract them during immunizations; however, it should be noted that lack of randomization makes this study at high risk of bias.[40] Interactive distraction interventions show some evidence for increased efficacy over more passive distraction for reducing distress during pediatric needle procedures.[5] Given the many highly interactive videos and games available on smart devices, their use for vaccine injections is worthy of future research.

Findings showed mixed benefit for the use of breathing with a toy, but no support for breathing without a toy or for a breathing intervention (cough). The type of breathing children and/or adolescents were instructed to do as part of these interventions (ie, blowing out air, coughing) may have been insufficient to induce any sort of relaxation response and/or distract children on their own. Research has shown that relaxation during breathing is an important mechanism for modulating physiological responses to stress and influencing pain perception, as compared with simply attending to the breath in the absence of efforts to relax.[51] It is likely that the small toys that assisted children during the "breathing with a toy" interventions also served as distracters (eg, bubbles, pinwheel, party blower), thereby potentially bolstering the effectiveness of the intervention on pain. As is noted in this review and in others, distraction is a generally effective strategy for reducing pain and pain-related outcomes during pediatric medical procedures.[5,49,52] Thus, the availability of a toy may have enhanced the efficacy of breathing alone by enhanced distraction. However, no trials provided a head-to-head comparison of breathing with and without a toy, making it difficult to conclude what components of the intervention were the most effective.

Behaviors of parents and other adults (eg, nurses) have received extensive study in the context of pediatric medical procedures, and have been shown repeatedly to exert helpful and unhelpful influences on children's pain and distress.[53] Although seemingly counterintuitive, a generally consistent finding is that reassurance seems to be unhelpful for children when they are in pain.[54,55] One reason may be because children perceive adults as being worried when they reassure, which may in turn increase child distress.[45] Although there may be forms of reassurance that are more helpful than others,[45] the lack of benefit for repeated reassurance found for vaccine injections in this review is consistent with extant research, and is thus, not recommended when other adult behaviors, such as distraction, are helpful. Although the evidence base consisted of children only, the counterintuitive relationship between reassurance and increased distress has been found in infants[54,56,57]; furthermore, although in a different context, medically focused reassurance has also been shown to be ineffective for adults with high levels of health anxiety.[58]

Included trials also assessed the impact of an adult (nurse or researcher) suggesting to the child that something was being done to help make the injection easier. As with repeated reassurance, false suggestion showed no benefit for reducing children's pain or distress. Suggestion showed no benefit in and of itself, indicating that there was no observed placebo effect induced by a simple statement that some sort of pain management was being used in the absence of a real intervention. There was also no benefit for suggestion used as a means of enhancing the efficacy of another intervention (ie, distraction or vapocoolant). Use of false suggestion as a placebo or to overstate the efficacy of an intervention may be perceived by the person being immunized as deceitful and may lead to distrust of immunizers and health care professionals more broadly, potentially leading to noncompliance with medical care. Thus, use of false or simplistic suggestion may be problematic for individuals of any age being immunized across the lifespan.

Other than the breathing intervention (cough), the only other psychological intervention studied in adolescents was music distraction. In contrast to the clear benefits of music distraction for children below 12 years old, no support was found for use of music distraction with adolescents above 12 years old. This is consistent with a recent systematic review and meta-analysis that found no evidence supporting use of distraction to reduce pain and distress in adolescents across all types of needle procedures.[5] Three of the 4 distraction interventions studied, in samples of predominantly adolescents, included music.[59-61] However, evidence for music distraction in adolescents based on a single trial in the current review, and the ability to detect differences between treatment and control groups may have been impeded by the very low levels of self-reported pain following the injection in both groups (ie, average pain $< 1/10$) in this study, potentially introducing floor effects.[31] Developmental differences are noted in coping strategies, preferences, and self-efficacy across childhood and adolescence.[62] In particular, adolescents seem to have different preferences in how they want to cope depending on the stressor, and they increasingly draw on cognitive strategies.[62] Although 70% to 80% of the adolescents in the music distraction trial identified using music to cope with emotional stress, only about half indicated they typically use music to cope with pain.[31] It may be that the requirement for adolescents to use music during the vaccine injection detracted from use of a more preferred (and effective) coping strategy (eg, positive self-talk). More research is needed to understand whether individual

treatment preference impacts the efficacy of a psychological intervention for managing pain and related outcomes from vaccinations.

All of the psychological interventions showing some benefit for reducing pain and/or pain-related outcomes included some form of distraction (ie, verbal, music, video, breathing with a toy). Distraction is the most commonly studied psychological intervention for all procedural pain in children,[49] and has been shown to be efficacious for reducing pain across all types of pediatric needle procedures, including vaccine injections.[5,52] Although it remains somewhat unclear what the effective components of distraction interventions are specifically, they generally require minimal instruction, and can be easily tailored given the cultural or resource considerations. Thus, while video distraction may have specific technological demands, verbal and music distraction, as well as breathing with a toy, do not. Moreover, the support for the efficacy of these interventions suggests that low-tech modalities can also be engaging and effective in children. This holds broad appeal for global implementation of psychological interventions, as part of a multifaceted approach to pain management. Furthermore, they may be accessible even in areas of the world where pharmacological interventions, such as topical anesthetics (lidocaine-prilocaine), are not. That being said, educating parents through knowledge translation initiatives before the vaccine injection itself, may be helpful given the need for parents to bring necessary distracters or toys (eg, bubbles).

A major limitation of this area of research is that there are several psychological interventions for which the evidence base is relatively limited and is outdated. Six of 9 clinical questions relied on data from only 1 or 2 trials, and half (n = 11) of the included studies were published before the year 2000. That being said, the psychological interventions showing benefit in the current review, generally relied on a larger number of trials, and more recent trials, overall. Of particular mention, is the paucity of research available for adolescents given that approximately up to 4 vaccinations are offered in Canada in grades 7 or later.[63] The typical setting in which adolescents (and slightly younger school-aged children) undergo vaccine injections is school-based immunization clinics. This setting brings very different circumstances as compared with primary care clinics where younger children are often immunized, perhaps most notably, the absence of parents and presence of peers.[64] Fear may be particularly high among children and adolescents receiving vaccine injections at school, and has the potential to spread quickly among peers, a phenomenon referred to as "fear contagion."[65] As a result, adolescents, in particular, are required to become much more autonomous in their use of pain management strategies. Although their confidence, self-reliance, and effective use of coping strategies is more developed than younger children,[42] additional research is needed to ensure implementation of effective psychological strategies that match the coping skills and preferences in this age group and for this setting.

Also of note is the very low to low quality of evidence available across all assessed outcomes.[10] In large part, this is due to high risk of bias arising from the lack of blinding of participants and outcome assessors, including children, parents, and immunizers. The generally poor quality of evidence has been previously noted, as it is a consistent finding for trials investigating psychological interventions across all types of needle procedures in children and adolescents.[5,52,66] This is concerning, as high risk of bias has been associated with exaggerated treatment effects.[67] While blinding of children, parents, and immunizers to study group can sometimes be difficult given the nature of psychological interventions (ie, it is difficult to hide the presence of a television or headphones), efforts can be made to blind individuals to study hypotheses, and researcher-ratings of the child's distress can readily be achieved. Several trials also noted contamination of treatment effects in control groups. Although this may be unavoidable due to the natural engagement of parents or other adults' in specific behaviors (ie, distraction), it does support the value of assessing the natural occurrence of the intervention in control groups. Future trials need to improve the quality of evidence by considering necessary design considerations a priori. A more detailed discussion of limitations of the available evidence and discussions for future research in all areas of pain management for vaccine injections is also available.[68]

Despite the unavoidable limitations posed by the available evidence in this area, the current systematic review and meta-analysis was very rigorous in its approach.[9] A thorough database search for all relevant studies was undertaken, with consistent a priori decisions for identifying relevant clinical questions and critically important outcomes as derived by a multidisciplinary national panel of experts in vaccination pain management (HELPinKids&Adults team). The application of high quality established methods for pooling data and evaluating the quality of evidence ensures confidence in the review's findings (GRADE[10]; Cochrane[11]). Furthermore, a unique strength arises from the inclusion of this review within a series of similar reviews examining psychological interventions for vaccine injections across the lifespan,[7,8] reviews examining physical, procedural, and pharmacological approaches to vaccine pain management, as well as a review on the management of high levels of needle fear.[12] The compilation of these reviews in clinical practice guidelines ensures the utility, feasibility, and practicality of a multipronged approach to vaccine pain management and long-term sequelae, and encourages uptake of these findings in clinical practice (also McMurtry CM, Taddio A, Noel M, et al., unpublished data, 2015).[69]

In summary, a number of psychological interventions show benefit for reducing pain and pain-related outcomes during vaccine injections in children. Effective interventions largely seem to include some degree of distraction, with music distraction being the most consistently beneficial across assessed outcomes for children. In general, effective psychological interventions require minimal training to be implemented by children, parents, and/or immunizers, and can draw from varied available resources, ensuring their clinical utility and appropriateness for children of different ages and at a global level.

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