OPEN

Process Interventions for Vaccine Injections

Systematic Review of Randomized Controlled Trials and Quasi-Randomized Controlled Trials

Rebecca Pillai Riddell, PhD, C Psych,†‡ Anna Taddio, BScPhm, MSc, PhD,§‖ C. Meghan McMurtry, PhD, C Psych,¶#** Vibhuti Shah, MD, MSc,††‡‡§§ Melanie Noel, PhD,‖‖ Christine T. Chambers, PhD, R Psych,¶¶## and HELPinKIDS&Adults Team*

Background: This systematic review evaluated the effectiveness of process interventions (education for clinicians, parent presence, education of parents [before and on day of vaccination], and education of patients on day of vaccination) on reducing vaccination pain, fear, and distress and increasing the use of interventions during vaccination.

Design/Methods: Databases were searched using a broad search strategy to identify relevant randomized and quasi-randomized controlled trials. Critical outcomes were pain, fear, distress (when applicable), and use of pain management interventions. Data were extracted according to procedure phase (preprocedure, acute, recovery, combinations of these) and pooled using established methods. Analyses were conducted using standardized mean differences (SMD) and risk ratios (RR).

Results: Thirteen studies were included. Results were generally mixed. On the basis of low to very low-quality evidence, the following specific critical outcomes showed significant effects suggesting: (1) clinicians should be educated about vaccine injection pain management (use of interventions: SMD 0.66; 95% confidence interval [CI]: 0.47, 0.85); (2) parents should be present (distress preprocedure: SMD −0.85; 95% CI: −1.35, −0.35); (3) parents should be educated before the vaccination day (use of intervention preprocedure: SMD 0.83; 95% CI: 0.25, 1.41 and RR, 2.08; 95% CI: 1.51, 2.86; distress acute: SMD, −0.35; 95% CI: −0.57, −0.13); (4) parents should be educated on the vaccination day (use of interventions: SMD 1.02; 95% CI: 0.22, 1.83 and RR, 2.42; 95% CI: 1.47, 3.99; distress preprocedure + acute + recovery: SMD −0.48; 95% CI: −0.82, −0.15); and (5) individuals 3 years of age and above should be educated on the day of vaccination (fear preprocedure: SMD −0.67; 95% CI: −1.28, −0.07).

Conclusions: Educating individuals involved in the vaccination procedure (clinicians, parents of children being vaccinated; individuals above 3 y of age) is beneficial to increase use of pain management strategies, reduce distress surrounding with vaccination, and to reduce fear. When possible, parent presence is also recommended for children undergoing vaccination.

Key Words: pain management, randomized controlled trial, systematic review, vaccination, parent presence, education, implementation science

(*Clin J Pain* 2015;31:S99–S108)

Pain and fear are unfortunate sequelae of vaccine injections. Evidence across varied participants in the process of vaccination, from clinicians[1] to parents of children being vaccinated[2] to the individual undergoing vaccination themselves[3–5] unequivocally demonstrates that these adverse events are major challenges to current vaccination practices. Addressing the mandate of the Help ELiminate Pain in Kids & Adults (HELPinKids&Adults) Team to provide a comprehensive update to the 2010 clinical practice guideline on reducing childhood vaccination pain,[6] this meta-analysis served to evaluate process interventions.[7] Other papers in this series of reviews examine pain management strategies directly, whether it be pharmacological,[8] psychological,[9–11] or physical and procedural.[12] This paper addresses the pedagogical implementation of the pain management strategies, or more specifically, the efficacy of teaching pain management strategies to clinicians, parents, and the individuals themselves.

The provision of information or education of individuals involved in painful medical procedures has been previously synthesized[13,14] without specific attention to vaccination. However, despite the almost 20 years between

Received for publication April 12, 2015; accepted June 29, 2015.

From the *Department of Psychology, York University; †Department of Psychiatry, the Hospital for Sick Children; ‡Department of Psychiatry, University of Toronto; §§Departement of Neonatology; ‖Child Health and Evaluative Sciences, Hospital for Sick Children; §Leslie Dan Faculty of Pharmacy, University of Toronto; ‡‡Faculty of Medicine, University of Toronto; ††Mount Sinai Hospital, Toronto; ¶Department of Psychology, University of Guelph, Guelph; #Children's Health Research Institute, Children's Hospital; **Department of Paediatrics, Western University, London, ON; ¶¶Department of Pediatrics and Psychology, Faculty of Science, Dalhousie University; ##IWK Health Centre, Halifax, NS, Canada; and ‖‖Center for Child Health, Behavior and Development, Seattle Children's Research Institute, Seattle, WA.

HELPinKIDS (Help ELiminate Pain in KIDS) Team: N.E. MacDonald, J. Rogers, L. Bucci, P. Mousmanis, E. Lang, S.A. Halperin, S. Bowles, C. Halpert, M. Ipp, G.J.G. Asmundson, M. Rieder, K. Robson, E. Uleryk, M.M. Antony, V. Dubey, A. Hanrahan, D. Lockett, J. Scott, E. Votta Bleeker.

Supported by the Canadian Institutes of Health Research (CIHR), Ottawa, ON, Canada (KRS 132031). Open access funding was provided by the Mayday Fund in the United States. A. T., declares a grant from Pfizer, and study supplies from Natus and Ferndale. C.T. C., declares consultation fees from Abbvie. E. L., is a member of the GRADE working group and declares consultation fees from the International Liaison Committee on Resuscitation ILCOR). L. B., declares a relationship with government agencies and grants from Merck, GSK, Novartis, Sanofi, and Pfizer. S.A.H., declares grants from GSK, Sanofi, Novartis, Pfizer, Merck, PREVENT, ImmunoVaccine, NovaVax, Janssen, and Folia.

Reprints: Rebecca Pillai Riddell, PhD, Department of Psychology, 4700 Keele Street, Toronto, ON, Canada M3H 4C4 (e-mail: rpr@yorku.ca).

Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Website, www.clinicalpain.com.

DOI: 10.1097/AJP.0000000000000280

the publications and somewhat different population focus, both reviews provide similar ideas about the structure, content, and caveats of education and preparation that readily apply to the vaccination context. Specifically, both reviews suggest that preparatory content should address both the sensory aspects and procedural details of painful medical procedures. Moreover, both reviews suggest that there is a clear interaction regarding the delivery of intervention and the individual undergoing the painful procedure. The amount of information, the timing of when the information is relayed, and the method of information delivery has been noted to vary depending on characteristics of the patient facing the medical procedure. Generally, it has been recommended that the majority of information be delivered ahead of time and that focus be given to coping strategies at the time of the procedure.

The current review adds to the body of literature on this topic through its specific focus on education recommendations for the vaccination setting. Juxtaposing the aforementioned factors (content, timing, and individual variability) with the literature available for synthesis, the meta-analysis was structured with 5 clinical questions relating to process strategies: (1) the education of vaccinating clinicians about vaccine injection pain management; (2) the instruction of parents to be present or absent during vaccination; (3) the education of parents about pain management before the vaccination; (4) the education of parents on the day of vaccination; and (5) the education of individuals undergoing vaccination.

METHODS

An overarching methodology was utilized in all the reviews in this series and has been described in detail in an accompanying manuscript.[15] However, it is of note that both the Grading of Assessments, Recommendations, Development and Evaluation (GRADE)[16] and Cochrane[17] methodologies guided the review. The search strategy was developed with the assistance of an experienced librarian and was executed in EMBASE, Medline, PsycInfo, CINAHL, and ProQuest Dissertations & Theses Global. Relevant citations were screened and included as previously described.

The review included studies whereby clinicians, parents, or individuals being vaccinated received information within a randomized or quasi-randomized study design. Through an electronic voting process, in advance of data analysis, every member of the HELPinKids&Adults team was asked to rate on a scale from 0 to 9 (higher scores reflect higher import) the importance of potential clinical outcomes for each question that was to be posed in the review. Outcomes that received a mean score in excess of 7 were ranked as critical, whereas outcomes with mean ratings between 4 and 6 were deemed important (see Table 1 for list of critical and important outcomes for the clinical questions contained within this review). Only critical outcomes (pain, fear, distress [when applicable], use of pain management strategies) for which data were available will be discussed under each clinical question. However, while not discussed herein, whenever possible, important outcomes were also analyzed with the relevant GRADE tables and forest plots provided in Supplemental Digital Content for this Paper (see Process Figs. 1 to 5, Supplemental Digital Content 1, http://links.lww.com/CJP/A280 and Process Tables 1 to 5, Supplemental Digital Content 2, http://links.lww.com/CJP/A281). In this review, a comment about the use of the term pain versus distress is necessary due to the predominance of work for pooling that dealt with children 7 years and below. Pain or fear were the critical outcomes when reliable self-report was obtained (ie, with individuals above 7 y of age). However, distress (a term we are using to delineate proxy reports of pain and distress for patients who are unable to reliably self-report) was included in analyses of patient populations for which self-report was not possible (eg, infants) or potentially unreliable (children below 7 years old).[18] In addition, given the focus of this review on education about pain management strategies, the actual increase in the use of a pain management strategy was deemed critical.

The Cochrane risk of bias tool (https://bmg.cochrane.org/assessing-risk-bias-included-studies) was used to evaluate methodological limitations and the RevMan software program (version 5.2, Cochrane Collaboration, Copenhagen, Denmark) was used to pool the data and create the forest plots. The effect of each intervention was expressed as a standardized mean difference (SMD) with accompanying 95% confidence interval (CI) or relative risk (RR) and CI, as appropriate. A random effects model was used for all analyses. Statistical heterogeneity was assessed using I^2 and χ^2 tests.

TABLE 1. Clinical Questions and Outcomes for Process Interventions

Clinical Questions	Critical Outcomes*	Important Outcomes
Should clinicians administering vaccine injections be educated about vaccine injection pain management?	Use of intervention	Pain, distress, fear, procedure outcome, parent fear, compliance, preference, satisfaction
Should parents be present during vaccine injections in children 0-10 y?	Pain, fear, distress	Procedure outcome, parent fear, compliance, memory, preference, satisfaction
Should parents be educated about vaccine injection pain management before the day of vaccination (ie, ahead of time)?	Use of intervention, pain, fear, distress	Procedure outcomes, parent fear, knowledge, compliance, memory, preference, satisfaction
Should parents be educated about vaccine injection pain management on the day of vaccination?	Use of intervention, pain, fear, distress	Procedure outcomes, parent fear, compliance, memory, preference, satisfaction
Should children above 3 y and adults be educated about vaccine injection pain management on the day of vaccination?	Pain, fear	Distress, procedure outcomes, use of intervention, parent fear, compliance, memory, preference, satisfaction

*Distress is the critical outcome only in the absence of data for pain, fear, or both in individuals incapable of self-report (eg, infants).

In an attempt to more precisely describe the effects of the intervention, outcomes that were evaluated at multiple time-points were analyzed according to the procedure phase: (1) the preprocedure phase, which occurred post-intervention but before vaccine injection(s); (2) the acute procedure phase (within the first minute of needle puncture and vaccine injection); and (3) the recovery procedure phase (1 to 5 min after vaccine injection(s)). When necessary, data from a combination of phases were presented to accommodate the study authors' use of measures. Pain that was not temporally proximal to the actual vaccination (eg, delayed pain occurring hours to days after injection) was not examined.

Data from multiple observers assessing the same outcome (eg, parent-rated child distress, clinician-rated child distress) and data from multiple time-points within the same procedure phase (eg, acute distress measured every 15 s within the first minute of vaccine injection) were pooled before inclusion in the meta-analysis using established methods.[19]

The means and SDs were calculated from the medians, the ranges, the standard errors, and 95% CI or were estimated from graphs. Authors of trials were contacted for further details and provision of original data if the published report contained insufficient information. Modification of original data was done (eg, range conversion to SD) on a very restricted predefined basis, as needed, according to established methods.[20]

The summary of findings tables (GRADE Tables) were created using the GRADE profiler software (version 3.6.1) in which all judgments pertaining to evaluation of quality of evidence were recorded. When findings demonstrated a benefit across critical outcomes, the intervention was said to have benefit across all measured outcomes. When the results were inconsistent across all measured outcomes, the results were said to be "mixed." Interventions without statistical evidence of benefit were said to have no evidence of a benefit.

RESULTS

A total of 114,251 references were retrieved from the databases. Another 138 were identified separately from reference sections of retrieved articles. All references were saved in an EndNote library that identified 32,155 duplicates. The remaining 82,234 references were reviewed by 2 of the authors (A.T., V.S.) against the inclusion criteria. From this overarching search, 13 studies investigating education and preparation interventions were included in the review.[21–33] In 2 cases, multiple citations were identified for the same study and in both cases it was a thesis that was later published.[28,29] The literature search flow is shown in Figure 1. Characteristics of included trials are displayed in Table 2. All studies focused on children, with the majority of studies focusing on children 7 years and below.

Quality of Studies and Risk of Bias

Table 3 shows the results for the risk of bias assessment for critical outcomes. All trials had a high overall risk of bias primarily due to lack of blinding of important personnel and lack of methodological rigor in relation to randomization procedures.

Overall Quality of Evidence and Treatment Effects

A quantitative summary of the treatment effects for available critical outcomes is provided below. Table 4 displays a qualitative summary of these results. Supporting GRADE Evidence Profiles and Summary of Findings tables for critically important and important outcomes is in the Supplemental Digital Content for this paper (Process Figs. 1 to 5, Supplemental Digital Content 1, http://links.lww.com/CJP/A280 and Process Tables 1 to 5, Supplemental Digital Content 2, http://links.lww.com/CJP/A281).

Should Clinicians Administering Vaccine Injections be Educated About Vaccine Injection Pain and Fear Management?

One trial examined the efficacy of training public health nurses (n = 53) who were immunizing children of all ages on a variety of evidence-based pain management strategies.[21] There was low-quality evidence due to methodological limitations related to randomization details and lack of blinding of both participants and outcome assessors. The trial addressed the critical outcome of use of interventions and results were in favor of clinician education (n = 459; SMD 0.66; 95% CI: 0.47, 0.85).

Should Parents be Present During Vaccine Injections in Children?

Four trials addressed the presence of parents during childhood vaccine injections,[22–24,33] with 1 trial[33] providing 2 arms as data were presented separately for toddlers (approximately 18 mo of age) and preschoolers (approximately 5 y of age). Only 3 trials[23,24,33] provided data on a critical outcome (distress: preprocedure, acute, recovery, preprocedure + acute + recovery) and all analyses were based on very low-quality data due to lack of blinding, selective data reporting, and small sample sizes. The results were mixed; data only supported the presence of parents for distress preprocedure (n = 67; SMD −0.85; 95% CI: −1.35, −0.35).

Should Parents be Educated About Vaccine Injection Pain and Fear Management Ahead of Time?

Five[25–29] trials studied the efficacy of parent pain management before the day of vaccination. All trials were performed in the context of vaccinations of children 2 years or below, only 4[25,27–29] of the trials provided data for the analysis of critical outcomes (use of intervention and distress). In regards to the critical outcome for parent use of intervention, 3 separate analyses had to be conducted due to the timing of the measurement or the type of data provided. Parent use of pain management strategies before the procedure was supported by data from 1 trial[25] of low quality (n = 50; SMD 0.83; 95% CI: 0.25, 1.41). During the procedure, parent use of interventions using continuous data from 1 moderate quality trial[27] did not support parent education, whereas a categorical analysis of 2 trials[28,29] of low quality did support advance education in improving parent use of pain management strategies (n = 300; RR 2.08; 95% CI: 1.51, 2.86).

Analyses on the critical outcome of distress were conducted on the acute and the acute + recovery phases using low-quality data. Results were mixed as only data on the acute distress outcome, based on 3 trials,[25,28,29]

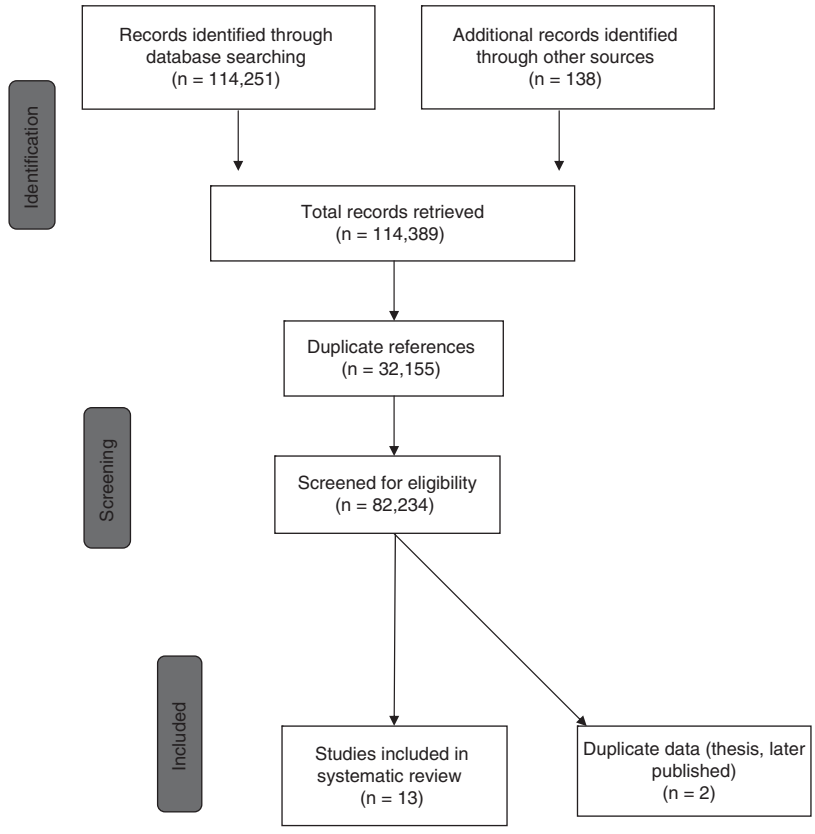

FIGURE 1. Flow chart of studies for process intervention trials.

supported educating parents in advance of education (n = 350; SMD −0.35; 95% CI: −0.57, −0.13).

Should Parents be Educated About Vaccine Injection Pain and Fear Management on the Day of Vaccination?

Four trials were reviewed for this clinical question,[26,28,30,31] with 1 study providing 2 separate arms for analysis[26] of critical outcomes. The quality of the evidence was low to very low, primarily due to issues, omissions related to randomization procedures, or both and the lack of blinding of participants and personnel. For the critical outcome parent use of intervention, both continuous data analysis[26,30] (n = 183; SMD 1.02; 95% CI: 0.22, 1.83) and categorical data analysis[28,31] (n = 239; RR 2.42; 95% CI: 1.47, 3.99) supported the education of parents on the day of vaccination. Because of the age of children in the analyses (6 and below), distress was considered (ie, acute, acute + recovery, preprocedure + acute + recovery, and preprocedure distress). Results were mixed. Only the analysis on the preprocedure + acute + recovery distress outcome supported parent education on the day of vaccination (n = 262; SMD −0.48; 95% CI: −0.82, −0.15).

Should Children Above 3 Years and Adults be Educated About Vaccine Injection Pain Management on the Day of Vaccination?

One very low-quality study (n = 17) contributed 2 arms to the analysis of the critical outcome of fear[32] (preprocedure, postprocedure) based on children 11 to 12 years of age. Analyses showed mixed support for the reduction of fear through education of patients on the day of immunization: fear preprocedure (SMD −0.67; 95% CI: −1.28, −0.07) and fear postprocedure (SMD −0.63; 95% CI: −1.62, 0.36).

DISCUSSION

This systematic review examined education strategies for clinicians, parents (before the day of vaccination, on the day of vaccination), and individuals being vaccinated (on the day of vaccination), in addition to an analysis of instructing a parent to be present or absent during the vaccination procedure. The results demonstrated evidence to support educating all groups (both in advance and on day of vaccination) and the parents present; however, the results were mixed for the majority of analyses. A discussion of each clinical question in turn will expand on these findings.

One low-quality trial[21] provided evidence that an education intervention (2-hour workshop on evidence-based pain management; online support) was able to increase nurse pain management strategy utilization. These effects were seen both in comparison with the no education group and in comparison with their own strategy utilization during the baseline phase. Although there was a large number of patients exposed to increased evidence-based pain management (n = 459) in this study, the actual number of nurses in the trial was quite small (n = 53). Nonetheless the uptake of pain management was significantly increased and the cost-benefit ratio was favorable. These results, coupled with the expectation that immunizing clinicians who are competent in vaccination administration techniques, including ways to

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 clinicians administering vaccine injections be educated about vaccine injection pain and fear management?				
Chan 2013,[21] Canada	Vaccines NR; no injection details	N = 53 nurses; children of all ages; multicenter cluster trial; public health clinics	Training of public health nurse immunizers (2 h educational workshop, supplies [eg, sucrose solution], online support) (n = 237) or Control (no intervention) (n = 222)	Use of interventions
Should parents be present during vaccine injections in children 0-10 y?				
Broome 1989,[22] USA	DT; no injection details	N = 138; children 3-9 y; between-groups design; single center, health screening clinic	Parent present (3 ft away) for interview and injection (n = 53) or Parent present for interview and absent for injection (n = 21) or Parent absent for interview and injection (n = 26)* or Parent absent for interview and present for injection (3 ft away) (n = 38)*	NA (this study was not included in the meta-analysis for critical outcomes)
Gonzalez et al 1989,[23] USA	Immunization (vaccine NR) or antibiotic injections (not specified); typically in arm	N = 47; children 13 mo-7 y; between-groups design; single center, pediatric primary care clinic of hospital	Parent present (6 ft away) for injection (n = 23) or Parent absent for injection (n = 24)	NA (this study was not included in the meta-analysis for critical outcomes)†
O'Laughlin 1995[24] (2), 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 (n = 11) or Mother absent for injection (n = 9) or Mother present for injection, instructed to watch only (n = 9)* or Parent present for injection, instructed to coach child in using distraction: counting, rhyme or poem recitation, singing, or looking at an object (n = 7)*	NA (this study was not included in the meta-analysis for critical outcomes)†
Shaw 1982[33] (1,2), USA	Oral polio, DPT; thigh	Shaw 1982 (1): N = 20; children 18-26 mo; between-groups design; single center, private pediatric practice Shaw 1982 (2): N = 20; children 4-5 y; between-groups design; single center, private pediatric practice	Shaw 1982 (1): parent present for injection (n = 10) or parent absent for injection (n = 10) Shaw 1982 (2): parent present for injection (n = 10) or Parent absent for injection (n = 10)	Shaw 1982 (1): distress: modified Frankl Scale Shaw 1982 (2): NA (this study was not included in the meta-analysis for critical outcomes)†
Should parents be educated about vaccine injection pain management before the day of vaccination (ie, ahead of time)?				
Bustos et al 2008,[25] Australia	Vaccines NR; no injection details	N = 50; infants 5-7 mo; between-groups design; single center, outpatient hospital clinic	Parent education (pamphlet about parent behaviors that reduce child distress) (n = 25) or Control (n = 25)	Use of Interventions Distress: NFCS, cry
Cramer-Berness 2005[26] (1,2), USA	Vaccines NR; no injection details	N = 123; children 2 mo-2 y; between-groups design; single center, outpatient clinic	Education of parents (parent instruction in distraction) (n = 40) or Education of parents (parent instruction in supportive care [verbal dialog encouraging parent existing strategies to soothe child's pain]) (n = 42) or Control (n = 41)	Use of interventions Distress: MBPS, VAS

(*Continued*)

TABLE 2. (*continued*)

First Author, Year, Country	Injection Details	Population Enrolled, Design, Setting	Intervention	Critical Outcomes
Taddio et al 2015[28] (2), Canada	DTaP-IPV-Hib, PCV IM; 25-gauge, 1-inch needle; thigh	N = 160; infants 2-6 mo;between-groups design; single center cluster trial, outpatient hospital clinic	Education of parents (parent viewed pamphlet and video about pain management while waiting in clinic on a previous appointment) (n = 80) or Control (parent viewed pamphlet with general information about immunization on a previous appointment) (n = 80)	Use of Interventions Distress: MBPS, VAS, cry
Taddio et al 2014,[29] Canada	Vaccines NR; no injection details	N = 197; expectant parents; between-groups design; single center cluster trial, hospital prenatal class	Education of parents (parent viewed a presentation about pain management during prenatal class, including viewing video, reviewing pamphlet, and "Question & Answer" period) (n = 101) or Control (n = 96)	Use of Interventions Distress: NRS
Taddio et al 2014,[27] Canada	Vaccines NR; no injection details	N = 178; newborns; between-groups design; multicenter, hospital	Parent education (pamphlet about pain management passively inserted in hospital discharge materials) (n = 92) or Control (n = 86)	Use of intervention
Should parents be educated about vaccine injection pain and fear management on the day of vaccination?				
Cramer-Berness 2005[26] (1,2), USA	Vaccines NR; no injection details	N = 123; children 2 mo-2 y; between-groups design; single center, outpatient clinic	Education of parents (parent instruction in distraction) (n = 40) or Education of parents (parent instruction in supportive care [verbal dialog encouraging parent existing strategies to soothe child's pain]) (n = 42) or Control (n = 41)	Use of interventions Distress: MBPS, VAS
Cohen et al 2015[30] (2), USA	DPTaP, MMR; no injection details	N = 90; children 4-6 y; between-groups design; single center, outpatient clinic	Distraction (parent viewed computer games while in waiting room; portable movie player provided for use during vaccination) (n = 30)* or Education of parents (parent viewed computer training program "Bear Essentials" while in waiting room which included information about parent behaviors that positively and negatively affect child distress; portable movie player provided for use during vaccination) (n = 30) or Control (n = 30)	Use of intervention Pain: FPS-R Distress: Behavior coding, VAS
Felt et al 2000,[31] USA	Vaccines NR; no injection details	N = 112; children 2-24 mo; single center, outpatient clinic	Education of parents (parent viewed pamphlet about distraction techniques) (n = 57) or Standard care (n = 45)	Use of Interventions Distress: Behavior coding, VAS
Taddio et al 2015[28] (1), Canada	DTaP-IPV-Hib, PCV IM; 25-gauge, 1-inch needle; thigh	N = 160 infant parent dyads; infants 2-6 mo; between-groups design; single center cluster trial, outpatient hospital clinic	Education of parents (parent viewed pamphlet and video about pain management while waiting in clinic) (n = 80) or Control (parent viewed pamphlet with general information about immunization) (n = 80)	Use of Interventions Distress: MBPS, VAS, cry

(*Continued*)

TABLE 2. (*continued*)

First Author, Year, Country	Injection Details	Population Enrolled, Design, Setting	Intervention	Critical Outcomes
Should children above 3 y and adults be educated about vaccine injection pain management on the day of vaccination?				
Klingman 1985[32] (1, 2), Israel	Rubella; no injection details	N = 51; children 11-12 y; between-groups design; school setting	Education (disease, procedure, cognitive coping techniques and practice) (n = 17) or Education (disease, procedure, cognitive coping techniques and question/answer) (n = 17) or Control (education about procedure, and then reading lesson from normal curriculum) (n = 17)	Fear: SAIC

Studies were identified using the following notation: "First Author" "Year of Publication" (eg, Taddio 2014). If studies contributed to multiple analyses, then "#" was added to enable their discernment (eg, Taddio 2014 [1]).

*Not included in analysis.

†Distress considered due to young age of children.

Route: IM, intramuscular; SC, subcutaneous. Outcomes: Cry, cry duration; FPS-R, Faces Pain Scale- Revised; MBPS, Modified Behavioral Pain Scale; modified Frankl Scale, Modified Frankl Behavior Rating Scale; NFCS, Neonatal Facial Coding Scale; NRS, Numerical Rating Scale; SAIC, self-report State Anxiety Inventory for Children (from the State Trait Anxiety Inventory for Children (STAIC); VAS, Visual Analog Scale. Vaccines: DPT, diphtheria, tetanus, pertussis; DPTaP, diphtheria, polio, tetanus, acellular pertussis; DT, diphtheria, tetanus; DTaP-IPV-Hib, diphtheria, tetanus toxoid, acellular pertussis, inactivated polio vaccine, *Haemophilus influenzae* type b; DTP, diphtheria, tetanus, pertussis; MMR, measles, mumps, rubella; PCV, pneumococcal conjugate vaccine. Other: NA, not applicable; NR, not reported.

prevent pain (ie, adverse events or harm), supports the notion that clinicians should be educated about these strategies. This study was conducted with nurses who were already practicing. Another important future direction will be to explore the specific benefits of providing pain management education during health professional training, through nursing and medical schools, with continuing education modules available after graduation. In addition, the paucity of trial data for this integral strategy suggest the need for more research.

Although there were more data for the education of parents, results were mixed for both educating parents before vaccination day and on the vaccination day for both critical outcomes where data were available (increase in use of strategies, distress). The only analysis of moderate quality[27] in the meta-analyses suggested that parent use of strategies did not increase with education before the immunization day, whereas 2 other separate analyses of use of strategies (based on trials of lower quality[25,28,29]) suggested prior parent education was efficacious. This difference was hypothesized to have been due to the format of the education. Specifically, the trial[27] that did not find significant effects educated parents through inclusion of a pamphlet in a postnatal information package when mothers left the hospital, whereas the other interventions involved interactive discussion, presentations, or both videos, information pamphlets, or both. Thus, educational efforts likely need to be more interactive rather than simply providing a brochure.[13] All of the analyses on educating parents on the vaccination day (very low to low quality) suggested an increase in parent use of pain management strategies. In terms of the impact of educating parents on the critical outcome of distress, mixed results were found for both prior and on-the-day-of education of parents. There was no apparent pattern to the findings but again, the heterogeneity of the interventions that were synthesized likely contributed to these mixed findings.

The mode of education used to teach parents included usual modalities, such as pamphlets, videos or computer-based education, and in person education. Prior work suggests that parents are accepting of these methods of instruction; in fact, video instruction has been reported as being particularly helpful in increasing their knowledge about how to implement pain strategies.[34] Little attention, however, has been given to individualizing education according to personal preference. None of the trials synthesized asked the parent for a preferred mode of education or preparation. This is an important factor in education and should be included in future studies. Moreover, the dominance of smart phone technology and app-based education tools, provide other novel and potentially engaging instructional formats that need to be empirically studied.

Another important consideration in targeting parents for education is the perception of parents regarding their role in mitigating pain and the support afforded to them by health care providers. In previous studies, it has been demonstrated that parents often look to health care providers to endorse and lead pain management efforts.[35,36] Even if parents actively seek advice and advocate for pain management, some clinicians may refuse to allow pain interventions.[27,28] This will likely lead to a more distressing procedure for children and a more negative experience for parents who are now aware that something could have been done to make their children more comfortable but was not. More generally, it may also lead parents to question the competence of their clinician. Conversely, messages and actions by clinicians that "dismiss" pain may falsely lead parents to believe that managing pain is unimportant, which puts children at risk for the adverse sequelae of pain (ie, development of needle fears and health care avoidance behaviors).[37] Any efforts to educate parents should also target clinicians administering vaccinations.

The education of individuals being vaccinated was based on very low-quality data with children. Although the

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

First Author, Year	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 clinicians administering vaccine injections be educated about vaccine injection pain management?								
Chan et al 2013[21]	Unclear	Unclear	No	No	Yes	Yes	No	High
Should parents be present during vaccine injections in children 0-10 y?								
Broome 1989[22]	No	No	No	No	No	Yes	Yes	High
Gonzalez et al 1989[23]	Unclear	Unclear	No	Yes	Unclear	No	Yes	High
O'Laughlin 1995[24] (2)	Unclear	Unclear	No	No	Unclear	No	No	High
Shaw 1982[33] (1,2)	Unclear	Unclear	No	No	Yes	No	No	High
Should parents be educated about vaccine injection pain management before the day of vaccination (ie, ahead of time)?								
Bustos et al 2008[25]	Yes	Unclear	No	Yes	Yes	Yes	Yes	High
Cramer-Berness 2005[26] (1,2)	Unclear	Unclear	No	Yes	Yes	Yes	Yes	High
Taddio et al 2015[28]	Yes	No	No	Yes	No	Yes	Yes	High
Taddio et al 2014[29]	Yes	Yes	No	Yes	Yes	Yes	Yes	High
Taddio et al 2014[27]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
Should parents be educated about vaccine injection pain management on the day of vaccination?								
Cramer-Berness 2005[26] (1,2)	Unclear	Unclear	No	Yes	Yes	Yes	Yes	High
Felt et al 2000[31]	No	No	No	No	No	Yes	No	High
Taddio et al 2015[28]	Yes	No	No	Yes	No	Yes	Yes	High
Cohen et al 2015[30] (2)	Yes	Yes	No	No	Yes	Yes	Yes	High
Should children above 3 y and adults be educated about vaccine injection pain management on the day of vaccination?								
Klingman 1985[32]	Unclear	Unclear	No	No	Unclear	No	Unclear	High

analysis on the 1 trial implementing education on the day of vaccination[32] supported efficacy for the critical outcome of fear, there were no data on increased use of strategies nor on pain. More research needs to be done across the lifespan that examines different modes of education and how they interact with individual preferences. The effects of education before the vaccination day are particularly worthy of study, especially in children who have a higher level of fear of needles.[37] In 1 before-and-after study that educated school-aged children about needles, a decrease in child self-reported fear of needles and an increase in willingness to be vaccinated were observed.[4] The results of this study suggest that these interventions hold promise for reducing future pain and improving vaccination compliance among this vulnerable group. Prior education also affords individuals with additional time to learn about how to implement interventions and reduces the potential for disappointment from not being able to optimally implement pain treatments of their choice (eg, topical anesthetics, which require prior purchase and time for application). Moreover, another important variable to consider in future trials is how far in advance to prepare and educate. It is clear that optimal timing will likely depend on both developmental and personality factors.

The remaining clinical question related to the presence of parents during vaccination injections.[22–24,33] The results were mixed regarding the impact on child distress. In 3 of the 4 analyses (distress acute, distress, distress recovery, preprocedure + acute + recovery), results appeared to support parent absence rather than presence. Only for the distress preprocedure outcome did results support presence. This question was based on the lowest quality of evidence due to issues with randomization, blinding, and selective outcome reporting. Together, the results suggest that in a lower distress situation (ie, in anticipation of a painful needle), parent presence seems to reduce distress. However, in a high distress situation (ie, after a painful needle), parent presence increases distress. Although at face value, this could be taken to suggest that parents should not attend vaccinations; consideration of additional factors is needed when interpreting the results. Firstly, children clearly report a strong preference for parental presence at vaccination.[7,23] Children's preferences should be taken into account when delivering vaccine injections. Secondly, from an attachment perspective, stronger pain signaling in the presence of parent is expected.[38] A recent observational study of infant vaccination pain and infant attachment status showed that secure babies signaled more distress than insecure babies[38] in the absence of any formalized pain management strategies. It is posited that the increased distress (in the absence of other formalized pain management strategies) reflects the attachment security of the infants. The patterns for expressing and regulating distress in the context of their caregiver represent a newly recognized source of distress variability in the infant vaccination context that should be considered in future studies.[39] Despite the mixed evidence base, our group strongly recommends parent presence for young children below 10 years of age. This is due to the developmental needs (ie, attachment needs) that have been clearly demonstrated in young children during periods of distress. However, recommendations regarding the role of parent presence with older children cannot be discerned at

TABLE 4. Summary of Results for Process Interventions' Critically Important Outcomes

Clinical Questions	Critical Outcomes*	Benefit of Intervention†	Quality of Evidence‡
Should clinicians administering vaccine injections be educated about vaccine injection pain management?	Use of intervention	Yes	Low
Should parents be present during vaccine injections in children 0-10 y?	Pain, fear	Mixed§	Very low
Should parents be educated about vaccine injection pain management before the day of vaccination (ie, ahead of time)?	Use of intervention, pain, fear, distress	Mixed	Low
Should parents be educated about vaccine injection pain management on the day of vaccination?	Use of intervention, pain, fear, distress	Mixed	Very low
Should children above 3 y and adults be educated about vaccine injection pain management on the day of vaccination?	Pain, fear	Yes	Very low

*Includes results for the critical outcomes that were evaluated in included studies only; distress, whereas not a critical outcome, was considered in analyses that predominantly analyzed children below 7 years of age.

†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 observed across all evaluated critical outcomes; Mixed, benefit was observed for one or more, but not all, 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 the evaluated critical outcomes whereby rankings range from high to moderate to low to very low.

§On the basis of the analysis of important outcome of distress; see text for details.

this time. Research in this age group seems to be nonexistent (likely because older children are often involved in school-based immunization programs where parents are not present) and older children may have differing preferences (peer support may play a larger role in the social context of these immunizations during the adolescent stage of development). The value of parental presence also may vary according to the distress levels of the parent themselves. More research must be done to explore the role of parental presence across childhood according to important covariates such as age, parental psychopathology, or parental comfort in medical settings.

Some limitations to this review must be reviewed. The paucity of evidence and low quality of existing evidence provided a weak foundation on which to make definitive conclusions. Moreover, the heterogeneity of educational strategies that were analyzed together, the lack of attention to individual preferences (eg, how information is delivered, how much information is given, when the information is given), and individual variability factors (eg, attachment status) also suggests this particular area is in dire need of strong trials that take a more sophisticated approach to study design. Strengths of the review include a thorough database search for all relevant studies, a priori decisions for identifying relevant clinical questions and critically important outcomes, and the use of state-of-the-art methods for pooling data and evaluating the quality of evidence.

In conclusion, in the first analysis of process interventions for pain management during vaccination, we found evidence for educational interventions directed at clinicians, parents, and individuals undergoing immunization, and parent presence during childhood vaccination. Educational interventions empower all stakeholders to take control of the pain, fear, and distress that is known to occur in relation to vaccine injections. More work is recommended in this area to inform society about better ways to translate and mobilize pain management strategies.

REFERENCES

1. Kikuta A, Gardezi F, Dubey V, et al. Practices and perceptions regarding pain and pain management during routine childhood immunizations: finding from a focus-group study with nurses working at Toronto Public Health, Ontario. *Can J Infact Dis Med Mircobiol*. 2011;22:43–48.
2. Taddio A, Hogan M-E, Gerges S, et al. Addressing parental concerns about pain during childhood vaccination: is there enough time to include pain management in the ambulatory setting? *Clin J Pain*. 2012;28:238–242.
3. Taddio A, Ilersich AF, Ilersich AN, et al. From the mouth of babes: getting vaccinated doesn't have to hurt. *Can J Infect Dis Med Micriobiol*. 2014;25(X):1–5.
4. Kajikawa N, Maeno T, Maeno T. Does a child's fear of needles decrease through a learning event with needles? *Issues Compr Pediatr Nurs*. 2014;37:183–194.
5. Dalley JS, McMurtry CM, Creary P. Pain tolerance of parents and children during needle procedures. Proceedings of the 35th Annual Scientific Meeting of the Canadian Pain Society, May 20-23, 2014, Quebec City, Quebec.
6. Taddio A, Appleton M, Bortolussi R, et al. Reducing the pain of childhood immunization—an evidence-based clinical practice guideline. *Can Med Assoc J*. 2010;182:E843–E855.
7. Taddio A, McMurtry CM, Shah V, et al. Reducing pain during vaccine injections: clinical practice guideline. *CMAJ*. 2015; Aug 24. [Epub ahead of print]. DOI:10.1503?/cmaj.150391.
8. Shah V, Taddio A, McMurtry M, et al. Pharmacological and combined interventions to reduce vaccine injection pain in children and adults: systematic review and meta-analysis. *Clin J Pain*. 2015;31(10S):S38–S63.
9. Pillai Riddell R, Taddio A, McMurtry CM. Psychological interventions for vaccine injections in young children 0 to 3 years: systematic review of randomized controlled trials and quasi-randomized controlled trials. *Clin J Pain*. 2015;31(10S): S64–S71.
10. Birnie KA, Chambers CT, Taddio A, et al. Psychological interventions for vaccine injections in children and adolescents: systematic review of randomized and quasi-randomized controlled trials. *Clin J Pain*. 2015;31(10S):S72–S89.
11. Boerner KE, Birnie KA, Chambers CT, et al. Simple psychological interventions for reducing pain from common needle procedures in adults: systematic review of randomized and quasi-randomized controlled trials. *Clin J Pain*. 2015; 31(10S):S90–S98.
12. Taddio A, Shah V, McMurtry CM. Procedural and physical interventions for vaccine injections: systematic review of randomized controlled trials and quasi-randomized controlled trials. *Clin J Pain*. 2015;31(10S):S20–S37.

13. Jaaniste T, Hayes B, von Baeyer CL. Providing children with information about forthcoming medical procedures: a review and synthesis. *Clin Psychol-Sci Pr*. 2007;14:124–143.
14. Suls J, Wan CK. The effects of sensory and procedural information on coping with stressful medical procedures and pain: a meta-analysis. *J Consult Clin Psych*. 1989;57:372–379.
15. Taddio A, McMurtry CM, Shah V, et al. Methodology for knowledge synthesis of the management of vaccination pain and needle fear. *Can Med Assoc J*. 2015.Forthcoming.
16. Guyatt GH, Oxman AD, Schunemann HJ, et al. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. *J Clin Epidemiol*. 2011;64:380–382.
17. Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from: http://www.cochrane-handbook.org.
18. von Baeyer CL. Children's self-reports of pain intensity: scale selection, limitations and interpretation. *Pain Res Manag*. 2006;11:157–162.
19. Borenstein M, Hedges LV, Higgins JPT, et al. *Introduction to Meta-analysis*. West Sussex, UK: John Wiley & Sons; 2009.
20. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol*. 2005;5:13.
21. Chan S, Pielak K, McIntyre C, et al. Implementation of a new clinical practice guideline regarding pain management during childhood vaccine injections. *Paediatr Child Health*. 2013;18:367–372.
22. Broome ME, Endsley RC. Maternal presence, childrearing practices, and children's response to an injection. *Res Nurs Health*. 1989;12:229–235.
23. Gonzalez JC, Routh DK, Saab PG, et al. Effects of parent presence on children's reactions to injections: behavioral, physiological, and subjective aspects. *J Pediatr Psychol*. 1989;14:449–462.
24. O'Laughlin E, Ridley-Johnson R. Maternal presence during children's routine immunizations: the effect of mother as observer in reducing child distress. *Child Health Care*. 1995;24:175–191.
25. Bustos T, Jaaniste T, Salmon K, et al. Evaluation of a brief parent intervention teaching coping-promoting behavior for the infant immunization context: a randomized controlled trial. *Behav Modif*. 2008;32:450–467.
26. Cramer-Berness LJ, Friedman AG. Behavioral interventions for infant immunizations. *Child Health Care*. 2005;34:95–111.
27. Taddio A, MacDonald NE, Smart S, et al. Impact of a parent-directed pamphlet about pain management during infant vaccinations on maternal knowledge and behavior. *Neonatal Netw*. 2014;33:74–82.
28. Taddio A, Parikh C, Yoon EW, et al. Impact of parent-directed education on parental use of pain treatments during routine infant immunizations: a cluster randomized trial. *Pain*. 2015;156:185–191.
29. Taddio A, Smart S, Sheedy M, et al. Impact of prenatal education on maternal utilization of analgesic interventions at future infant vaccinations: a cluster randomized trial. *Pain*. 2014;155:1288–1292.
30. Cohen LL, Rodrigues NP, Lim CS, et al. Automated parent-training for preschooler immunization pain relief: a randomized controlled trial. *J Pediatric Psychol*. 2015:1–9.
31. Felt BT, Mollen E, Diaz S, et al. Behavioral interventions reduce infant distress at immunization. *Arch Pediatr Adolesc Med*. 2000;154:719–724.
32. Klingman A. Mass inoculation in a community: the effect of primary prevention of stress reactions. *Am J Community Psychol*. 1985;13:323–332.
33. Shaw EG, Routh DK. Effect of mother presence on children's reaction to aversive procedures. *J Pediatr Psychol*. 1982;7:33–42.
34. Taddio A, Shah V, Leung E, et al. Knowledge translation of the HELPinKIDS clinical practice guideline for managing childhood vaccination pain: usability and knowledge uptake of educational materials directed to new parents. *BMC Pediatr*. 2013;13:23.
35. Taddio A, Manley J, Potash L, et al. Routine immunization practices: use of topical anesthetics and oral analgesics. *Pediatrics*. 2007;120:e637–e643.
36. Parvez E, Stinson J, Boon H, et al. Mothers' beliefs about analgesia during childhood immunization. *Paediatr Child Health*. 2010;15:289–293.
37. McMurtry CM, Pillai Riddell R, Taddio A, et al. HELPinKids&Adults Team. Far from "just a poke": common painful needle procedures and the development of needle fear. *Clin J Pain*. 201531(10S):S3–S11.
38. Horton R, Pillai Riddell R, Flora D, et al. Distress regulation in infancy: attachment and temperament in the context of pain of acute pain. *J Dev Behav Pediatr*. 2015;36:35–44.
39. Pillai Riddell RR, Flora DB, Stevens SA, et al. Variability in infant acute pain responding meaningfully obscured by averaging pain responses. *Pain*. 2013;154:714–721.