PAIN-RELATED ANTICIPATORY DISTRESS IN PRESCHOOLERS: LONGITUDINAL AND CONCURRENT PREDICTORS

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A DISSERTATION SUBMITTED TO
THE FACULTY OF GRADUATE STUDIES
IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

GRADUATE PROGRAM IN PSYCHOLOGY
YORK UNIVERSITY
TORONTO, ONTARIO

July 2016

ABSTRACT

Pain-related anticipatory distress prior to a painful medical procedure can lead to negative sequelae including heightened pain experiences, avoidance of future medical procedures, and potential non-compliance with preventative healthcare such as vaccinations. No study to date has examined the longitudinal and concurrent predictors of preschool pain-related anticipatory distress in the vaccination context. This dissertation consists of three studies examining the longitudinal factors from infancy as well as concurrent factors from preschool age that predict pain-related anticipatory distress at the preschool age. Study 1 is a large-scale, published systematic review of the factors predicting pain-related anticipatory distress to painful medical procedures in children using a developmental psychopathology framework. A narrative synthesis of the evidence, which appears to predict anticipatory distress, was presented. Study 2 and 3 were published in an extended research paper. A sample of 202 caregiver-child dyads (OUCH Cohort) was observed during their infant and preschool vaccinations and was used for both Study 2 and Study 3. Study 2 examined how well preschool pain-related anticipatory distress was predicted by infant pain responding at 2, 4, 6 and 12 months of age. Study 3, using a developmental psychopathology framework, examined the predisposing, precipitating, perpetuating, and present factors that led to the development of anticipatory distress during routine preschool vaccinations. In Study 2, pain responding during infancy did not significantly predict pain-related anticipatory distress at preschool. However, a strong explanatory model was created in Study 3 whereby parental behaviours from infancy and preschool were the strongest predictors of child anticipatory distress at preschool, underscoring the importance of parents during the preschool vaccination. Clinical implications and suggestions for future research are discussed.

DEDICATION

This thesis is dedicated to the children and families who participated in our research. Thank you for allowing us to be part of your lives and to observe your interactions for the last 7 years. Your openness and willingness to participate in our work has provided a richness of information and an understanding that we are eternally grateful for.

ACKNOWLEDGMENTS

Dr. Donald Winnicott, a pioneer in the area of relational theory, said, “There is no such thing as a baby, there is a baby and someone”. Over the last 7 years I have been fortunate to study babies and their “someone”. Similar to a baby, a graduate student also has someone, or in my case, several someones who accompanied me on my journey through graduate school. I would like to take this opportunity to thank all the “someones” who have taken the time to be with me and support me through my journey.

First and foremost, thank you to Dr. Rebecca Pillai Riddell for your endless guidance, support, and mentorship over the last 7 years. It has been a pleasure to spend my formative years as a researcher with you and I sincerely look forward to our continued work together. Thank you for consistently recognizing and fostering a “holding environment” where I could learn, develop, and grow. I am incredibly grateful for both the professional and personal guidance you have provided me through my time as a graduate student. Thank you for creating such a supportive environment within the OUCH lab by selecting individuals with intelligent and collaborative minds. I attribute so much of the joy and success I have experienced over the last 7 years to the amazing individuals I have had the opportunity to work. To my fellow graduate students (Rachel Horton, Laila Din Osmun, Sara Ahola Kohut, Jessica Hillgrove, Lauren Campbell, Jordana Waxman, Monica O’Neill, Hannah Gennis, and Miranda DeLorenzo), thank you for being my sounding board, my support, and fellow “wolf-pack” members. You made graduate school stimulating and fun. A special thank you to the lab managers and research assistants over the years, in particular Diana Lisi, Paula Tablon, and Maria Khan for your hard work, positive attitude, and diligence. I am forever indebted to your contributions.

To my committee members, Dr. David Flora and Dr. Anna Taddio, thank you for thoughtful comments and insights with regards to this project. To the other members of my dissertation committee (Dr. Jonathan Weiss and Dr. Alison McPherson), thank you for your time and helpful comments. I would also like to extend a sincere thank you to Dr. Heidi Bailey for being my external examiner. I am grateful for your contributions and for the stimulating discussion during my defense.

There are several “someones” who have been there for me long before I started my graduate education. To my mother, Cecilia Freiburger, thank you for being a model of hard work, for instilling the value of pursuing my academic goals, and for your eternal love and support (including reading every published work I have ever written with interest and enthusiasm). To my sisters, Mary Motz, Jane Motz-Hayes, and Michelle Racine, thank you for your unwavering love and guidance and for raising four beautiful children who have been the biggest source of joy during my time in graduate school. Thank you to the late Adam Coules who encouraged me to embark on this journey and supported me with love and compassion. Finally, thank you to my partner, Zhaodi Culbreath, who picked up the torch, ran beside me, and held my hand at the finish line. I am eternally grateful for your love and support.

PUBLICATION DISCLOSURE

The work submitted in this dissertation has been published under the following citations:

Racine, N., Pillai Riddell, R., Khan, M., Calic, M., Taddio, A. & Tablon, P. (2016). Systematic review: Predisposing, precipitating, perpetuating, and present factors predicting anticipatory distress to painful medical procedures in children. *Journal of Pediatric Psychology, 41*(2):159-181. doi: 10.1093/jpepsy/jsv076.

Racine, N., Pillai Riddell, R., Flora, D., Taddio, A., Garfield, H., Greenberg, S. (in press). *Predicting preschool pain-related anticipatory distress: The relative contribution of longitudinal and concurrent factors*. Manuscript accepted for publication in Pain. doi: 10.1097/j.pain.0000000000000590.

Conceptual ideas from the current dissertation were also invited to be included in the following publication:

McMurtry, C.M., Pillai Riddell, R., Taddio, A., **Racine**, N., Asmundson, G.J.G., Noel, M., Chambers, C., Shah, V., & HELPin KIDS&Adults Team. (2015). Far from "Just a Poke": Common painful needle procedures and the development of needle fear. *Clinical Journal of Pain, 31*(10S), S3-S11. doi: 10.1097/AJP.0000000000000272.

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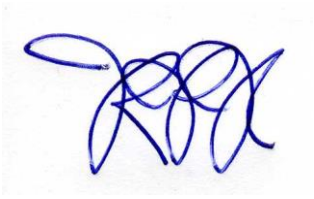

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DISSERTATION SYNOPSIS

Infants and young children undergo frequent routine painful procedures in the first five years of life, yet adequate pain management strategies are seldom employed (Lisi, Campbell, Pillai Riddell, Garfield, & Greenberg, 2013). In addition to the pain associated with the procedure, many young children experience fear and distress prior to the procedure (Howe, Ratcliffe, Tuttle, Dougherty, & Lipman, 2011). Research has shown that fear of vaccinations can have acute and long-term impacts including increased pain, difficulties managing behaviour during the procedure, and avoidance of future preventative health measures, which have striking impacts from a public health perspective (McMurtry et al., 2015). Despite these negative outcomes, little research has examined the longitudinal factors in early childhood that may predict the development of pain-related anticipatory distress and needle fear in preschool age children. Additionally, the onset of severe needle fears is thought to occur in early childhood between five and six years of age (Bienvenu & Eaton, 1998), highlighting the importance of studying the preschool period. Examination of factors in early childhood prior to the development of severe needle fear may inform prevention efforts and interventions.

Using the developmental psychopathology perspective (Cicchetti & Cohen, 1995; Sroufe & Rutter, 1984) as a guide, three broad research questions were developed for the dissertation: (1) Which factors have already been identified in the literature as predicting child pain-related anticipatory distress in preschool children? (2) Does infant pain responding from the first year of life predict child pain-related anticipatory distress at preschool age? and (3) Using a longitudinal design, do longitudinal and concurrent predisposing, precipitating, perpetuating, and present factors predict pain-related anticipatory distress to vaccinations at preschool age? These research questions were addressed as three separate studies within two published manuscripts (Racine et

al., 2016; Racine et al., in press), which built upon each other. The first study was a large-scale systematic literature review of the factors predicting anticipatory distress. These findings then informed the analyses of the second and third study. The second study examined whether infant pain responding predicted preschool anticipatory distress and the third study examined the relative value of broader longitudinal and concurrent factors in predicting preschool anticipatory distress. A subsample of 202 caregiver-child dyads from an ongoing longitudinal cohort study was used in both analyses. Dyads were videotaped during their 2-, 4-, 6-, and 12-month vaccination appointments and pain-related distress as well as caregiver and infant behaviours were coded. Caregivers and children were invited to participate again during their preschool vaccinations (at 4 to 5 years of age). Structural equation modeling (SEM) was used to answer the research questions. It was hypothesized that infant pain-responding from the first year of life, child age, previous and concurrent parent behaviour, previous pain events, healthcare provider behaviour, child sex, parent worry, and parent report of child worry would all predict pain-related anticipatory distress during the preschool vaccination appointment.

In the systematic review (Study 1), a narrative synthesis of the evidence showed that factors which appear to predict anticipatory distress are child psychopathology, difficult child temperament, parent distress-promoting behaviours, parent situational distress, previous pain events, parent anticipation of distress, and parent anxious predisposition. In Study 2, hypotheses were not supported in that infant-pain responding from the first year of life did not predict anticipatory distress at the preschool age. In Study 3, an explanatory model was developed whereby 40% of the variance in preschool anticipatory distress was explained. Parental behaviours from infancy and preschool were the strongest predictors of child anticipatory distress at preschool. Child age also positively predicted child anticipatory distress.

These novel results extend previous research to demonstrate parent behaviour as the most salient predictor of child anticipatory distress to vaccination needles. This is the first study to show that pain-related distress from vaccination during infancy does not predict child pain-related anticipatory distress at the preschool age, nor do previous painful events as measured in the current study. Parent behaviour from both infancy and preschool were predictors of anticipatory distress at 4-5 years of age, thus underscoring the critical need to support parents to better soothe their young child's pain during vaccinations across early childhood to potentially modify trajectories of maladaptive anticipatory distress.

Chapter 1: Introduction

Painful Procedures in Infants and Young Children

Healthy children experience frequent painful medical procedures over the first five years of life such as vaccinations and blood-draws (Public Health Agency of Canada, 2006). Although these procedures are part of routine preventative healthcare, many young children experience high levels of pain and distress during these procedures and adequate pain management strategies are seldom used (Lisi et al., 2013). It has been well established that painful experiences in early infancy have long-term developmental implications (Schwaller & Fitzgerald, 2014). There is substantial evidence that suggests that although a declarative memory may not be preserved and therefore cannot be reported by infants, repeated painful procedures can lead to alterations in the infant's nociceptive sensory thresholds and is expressed by their behavioural responses to future painful stimuli (Taddio, Katz, Ilersich, & Koren, 1997; Fitzgerald, Millard, & McIntosh, 1989, Schwaller & Fitzgerald, 2014). The negative impact of pain on developmental outcomes behooves parents and clinicians to adequately manage pain in infants and young children.

Fear of Painful Procedures in Young Children

In addition to the pain and distress associated with routine medical procedures, young children also experience high levels of fear and distress prior to the procedure beginning (Taddio et al., 2012, Jacobson et al., 2001). Studies have systematically demonstrated that infants and young children can learn to anticipate pain and exhibit altered pain responses as a result of cumulative exposures to pain over time. A seminal study by Taddio and colleagues (2002) found that newborns exposed to repeated heel lances in the first 24 to 26 hours of life learned to anticipate the pain of an impending venipuncture compared with infants who had not undergone

repeated painful procedures. This study set the stage for future research on fear and distress prior to medical procedures in infants and young children.

Although fear of pain has been reported in children with chronic illnesses such as diabetes who undergo frequent painful procedures (Howe, Ratcliffe, Tuttle, Dougherty, & Lipman, 2011), high levels of anticipatory distress and fear to painful medical procedures have also been reported in healthy children who do not have chronic health conditions. A recent study found that 63% of healthy children under the age of 8 years have needle fear (Taddio et al., 2012), while adult prevalence has been estimated to be between 14 and 38% (McMurtry et al., 2015). These findings are particularly concerning as anticipatory distress and fear of painful medical procedures have been associated with several negative proximal and distal sequelae. A review by McMurtry and colleagues (2015) outlined some of the key consequences that are associated with needle fear in children during the painful medical procedure itself, including increased pain and distress during painful medical procedures, increased risk of experiencing physiological symptoms such as fainting during the procedure, and increased difficulties with managing child behaviour such as flailing or running away. Additional negative consequences that may develop following the needle procedure include negative pain memories (Noel, Chambers, McGrath, Klein, & Stewart, 2012), fear of future medical procedures (Wright Yelland, Heathcote, Ng, & Wright, 2009), and potential non-compliance with healthcare procedures such as vaccinations (Taddio et al., 2012). McMurtry et al. (2015) argued that fear of needles can lead to a significant economic burden on the healthcare system as a result of managing illnesses that could have been prevented such as those that can be prevented through vaccination. Despite the important implications of fear and anticipatory distress to painful

medical procedures for children, little empirical work has investigated the factors that lead to its development.

Operational Definitions of Fear, Anxiety, and Distress

Historically, "anxiety" and "fear" have been used interchangeably within the pain literature, although McMurtry et al. (2015) clarified the distinction between these terms. Fear is defined as a response to an immediate threat (real or perceived) and is typically adaptive in dangerous situations. Some fear is typically expected with regards to needle procedures; however, high levels of needle fear are considered largely atypical (McMurtry et al., 2015). Anxiety is described as a negative emotive state and involves threat in anticipation of a future event. Similar to fear, high levels of anxiety regarding needles is considered atypical. Phobias have typically been defined using the criteria for the Diagnostic and Statistical Manual of Mental Disorders-5th Edition (APA, 2013) and usually involve persistent and severe anxiety and fear regarding a feared stimulus. With phobias, the reaction is considered disproportionate to the actual danger posed. Thus, extreme fear and anxiety regarding needles and needle procedures is not normative and involve a degree of distress that is impairing to the individual. Finally, "distress" is a general term used to describe the response to an unpleasant or negative event that traditionally incorporates multiple negative states such as pain, fear, distress, or anxiety. Since most children under 8 or 9 years of age have difficulty distinguishing between negative affective states such as fear, anxiety, or pain (von Baeyer & Spagrud, 2007), using distress as an outcome construct can capture the negative affectivity associated with painful procedures.

Development of Needle Phobia

According to the literature on child phobias, children can develop specific fears to medical procedures that are so severe that they interfere with their normal functioning and a

diagnosis of a specific phobia can be considered (Muris & Merckelbach, 2001). In most cases of specific phobia, a discrete learning experience interacts with normal development to produce severe and persistent fears (Muris & Merckelbach, 2001). Studies of prevalence and etiology of needle phobia have identified a median age of onset of 5.5 years (Bienvenu & Eaton, 1998). Rachman (1977) conducted pioneering research to identify the primary learning pathways for specific phobias, such as needle phobia. He proposed several pathways that lead to the acquisition of a phobia including the environmental learning pathway (i.e. direct conditioning, vicarious learning, and negative information). Newer work has described non-associative pathways (e.g. genetic mechanisms; Neale, Walter, Eaves, Kessler, Heath, & Kendler, 1994). Direct conditioning implies that exposure to cues associated with a negative stimulus can cause an individual to remain fearful of that stimulus. In the case of needle fear, many of these pathways are activated. Almost all children are conditioned to associate a needle with subsequent pain. The pairing of a needle and pain over time eventually leads to a fear of the needle and avoidance of the needles perpetuates the fear (Du, Jaaniste, Champion, & Yap, 2008). However, direct conditioning is by no means a universal predictor of needle phobia, as many children who are exposed to needles do not subsequently develop a fear. Children often watch older siblings get immunizations (vicarious learning) and receive negative information from cartoons and other media about needles from medical professionals without developing a fear or phobia. Needle phobia, more broadly encapsulated under the category of blood/injury phobia, has also been shown to have a greater genetic component than other phobias (Marks, 1988). Thus, associative and genetic pathways to the development of phobia are unlikely to function independently and likely combine to lead to the development of needle fear and phobia.

Although many children are fearful or are distressed prior to a painful medical procedure, not all children display notable distress prior to a painful medical procedure and the majority of children display developmental fears that decrease with age (Blount, Sturges, Powers, 1990; Muris & Merckelbach, 2001). McMurtry et al. (2015) explained that there is likely a spectrum of needle fear that varies on the level of distress experienced and the amount of impairment to daily life. Thus, although a small group of our sample likely had needle phobia per se, we are not focusing on this group but rather predicting the broader presence of anticipatory distress prior to vaccination during a needle. The discussion will now turn to the pediatric pain literature and anxiety literature for conceptual models to understand the development of anticipatory distress in young children.

Development of Pain-Related Anticipatory Distress

A Pediatric Pain Perspective

Pioneering work in the field of pain by Melzack and Wall (1965) highlighted the interplay between psychosocial and biological features of the pain experience. The gate control theory of pain was the first biopsychosocial model of pediatric pain to emphasize the affective and emotional components of pain, stressing that the pain experience involves more than the sensory stimulus and includes cognitive, affective, social, and environmental components (Craig, Lilley, & Gilbert, 1996). The gate control theory of pain paved the way for subsequent biopsychosocial models of pediatric pain which purported that pain, distress, and anxiety are part of the pain experience. One model that outlines the impact of pre-procedural factors on the pain experience is Young's (2005) model for conceptualizing and studying pediatric procedural pain. This model breaks down the child's pain experience into three distinct phases: pre-procedure, procedure, and post-procedure. This model indicates that the experience following the painful

stimuli is influenced by pre-procedural factors such as individual child factors (the child's past pain experience, child fear or anxiety, child temperament), psychobiological factors (pain receptor density), cultural and familial factors (pain beliefs), and societal or environmental factors (e.g. peer influences). Both pre-procedure and post-procedure factors continue to influence the child long after the procedure has been completed. The model also includes the indirect influences of parent and healthcare provider interactions with the child on the child's pain experience, highlighting the importance of caregivers within the acute pain context. Most important and relevant to the current dissertation, the model acknowledges that the pain response and the long-term effects of pain and distress influence individual child factors such as fear and anxiety in subsequent pre-procedure phases. This model of pediatric pain is one of the first to demonstrate a reciprocal relation between child fear and anxiety and the subsequent pain response. A gap in Young's model, however, is that it does not consider relationships among pre-procedure factors or the impact of individual factors such as age, sex, development, or temperament on fear and anxiety prior to an acute painful medical procedure. A broader model is needed to incorporate variables that may predict anticipatory distress.

A Developmental Psychopathology Perspective

The literature on the development of phobias has outlined pathways by which fear acquisition occurs (Rachman, 1977; Muris & Merckelbach, 2001); however, specific phobias are rare and a broader perspective to understand the development of anticipatory distress to painful procedures in needed. Additionally, to date, pediatric pain models have not incorporated the many factors that could lead to the development of fear and anticipatory distress. A broader perspective that has emerged as an organizational framework for the study of psychological maladaptation in childhood is the developmental psychopathology perspective (Cicchetti &

Cohen, 1995; Sroufe & Rutter, 1984) which can be used to comprehensively represent the factors that lead to anticipatory distress and fear to painful medical procedures in children.

The developmental psychopathology perspective emphasizes the importance of the complex transactional interactions among various factors across development to explain the success or maladaptive adaptation of a child, in this case with regards to anticipatory distress to painful medical procedures. In the seminal article by Sroufe and Rutter (1984), developmental psychopathology was initially defined as "the study of the origins and course of individual patterns of behavioural maladaptation" (p. 18). More recently, the developmental psychopathology perspective has been applied to the development of anxiety disorders in children. Vasey and Dadds (2001) review the tenets of developmental psychopathology as they relate to the development, maintenance, and amelioration of anxiety disorders. They argue that understanding the pathways by which childhood anxiety disorders develop, persist, and remit requires consideration of a wide range of influences and their dynamic interaction across development.

The theory of Vasey and Dadds (2001) also specifies that there are numerous pathways to the development of childhood anxiety. For example, multiple paths can lead to the same outcome (equifinality) or one path can lead to diverse outcomes (multifinality). Vasey and Dadds further argued that in addition to simple main-effect models, the onset, maintenance, and improvement of anxiety in children is likely the product of interactions among predictors. For example, direct classical conditioning alone has been inadequate for explaining the development of specific phobias (Rachman, 1977). From this perspective, anxiety disorders are conceptualized as emerging from multiple pathological pathways, which potentially reflect complex transactions across time between diverse children and their environments (Vasey & Dadds, 2001).

The second key concept in the developmental psychopathology model is the examination of risk, vulnerability, and protective factors as indicators of complex processes and mechanisms, which impact an individual's development. These factors can be transient or consistent in nature and, thus, have varying influences. Risk and protective factors can predispose to, precipitate, maintain, perpetuate, or protect against the development of anxiety (Vasey & Dadds, 2001; Carr, 1999). While risk factors contribute to the development of an anxiety disorder, protective factors encourage a return to normal development (Vasey & Dadds, 2001). Considering the multitude of predictors and how their interactions lead to particular outcomes is crucial to understanding the development of maladaptive behaviour in children (Cicchetti & Cohen, 1995).

Third, the field of developmental psychopathology focuses on the interplay between normal and atypical development, whereby both pathways of development are seen as mutually informative. In other words, if one wishes to explore maladaptive behaviour (i.e. the development of high pain-related anticipatory distress), one must first understand normal functioning as a comparison.

The developmental psychopathology model provides a comprehensive perspective that can be applied to understanding the development of fear and distress to painful medical procedures in children. Its application includes the interplay of multiple factors, which have previously been excluded from pediatric pain models. It should be noted that the use of this model does not imply that pain-related anticipatory distress is considered pathological, because fear of unknown and painful stimuli is adaptive. Rather, the framework is used conceptually to understand the combination of factors that lead to the development of pain-related anticipatory distress.

Factors predicting pain-related anticipatory distress in children.

Vasey and Dadds (2001) proposed a framework using the developmental psychopathology perspective to understand the development of anxiety disorders in children. The model suggests that risk and protective factors (cumulative risk) combine dynamically to lead to the onset of an anxiety disorder. Cumulative risk and precipitating influences are hypothesized as the two pathways to onset of anxiety disorders. Long-term risk factors are hypothesized to function as maintaining factors while long-term protective factors function as ameliorating factors. Research has suggested an extensive list of factors which predispose, precipitate, perpetuate, and protect against the development of anxiety. These factors can be applied to the development of pain-related anticipatory distress and are hypothesized to include risk and protective factors individual to the child, parent factors, and broader contextual or environmental factors. The combination of these factors is thought to contribute to the development of anxiety symptoms in children. For example, difficult temperament in combination with exposure to a feared stimulus may increase the likelihood of developing anxiety. The following sections briefly review these categories of factors.

Child factors. Factors individual to the child that predispose a child to developing anxiety include genetic factors, neurobiological factors, temperament (e.g. behavioural inhibition), emotion regulation skills, and cognitive biases or distortions (Vasey & Dadds, 2001; Hirshfeld-Becker et al., 2007; Hudson & Rapee, 2004). These factors are hypothesized to combine over time and change with development to predict the development of anxiety problems in children.

Parent factors. It has been hypothesized that parents influence the fear acquisition of their children. Children develop fear through vicarious learning and the modeling of threat whereby fear occurs by observing the fear response of their parents (Rachman, 1977). Additional

parent-related risk factors for the development of anxiety include overprotective and controlling parenting behaviour, low parental warmth, negative parent affectivity, and negative verbal transmission whereby feared stimuli are discussed or experienced in negative and frightening ways (Rapee, Schniering, & Hudson, 2009; Edwards, Rapee, & Kennedy, 2010; DiBartolo & Helt, 2007). Both anxiety and pediatric pain literatures have suggested that parental autonomy granting or giving control to a child is positively related to child fear and anxiety (Bogels & van Melick, 2004; Blount, Cohen, Frank, Bachanas, 1997), which indicates that having too much control or influence over one's environment as a child may in fact be anxiety-provoking. An important factor to consider regarding parental influences on the development of fear or anxiety is that children with high anxiety sensitivity may be more susceptible to parenting influences than children who are less sensitive (Vander Bruggen, Stams, & Bogels, 2008). In addition to parent behaviour, parent anxiety has also been found to be associated with child anxiety both generally and in the pediatric pain context. Vander Bruggen et al. (2008) hypothesized that high parent anxiety may result in a reduced effort or ability for parents to interact and support their child who has anxiety.

Experimental studies have shown that children of parents who modeled anxious behaviours and cognitions endorse higher anxiety levels, anxious cognitions, and avoidance behaviours. In one study where parents were trained in either an anxious condition or non-anxious condition, children of parents who modeled anxious behaviour, transmitted threat information, and communicated negative expectations had children who endorsed higher anxiety levels and anxious cognitions (Burstein & Gindburg, 2010). A recent study in the vaccination context showed that parent anxiety prior to the immunization heightened the child's anxiety during the procedure, which in turn resulted in higher pain for the child (Bearden, Feinstein, &

Cohen, 2012). Another study also found that parent distress-promoting behaviours including reassurance, apologies, empathy, giving control, and criticism were associated with parent reports of child fear (Blount et al., 1997). While factors specific to the child are thought to directly predict the development of child anxiety, parental variables are hypothesized to function as mediators (Degnas, Almas, & Fox, 2010) between individual child factors (i.e. temperament) and later development of child anxiety or fear. Parents play a key role in the development and maintenance of child anxiety behaviours.

Contextual factors. Contextual factors that may contribute to the development of anxiety and fear include experience with conditioned stimuli and the level of exposure with the feared stimuli (Vasey & Dadds, 2001). Rachman's (1977) theory of fear acquisition states that fear can be acquired through conditioning, vicarious exposures, and transmission of information and instruction. Direct conditioning may occur whereby a stimulus such as a needle is repeatedly paired with pain. However, research has shown that modeling and information transmission were the most common modes of fear acquisition reported by children, with a minority reporting direct conditioning experiences (Vasey & Ollendick, 2000). Contextual factors play a key role in the development of child anticipatory distress to painful medical procedures.

Current Dissertation

Although comprehensive reviews of the risk and protective factors associated with general anxiety have been well documented (Vasey & Dadds, 2001), a comprehensive and systematic review of the factors that are associated with pain-related anticipatory distress to painful medical procedures in children has yet to be conducted. Furthermore, in addition to a lack of a comprehensive review, a systematic examination of multiple concurrent and longitudinal factors, which may predict anticipatory distress in young children was missing from

the literature. As such, the current dissertation had two primary goals: first, to conduct a systematic review of the findings of studies that examine the factors that predict anticipatory distress to painful medical procedures in children, and second, to use participants from a longitudinal cohort of children receiving vaccinations across the first five years of life to systematically test predisposing, precipitating, perpetuating, and present factors that predict pain-related anticipatory distress in young children. This dissertation is the compilation of three studies over two published manuscripts: the first is a large-scale systematic review of the factors predicting anticipatory distress to painful medical procedures (Racine et al., 2016) and the second includes two studies, which systematically test the longitudinal and concurrent factors that predict anticipatory distress in preschoolers (Racine et al., in press). All the research questions, analyses, and results across the three studies are conveniently summarized in a two-page outline created for dissertation readers (see Appendix A).

In Chapter 2 (Study 1), factors that predict child pain-related anticipatory distress were examined through a systematic review. Based on the developmental psychopathology perspective, factors in the review were hypothesized to fall under the four Ps of case formulation: predisposing (e.g. genetics, temperament), precipitating (e.g. negative pain experiences), perpetuating (e.g. parent behavior, parent anxiety, child behavior, child cognitions), and present factors (e.g. healthcare professional behavior). Chapter 2 is the author-version of the manuscript published this year by the *Journal of Pediatric Psychology*.

Chapter 3 is a brief bridge that explains how Study 2 and 3 of the dissertation built upon Study 1. Chapter 4 (Study 2 and Study 3) is the author-version of the extended-length manuscript in the journal *Pain*. Study 2 included a fine-grained analysis of infant vaccination pain responding, a potentially critical child factor, as a predictor of pain-related anticipatory

distress at preschool age. Discrete infant pain response epochs were analyzed separately from each of the 2-, 4-, 6-, and 12-month vaccinations for their predictive relationships with anticipatory anxiety at the preschool vaccination. Specifically, SEM was used to predict preschool anticipatory anxiety from the pre-needle phase, immediately post- needle phase, and the change in behavioural pain responding over the first three minutes post-needle phases during their infant immunizations. It was hypothesized that higher levels of pain-related distress during infancy would positively predict pain-related anticipatory distress at the preschool age as greater pain during infancy would have a greater likelihood of directly conditioning anticipatory distress later in childhood.

In Study 3 (also in Chapter 4), a broader perspective was taken to accommodate parent and contextual factors that may play a role in the development of anticipatory anxiety during preschool. Thus, the predisposing, precipitating, perpetuating, and present factors that may longitudinally predict pain-related anticipatory distress to vaccinations at preschool were examined. Specifically, Study 3 included tests of whether child age, cumulative pain-related distress at 2 and 12 months of age, child sex, caregiver distress-promoting behaviour, healthcare provider distress-promoting behaviour, parent report of child worry, and parent worry predict pain-related anticipatory distress at preschool.

Based on the findings from Study 1, we hypothesized that cumulative pain experiences at 2 and 12 months of age and previous pain events would positively predict pain-related anticipatory distress at preschool. Based on previous work (Pillai Riddell et al., 2011) and classic child-development literature that demonstrates patterns of sensitive contingent soothing results in children who regulate from distress more optimally (Ainsworth, Blehar, Waters, & Wall, 1978; Bowlby 1969/82), we also hypothesized that caregiver emotional availability at 2 and 12 months

of age would negatively predict pain-related anticipatory distress at preschool. Age was hypothesized to negatively predict pain-related anticipatory distress in preschool because, although findings have been inconclusive in previous work, a recent summary indicated that younger children likely express more anticipatory distress (Racine et al., 2016). Perpetuating factors such as parent worry, parent report of child worry, and parent distress-promoting behaviours were hypothesized to positively predict pain-related anticipatory distress based on past work (Bearden et al., 2012, Blount et al., 1997; Mahoney, Ayers, & Seddon, 2010). Finally, previous research has suggested that healthcare professional distress-promoting behaviour positively predicts pain-related anticipatory distress at preschool (Blount et al., 1997); thus, we hypothesized similar findings.

An important labeling note is required for Chapter 4. As aforementioned, Chapter 4 is the author-version of the manuscript accepted for publication by the journal *Pain* in March 2016 (http://www.ncbi.nlm.nih.gov/pubmed/27276117). Thus, while for the purposes of the dissertation the analyses contained therein are Study 2 and Study 3, in the published manuscript they are referred to as Study 1 and 2.

Chapter 2: Systematic Review: Predisposing, Precipitating, Perpetuating, and Present Factors Predicting Anticipatory Distress to Painful Medical Procedures[1]

Healthy children experience frequent medical procedures such as immunization and blood-draws (Public Health Agency of Canada, 2006). Many young children experience high levels of pain and distress during these procedures and adequate pain management strategies are seldom used (Lisi, Campbell, Pillai Riddell, Garfield, & Greenberg, 2013). Many children also experience distress and anxiety before the procedure even begins (Blount, Sturges, & Powers, 1990). This is called anticipatory distress. Anticipatory distress has been identified as occurring as early as infancy. Newborn infants who have been exposed to several painful procedures can learn to anticipate pain and exhibit more intense pain responses (Taddio, Shah, Gilbert-MacLeod, & Katz, 2002). Anticipatory distress and fear of medical procedures have also been identified as concerns in preschool and school-aged children. One study found that 22% of 4-6 year old children experience serious distress during the preparatory phase of an immunization (Jacobson et al., 2001). Another recent study found that more than half of children under the age of 8 years have needle fear (Taddio et al., 2012). This finding is particularly concerning as anticipatory distress has been associated with several negative sequelae (Palermo & Drotar, 1996; Tsao et al., 2004; Bijttebier & Vertommen, 1998; Wright, Yelland, Heathcote, Ng, & Wright, 2009). These negative outcomes could lead to avoidance of painful medical procedures and reduced compliance with preventative medical care (Taddio et al., 2012). Despite the

[1] This is the author's version of the published manuscript:
Racine, N., Pillai Riddell, R., Khan, M., Calic, M., Taddio, A. & Tablon, P. (2016). Systematic Review: Predisposing, Precipitating, Perpetuating, and Present Factors Predicting Anticipatory Distress to Painful Medical Procedures in Children. *Journal of Pediatric Psychology, 41*(2):159-181. Doi: 10.1093/jpepsy/jsv076.

important implications of anticipatory distress to painful medical procedures for children, little empirical work has investigated the factors that lead to its development.

Several models in the developmental literature have outlined the pathways that lead to the development of maladaptive anxiety and anxiety-related problems (Rachman, 1977; Vasey & Dadds, 2001; Cicchetti & Cohen, 1995). Within the pediatric pain literature, some work has examined the pre-procedural child factors that impact a child's pain response (Young, 2005; Kleiber & McCarthy, 2006); however, these models focus on pain responses rather than anxiety and anticipatory distress. Previous models share a common emphasis on the transactional and developmental nature of anxiety or fear over time and highlight the dynamic interaction between the individual child and his/her environment. The four "Ps" of case formulation (predisposing, precipitating, perpetuating, and protective factors) also provide a useful framework for organizing the factors that may contribute to the development of anticipatory distress (Barker, 1988; Carr, 1999; Winters, Hanson, & Stoyanova, 2007). Predisposing factors are those that put a child at risk of developing a problem (in this case, high anticipatory distress). These may include genetics, life events, or temperament. Precipitating factors refer to a specific event or trigger to the onset of the current problem. Perpetuating factors are those that maintain the problem once it has become established. Finally, protective factors are strengths of the child or reduce the severity of problems and promote healthy and adaptive functioning. Another 'P' that can be relevant in case formulation are "present" factors. i.e., those that are operating during the time of the event eliciting distress. Present factors are relevant due to the emphasis on "procedure" or context in the literature. Additionally, factors that are considered protective can be collapsed within predisposing, perpetuating, and present factors.

The objective of the current review is to summarize the findings of studies that examine factors that predict anticipatory distress to painful medical procedures in children. This systematic review is a qualitative synthesis and summarizes the findings from the search in a summary figure. The goal of the summary figure (Figure 2) is to provide an overview for researchers and clinicians of the current literature as well as highlight gaps in the literature. Based on the developmental psychopathology perspective, factors in the current review were hypothesized to fall under the four Ps of case formulation: predisposing (e.g. genetics, temperament), precipitating (e.g. negative pain experiences), perpetuating (e.g. parent behavior, parent anxiety, child behavior, child cognitions), and present factors (e.g. health care professional behavior). This review also evaluated the included studies for risk of bias and identified methodological limitations of current studies. Promising directions for future research in this area are outlined.

Method

Criteria for Considering Studies for This Review

Types of Studies. Studies examining factors that are related to or predict anticipatory distress (anxiety, fear, distress) to painful medical procedures that were published in peer-reviewed journals were considered for inclusion. Although the goal of the study was to examine anticipatory distress, not pain, pain studies that measured anticipatory distress, anxiety or fear were included in the review. Given the study of fear and anxiety is a bourgeoning area in the field of pediatric pain and the goal was not to summarize treatment efficacy, nonrandomized studies were included in this review and formed the preponderance of the literature base. Non-randomized studies were included following guidelines of the Cochrane Collaboration that a systematic review should include the best available study designs with the least risk of bias

(Reeves, Deeks, Higgins, & Wells, 2011). RCTs were included when appropriate, however, the variables predicting anticipatory distress were the focus, not the treatment effect. Pharmacological (e.g. sedatives) and physical (e.g. needle type) predictors of anticipatory distress were not examined in the current review. All studies were examined for potential sources of bias.

Types of Participants. To be considered in the review, the study had to examine a painful procedure in children from birth through 18 years of age. The study also had to measure anticipatory distress (including anxiety/fear rated before or after the procedure or in some cases pain scores *prior* to the application of pain) to a painful medical procedure or operation (laboratory pain tasks were excluded from the review). Exclusion criteria for studies were: no painful medical procedure, incorrect age (i.e. not children 0 to 18), and studies where no factor was analyzed for its relationship to anticipatory distress.

Types of Measures of Anticipatory Distress. Studies that used an objective behavioral measure, observer reported (e.g. parent, nurse, physician, research assistant), or self-report measure of distress prior to a painful medical procedure or operation were included in the current review. In addition to distress prior to painful medical procedures, for the purpose of the current review, the term anticipatory distress was operationalized to be an umbrella term that also included ratings of fear or anxiety about a procedure provided after the procedure or operation as well as a retrospective report of anxiety/fear about a procedure. In circumstances where more than one measure of anticipatory distress was provided, self-report measures of anxiety, fear, and distress were prioritized. Behavioral measures and observer report measures were used when self-report was not available or was not developmentally appropriate. Additionally, measures that were most specific to anxiety and fear were used. For example, using the State Trait Anxiety

Inventory over a general distress measure. Measures of anticipatory distress most proximal to the painful medical procedure were used. For pre-operative studies, ratings in holding areas or during induction were used rather than during separation from parents as not to confound fear and distress of the medical procedure with fear and distress from separation.

Search Methods for Identification of Studies

A review protocol was not registered for this review. A librarian from a tertiary hospital with specialized training in conducting systematic reviews conducted a systematic search in MEDLINE, EMBASE, and EBM Reviews – Cochrane Central Register of Controlled Trials (CCTR) and PsycINFO to include articles indexed as of November 20, 2013. Separate search strategies and terms were developed for each of the databases. Search results were limited to publication years (1946+) and age group (children 0-18 years). Search terms related to anticipatory distress, medical procedures, pain procedures, and children were systematically paired (See online Appendix 1). A manual database search was also conducted for new articles published after 2013 to update the search in November 2014. Prior meta-analyses and reference lists from identified studies were also reviewed. Authors of studies that could not be found were contacted.

Data Collection and Analysis

Selection of Studies. Three authors (NR, RPR, AT) and the librarian from a tertiary hospital identified studies through database searching as described above, and duplicates were removed using reference management software (Endnote X7). Two review authors (NR and RPR) initially screened 1000 abstracts to pilot the initial search strategy. Five review authors (NR, RPR, PT, MC, and MK) screened titles and abstracts of studies from the final database searches for inclusion in the review based on predetermined inclusion and exclusion criteria

listed above. Figure 1 provides the PRISMA (Moher, Liberati, Tetzlaff, & Altman, 2009) chart outlining the flow of study selection.

Data Extraction and Management

Four authors conducted data extraction independently for all included studies using a data extraction form created by the lead author designed for this review, which was approved by the senior author (RPR). The lead author conducted training sessions with the review authors to explicitly outline the exclusion criteria and how to use the data extraction form. Decision-making reliability was evaluated for 20% of all studies screened. Percent agreement, calculated as the percentage of studies that were agreed upon between two authors, ranged from 0.83 to 0.95 indicating strong inter-rater agreement.

Assessment of Risk of Bias

A nuanced approach was necessary as the purpose of this review was not to evaluate treatment outcomes or to make recommendations about practice. The state of the literature in the area of anticipatory distress is such that the preponderance of research is observational, not experimental, in nature. However, assessment of risk of bias within observational studies was deemed necessary despite the lack of randomization. Risk of bias was assessed for the 77 included studies using the Cochrane Collaboration methodology for systematic reviews (Reeves et al., 2011). The majority of the studies included in the review (70 studies) were not randomized controlled trials. In the Risk of Bias tool created by the Cochrane Collaboration, the first three criteria (random sequence generation, allocation concealment, and blinding of participants) are only relevant for randomized controlled trials. As such, for observational and retrospective studies, only the last four criteria were used to make judgments: blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. This adaptation was

based on the decision not to penalize non-randomized observational studies for being evaluated against criteria for randomization. The Cochrane collaboration recently launched a risk of bias tool for non-randomized studies of interventions (Sterne, Higgins, & Reeves, 2014), however, at the time of this manuscript, trainings were only beginning to be offered and the tool was not yet widely used. Established tools to evaluate risk of bias in non-randomized studies were also considered (e.g. Downs & Black, 1998). However, given the number of studies in the review, an abbreviated tool was selected. Two authors evaluated risk of bias and consensus decisions were made where authors disagreed. All studies were classified as high, unclear, or low risk of bias. If one of the criteria was rated as "high", the overall study rating was considered to be high risk. "Unclear risk of bias" was indicated when one of the four criteria was missing, not mentioned, or did not meet the criteria for low or high risk of bias. To be evaluated as low risk of bias, all the criteria had to be rated as low.

Data Synthesis

Due to the diversity of medical procedures, outcome measures used, and participant ages included in the studies, a meta-analysis was not deemed appropriate for the current review and, rather, a narrative synthesis framework (Popay et al., 2005) was applied. Influenced by developmental psychopathology theory and by the four Ps for case conceptualization (Vasey & Dadds, 2001; Winters et al., 2007), this review categorized factors related to anticipatory distress to painful medical procedures as predisposing, precipitating, perpetuating, or present factors. Present factors were chosen (instead of protective factors) due to the emphasis on "procedure" or contextual factors in the literature. Additionally, factors that could be considered protective factors were collapsed within predisposing, perpetuating, and present factors as it made more conceptual sense based on how these factors were operationalized in the medical literature. For

the purposes of the current review, predisposing factors were operationalized as inherent variables that increase the child's risk for anticipatory distress, for example, pre-existing aspects of the child such as age, gender, or temperament as well as socio-demographic variables of the parent or environment. Precipitating factors were conceptualized as factors that lead to the onset of anticipatory distress to painful medical procedures such as a negative pain event or previous experience with pain. Perpetuating or maintaining factors (Carr, 1999) were factors that likely extend or preserve the problem such as parent behavior that maintains the child's distress both inside and outside the medical procedure. Finally, present factors were variables that occurred at the time of the procedure and could positively or negatively influence the child's anticipatory distress. It should be noted that predisposing, precipitating, perpetuating, and present factors are not mutually exclusive categories as some factors may apply to multiple categories. These factors may also interact to compound anticipatory distress. For the purposes of the review, the lead author and senior author categorized each factor for parsimony and ease of interpretation.

Results

Results of the Search

The search strategy retrieved 7088 abstracts to review against the inclusion criteria. Four individuals screened the initial 7088 abstracts against inclusion criteria. Based on these criteria, the full article was retrieved for 159 studies. Eighty-two articles for which the full text was retrieved were excluded from the review. A total of 77 full-text studies were included in the review. The review process followed PRISMA guidelines (Moher et al., 2009; Figure 1). Tables 1-4 provide detailed overviews of the included studies including age range, sample size, country of origin, procedure, design, and risk of bias rating. In summary, most included studies were observational, from North America, encompassed a broad age range, and were based on surgical

or needle-related procedures. The most common procedures included surgery or operative procedures (29), immunizations/injections (13), dental procedures (11), and venipuncture procedures (8). A total of 15,106 participants were included in the review.

In terms of the types of outcome measures, 43 measured anxiety, 15 measured fear, 13 measured distress, and 6 measured baseline pain. The majority of outcome measures were self-report (35), while the remaining outcome measures were behavioral (11), or observer reported (31).

Risk of Bias

Risk of bias was assessed for the 77 studies included in the review using the Cochrane Collaboration methodology for systematic reviews. As all but 7 studies were non-randomized control trials, 15 studies were evaluated to have high risk of bias, 16 studies had unclear risk of bias, and 46 studies had low risk of bias (See Table 1-4).

Factors Included in the Review

The list of factors that predict anticipatory distress to painful medical procedures can be found in the left-most column of Tables 1-4. Overall, there were 31 factors that were examined for their relationship to predict anticipatory distress.

Overall Findings

The overall goal of the review was to synthesize the literature on factors that predict anticipatory distress to painful medical procedures. Following data extraction, the lead and senior authors synthesized the results into the summary figure. The summary figure (see Figure 2) includes most of the information from Table 1-4 and highlights the contribution of predisposing, precipitating, perpetuating, and present factors influencing the child's anticipatory distress. Only factors with two studies or more that were similar in nature were included in Figure 2. Moreover,

in the summary figure, factors were subcategorized according to child, parent, healthcare professional, and/or contextual domains. Finally, the risk of bias and overall findings synthesis have been presented in Tables 1-4 as well as in Figure 2.

Predisposing Factors

Child. As seen in Table 1, ten variables were identified for child predisposing factors (See Table 1). Results suggest the data regarding age was inconclusive with almost half the studies showing no age effect, and the vast majority of the other studies suggesting younger children have higher anticipatory distress. The overall risk of bias for age was unclear (See Table 1). For gender, although results were varied, most studies (20/26) reported there was no effect of gender on anticipatory distress in children, while six studies found that girls experienced more anticipatory distress than boys. The overall risk of bias for gender was unclear (See Table 1). Four studies examined the effect of race on anticipatory distress, with the majority suggesting no effect. The overall risk of bias was unclear (See Table 1). Birth order was not found to have an effect on child anticipatory distress as indicated by two studies. The effect of number of siblings and sibling order was investigated by three studies and was found to have no effect. Child illness and child intelligence were both investigated by one study and were both found to positively predict child anticipatory distress.

For child psychopathology, the overall findings (6/8) supported the positive relationship between pre-existing child psychopathology and increased child anticipatory distress to painful medical procedures. The overall risk of bias rating was unclear (See Table 1). For child temperament, the overall findings (8/11 studies) support a positive relationship between difficult child temperament and increased child anticipatory distress. The overall risk of bias score for temperament was unclear (See Table 1). Finally, there were inconclusive results for child

attachment from two low risk of bias studies. One study (Horton et al., 2015) indicated that infants with avoidant infant attachment had lower anticipatory distress where as another study (Lumley, Melamed, & Abeles, 1993) found no effect.

Parent. A total of 12 studies provided evidence for parent predisposing factors that are associated with child anticipatory distress to painful medical procedures. Results are found in Table 1. Overall findings suggest that parent anxious predisposition, and pain experience or fear of pain were all associated with increased anticipatory distress. The results for parent education and coping style were found to be inconclusive.

Health Professional. No health professional factors were found under the predisposing domain.

Contextual. Two factors were identified as contextual predisposing factors: previous hospitalization of the child or sibling (5 studies) and other contextual factors (4 studies). For previous hospitalization, four of the five studies found no effect of previous hospitalization on child anticipatory distress; however, one study (Broome & Hellier, 1987) found that hospitalization of a sibling (but not of self) was associated with higher anticipatory distress. The overall risk of bias for this factor was unclear. In terms of other contextual factors, the overall findings showed that having never visited a dentist and having irregular visits to the dentist are positively associated with child anticipatory distress. Other demographic variables had mixed results. The evidence for this factor was unclear.

Precipitating Factors

Child. Two broad factors were identified as precipitating factors that contributed to the onset of anticipatory distress to painful medical procedures (See Table 2). The first factor was general and specific negative pain events (33 studies). The results showed that 17 studies found

that previous negative experiences positively predict child anticipatory distress, while 12 studies found no effect of previous painful events. Four studies indicated that history of painful procedures was in fact associated with decreased child anticipatory distress. Overall the evidence points towards a positive relationship between previous pain events and child anticipatory distress based on unclear risk of bias.

The second precipitating child factor that was identified was previous child/adolescent behavior (5 studies). Overall results indicate that previous pain behavior positively predicts child anticipatory distress. The risk of bias was unclear.

Parent. No parent factors were found under the precipitating domain.

Health professional. No health professional factors were found under the precipitating domain.

Contextual. No contextual factors were found under the precipitating domain.

Perpetuating Factors

Child. As seen in Table 3, four factors were identified as child perpetuating factors: child knowledge (7 studies), child coping style (4 studies), child cognitions (3 studies) and other child behaviors (2 studies). For child knowledge, the results were inconclusive. This was based on unclear evidence. The evidence for child coping style was inconclusive based on unclear risk of bias. For child cognitions (3 studies), overall results suggest that child cognitions including high threat appraisal, lower perceived control, and high aversion to the procedure were all associated with higher child anticipatory distress, based on studies with unclear risk of bias. Finally, the evidence for other child behaviors (2 studies) was inconclusive as studies highlighted different child behaviors associated with increased or decreased anticipatory distress.

Parent. Four factors were identified as parent perpetuating factors: parent behavior (7 studies), parent situational distress (19 studies), parent anticipation of child distress (5 studies), and parent self-efficacy/attitudes (two studies). See Table 3. Overall findings suggest that parent behavior, parent situational distress, and parent anticipation of child distress were associated with increased anticipatory distress. See Table 3.

Health professional. No health professional factors were found under the perpetuating domain.

Contextual. No contextual factors were found under the perpetuating domain.

Present Factors

Child. As seen in Table 4, one factor was identified for child present factors: idiosyncratic needs. One study (Ameringer, Elswick Jr, Shockey, & Dillon, 2013) showed that fatigue and nausea were positively associated with child anticipatory distress prior to chemotherapy with a low risk of bias.

Parent. One parent present factor was identified: parental presence during a painful medical procedure. The overall results for this factor are inconclusive. See Table 4. The risk of bias for this factor was unclear.

Health professional. One factor was identified as a health professional present factor: health professional behavior (3 studies). Overall, evidence suggests that distress promoting behavior by health care professionals is associated with higher child anticipatory distress. The overall risk of bias was unclear.

Contextual. One broad factor, environmental factors, was identified for contextual present factors. Fifteen studies investigated the effects of various contextual factors on child

anticipatory distress during the painful medical procedure (e.g. type of admission, severity of procedure, etc.). Results vary based on the study.

Discussion

The purpose of the current review was to summarize the findings of studies that examine the factors that predict anticipatory distress to painful medical procedures in children. The overarching goal of this review was to qualitatively synthesize the literature on the factors that predict anticipatory distress to painful medical procedures into a summary figure using predisposing, precipitating, perpetuating, and present factors as a framework. The following paragraphs will discuss key findings and patterns from the summary figure (Figure 2) of the review in the context of methodological differences and risk of bias within studies. Only factors with two or more included studies of a similar nature that can be found in the summary figure will be discussed. Finally, clinical implications, areas for future research based on the summary figure and limitations of the review will be highlighted.

Predisposing Factors

Child. There were some interesting patterns among the child predisposing factors. First, there is clear evidence that child psychopathology and difficult, fearful, or shy child temperament are individual child factors that increase the risk of child anticipatory distress. This finding is in line with developmental literature suggesting that children who have internalizing or externalizing problems have more difficulty regulating their affect (Bradley, 2003). Pre-existing psychopathology or difficult temperament may be important factors to screen for prior to a medical procedure or surgery to have an understanding of how a child might respond or cope with the procedure. The risk of bias subsuming this factor was generally unclear because there were 6 low and 2 high rated studies included.

Second, gender does not appear to play an important role in predicting anticipatory distress. Although some studies did find that girls experience higher anticipatory distress to medical procedures, the majority of studies did not find an effect. The studies that found an effect for girls had participants closer to pubertal age, which may have played a role.

Some predisposing child factors yielded inconclusive results. Despite the large body of research (43 studies) that examined the effect of age on child anticipatory distress, the research on this factor does not seem to converge. Almost half the studies showed no effect of age while the other half suggests younger children experience higher anticipatory distress. The type of medical procedure did not seem to systematically differ between the two groups. Although the studies that did not find an effect of age were more likely to have a low risk of bias, it is difficult to make conclusions based on this. Methodological factors may also have contributed to differences in results as the majority of studies did not examine a discrete age range but rather averaged over large age ranges of up to 15 years. Examining a restricted age range may also have contributed to the lack of an effect. At this point, the results on age remain largely inconclusive, although the results from this review point towards younger children experiencing more anticipatory distress than older children. This is in line with the literature that indicates that younger children are more likely to be fearful and distressed and that this fear may increase and decrease over the course of childhood (American Psychiatric Association, 2013). It may also be the case that the relationship between age and anticipatory distress is non-linear or co-varies with other factors. Future longitudinal or cross-sectional studies could provide some insight into whether age is an important factor in predicting child anticipatory distress.

Parent. Two parent predisposing factors that emerged as predicting increased child anticipatory distress are parent anxious predisposition and previous parent pain experience. The

fact that a parent's own anxiety and fear/experiences with pain are related to the child's anticipatory distress directly supports the transmission of anxiety from parent to child. Previous work has hypothesized the mechanisms by which this occurs, such as through modeling and information transmission (Rachman, 1977; Vasey & Ollendick, 2000). It may be that parents are discussing or demonstrating their fear of pain as it relates to painful medical procedures, impacting the anticipatory distress of their children. Future experimental research could examine how transmission of fear of painful medical procedures occur in order to develop targets for intervention. Risk of bias was variable across factors ranging the full gamut from low to unclear to high. Of note, the anxious predisposition has low risk of bias; thus, there is increased confidence in this finding.

Inconclusive results were found for the impact of parent education level on child anticipatory distress. The difference in finding may be due to the differences in education levels included in the studies. More research is needed in this area.

Context. Two contextual factors emerged under the predisposing domain. First, previous hospitalization was overall not found to have an effect on child anticipatory distress (only previous hospitalization of siblings did). It may be that hospitalization itself is not sufficient to lead to the development of fear, but rather that negative experiences or vicarious fear are much more salient. The risk of bias for this factor was unclear as there was a mix of high and low rated studies. Few predisposing contextual factors have been examined and more research is needed.

Precipitating Factors

Child. Two broad factors were identified as factors that contributed to the onset of anticipatory distress to painful medical procedures. The first factor is general and specific negative pain events. Although the overall result is that previous negative pain events predict

anticipatory distress, this was not uniformly the case across studies. Some reasons for this include risk of bias and sample size. The studies that found an effect of previous negative procedures largely had low risk of bias and large sample sizes. The studies that found a negative relationship between previous pain events and anticipatory distress, were methodologically different in that they all involved short routine medical procedures such as insulin injections (Hanas et al., 2002; Howe, Ratcliffe, Tuttle, Dougherty, & Lipman, 2011) and immunotherapy injection (deVos et al., 2012). These types of procedures provide repeated exposure to the stimuli whereby eventually extinction of the fear occurs. Typically developing children do not usually have daily exposure to needles or surgery in order to facilitate extinction, which may explain the difference in finding for the studies. Furthermore, previous work in child anxiety has demonstrated that direct conditioning is only one pathway to the development of anxiety problems in children (Vasey & Dadds, 2001). According to retrospective reports of adults with phobia, modeling and information transmission were the most common modes of fear acquisition with a minority reporting direct conditioning experiences (Vasey & Ollendick, 2000). This highlights that, although direct conditioning of a general or specific negative pain event may precipitate anticipatory distress for some children, multiple factors are at play, including the frequency and severity of the painful medical procedure.

The second factor that was identified as a child precipitating factor is previous child/adolescent behavior (5 studies). There is evidence that a child or adolescent's previous behavior during a painful medical procedure will predict anticipatory distress at a future medical procedure. The risk of bias was rated as unclear due to one study with an unclear rating.

Perpetuating Factors

Child. Four child factors were identified as maintaining child anticipatory distress. First, child maladaptive cognitions were found to positively predict distress prior to a procedure with overall low risk of bias studies. Overall, children who perceived less control, expected an aversive experience, and appraised procedures as more threatening were more inclined to be distressed prior to those procedures. Given that child threat appraisal and perceived control predict child anticipatory distress, this highlights the importance of teaching children cognitive and behavioral coping strategies to manage their anticipatory distress. The overall risk of bias is unclear, reducing our confidence in these findings.

In terms of having more knowledge about the procedure, the overall results were inconclusive, however, 3 studies did show a decrease in anticipatory distress. The method, type of information, and developmental level of the knowledge provided may be important variables in whether the knowledge presented works. The overall risk of bias was unclear for this factor, reducing our confidence in the findings. There was inconclusive evidence for child coping style with unclear risk of bias, reducing confidence in these findings. There are specific child behaviors such as using non-procedural talk, humor and talking to a parent that were related to child coping before a procedure while verbal resistance was found to be positively associated to child preoperative anxiety. The child behavior factor had an overall unclear risk of bias, reducing our confidence in these findings. More research on the child behaviors that are associated with coping before a painful medical procedure will help inform targets for intervention.

Parent. When examining the parent factors that perpetuate a child's anticipatory distress to painful medical procedures, an important pattern emerges. Across three factors examined, there was evidence that parent factors play a key role in maintaining the distress of children

during painful medical procedures. Parent behavior during the procedure, parent situational distress/state anxiety, and parent anticipation of child distress had overall results predictive of child anticipatory distress. Although the findings of the studies were not completely uniform, the majority of studies highlighted the role that parents play in continuing child anticipatory distress. It has been argued that, particularly for infants and young children, the caregiver is the most important context in the pediatric pain setting (Pillai Riddell & Racine, 2009). Parental responding (modeling, overprotection, reinforcement, and encouragement) plays a key role in the development of anxiety (Vasey & Dadds, 2001). These results highlight the importance of engaging parents in interventions to help reduce child anticipatory distress. The risk of bias for the parent perpetuating factors was unclear, indicating reduced confidence in these findings.

Present Factors

Parent. A trend towards family-centered care has led to the increase of parental presence within pediatric healthcare settings. While parent presence during child hospital stays have been associated with positive outcomes (Wright, Stewart, & Finley, 2010), parent presence during a painful medical procedure in the current review had inconclusive results. However, two studies pointed to mechanisms that may underlie the effect of parental presence. Kain and colleagues (2006) found that the presence of a calm parent reduces preoperative anxiety while the presence of an overly anxious parent does not. Given the transactional and individual factors that predict anticipatory distress, clinical recommendations for parental presence during a procedure should be based on characteristics of the parent and their ability to provide calm support rather than the blanket assumption that all parents should consistently be present or not present. More research should investigate the conditions under which parental presence is beneficial in reducing child anticipatory distress.

Health professional. Our synthesis demonstrates that health care professional behavior does play an important role in predicting child anticipatory distress. Given the crucial role that healthcare professionals can play in the experience of children and families during painful medical procedures (Mahoney, Ayers, & Seddon, 2010), researchers should continue to examine distress reducing behaviors such as distraction that could be taught to health care professionals, as well as parents, as an intervention to reduce procedural distress prior to a painful medical procedure.

Contextual. Fifteen studies investigated the effects of various contextual factors on child anticipatory distress during the painful medical procedure. It is difficult to synthesize this research due to the varied contextual factors, however, some environmental factors (e.g. induction location and sensory stimulation) do seem to impact anticipatory distress. More research is needed to determine which contextual factors should be addressed in clinical practice.

Author's Conclusions and Clinical Implications

As outlined in developmental psychopathology theory (Cicchetti & Cohen, 1995), the development of anticipatory distress occurs through a dynamic interplay of factors, including individual child factors, parent factors, health professional factors, and their environment. There is no unique pathway that leads to the development of anticipatory distress but rather the interaction of predisposing, precipitating, perpetuating, and present factors over time leads to the onset and maintenance of distress.

In the current review, we examined 31 factors that predict anticipatory distress. Children with pre-existing anxiety and a difficult temperament were more likely to have anticipatory distress. Parents and children should examine patterns of past child behavior during painful procedures in order to better support and prepare children with these risk factors. Parent anxiety

and parent's previous experiences with pain are also important predictors of anticipatory distress. This suggests that parents need to be aware of their own subjective experience of medical procedures and how to manage their own anxiety in medical contexts. Past pain events and previous child behavior are indicators of future anticipatory distress. Using adequate pain management is of utmost importance in reducing the likelihood of conditioning fear and anxiety. Child and parent emotional and cognitive factors serve to maintain or fuel anticipatory distress. These areas will be important targets for interventions. Finally, health professionals should be wary of engaging in distress promoting behavior such as verbal reassurance and criticism and are encouraged to use coping promoting behavior such as talking about things other than the procedure and engaging in distraction.

Limitations and Implications for Research

The current review highlights important gaps where additional research is needed. As seen in Figure 2, factors that are depicted with a question mark have inconclusive evidence. All of these areas would benefit from additional research to investigate their impact on anticipatory distress. Additionally, there is a need for longitudinal and more complex methodologies to investigate the transactional nature of these factors. Future studies should also examine the interaction of multiple factors (i.e. temperament, previous pain experience, parent behavior) in order to determine the relative contribution of these factors. Furthermore, many of the studies included in the review were found to have high risk of bias often through biased outcome assessors or poor quality measures used. Many of the factors (e.g. child level of anxiety, age, gender, parent anxiety, previous pain experiences) cannot be randomized to participants to improve the quality of the methodology to test these factors. However, the knowledge of these proposed factors should be incorporated in randomized trials that test the efficacy of treatments

of anticipatory distress. Having large age ranges in studies and not controlling for factors such as psychopathology (parent/child), previous pain experiences (parent/child) and parent soothing behaviors/coping strategies will continue to limit the value of RCTs because they do not attempt to accommodate the inherent variability of pain responses and the causes for the variability (Pillai Riddell et al., 2013).

Funding

This research was funded by awards to Dr. Pillai Riddell from the Canadian Institutes of Health Research, the Ontario Ministry of Research and Innovation, the Canadian Foundation for Innovation, and the York Research Chairs Program. Ms. Racine received awards from the Canadian Institutes of Health Research, the Government of Ontario, the Lillian and Don Wright Foundation, and the Canadian Pain Society. Ms. Racine is also a trainee member of Pain In Child Health (PICH), a strategic research training initiative of the Canadian Institutes of Health Research.

Acknowledgements

The authors thank Noam Bin-Noon for her contribution to this review in conducting some of the initial article screening and Elizabeth Uleryk for performing the data searches and Zhaodi Culbreath for assistance with figures.

Conflicts of interest: None declared.

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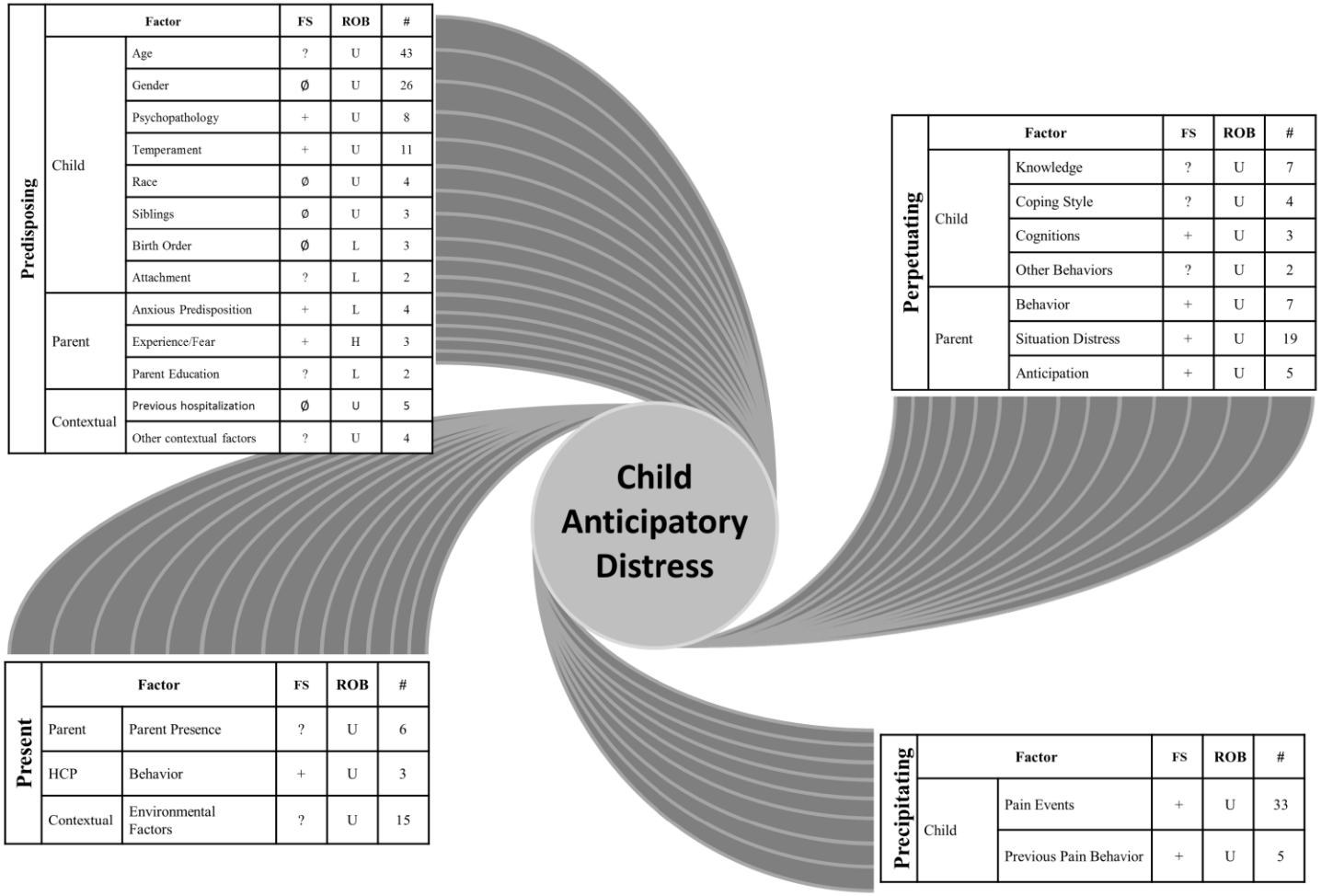

Figure 2. Summary figure of results.

Note. FS: Findings synthesis, ROB; risk of bias, + Factor has a positive relationship with anticipatory distress; - Factor has a negative relationship with anticipatory distress; ∅ No effect or significant relationship; ? inconclusive results; U unclear risk of bias; L low risk of bias; H high risk of bias; # indicates number of studies.

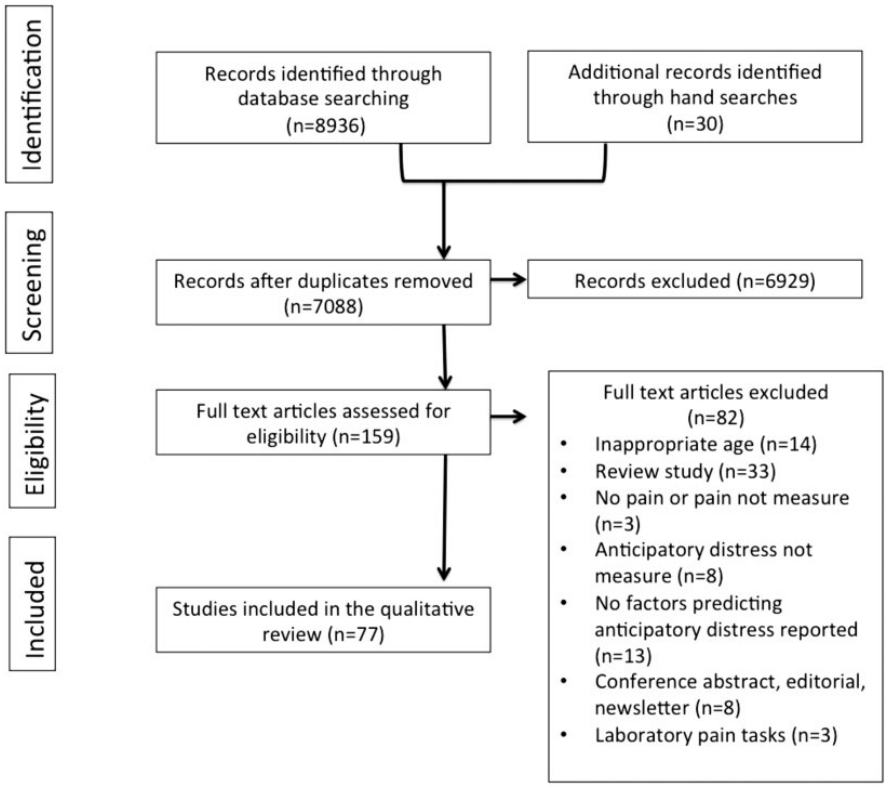

Figure 1. Included study flow chart from PRISMA guidelines.

Table 1
Predisposing Factors of Anticipatory Anxiety

Study	Age (years)	N	Country	Procedure	Design	Risk of bias	Result	Summary of bias	Results summary
Child predisposing factors									
1. Age (43 studies; N=9890)									
Bevan1990	2-10	134	Canada	Pre-op	E	Unclear	-	Unclear	Inconclusive
Broome 1987	5-11	84	USA	Medical	R	Low	-	(25 low, 8	
Caldwell-Andrews 2005	2-12	289	USA	Pre-op	O	Unclear	-	high, 10 unclear)	
Carpenter 1992	4-18	73	USA	Venipuncture	O	Low	-		
Chen 2000	3-18	55	USA	LP	RCT	High	-		
Chorney 2009	2-10	293	USA	Pre-op	O	Low	-		
Chorney 2009b	2-10	293	USA	Pre-op	O	Unclear	-		
Dahlquist 1994	2-7 8-17	63	USA	BMA	O	Low	-		
Dahlquist 2001	5-15	45	USA	Intramuscular injection and LP	O	Low	-		
Dahlquist 2005	2.4-5.1	29	USA	Immunization	RCT	High	-		
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	-		
Fukuchi 2005	2-12	78	Brazil	Pre-op	O	Unclear	-		
Hatava 2000	2-10	160	Sweden	Pre-op	E	Unclear	-		
Holm-Knudgsen	0-14	2122	Australia	Pre-op	O	Unclear	-		

1998							
Hosey 2006	2-14	407	UK	Dental	O	Low	-
Howe 2011	4.9-16.2	23	USA	Injection, Finger sticks	O	Unclear	-
Kain 2000	3-10	60	USA	Pre-op	O	High	-
Lilley 1997	0.17-1.5	75	Canada	Immunization	O	Low	-
Mahoney 2010	7-16	50	UK	Venipuncture	O	Low	-
Melamed 1993	4-12	46	USA	Pre-op	O	Low	-
Olak 2013	8-10	344	Estonia	Dental	R	Low	-
Taddio 2012	6-17	1024	Canada	Immunization	R	High	-
Tyc 2002	2-7	80	USA	Radiation Therapy	O	Low	-
Kain 1996	2-10	163	USA	Pre-op	O	Low	+
Tickle 2009	5-9	799	UK	Dental	O	High	+
Al-Jundi 2010	2-12	118	Jordan	Dental	O	High	ø
Bijtterbier 1998	2.75-12.75	47	Belgium	Venipuncture	O	High	ø
Carr 1998	3-12	62	USA	Allergy skin testing	O	Low	ø
Claar 2002b	8-18	100	USA	EGD	O	Low	ø
deVos 2012	M = 3.1	18	USA	Immunotherapy Injections	O	High	ø
Field 1988	4-10	56	USA	Pre-op	O	Low	ø
Fox 2006	5-17	38	UK	Dental	RCT	Low	ø
Goodenough 1998	3-17	117	Australia	Venipuncture	O	Unclear	ø
Jacobson 2001	1 - 6	150	USA	Immunization	O	Low	ø

Lumley 1993	4-10	50	USA	Pre-op	O	Low	ø		
Ortiz 2014	8-16	437	Mexico	Dental	O	Unclear	ø		
McMurtry 2011	5-10	100	Canada	Venipuncture	O	Low	ø		
Mekarski 1997	2.5-13	324	Canada	Dental	O	Low	ø		
Messeri 2004	2-14	39	Italy	Pre-op	O	Low	ø		
Siaw 1986	3.5-12.8	30	USA	Pre-op	O	Unclear	ø		
Thompson 1994	8-12	43	USA	Pre-op	O	Low	ø		
Wright 2010	3-6	61	Canada	Pre-op	E	Low	ø		
Wright 2013	3-6	61	Canada	Pre-op	O	Low	ø		
2. Gender (26 studies; N=6483)									
Al-Jundi 2010	2-12	118	Jordan	Dental	O	High	ø	Unclear (18 low, 6 high, 2 unclear)	No effect
Bearden 2012	3-5	90	USA	Immunization	O	Low	ø		
Bijtterbier 1998	2.75-12.75	47	Belgium	Venipuncture	O	High	ø		
Carr 1998	3-12	62	USA	Allergy test	O	Low	ø		
Colares 2013	5-12	970	Brazil	Dental	R	Low	ø		
Dahlquist 2001	5-15	45	USA	Intramuscular injection and LP	O	Low	ø		
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	ø		
Fortier 2011	11-18	59	USA	Pre-op	O	Low	ø		
Fox 2006	5-17	38	UK	Dental	RCT	Low	ø		
Gazal 2007	2-12	201	UK	Dental	O	Low	ø		
Goodenough 1998	3-17	117	Australia	Venipuncture	O	Unclear	ø		
Hanas 2002	1-15	41	Sweden	Insulin injection	RCT	High	ø		

Horton 2015	1-1.5	130	Canada	Immunization	O	Low	Ø		
Jacobson 2001	1-6	150	USA	Immunization	O	Low	Ø		
Kain 2000	3-10	60	USA	Pre-op	O	High	Ø		
Lumley 1993	4-10	50	USA	Pre-op	O	Low	Ø		
Ortiz 2014	8-16	437	Mexico	Dental	O	Unclear	Ø		
Thompson 1994	8-12	43	USA	Pre-op	O	Low	Ø		
Wright 2010	3-6	61	Canada	Pre-op	E	Low	Ø		
Wright 2013	3-6	61	Canada	Pre-op	O	Low	Ø		
Broome 1987	5-11	84	USA	Medical	O	Low	+Girls		
Logan 2004	12-18	102	USA	Pre-op	O	Low	+Girls		
McMurtry 2011	5-10	100	Canada	Venipuncture	O	Low	+Girls		
Olak 2013	8-10	344	Estonia	Dental	R	Low	+Girls		
Taddio 2012	6-17	1024	Canada	Immunization	R	High	+Girls		
Tickle 2009	5-9	799	UK	Dental	O	High	+Girls		
3. Child psychopathology (8 studies; N=2053)									
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	+	Unclear (6 low, 2 high)	Positively predicts anticipatory distress.
Ericsson 2006	5-15	92	Sweden	Pre-op	RCT	High	+		
Fortier 2011	11-18	59	USA	Pre-op	O	Low	+		
Hosey 2006	2-14	407	UK	Dental	O	Low	+		
Kain 2000	3-10	60	USA	Pre-op	O	High	+		
Wright 2013	3-6	61	Canada	Pre-op	O	Low	+		
Kiley 1997	School age	74	USA	Immunization	E	Low	Ø		
Lumley 1993	4-10	50	USA	Pre-op	O	Low	Ø		
4. Temperament (11 studies; N=2235)									
Arnrup 2003	4-12	86	Sweden	Dental	E	High	+	Unclear (7 low, 3 high,	Positively predicts
Chen 2000	3-18	55	USA	LP	RCT	High	+		

Cropper 2011	4-7	84	UK	GA (Cochlear Implant)	O	Low	+	1 unclear) .	anticipatory distress
Fortier 2011	11-18	59	USA	Pre-op	O	Low	+		
Jacobson 2001	1 -6	150	USA	Immunization	O	Low	+		
Kain 1996	2-10	163	USA	Pre-op	O	Low	+		
Kain 2000	3-10	60	USA	Pre-op	O	High	+		
Lee 1996	3-7	137	USA	Venipuncture	O	Unclear	+		
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	Ø		
Horton 2015	1-1.5	130	Canada	Immunization	O	Low	Ø		
Wright 2013	3-6	61	Canada	Pre-op	O	Low	Ø		
5. Race (4 studies; N=296)									
Broome 1987	3-15	140	USA	Medical	R	Low	Ø	Unclear (3 low, 1 high)	No effect
Kain 2000	3-10	60	USA	Pre-op	O	High	Ø		
Lumley 1993	4-10	50	USA	Pre-op	O	Low	Ø		
Melamed 1993	4-12	46	USA	Pre-op	O	Low	+		
6. Birth order (3 studies; N=1352)									
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	Ø	Low (3 low)	No effect
Fortier 2011	11-18	59	USA	Pre-op	O	Low	Ø		
Thompson 1994	8-12	43	USA	Pre-op	O	Low	Ø		
7. Number of Siblings/Sibling order (3 studies; N=1369)									
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	Ø	Unclear (2 low, 1 high)	No effect
Fortier 2011	11-18	59	USA	Pre-op	O	Low	Ø		
Kain 2000	3-10	60	USA	Pre-op	O	High	Ø		
8. Child Illness (1 study; N=80)									
Tyc 2002	2-7	80	USA	Radiation Therapy	O	Low	+	Low	CNS disease positively predicts.
9. Attachment (2 studies; N=180)									
Horton 2015	1-1.5	130	Canada	Immunization	O	Low	-	Low	Inconclusive

Lumley 1993	4-10	50	USA	Pre-op	O	Low	Ø		
10. Intelligence (1 study; N=60)									
Kain 2000	3-10	60	USA	Pre-op	O	High	+	High	+
								.	
Parent predisposing factors									
1. Anxious predisposition (4 studies; N=1532)									
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	+	Low	+
Kain 1996	2-10	163	USA	Pre-op	O	Low	+		.
Messeri 2004	2-14	39	Italy	Pre-op	O	Low	+		
Tyc 2002	2-7	80	USA	Radiation Therapy	O	Low	Ø		
2. Beliefs about Coping and Coping style (2 studies; N=349)									
Caldwell-Andrews 2005	2-12	289	USA	Pre-op	O	Unclear	-	Unclear	Inconclusive.
Kain 2000	3-10	60	USA	Pre-op	O	High	+		
3. Pain experience and fear of pain (3 studies; N=1185)									
Ellerton 1994	3-15	75	Canada	Pre-op	R	Unclear	+	High	+
Arnup 2003	4-12	86	Sweden	Dental	E	High	Ø	(1 unclear,	
Taddio 2012	6-17	1024	Canada	Immunization	R	High	+	2 high)	
4. Parental Education (2 studies; N=1029)									
Colares 2013	5-12	970	Brazil	Dental	R	Low	+	Low (2 low)	Inconclusive
Fortier 2011	11-18	59	USA	Pre-op	O	Low	Ø		
5. Parent Gender (1 study; N=437)									

Ortiz 2014	8-16	437	Mexico	Dental	O	Unclear	+	Unclear	Mothers+
Contextual predisposing factors									
1. Previous hospitalization of child or sibling (5 studies; N=1451)									
Broome 1987	5-11	84	USA	Medical	R	Low	Ø	Unclear (4 low, 1 high)	No effect of previous hospitalization
Field 1988	4-10	56	USA	Pre-op	O	Low	Ø		
deVos 2012	M = 3.1	18	USA	Immunotherapy Injections	O	High	Ø		
Thompson 1994	8-12	43	USA	Pre-op	O	Low	Ø		
Broome 1987	5-11	84	USA	Medical	R	Low	+(sib)		
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	+		
2. Other Contextual factors (4 studies; N= 3079)									
Colares 2013	5-12	970	Brazil	Dental	R	Low	+ (no visits)	Unclear (2 low, 2 high)	No/irregular dental visits positively predicted.
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	Ø (SES)		
Kain 2000	3-10	60	USA	Pre-op	O	High	Ø (demographics)		
Tickle 2009	5-9	799	UK	Dental	O	High	+ (visits)		

Note. + Factor has a positive relationship with anticipatory distress; - Factor has a negative relationship with anticipatory distress; Ø No effect or significant relationship; O-Observational study; E-Experimental study; R-retrospective study; RCT- randomized control trial; Pre-op- pre-operative; LP-lumbar puncture; BMA- bone marrow aspiration; CNS- central nervous system.

Table 2

Precipitating Factors of Anticipatory Anxiety

Study	Age (Years)	N	Country	Procedure	Design	Risk of bias	Result	Summary of bias	Result Summ-ary
Child precipitating factors									
1. General and specific negative pain events (33 studies; N=5145)									
Al-Jundi 2010	2-12	118	Jordan	Dental	O	High	+	Unclear	+.
Bijtterbier 1998	2.75-12.75	47	Belgium	Venipuncture	O	High	+	(20 low, 7 high,	
Caes 2014	0.6-15	28	Canada	BMA or LP	O	Unclear	+	6	
Carrilo-Diaz 2013	8-18	179	Spain	Dental	R	Unclear	+	unclear)	
Colares 2013	5-12	970	Brazil	Dental	R	Low	+		
Cropper 2011	4-7	84	UK	Pre-op	O	Low	+		
Ellerton 1994	3-15	75	Canada	Pre-op	R	Unclear	+		
Hatava 2000	2-10	160	Sweden	Pre-op	E	Unclear	+		
Jacobson 2001	1 - 6	150	USA	Immunization	O	Low	+		
Kain 1996	2-10	163	USA	Pre-op	O	Low	+		
Lee 1996	3-7	137	USA	Venipuncture	O	Unclear	+		
Lumley 1993	4-10	50	USA	Pre-op	O	Low	+ (quality)		
Noel 2010	5-10	48	Canada	Venipuncture	O	Low	+		
Olak 2013	8-10	344	Estonia	Dental	R	Low	+		
Pillai Riddell 2011	0-1	731	Canada	Immunization	O	Low	+		
Taddio 2002	Newborns (>1 month)	66	Canada	Venipuncture, Vitamin K injections	O	Low	+		
Tickle 2009	5-9	799	UK	Dental	O	High	+		
Arnrup 2003	4-12	86	Sweden	Dental	E	High	Ø		

Broome 1994	3-15	14	USA	LP	O	Low	Ø		
Carr 1998	3-12	62	USA	Allergy testing	O	Low	Ø		
Chorney 2009	2-10	293	USA	Pre-op	O	Low	Ø		
Ericcson 2006	5-15	92	Sweden	Pre-op	RCT	High	Ø		
Dahlquist 2001	5-15	45	USA	Intramuscular injection and LP	O	Low	Ø		
Fortier 2011	11-18	59	USA	Pre-op	O	Low	Ø		
Goubet 2001	0-0.04	12	USA	Heel-lance	O	Low	Ø		
Owen 1984	Newborns (>1 month)	20	USA	Heel-lance	O	Low	Ø		
McMurtry 2011	5-10	100	Canada	Venipuncture	O	Low	Ø		
Wright 2010	3-6	61	Canada	Pre-op	E	Low	Ø		
Wright 2013	3-6	61	Canada	Pre-op	E	Low	Ø		
Mahoney 2010	7-16	50	UK	Venipuncture	O	Low	-		
deVos 2012	*M* = 3.1	18	USA	Immunotherapy Injections	O	High	-		
Howe 2011	4.9-16.2	23	USA	Insulin injection and Finger sticks	O	Unclear	-		
Hanas 2002	1-15	41	Sweden	Insulin injection	RCT	High	-		
2. Previous pain behavior (5 studies; N=3681)									
Holm-Knudsen 1998	0-14	2122	Australia	Pre-op	O	Unclear	+	Unclear (4 low, 1 unclear)	+.
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	+		
Jacobson 2001	1 - 6	150	USA	Immunization	O	Low	+		
McMurtry 2011	5-10	100	Canada	Venipuncture	O	Low	+		
Fortier 2011	11-18	59	USA	Pre-op	O	Low	Ø		

Note. + Factor has a positive relationship with anticipatory distress; - Factor has a negative relationship with anticipatory distress; Ø No effect or significant relationship; O-Observational study; E-Experimental study; R-retrospective study; RCT- randomized control trial; Pre-op- pre-operative; LP-lumbar puncture; BMA- bone marrow aspiration.

Table 3

Perpetuating Factors of Anticipatory Anxiety

Study	Age (years)	N	Country	Procedure	Design	Risk of Bias	Result	Summary of Bias	Results Summary
Child Perpetuating Factors									
1. Child knowledge (7 studies; N=1850)									
Claar 2002	8-17	100	USA	EGD	O	Low	∅	Unclear (5 low, 2 unclear)	Inconclusive
Crandall 2008	7-13	60	USA	Pre-op	E	Low	∅		
Jacobson 2001	1 - 6	150	USA	Immunization	O	Low	∅		
Claar 2002b	8-18	100	USA	EGD	O	Low	∅		
Davidson 2005	3-12	1250	Australia	Pre-op	O	Low	-		
Hatava 2000	2-10	160	Sweden	Pre-op	E	Unclear	-		
Siaw 1986	3.5-12.8	30	USA	Pre-op	O	Unclear	-		
2. Child coping style (4 studies; N=174)									
Bijtterbier 1998	2.75-12.75	47	Belgium	Venipuncture	O	High	+	Unclear (1 high, 3 low)	Inconclusive
Field 1988	4-10	56	USA	Pre-op	O	Low	∅		
Smith 1989	6-18	28	USA	BMA and LP	O	Low	∅		
Thompson 1994	8-12	43	USA	Pre-op	O	Low	-		
3. Other child behaviours (2 studies; N=368)									
Chorney 2009	2-10	293	USA	Pre-op	O	Low	+	Unclear (1 low, 1 unclear)	More research needed.
Kain 1998	2-12	75	USA	Pre-op	RCT	Unclear	-		
4. Child cognitions (3 studies; N=352)									
Carillo-Diaz 2013	8-18	179	Spain	Dental	R	Unclear	+ (expectancy)	Unclear (2 low, 1 unclear)	Neg. child cognitions pos. predict child ant.
Claar 2002b	8-18	100	USA	EGD	O	Low	+		

Carpenter1992	4-18	73	USA	Venipuncture	O	Low	_		distress.
Carillo-Diaz 2013	8-18	179	Spain	Dental	R	Unclear	+ (appraisal)		
Parent Perpetuating Factors									
1. Parent behaviour (7 studies; N=1962)									
Blount 1990	5-13	22	USA	BMA or LP	O	Unclear	+	Unclear (5 low, 2 unclear)	Parent behaviour associated w/ ant. distress. Direction dependent on type behavior.
Chorney 2009b	2-10	293	USA	Pre-op	O	Unclear	+, - (distraction)		
Dahlquist 1994	2-7, 8-17	63	USA	BMA	O	Low	+		
Dahlquist 2001	5-15	45	USA	Intramuscular injection and LP	O	Low	+		
Lisi 2013	0-1	760	Canada	Immunization	O	Low	+		
Noel 2010	5-10	48	Canada	Venipuncture	O	Low	+		
Pillai Riddell 2011	0-1	731	Canada	Immunization	O	Low	∅		
2. Parent situational distress (19 studies; N=4998)									
Arnrup 2003	4-12	86	Sweden	Dental	E	High	+	Unclear (7 high, 9 low, 3 unclear)	Positively predicts anticipatory distress.
Bearden 2012	3-5	90	USA	Immunization	O	Low	+		
Bevan 1990	2-10	134	Canada	Pre-op	E	Unclear	+		
Caes 2014	0.6-15	28	Canada	BMA or LP	O	Unclear	+		
Colares 2013	5-12	970	Brazil	Dental	R	Low	+		
Dahlquist 1994	2-7, 8-17	63	USA	BMA	O	Low	+		
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	+		
Gazal 2007	2-12	201	UK	Dental	O	Low	+		
Hatava 2000	2-10	160	Sweden	Pre-op	E	Unclear	+		
Kain 2000	3-10	60	USA	Pre-op	O	High	+		
LaMontagne	8-17	90	USA	Pre-op	O	High	+		

1996									
Messeri 2004	2-14	39	Italy	Pre-op	O	Low	+		
Olak 2013	8-10	344	Estonia	Dental	R	Low	+		
Tickle 2009	5-9	799	UK	Dental	O	High	+		
Tourigny 1992	2-10	50	Canada	Pre-op	O	High	+		
Al-Jundi 2010	2-12	118	Jordan	Dental	O	High	∅		
Dahlquist	2.4-5.1	29	USA	Immunization	RCT	High	∅		
2005	2-14	407	UK	Dental	O	Low	∅		
Hosey 2006									
Tyc 2002	2-7	80	USA	Radiation Therapy	O	Low	∅		
3. Parent anticipation of child distress (5 studies; N=742)									
Jacobson 2001	1 - 6	150	USA	Immunization	O	Low	+	Unclear (1 unclear, 4 low)	Positively predicts anticipatory distress.
Ortiz 2014	8-16	437	Mexico	Dental	O	Unclear	+		
Lumley 1993	4-10	50	USA	Pre-op	O	Low	+		
Tyc 2002	2-7	80	USA	Radiation Therapy	O	Low	+		
Srivastava 2001	0- 6.5	25	Australia	Micturating cystourethrogram	O	Low	∅		
4. Parent self-efficacy/Attitude toward procedure (2 studies; N=236)									
Arnrup 2003	4-12	86	Sweden	Dental	E	High	∅	Unclear	More research is needed.
Jacobson 2001	1 - 6	150	USA	Immunization	O	Low	∅		

Note. + Factor has a positive relationship with anticipatory distress; - Factor has a negative relationship with anticipatory distress; ∅ No effect or significant relationship; O-Observational study; E-Experimental study; R-retrospective study; RCT- randomized control trial; Pre-op- pre-operative; LP-lumbar puncture; BMA- bone marrow aspiration; EGD- Esophagogastroduodenoscopy.

Table 4

Present Factors of Anticipatory Anxiety

Study	Age (years)	N	Country	Procedure	Design	Risk of Bias	Result	Summary of Bias	Results Summary
Child Present Factors									
1. Idiosyncratic needs (1 study; N=9)									
Ameringer 2013	13-18	9	USA	Chemotherapy	O	Low	+	Low	More research is needed.
Parent Present Factors									
1. Parent presence (6 studies; N=2159)									
Al-Jundi 2010	2-12	118	Jordan	Dental	O	High	Ø	Unclear (3 low, 2 high, 1 unclear)	Inconclusive
Bevan 1990	2-10	134	Canada	Pre-op	E	Unclear	Ø		
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	Ø		
Tourigny 1992	2-10	50	Canada	Pre-op	O	High	+		
Messeri 2004	2-14	39	Italy	Pre-op	O	Low	-		
Kain 2006	2-12	568	USA	Pre-op	O	Low	-,+		
Health Care Professional Factors									
1. Health professional behaviour (3 studies; N=386)									
Noel 2010	5-10	48	Canada	Venipuncture	O	Low	+	Unclear (2 low, 1 unclear)	Distress promoting behaviour positively predicts child anticipatory distress.
Chorney 2009b	2-10	293	USA	Pre-op	O	Unclear	+		
Dahlquist 2001	5-15	45	USA	Intramuscular injection and LP	O	Low	+ (nurse) Ø (MD)		
Contextual Present Factors									
1. Environmental factors (15 different studies; N=4926)									
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	- admission type	Unclear (9 low, 4 high, 2 unclear)	More research needed.
Holm-Knudsen 1998	0-14	2122	Australia	Pre-op	O	Unlcear	- induction location		
Kain 2001	2-7	70	USA	Pre-op	RCT	High	- reduced		

							sensory stimulation
Mekarski 1997	2.5-13	324	Canada	Dental	O	Low	+ dental work severity
deVos 2012	*M* = 3.1	18	USA	Immunotherapy Injections	O	High	∅ injection personnel
Horton 2015	1-1.5	130	Canada	Immunization	O	Low	∅ number of needles
Davidson 2006	3-12	1250	Australia	Pre-op	O	Low	+ longer procedure
deVos 2012	M = 3.1	18	USA	Immunotherapy Injections	O	High	+ intervals between needles
Holm-Knudsen 1998	0-14	2122	Australia	Pre-op	O	Unclear	∅ fasting time
Al-Jundi 201	2-12	118	Jordan	Dental	O	High	+ referral reason
Dahlquist 1994	2-7, 8-17	63	USA	BMA	O	Low	∅ time since diagnosis
Dahlquist 2001	5-15	45	USA	Intramuscular injection and LP	O	Low	∅ time since diagnosis
Tyc 2002	2-7	80	USA	Radiation Therapy	O	Low	∅ time since diagnosis
Dahlquist 2005	2.4-5.1	29	USA	Immunization	RCT	High	- time since diagnosis
Holm-Knudsen 1998	0-14	2122	Australia	Pre-op	O	Unclear	∅ type of case
Ortiz 2014	8-16	437	Mexico	Dental	O	Unclear	∅ procedure
Wright 2010	3-6	61	Canada	Pre-op	E	Low	∅ surgery type
Wollin 2004	5-12	120	Australia	Pre-op	O	Low	+ various

							factors
deVos 2012	*M* = 3.1	18	USA	Immunotherapy Injections	O	High	Ø number of needles
Fortier 2011	11-18	59	USA	Pre-op	O	Low	Ø preadmission visit

Note. + Factor has a positive relationship with anticipatory distress*;* - Factor has a negative relationship with anticipatory distress*;* Ø No effect or significant relationship*;* O-Observational study*;* E-Experimental study*;* R-retrospective study*;* RCT- randomized control trial*;* Pre-op- pre-operative*;* LP-lumbar puncture*;* BMA- bone marrow aspiration.

Chapter 3: Bridging Study 1 (Systematic Review) with Study 2 and 3 (Empirical Analyses)

Using a developmental psychopathology perspective (Cicchetti & Cohen, 1995; Sroufe & Rutter, 1984), the systematic review that comprised Study 1 (Chapter 2) found 31 factors that predicted pain-related anticipatory distress in children. The results synthesis in Figure 2 of Chapter 2 outlined the various individual child factors, parent factors, healthcare provider factors, and contextual factors that are associated with pain-related anticipatory distress in children.

Individual child factors associated with increased pain-related anticipatory distress were child psychopathology, difficult child temperament, child cognitions, previous child pain behaviour, and having experienced previous pain events. Parent factors associated with increased pain-related anticipatory distress included parent distress-promoting behaviour, parent situational distress, parent anticipation of distress, parent anxious predisposition, and previous parent experiences of fear. Healthcare distress-promoting behaviour was also associated with increases in pain-related anticipatory distress. There was a number of factors that either had no association or had inconclusive findings. In particular, child sex had no association, while the results for child age and attachment style were inconclusive.

Despite the large number of studies included in the review, there were limitations to the studies included. First, most of them only reported concurrent associations, meaning that the predictor and outcome were measured at the same point in time. Importantly, there was a limited number of longitudinal studies which could attest to whether factors from an earlier time point predicted subsequent anticipatory distress, thus informing the field on the development of anticipatory distress. Second, some studies included participants of very diverse ages, making it

difficult to make developmental attributions. Lastly, there were few studies which tested the relative contribution of a number of factors simultaneously, making it difficult to know which factors were uniquely predictive of pain-related anticipatory distress.

Given the limitations of the studies included in the Chapter 2 (systematic review), the goal of Chapter 4 (Study 2 and Study 3) was to systematically examine the concurrent and longitudinal factors that may predict pain-related anticipatory distress in preschool-age children. These analyses were conducted using a large subsample of the OUCH cohort. The OUCH cohort is the largest cohort to date naturalistically observing parents and their children during routine well-baby visits in early childhood. Seven hundred and sixty parent-infant dyads were originally observed at their 2-, 4-, 6-, and 12-month vaccination appointments (or some subset of these appointments) and a subset of these were observed again at the preschool age. The longitudinal nature of this cohort provides a unique opportunity to systematically examine whether pain responses to vaccination over the first year of life predict anticipatory distress at the preschool age. Furthermore, individual child, parent, and contextual factors observed in the first year of life and concurrently at the preschool age can also be systematically evaluated as predictors. The ultimate goal of Chapter 4 is to systematically build on the findings from the review using the developmental psychopathology framework. Using the OUCH Cohort, Chapter 4 sets out to determine which factors are most predictive of pain-related anticipatory distress at the preschool immunization through two separate sets of analyses.

Chapter 4. Dissertation Study 2 and 3: Predicting Preschool Pain-Related Anticipatory Distress: The Relative Contribution of Longitudinal and Concurrent Factors[2]

1. Introduction

Healthy children commonly experience procedural pain from vaccinations and routine blood draws throughout childhood [37]. In addition to experiencing pain, many children also experience fear and pain-related anticipatory distress before the procedure even begins [24]. Pain-related anticipatory distress encompasses negative affect that may result in behavioural responses (e.g., crying, screaming, flailing) and physiological changes (e.g. increased heart rate, cortisol levels) displayed by a child prior to a painful medical procedure [32]. Higher fear and distress before a painful procedure have been associated with a number of negative sequelae including heightened pain experiences, avoidance of future painful medical procedures, and potential non-compliance with preventative healthcare such as vaccinations [5,35,36,47,49,53]. Despite the negative impact of pain-related anticipatory distress, there is a lack of research using longitudinal methodology examining the factors that contribute to its development.

Prior to undertaking the two studies presented in the current paper, an in-depth systematic review synthesized the factors that predict the development of pain-related anticipatory distress in children [44]. In particular, a developmental psychopathology framework [14] was used to examine predisposing, precipitating, perpetuating, and present factors to understand the development of pain-related anticipatory distress in children and adolescents. While some degree

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[2] This chapter is the author version of the following 'in press' manuscript:

Racine, N., Pillai Riddell, R., Flora, D., Taddio, A., Garfield, H., Greenberg, S. (in press). *Predicting Preschool Pain-Related Anticipatory Distress: The Relative Contribution of Longitudinal and Concurrent Factors*. Manuscript accepted for publication in PAIN. Doi: 10.1097/j.pain.0000000000000590.

Please note that the Study labeled as 'Study 1' in this chapter, is the 2nd study of the dissertation. The Study labeled as 'Study 2' in this chapter is the 3rd and final study of the dissertation.

of pain-related anticipatory distress would be considered normative, this framework still provided a strong theoretical framework for organizing possible variable relationships for the review and the current analysis. The overarching goal of the current paper is to systematically test the factors that contribute to the development of pain-related anticipatory distress to vaccination in early childhood using data from an established longitudinal cohort (the OUCH [Opportunities to Understand Childhood Hurt] cohort). The current paper includes two companion studies: the first examines the relative contribution of pain from the first year of life on preschool pain-related anticipatory distress to vaccination, while the second examines broader predisposing, precipitating, perpetuating, and present factors in one large model.

1.1. The Current Study.

Starting directly with pain experiences, the goal of Study 1 was to examine how infant pain-related distress variables from vaccinations during the first year of life predict pain-related anticipatory distress at the preschool vaccination. The goal of Study 2 was to examine longitudinal predisposing, precipitating, perpetuating, and present factors that may predict pain-related anticipatory distress at the preschool immunization. For the first study, we hypothesized that pre-needle distress and initial reactivity in infancy would positively predict pain-related anticipatory distress at the preschool age. We further hypothesized that less pain regulation during vaccination appointments over the first year would predict increased pain-related anticipatory distress at the preschool vaccinations. In Study 2, based on our earlier review [44] and the findings from Study 1, we hypothesized that cumulative pain experiences at 2 and 12 months of age and previous pain events would positively predict pain-related anticipatory distress at preschool. Based on previous work [38], we also hypothesized that caregiver emotional availability at 2 and 12 months of child age would negatively predict pain-related

anticipatory distress. Age was hypothesized to negatively predict pain-related anticipatory distress. Perpetuating factors such as parent worry [4], parent report of child worry, and parent distress-promoting behaviours [7, 29] were hypothesized to positively predict pain-related anticipatory distress. Finally, healthcare professional distress-promoting behaviour was a hypothesized to positively predict pain-related anticipatory distress at preschool.

2. Methods

2.1. Study sample

Participants from this study were recruited from the OUCH cohort, which has been observing caregiver-infant dyads from infancy to preschool [42]. At the time of the current study, the infancy waves were completed with a total sample size of 760 caregiver-infant dyads. Caregiver-child dyads were initially recruited from three pediatric clinics in the Greater Toronto Area, Canada. Infants and their caregivers were recruited at their 2, 4, 6, or 12 month vaccinations. At the time of the current analysis, 202 parent-child dyads were observed at the preschool time point (age 4 to 6 years) with data collection ongoing. Of the 202 parent-child dyads that were observed at preschool, 133 had 2-month data, 170 had 4-month data, 175 had 6-month data, and 177 had 12-month data. The vast majority had 3 or 4 time points (n=170), with 32 participants having data from one or two time points. Full-information maximum likelihood estimation [2] was used so that all cases could be included, which resulted in 202 cases contributing to model estimations.

Inclusion criteria for the study were that caregivers could read and speak English, that the infants had no suspected developmental delays or impairments or chronic illnesses, and had never been admitted to a neonatal intensive care unit. All children were considered healthy, from middle class families, low-risk, and developmentally typical. At the preschool appointment,

parents were predominantly mothers (85.1%) with some fathers (13.9%) and other caregivers (1.0%), and an average age of 38.91 years (SD = 5.29). The preschool sample was 46.5% female (94) and 53.5% male (108) and was an average of 4.61 years (SD = 0.55). The caregivers were asked an open-ended question about the heritage culture that had most influenced them or an earlier generation of their family. A broad classification of their responses is 13.9% Canadian, 42.1% European (e.g. British, Italian, Polish), 11.4% Jewish, and 18.3% Asian (e.g. Chinese, Indian, Vietnamese). At the preschool time point, 4.5% of children were given Tylenol or EMLA before the needle procedure.

2.2. Procedure

Ethics approval was received from York University. Details of the procedure from the infant wave of the study have been published elsewhere [38] and here we describe the procedure for the preschool vaccinations. Parents who were observed during their child's vaccinations were given a flyer by a medical receptionist and asked whether they would like to learn more about a new study. If interested, informed consent was obtained and the parent completed a demographic information form. Ninety percent of approached parents allowed us to videotape their child's preschool vaccination. Once in the examination room, two video cameras were set up to capture a close-up face shot of the preschooler as well as a wide shot to obtain a full view of the parent and the child, both 5 minutes prior and 5 minutes post-needle. This footage was used to code preschool anticipatory distress behaviours and child verbalizations. Parents received a $5.00 coffee shop gift certificate for participation. At the 2, 4, 6, and 12-month vaccination appointments, infants received between 1 and 3 needles, with a means of 2.01 needles (SD=0.25).

2.3 Apparatus

At the preschool appointment, two Sony HDRXR260V High-Definition Handycam Camcorders (2012 Model) were used to record parent and child behaviour. One camera was hand-held by a research assistant to record the close-up image of the child's face, body movements, and verbalizations. The second camera was mounted on a tripod and fitted with a wide-angle lens to record parent-child interactions from a distance.

2.4 Measures

2.4.1. Parent and child demographic information

Caregivers were asked to complete a short demographic form prior to their child's vaccination. Questions pertained to their age, their child's age, their child's sex (male coded as 1, female coded as 2), the child's previous medical history, their relationship to the child, their education level, and their self-reported heritage culture.

2.4.2. Pain-Related Anticipatory Distress (Latent dependent variable; Study 1 and 2)

As will be described in greater detail in the results section, child behaviour (FLACC), proportion of child distress verbalizations (CAMPIS-R), and child cry duration were used as observed indicators of a latent variable representing pain-related anticipatory distress in Study 1 and Study 2. Using this latent variable accounts for measurement error with respect to the relations of the observed indicators to the hypothetical construct of pain-related anticipatory distress [9]. This variable is the dependent variable in all the models presented in the current paper. The three indicator variables (FLACC, child distress verbalizations, and cry) all demonstrated appropriate range and variance.

2.4.2.1. Face, Legs, Activity, Cry, and Consolability Scale

This measure was used as a component of our latent variable. The FLACC is also known as the Face, Legs, Activity, Cry, and Consolability scale [33]. The FLACC is a behavioural

rating scale that is a valid and reliable measure of procedural pain in infants and young children [51] and has also demonstrated reliability, construct validity, and concurrent validity for baseline measurements of pain-related distress [46]. The FLACC consists of five behavioural indices: face, legs, arms, cry, and consolability, which are each rated using a scale from 0 to 2. These ratings are added together for an overall score between 0 and 10 for each 15-second epoch (in the current analyses it was scored for four epochs). Higher scores indicate higher distress intensity. For the current analyses, FLACC scores are presented as proportions ranging from 0 to 1. The FLACC scale was coded by trained coders and interrater reliability coefficients for the current study all exceeded .85 for the five total behaviour indices.

2.4.2.2. Preschool distress verbalizations and cry

The CAMPIS-R also provided two components to our latent variable for pain-related preschool anticipatory distress. Child distress verbalizations and cry from the CAMPIS-R [7] were also included as indicators of the latent pain-related anticipatory distress variable. Videos were transcribed by research assistants and each transcript was reviewed by one research assistant trained in coding the CAMPIS to ensure it accurately reflected the content and to ensure vocalizations were spliced into codeable CAMPIS units. One child-caregiver dyad was excluded because no English was spoken during the entire interaction and the language could not be translated. The child distress verbalizations variable is a proportion ranging from 0 to 1 of the total number of child verbalizations that were distress verbalizations. Cry is presented as a proportion of the total time coded with scores ranging between 0 and 1. Videos were first coded on paper using the spliced transcript. The Observer XT (Noldus Inc.) was subsequently used to facilitate coding the video data. Timed-event data coding was used to capture data on frequency, duration, and timing of codes [3]. There were two coders for the study. For verbal behaviours,

percent agreements were calculated from the transcripts that were coded with a percent agreement of 85% with a range of 71% to 98% agreement. For non-verbal behaviours, reliability statistics were calculated using Noldus Observer XT version 11. A tolerance window of 2 seconds was used including gaps with an overall average percent agreement of 86% with a range of 74% to 97%.

2.4.3. Infant predictor variables

2.4.3.1. Infant pain-related distress (Study 1 and Study 2)

The Modified Behaviour Pain Scale (MBPS) [48] was used to assess infant pain-related distress for a 15-second epoch immediately prior to the first vaccination needle, immediately after the vaccination, 1-minute, 2 minutes, and 3 minutes after the vaccination. This was completed for the 2, 4, 6 and 12-month vaccinations. There are three subsections of the scale (facial expression, cry, and body movement), each requiring the coder to decide on what the maximal score based on the infant's overt behaviour during the 15-second epoch. All sections of the measure are summed to get an infant pain score out of ten. Moderate to high concurrent validity as well as item-total and inter-rater reliability have all been demonstrated in the vaccination context [48]. Inter-rater reliability was high with intraclass correlations ranging from .93 to .96.

In Study 1, the MBPS scores were used as indicators of the latent slope factor (operationalizing pain regulation) and intercept (operationalizing pain reactivity) factors in the four latent growth models (LGMs) using structural equation modeling [10]. Using a separate model within each age (2, 4, 6, and 12 months; see Figure 1), a latent slope factor represents the change in MBPS pain scores (i.e., pain regulation) from the needle observation across the 1-minute, 2-minute, and 3-minutes post-needle observations, whereas the latent intercept

represents the needle pain score (i.e., reactivity or the first pain score immediately after the last needle). Pain-related anticipatory distress prior to the needle was used as a separate covariate in each model.

In Study 2, greater parsimony was needed to represent pain experience due to the number of relationships to be tested in the broader model. Thus, a cumulative pain score from the two most painful vaccinations (the 2- and 12-month cumulative pain scores) were used, as it was felt these two time points would have the highest chance of predictive power for preschool outcomes. In addition, both initial reactivity (intercept) and change in pain scores (slope) were not found to have significant predictive value in Study 1. Rather, than insert variables we knew not to have a relationship with the final dependent variable into our model, a cumulative sum score of the three pain scores were used such that the pain scores were reflective of the total distress expressed during the 2-month or 12-month appointment.

2.4.3.2. Caregiver Emotional Availability in infancy (Study 2 only)

The emotional availability scale (EAS) [6] provides a global clinical judgment of caregiving behaviour. The EAS consists of four main caregiver subscales (sensitivity, structuring, non-intrusiveness, and non-hostility), which are summed to form an overall score [6]. Inter-rater reliability for the total score was calculated between each main coder and each of the reliability coders and intraclass correlations ranged from .80 to .93. Only the 2 and 12-month EAS scores were used in this study to logically parallel the infant pain scores used for Study 2 [38].

2.4.4. Preschool Predictors (Study 2 only)

2.4.4.1. Parent distress promoting verbalizations and healthcare provider verbalizations at preschool

Parent and healthcare professional verbalizations for three minutes prior to the needle were videotaped, transcribed, and later coded using the Child-Adult Medical Procedure Interaction Scale-Revised (CAMPIS-R) [7]. For this study, the categories used from the CAMPIS-R were parent distress-promoting behaviours and healthcare professional distress-promoting behaviours. Scores for both categories were calculated as the proportion of total behaviour for each individual. These variables were created by summing the criticism, reassuring comment, giving control to the child, apology, and empathy verbalization codes that occurred three minutes prior to the vaccination. As above, Observer XT software (Noldus Inc, The Netherlands) was used to facilitate the video coding. Timed-event data coding was used to capture data on frequency, duration, and timing of codes [3]. Reliability for these variables had an average of 85% agreement with a range of 71% to 98% agreement.

2.4.4.2. Parent report of child and self-worry pre-needle (Study 2 only)

Parents were asked to rate their own child's worry and their own worry using a scale from 0 to 10, where 0 was no worry and 10 was the most worry possible.

2.4.4.3. Number of significant painful procedures between 12 months and preschool (Study 2 only)

Parents were asked to report their child's medical history since 12 months of age by checking off which illnesses or conditions their child had experienced [45]. From this list, four significant events that are hypothesized to be painful were used to create a cumulative score of significant painful events. These four painful events were circumcision, broken bones, hospitalization, and operations. The cumulative painful event score ranged from 0 to 4, with a higher score indicating more previously experienced painful events.

2.5 Data analysis plan

2.5.1. Study 1: Impact of pain regulation over the first year of life on pain-related anticipatory distress at preschool age.

We fitted four separate models (2, 4, 6 and 12 months) to examine whether infant pain-related distress reactivity (represented using a latent *intercept* factor described above) and regulation (represented using latent *slope* factors described above) at each of these age predicted child pain-related anticipatory distress at preschool. Each model was estimated using full-information maximum likelihood with Mplus version 7 software [34]. The comparative fit index (CFI), the root mean square error of approximation (RMSEA), and the Standardized Root Mean Square Residual (SRMR) evaluated goodness of fit for the models. CFI values of 0.95 or higher and RMSEA and SRMR values of 0.05 or less indicate that a model fit the data well [11].

All four models (i.e., using data from each of the 2, 4, 6, and 12 month vaccination appointments) were specified such that pain-related anticipatory distress at preschool was conditioned on the pre-needle pain-related distress score, the intercept factor (needle pain reactivity), and the change in infant pain-related distress across the appointment (i.e. infant pain regulation or slope factor from immediately after the needle to 3-minutes post needle). To account for the non-linear pattern in the MBPS scores across the vaccination appointment, the slope factor loadings were set to 0 at needle, freely estimated for 1 and 2 minutes post-needle, and set to 1 for 3 minutes post-needle (i.e., a "freed-loading" model to produce a series of linear splines)[10]. Because the slope factor loading was set to zero for the needle pain score, the intercept factor represents the pain-related distress mean at needle in all models. Given multiple comparisons made in the LGM analyses, a Bonferroni correction was applied. Using a family-wise error rate of $\alpha = .05$ and four analyses, the criteria of $p < .0125$ was used for the LGM analyses. See Figure 1 for details.

2.5.2. Study 2: Impact of predisposing, precipitating, perpetuating, and present factors on pain-related anticipatory distress at preschool age.

First, correlations among the independent variables (MBPS baseline at 2 and 12 months, MBPS post-needle at 2 and 12 months, MBPS 1 minute at 2 and 12 months, healthcare professional distress-promoting behaviour, caregiver distress-promoting behaviour, sex, age, child worry, parent worry, painful events, caregiver sensitivity at 2 months, and caregiver sensitivity at 12 months) were examined to determine which relationships to include in the final model. The prediction of pain-related anticipatory distress from longitudinal and concurrent factors was then modeled using SEM so that certain constructs (child pain-related anticipatory distress at preschool, 2 month cumulative distress, and 12 month cumulative distress) could be represented by latent variables with multiple observed indicators [11]. The models were estimated using full-information maximum likelihood with Mplus version 7.31 [34]. Model fit was evaluated using the comparative fit index (CFI), the root mean square error of approximation (RMSEA), and standardized root mean square residual (SRMR). CFI values of 0.95 or higher and RMSEA and SRMR values of 0.05 or less indicate that a model has a good fit to the data [11].

The final model was specified such that the preschool pain-related anticipatory distress latent variable was conditioned on infant cumulative distress at 2 and 12-months, caregiver emotional availability at 2 months, caregiver emotional availability at 12 months, age, sex, pain events, parent worry, child worry, parent distress promoting behaviours, and healthcare professional distress promoting behaviours. See Figure 2.

3. Results

3.1 Study 1: Predicting pain-related anticipatory distress from infant pain responses

The means, standard deviations, and correlations among variables at 2, 4, 6, and 12 months of age are presented in Tables 1 to 4. Four models (one for each age of infant vaccination) were estimated with slope (pain regulation) and intercept (pain reactivity) latent growth factors. These four models were expanded to include the latent preschool pain-related anticipatory distress variable as the outcome. Figure 1 shows a visual of the Latent Growth Models estimated at each age (2, 4, 6, and 12 months of age).

3.1.1. Impact of pre-needle pain-related distress, pain reactivity, and pain regulation at 2 months on preschool pain-related anticipatory distress to vaccination.

The mean MBPS scores for infant pain-related distress at 2 months of age decreased from 8.79 at needle to 5.47 at 3 minutes post-needle. Pre-needle pain-related distress at 2 months was also included as a predictor of preschool pain-related anticipatory distress. Because there was minimal variability in infant needle pain at the two-month time point (the majority of infants had high pain-related distress), the residual variance for MBPS at needle was constrained to zero to avoid obtaining an improper negative residual variance estimate. The combination of fit indices suggested that this model fit the data well (CFI= 1.0, RMSEA = .01, SRMR=. 05). Both standardized and unstandardized estimates are represented in Table 5.

The mean of the linear slope factor was negative and significant ($p < .001$), indicating that the change in pain-related distress scores decreased on average following the needle. There was no significant relationship between the pain reactivity and pain regulation. Pain reactivity and pain regulation did not predict pain-related anticipatory distress ($p = .06$ and $p = .25$). The pre-needle pain-related distress score at two months did not predict pain-related anticipatory distress at preschool ($p = .82$). This model accounted for only 3% of the variance in pain-related anticipatory distress at preschool.

3.1.2. Impact of pre-needle pain-related distress, pain reactivity, and pain regulation at 4 months on preschool pain-related anticipatory distress to vaccination.

The mean values for infant pain-related distress at 4 months of age decreased from 8.47 at needle to 4.30 at 3 minutes post-needle. Pre-needle pain-related distress at 4 months was also entered as a predictor of preschool pain-related anticipatory distress. Since there was minimal variability in infant needle pain-related distress at the 4-month time point (the majority of infants displayed high pain-related distress), the residual variance for pain-related distress at needle was constrained to zero to avoid obtaining an improper negative residual variance estimate. The combination of fit indices suggested that this model fit the data well (CFI= 1.0, RMSEA = .002, SRMR=. 04). Both standardized and unstandardized estimates are represented in Table 6.

The mean of the linear slope factor was negative and significant ($p < .001$), indicating that the change in pain-related distress scores decreased on average following the needle. The pain reactivity and pain regulation were not significantly related at 4 months of age ($p = .04$). Using the Bonferroni-corrected α of .0125, pain reactivity did not predict preschool pain-related anticipatory distress ($p =. 03$) and neither did pain regulation ($p = .01$). It should be noted that although the p-value for pain regulation was below .125 for the standardized estimate, it was not for the unstandardized estimate ($p = .014$). As such a conservative approach was taken to not deem this value significant. The pre-needle pain-related distress score at 4 months did not predict pain-related anticipatory distress at preschool ($B = .06$, $p = .54$). This model accounted for 10% of the variance in pain-related anticipatory distress at preschool.

3.1.3. Impact of pre-needle pain-related distress, pain reactivity, and pain regulation at 6 months on preschool pain-related anticipatory distress to vaccination.

The mean values for infant pain-related distress at 6 months of age decreased from 8.50 at needle 3.97 at 3 minutes post-needle. Pre-needle pain-related distress at 6 months was also included as a predictor of preschool pain-related anticipatory distress. Since there was minimal variability in infant needle pain at the six-month time point (the majority of infants had high pain-related distress), the residual variance for pain-related distress at needle was constrained to 0 to avoid obtaining an improper negative residual variance estimate. The combination of fit indices suggested that the model fit was good (CFI = .98, RMSEA = .05, SRMR = .05). Both standardized and unstandardized estimates are represented in Table 7.

The mean of the linear slope factor was negative and significant ($p < .001$), indicating that the change in pain-related distress scores decreased on average following the needle. There was no significant relationship between pain reactivity and pain regulation at 6 months. The intercept ($p = .29$), slope ($p = .22$) and pre-needle pain-related distress score ($p = .60$) at 6 months did not significantly predict pain-related anticipatory distress. This model accounted for only 3% of the variance in pain-related anticipatory distress at preschool.

3.1.4. Impact of pre-needle pain-related distress, pain reactivity, and pain regulation at 12 months on preschool pain-related anticipatory distress to vaccination.

The mean values for infant pain-related distress at 12 months decreased from 8.23 at needle to 4.38 at 3 minutes post needle. Pre-needle pain-related distress at 12 months was also entered as an independent predictor of preschool pain-related anticipatory distress. The combination of fit indices suggested that this model fit the data relatively well (CFI = .96, RMSEA = .07, SRMR = .06). Both standardized and unstandardized estimates are represented in Table 8.

The mean of the linear slope factor was negative and significant ($p < .001$), indicating that the change in pain-related distress scores was decreasing over time. There was no significant relationship between the pain reactivity and pain regulation at 12 months. Pain reactivity ($p = .06$) and the pain regulation did not predict preschool pain-related anticipatory distress ($p = .75$). The pre-needle pain-related distress score at 12 months did not predict pain-related anticipatory distress at preschool ($p = .98$). This model accounted for 3% of the variance in pain-related anticipatory distress at preschool.

3.2 Study 2: Predicting pain-related anticipatory distress from predisposing, precipitating, perpetuating, and present factors.

3.2.1. Relationships among key variables

Correlations among key variables are presented in Table 9 for completeness. There were positive relationships among the baseline, needle, and one-minute pain scores at 2 months of age and at 12 months of age (see Table 9). Significant correlations were used to determine the relationships included in the final SEM model.

3.2.2. Measurement model of latent variables

Baseline MBPS, needle MBPS scores, and one-minute post-needle MBPS scores at 2-months were used as observed indicators of a 2-month cumulative distress latent variable whereas baseline MBPS, needle MBPS scores, and one-minute post-needle MBPS scores at 12-months were used as indicators of a 12-month cumulative distress latent variable. For the preschool pain-related anticipatory distress latent variable, FLACC scores, child distress behaviours, and cry were used. The combination of fit indices suggested that this model fit the data well (RMSEA = <.001, SRMR=.04, CFI=1.0). Parameter estimates are presented in Table 10.

3.2.3. Final model predicting pain-related anticipatory distress

The final model was specified such that the preschool pain-related anticipatory distress latent variable was regressed on the 2- and 12-month cumulative distress latent variables as well as pain events, caregiver EA at 2 months, caregiver EA at 12 months, child age, child sex, caregiver distress-promoting behaviour, healthcare provider distress-promoting behaviour, child worry, and parent worry. The final model depicted in Figure 2 fit the data well (CFI = 1.0; RMSEA = <.001, SRMR = .06). Completely standardized parameter estimates and correlations are presented in the text and Figure 1, while both standardized and unstandardized estimates are represented in Table 11.

3.2.4. Relationships among predictor variables

Based on a systematic review [44], the model was specified to include certain directional relationships among predictors. As was seen in the simple bivariate correlations, there were several significant relationships among predisposing, precipitating, perpetuating, and present factors (see Table 9). Both theoretical and statistical (i.e. significant bivariate correlations) were the criteria used for including a variable in the final model and for examining directional relationships among predictors. Cumulative distress at 12-months of age positively predicted parent report of child worry at preschool (B = .23, p = .01), whereby children who expressed more distress at 12-months had parents who rated them as more worried at preschool. In addition, parent self-report of worry was positively related to parent report of child worry (B = .23, p = .002). Parent worry at preschool negatively predicted healthcare provider distress-promoting behaviour (B = -.13, p = .01). Caregiver emotional availability at 2 months was negatively related to cumulative distress at 2 months (B = -.36, p = .001). Caregiver EA at 12

months was negatively related to cumulative distress at 12 months (B = -.41, p < .001). Caregiver EA and 2 and 12 months were positively related (B = .42, p < .001).

3.2.5. Factors predicting pain-related anticipatory distress at preschool

The R^2 for child pain-related anticipatory distress at preschool was .404 (p < .001), thus 40.4% of the variance in child pain-related anticipatory distress at preschool was explained by the set of latent and observed predictors. As seen in Table 11, caregiver distress-promoting behaviour positively predicted child pain-related anticipatory distress at preschool (B = .49, p < .001), whereby caregivers who used more distress-promoting behaviour had children who displayed more pain-related anticipatory distress. Caregiver distress-promoting behaviour at the preschool vaccination appointment uniquely accounted for 19.3% of the variance in child pain-related anticipatory distress at preschool. Child age positively predicted preschool pain-related anticipatory distress (B = .15, p = .01), uniquely accounting for 2.0% of pain-related anticipatory distress variance. Caregiver EA from the 2-month vaccination appointment positively predicted preschool pain-related anticipatory distress (B = .35, p = .02) and 12-month vaccination appointment negatively predicted child pain-related anticipatory distress (B = -.33, p = .01), explaining 6.4% and 6.1% of the variance in preschool pain-related anticipatory distress, respectively.

4. Discussion

The objective of the current paper using two companion analyses was to examine the relative contribution of vaccination pain and distress responses from the first year of life (Study 1) as well as broader longitudinal factors (predisposing, precipitating, perpetuating, and present) on pain-related anticipatory distress to vaccination at the preschool age (Study 2). In Study 1, using a sequential cohort design and a substantial sample of over 200 participants, our results

demonstrated that vaccination pain and distress responses over the first year of life did not predict preschool pain-related anticipatory distress. In Study 2, which tested a model that encompassed broader child and contextual factors, 40% of the variance in preschool pain-related anticipatory distress was accounted for. Ultimately, concurrent parent behaviours during the preschool pre-needle epoch predicted the majority of the variance, followed by parent emotional availability during 2 and 12 months, and finally child age at preschool (ranging between 4 and 6 years of age).

4.1. Study 1: Impact of infant pain responses on preschool pain-related pain-related.

The four models from Study 1 showed that pre-needle pain-related distress, pain reactivity, and pain regulation at 2, 4, 6, and 12 months of age did not predict pain-related anticipatory distress at preschool. These findings were not in line with hypotheses, which predicted that higher pre-needle pain-related distress, higher pain reactivity, and poor pain regulation during infancy would be associated with increased pain-related anticipatory distress at the preschool age. These findings suggest that pain-related anticipatory distress does not demonstrate continuity in its development (i.e. infant pre-needle distress was not related to preschool pre-needle distress). With regards to pain reactivity, infants during the first year of life may not have yet developed the ability to build lasting cognitive schemas to make the association from relatively rare events in infancy to preschool events. Although pain regulation across infancy was not found to predict pain-related anticipatory distress at preschool, it should be noted that the relationship just missed significance at 4 months using our stringent alpha level (explaining roughly 10% of the variance in pain-related anticipatory distress at preschool) suggesting that experiencing high levels of distress immediately following routine vaccination and not demonstrating a capacity towards regulation at 4 months may have some relationship

with pain-related anticipatory distress at preschool. Four months of age is a critical time in infant development when the inhibitory mechanisms of the central nervous system are beginning to develop, yet the infant does still not seem to yet have the cognitive capacity to directly encode a complex emotional reaction such as experiencing distress from anticipating future pain based on past pain [28]. This reinforces the need to start scaffolding the regulation of infant distress (i.e. pain management strategies) from the very beginning of life.

4.2 Study 2: Longitudinal and concurrent factors predicting pain-related anticipatory distress

Ultimately the results from Study 1 demonstrate the importance of taking a broader approach to examining the predictors of pain-related anticipatory distress at the preschool age [44]. In line with the developmental psychopathology framework, Study 2 examined which predisposing, precipitating, perpetuating, and present factors predicted child pain-related anticipatory distress at preschool.

4.2.1. Predisposing factors

Similar to findings in Study 1, cumulative distress from infancy did not predict pain-related anticipatory distress at preschool. It may be that these pain experiences occurred when the infant was too young to form declarative memories (or too infrequent and brief to trigger a lasting non-declarative memory) to have an impact on the child's cognitive appraisal of the vaccination as threatening at preschool. Additionally, previous research on needle phobia has demonstrated onset at the preschool age, indicating that direct conditioning from events at that age, rather than earlier, may be a significant contributor [32, 17]. The lack of a sex effect is in line with findings from a previous review [44]. Our findings regarding age may be related to older children having more ability to retrieve and experience a complex emotional reaction such as expressing distress in anticipation of pain based on previous experience with pain.

The only variable from the infant vaccinations that predicted pain-related anticipatory distress was caregiver emotional availability (EA) both at 2 and 12 months of age. The finding for 12 month EA is consistent with developmental literature suggesting that caregiver sensitivity to distress is related to fewer behavioural problems, higher social competence, and better affect regulation [27]. Contrary to hypotheses, higher emotional availability at 2-months predicted higher pain-related anticipatory distress at preschool. We know from previous work there is minimal variability in pain scores at the 2-month vaccination [40] and that caregiver sensitivity is strongly related over the first year of life [38]. Perhaps being highly reactive at 2 months reflects a predisposition to amplify distress signaling in later childhood. It is clear that over time by meeting their child's needs through subsequent vaccinations, dyads often develop secure attachment relationships and lead to EAS at 12 months of age predicting lower anticipatory distress. This discrepancy in findings between 2 and 12 months may also be a random association due to type I error.

4.2.2. Precipitating factors

Having more painful events during childhood (i.e. surgery, circumcision, hospitalization, and broken bones) did not significantly predict pain-related anticipatory distress. Previous research has shown that general and specific negative pain events can generalize to the development of fear and anxiety to painful medical procedures [5,24, 36], although this is not uniformly the case [21, 23,29, 31]. Perhaps rare painful medical events over early childhood are not predictive of pain-related anticipatory distress to vaccination.

4.2.3.Perpetuating factors.

The perpetuating or concurrent factors that would maintain the anticipatory anxiety at preschool included parent worry prior to vaccination, parent report of child worry prior to

vaccination, and parent distress-promoting behaviours during the pre-needle period, which were all hypothesized to positively predict pain-related anticipatory distress. Study 2 found that only parent behavior positively predicted pain-related anticipatory distress at preschool. This result is consistent with previous research demonstrating that caregiver distress-promoting verbalizations are strong predictors of worry and anxiety in children [13, 15].

In terms of relationships among the perpetuating variables, parental worry negatively predicted healthcare provider distress-promoting behaviour. This suggests that healthcare providers may be more attuned to avoid distress-promoting behaviors towards the child when parents communicate worry. Parents' own worry also positively predicted their report of their child's worry. This finding supports previous research with the same sample that has shown that parental factors have an impact on parental report of child pain-related distress [39].

4.2.4. Present factors

Finally, findings Study 2 did not support the hypothesis that healthcare professional distress-promoting behaviour positively predicts pain-related anticipatory distress at preschool. This may be a result of low healthcare professional interaction and the limited sample of health care professionals coded in this study. Future research should include a larger number of health professionals that can better represent the population of immunizing health professionals.

4.3. Conclusions

To our knowledge, this paper is the first to examine both longitudinal and concurrent factors that predict pain-related anticipatory distress in preschool-aged children. Results from the two companion analyses indicate that early pain responses have a limited impact on the development of pain-related anticipatory distress. During infancy, the caregiver has been described as the most important context for the infant in pain [41]. Results from Study 2 suggest

that at preschool age, the caregiver continues to be one of the most important factors in predicting pain-related anticipatory distress. Concurrent parent behaviour has been shown to be associated with pain-related anticipatory distress during painful medical procedures across childhood [8,15,16,20,29]. However, this study is the first to establish using longitudinal data that caregiver behaviour during vaccination from the first year of life and at the preschool age are *both* associated with pain-related anticipatory distress at preschool- significantly more than the child's own behaviours. Concurrent parent distress promoting behaviour at preschool was by far the most significant predictor of child pain-related anticipatory distress at preschool, which substantiates the critical role of parents during vaccination appointments in early childhood. The directionality of this relationship should be the subject of future research. We have established in earlier work that pain-related anticipatory distress increases pain-related distress post-needle [1], yet there is currently little evidence that parent-led interventions can be effective for reducing child distress during vaccinations [30, 43]. Interventions that target increasing caregiver sensitivity in the first year of life and increasing coping promoting behaviours at the preschool age are needed. More research is needed on interventions relating to parental coaching for their children's vaccinations.

4.4. Limitations and future directions

Caregivers from the current study self-selected to be associated with a longitudinal study and had higher education, affecting the potential generalizability of the study. Additionally, previous research has shown that temperament [22, 26] and pre-existing child psychopathology [12,18,19,25,52] may be important predisposing factors of child pain-related anticipatory distress that were not examined in the current study. Given challenges of self-report on anxiety and pain scales for preschool-aged children [50], child self-report was not used in the current study.

Alternate methods of assessing child distress, including age-appropriate self-report tools and physiology (e.g., heart rate) will be important areas for future investigation.

Conflict of interest statement

The authors report no conflict of interest.

Acknowledgments

This research was funded by salary support awards and/or research grants to Dr. Pillai Riddell from the Canadian Institutes of Health Research, the Ontario Ministry of Research and Innovation, the Canadian Foundation for Innovation and the York Research Chairs program. Ms. Racine received awards from the Canadian Institutes of Health Research, the Government of Ontario, the Lillian and Don Wright Foundation, and the Canadian Pain Society. Ms. Racine is also a trainee member of Pain In Child Health (PICH), a strategic research training initiative of the Canadian Institutes of Health Research. The authors would like to thank the staff at both Dr. Greenberg's and Dr. Garfield's clinics, and all OUCH lab research assistants for their assistance and ongoing support. Particular thanks to Maria Khan for her coding efforts and Zhaodi Culbreath for assistance with graphics. We would also like to thank all the families who have participated in this research.

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Table 1

Means, standard deviations, and correlations among the pain response variables at 2 months and preschool vaccinations

	1	2	3	4	5	6	7	8
1. Pre-needle distress 2-months	-	**.19** (.03)	**.22** (.01)	**.19** (.04)	**.24** (.02)	.10 (.92)	.04 (.67)	.03 (.70)
2. Needle pain 2-months	-	-	**.27** (.002)	**.22** (.02)	.16 (.11)	.12 (.24)	.04 (.63)	.15 (.09)
3. 1 minute pain 2-months	-	-	-	**.44** (<.001)	**.41** (<.001)	.04 (.74)	.12 (.20)	.11 (.23)
4. 2 minute pain 2-months	-	-	-	-	**.65** (.00)	-.07 (.51)	-.11 (.24)	.02 (.83)
5. 3 minute pain 2-months	-	-	-	-	-	-.19 (.09)	-.10 (.34)	-.08 (.43)
6. FLACC	-	-	-	-	-	-	**.79** (<.001)	**.57** (<.001)
7. Cry	-	-	-	-	-	-	-	**.48** (<.001)
8. Child distress behaviour	-	-	-	-	-	-	-	-
Mean	2.89	8.78	5.94	5.80	5.43	.14	.06	.33
SD	1.95	.85	2.47	2.50	2.61	.21	.17	.33
Range	0-10	0-10	0-10	0-10	0-10	0-1	0-1	0-1
N	132	133	123	118	96	156	202	202

Note. p-values are in parentheses. Significant correlations are bolded.

Table 2

Means, standard deviations, and correlations among the pain response variables at 4 months and preschool vaccinations

	1	2	3	4	5	6	7	8
1. Pre-needle distress 4-months	-	**.24** (.002)	**.26** (.001)	**.25** (.001)	**.27** (.002)	.12 (.20)	**.16** (.04)	.04 (.60)
2. Needle pain 4-months	-	-	**.31** (<.001)	**.19** (.02)	.16 (.08)	.13 (.15)	.09 (.24)	.08 (.28)
3. 1 minute pain 4-months	-	-	-	**.49** (<.001)	**.37** (<.001)	.18 (.05)	**.17** (.03)	.08 (.34)
4. 2 minute pain 4-months	-	-	-	-	**.59** (<.001)	.16 (.09)	.14 (.07)	.12 (.15)
5. 3 minute pain 4-months	-	-	-	-	-	**.29** (.003)	**.20** (.02)	.14 (.10)
6. FLACC	-	-	-	-	-	-	**.79** (<.001)	**.57** (<.001)
7. Cry	-	-	-	-	-	-	-	**.48** (<.001)
8. Child distress behaviour	-	-	-	-	-	-	-	-
Mean	2.75	8.48	4.75	4.65	4.22	.14	.06	.33
SD	1.79	.88	2.49	2.64	2.66	.21	.17	.33
Range	0-10	0-10	0-10	0-10	0-10	0-1	0-1	0-1
N	167	168	162	158	132	156	202	202

Note. p-values are in parentheses. Significant correlations are bolded.

Table 3

Means, standard deviations, and correlations among the pain response variables at 6 months and preschool vaccinations

	1	2	3	4	5	6	7	8
1. Pre-needle distress 6-months	-	**.38** (<.001)	**.22** (.01)	**.36** (<.001)	**.38** (<.001)	-.07 (.43)	.06 (.41)	.11 (.17)
2. Needle pain 6-months	-	-	**.31** (<.001)	**.35** (<.001)	**.28** (.002)	.04 (.62)	.07 (.35)	.07 (.37)
3. 1 minute pain 6-months	-	-	-	**.44** (<.001)	**.34** (<.001)	.12 (.18)	.14 (.07)	**.21** (.01)
4. 2 minute pain 6-months	-	-	-	-	**.64** (<.001)	-.02 (.83)	.05 (.52)	.07 (.39)
5. 3 minute pain 6-months	-	-	-	-	-	.04 (.68)	.07 (.43)	.02 (.83)
6. FLACC	-	-	-	-	-	-	**.79** (<.001)	**.57** (<.001)
7. Cry	-	-	-	-	-	-	-	**.48** (<.001)
8. Child distress behaviour	-	-	-	-	-	-	-	-
Mean	3.12	8.50	5.09	4.50	3.85	.14	.06	.33
SD	2.16	.89	2.59	2.70	2.47	.21	.17	.33
Range	0-10	0-10	0-10	0-10	0-10	0-1	0-1	0-1
N	172	173	161	153	117	156	202	202

Note. p-values are in parentheses. Significant correlations are bolded

Table 4

Means, standard deviations, and correlations among pain response variables at 12 months and preschool immunizations

	1	2	3	4	5	6	7	8
1. Pre-needle distress 12-months	-	**.36** (<.001)	**.28** (<.001)	**.26** (.001)	.17 (.05)	.05 (.56)	.04 (.65)	.11 (.16)
2. Needle pain 12-months	-	-	**.46** (<.001)	**.60** (<.001)	**.26** (<.001)	.13 (.14)	.09 (.24)	**.17** (.02)
3. 1 minute pain 12-months	-	-	-	**.39** (<.001)	**.26** (.002)	.11 (.22)	.10 (.21)	**.17** (.02)
4. 2 minute pain 12-months	-	-	-	-	**.52** (<.001)	.10 (.26)	.05 (.57)	.12 (.13)
5. 3 minute pain 12-months	-	-	-	-	-	.09 (.34)	.07 (.46)	.01 (.90)
6. FLACC	-	-	-	-	-	-	**.79** (<.001)	**.57** (<.001)
7. Cry	-	-	-	-	-	-	-	**.48** (<.001)
8. Child distress behaviour	-	-	-	-	-	-	-	-
Mean	3.63	8.21	5.98	4.99	4.44	.14	.06	.33
SD	2.37	1.30	2.36	2.56	2.72	.21	.17	.33
Range	0-10	0-10	0-10	0-10	0-10	0-1	0-1	0-1
N	171	176	172	158	134	156	202	202

Note. p-values are in parentheses. Significant correlations are bolded.

Table 5

Estimates from 2-month model predicting pain-related anticipatory distress at preschool

Variable	Un-standardized estimate	*SE*	*Z*	*p*	Standardized estimate	*SE*	*Z*	*p*
Indicators of preschool pain-related anticipatory distress factor								
FLACC	1.00	.00	-	-	.98	.03	32.71	<.001
Child distress verbalizations	.97	.08	12.79	<.001	.59	.05	12.41	<.001
Cry	.68	.09	7.99	.00	.80	.04	18.26	<.001
Indicators of pain reactivity at 2 months								
2-month needle MBPS	1.00	.00	-	-	1.00	.00	-	-
2-month 1 min MBPS	1.00	.00	-	-	.32	.08	3.91	.00
2-month 2 min MBPS	1.00	.00	-	-	.34	.09	3.96	.00
2-month 3 min MBPS	1.00	.00	-	-	.33	.08	3.96	.00
Indicators of pain regulation at 2 months								
2-month needle MBPS	.00	.00	-	-	.00	.00	-	-
2-month 1 min MBPS	.79	.05	15.20	.00	.61	.05	12.32	.00
2-month 2 min MBPS	.90	.05	17.66	.00	.73	.06	13.38	.00
2-month 3 min MBPS	1.00	.00	-	-	.78	.05	15.65	.00
Prediction of anticipatory distress				.				.
Intercept (reactivity)	.03	.01	1.90	.06	.11	.05	2.43	.02
Slope (regulation)	-.01	.01	-1.15	.25	-.10	.09	-1.16	.25
Pre-needle pain score	.002	.01	.23	.82	.02	.10	.23	.82

Note. p-value for significance is p< .0125 based with the Bonferonni correction.

Table 6

Estimates from 4-month model predicting pain-related anticipatory distress at preschool

Variable	Un-standardized estimate	*SE*	*Z*	*p*	Standardized estimate	*SE*	*Z*	*p*
Indicators of preschool pain-related anticipatory distress factor								
FLACC	1.00	.00	-	-	.99	.03	30.45	<.001
Child distress verbalizations	.95	.08	12.73	<.001	.59	.05	12.08	<.001
Cry	.66	.08	8.06	<.001	.79	.05	17.50	<.001
Indicators of pain reactivity at 4 months								
4-month needle MBPS	1.00	.00	-	-	1.00	.00	-	-
4-month 1 min MBPS	1.00	.00	-	-	.34	.04	9.50	.00
4-month 2 min MBPS	1.00	.00	-	-	.35	.04	9.74	.00
4-month 3 min MBPS	1.00	.00	-	-	.33	.04	9.44	.00
Indicators of pain regulation at 4 months								
4-month needle MBPS	.00	.00	-	-	.00	.00	-	-
4-month 1 min MBPS	.87	.05	18.01	.00	.64	.04	14.44	.00
4-month 2 min MBPS	.93	.04	21.40	.00	.69	.06	12.41	.00
4-month 3 min MBPS	1.00	.00	-	-	.70	.05	13.48	.00
Prediction of anticipatory distress				.				.
Intercept (reactivity)	.04	.02	2.21	.03	.16	.07	2.28	.02
Slope (regulation)	.03	.01	2.45	.014	.27	.10	2.71	.01
Pre-needle pain score	.01	.01	.62	.54	.06	.09	.61	.54

Note. p-value for significance is p< .0125 based with the Bonferonni correction.

Table 7

Estimates from 6-month model predicting pain-related anticipatory distress at preschool

Variable	Un-standardized estimate	*SE*	*Z*	*p*	Standardized estimate	*SE*	*Z*	*p*
Indicators of preschool pain-related anticipatory distress factor								
FLACC	1.00	.00	-	-	.98	.03	28.85	<.001
Child distress verbalizations	.98	.08	13.02	<.001	.60	.05	12.36	<.001
Cry	.68	.09	7.80	<.001	.80	.05	16.90	<.001
Indicators of pain reactivity at 6 months								
6-month needle MBPS	1.00	.00	-	-	1.00	.00	-	-
6-month 1 min MBPS	1.00	.00	-	-	.33	.03	11.76	.00
6-month 2 min MBPS	1.00	.00	-	-	.35	.03	12.06	.00
6-month 3 min MBPS	1.00	.00	-	-	.35	.03	11.03	.00
Indicators of pain regulation at 6 months								
6-month needle MBPS	.00	.00	-	-	.00	.00	-	-
6-month 1 min MBPS	.75	.05	14.88	.00	.51	.04	11.66	.00
6-month 2 min MBPS	.90	.04	21.93	.00	.65	.05	12.29	.00
6-month 3 min MBPS	1.00	.00	-	-	.73	.06	12.30	.00
Prediction of anticipatory distress				.				.
Intercept (reactivity)	.02	.02	1.06	.29	.10	.09	.1.08	.28
Slope (regulation)	.02	.01	1.24	.22	.15	.12	1.22	.22
Pre-needle pain score	-.005	.01	-.53	.60	-.06	.11	-.52	.60

Note. p-value for significance is p< .0125 based with the Bonferonni correction.

Table 8

Estimates from 12-month model predicting pain-related anticipatory distress at preschool

Variable	Un-standardized estimate	*SE*	*Z*	*p*	Standardized estimate	*SE*	*Z*	*p*
Indicators of preschool pain-related anticipatory distress factor								
FLACC	1.00	.00	-	-	.97	.03	34.01	<.001
Child distress verbalizations	.99	.08	13.29	<.001	.60	.05	12.67	<.001
Cry	.69	.09	8.01	<.001	.81	.05	17.98	<.001
Indicators of pain reactivity at 12 months								
12-month needle MBPS	1.00	.00	-	-	.87	.16	5.42	.00
12-month 1 min MBPS	1.00	.00	-	-	.49	.10	4.94	.00
12-month 2 min MBPS	1.00	.00	-	-	.46	.10	4.84	.00
12-month 3 min MBPS	1.00	.00	-	-	.38	.08	4.47	.00
Indicators of pain regulation at 12 months								
12-month needle MBPS	.00	.00	-	-	.00	.00	-	-
12-month 1 min MBPS	.61	.06	10.53	.00	.47	.07	6.87	.00
12-month 2 min MBPS	.88	.06	15.07	.00	.64	.09	6.97	.00
12-month 3 min MBPS	1.00	.00	-	-	.59	.09	6.78	.00
Prediction of anticipatory distress				.				.
Intercept (reactivity)	.03	.01	1.89	.06	.15	.07	2.21	.03
Slope (regulation)	.01	.01	.32	.75	.04	.13	.32	.75
Pre-needle pain score	.00	.01	.02	.98	.002	.10	.02	.98

Note. p-value for significance is p< .0125 based with the Bonferonni correction.

Table 9. Correlations and Means

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Baseline pain 2-months	1	**.19** (0.03)	**.22** (.01)	.127 (.19)	-.059 (.53)	.075 (.44)	.14 (.10)	-.07 (.43)	-.01 (.89)	.05 (.58)	.01 (.89)	.08 (.35)	-.02 (.85)	.07 (.44)	**-.19** (.03)
2. Needle pain 2-months	-	1	**.27** (<.001)	.103 (.28)	-.01 (.96)	-.06 (.51)	.07 (.40)	.11 (.22)	-.102 (.24)	-.12 (.16)	.08 (.39)	-.04 (.68)	**-.21** (.02)	.01 (.96)	-.12 (.17)
3. One minute pain 2-months	-	-	1	.09 (.38)	.09 (.37)	.06 (.54)	.02 (.87)	.09 (.31)	.15 (.11)	-.03 (.77)	.04 (.65)	**.21** (.02)	-.00 (.97)	-.01 (.93)	**-.22** (.02)
4. Baseline pain 12-months	-	-	-	1	**.29** (<.001)	**.35** (<.001)	-.10 (.21)	.05 (.56)	.05 (.53)	-.06 (.45)	.15 (.05)	.11 (.14)	**-.17** (.03)	**-.34** (<.001)	-.02 (.87)
5. Needle pain 12-months	-	-	-	-	1	**.45** (<.001)	**-.16** (.04)	.07 (.36)	.06 (.40)	-.06 (.45)	**.20** (.01)	**.17** (.02)	.01 (.90)	**-.21** (<.001)	.03 (.78)
6. One minute pain 12-months	-	-	-	-	-	1	-.10 (.20)	.09 (.24)	.03 (.66)	-.02 (.78)	**.19** (.01)	.11 (.15)	.00 (.97)	**-.28** (<.001)	-.02 (.82)
7. HCP Distress Promoting	-	-	-	-	-	-	1	.02 (.84)	.11 (.12)	.10 (.17)	-.11 (.11)	**-.16** (.03)	-.10 (.23)	.02 (.90)	-.04 (.65)
8. Caregiver Distress Promoting	-	-	-	-	-	-	-	1	.11 (.13)	.01 (.93)	.07 (.33)	-.02 (.77)	-.04 (.54)	-.06 (.45)	.08 (.36)
9. Sex	-	-	-	-	-	-	-	-	1	-.01 (.91)	.05 (.46)	-.02 (.80)	-.08 (.27)	-.05 (.51)	-.03 (.75)
10. Age	-	-	-	-	-	-	-	-	-	1	.06 (.44)	-.06 (.37)	.05 (.46)	-.10 (.18)	-.05 (.57)
11. Child Worry	-	-	-	-	-	-	-	-	-	-	1	**.27** (<.001)	.03 (.65)	.01 (.95)	.09 (.33)
12. Parent Worry	-	-	-	-	-	-	-	-	-	-	-	1	.04 (0.54)	.05 (.51)	-.04 (.65)
13. Events	-	-	-	-	-	-	-	-	-	-	-	-	1	.14 (.07)	.07 (.45)
14. Caregiver EAS 12months	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**.46** (<.001)
15. Caregiver EAS 2 months	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1
Means	2.89	8.78	5.94	3.63	8.21	5.97	.04	.07	94-F 108-M	4.61	3.96	2.37	.17	93.58	91.90
SD	1.95	.85	2.47	2.36	1.30	2.36	.07	.09	-	.55	3.30	2.89	.50	11.23	12.19
Range	0-10	0-10	0-10	0-10	0-10	0-10	0-1	0-1	1-M 2-F	3.92-6.58	0-10	0-10	0-4	28-116	28-116
N	132	133	123	171	176	172	202	202	202	202	201	201	202	176	132

Note: P-values in parentheses. Significant correlations are bolded.

Table 10

Completely standardized results of measurement model

Variable	Standardized estimate	SE	*Z*	*p*
2-month cumulative distress				
Baseline pain 2-months	.40	.10	4.07	<.001
Needle pain 2-months	.47	.14	3.32	.001
One-minute pain 2-months	.59	.18	3.26	.001
12-month cumulative distress				
Baseline pain 12-months	.48	.06	8.27	<.001
Needle pain 12-months	.61	.07	8.88	<.001
One-minute pain 12-months	.74	.08	9.87	<.001
Preschool anticipatory distress				
FLACC	.96	.03	33.05	<.001
Child distress verbalizations	.60	.05	12.67	<.001
Cry	.81	.05	17.91	<.001

Table 11

Estimates from final model predicting pain-related anticipatory distress at preschool

Variable	Un-standardized estimate	*SE*	*Z*	*p*	Standardized estimate	*SE*	*Z*	*p*
2-month cumulative distress								
Baseline pain 2-months	1.00	.00	-	-	.46	.10	4.42	<.001
Needle pain 2-months	.37	.18	2.00	.05	.38	.10	3.84	.002
One minute pain 2-months	1.60	.73	2.20	.03	.58	.14	4.22	<.001
12-month cumulative distress								
Baseline pain 12-months	1.00	.00	-	-	.55	.07	7.96	<.001
Needle pain 12-months	.61	.18	3.38	.001	.62	.08	8.14	<.001
One minute pain 12-months	1.23	.26	4.69	<.001	.68	.08	8.66	<.001
Preschool anticipatory distress								
FLACC proportion	1.00	.00	-	-	.97	.04	27.90	<.001
Child distress behaviour	.995	.09	11.15	<.001	.60	.05	12.14	<.001
Cry proportion	.68	.10	6.86	<.001	.79	.06	13.42	<.001
Predicting preschool anticipatory distress								
2 month cumulative distress	.06	.03	1.76	.08	.25	.14	1.77	.08
12 month cumulative distress	-.008	.02	-.41	.68	-.05	.13	-.41	.68
Healthcare provider distress promoting	.19	.18	1.05	.29	.06	.06	1.05	.29
Caregiver distress promoting	1.03	.23	4.44	<.001	.49	.10	4.84	<.001
Sex	.02	.03	.83	.40	.05	.06	.83	.40

Variable	Un-standardized estimate	*SE*	*Z*	*p*	Standardized estimate	*SE*	*Z*	*p*
Age	.05	.02	2.47	.01	.15	.06	2.49	.01
Child worry	.004	.005	.89	.38	.07	.08	.87	.39
Parent worry	.002	.005	.38	.70	.03	.07	.39	.70
Events	.05	.03	1.83	.07	.13	.07	1.91	.06
Emotional Availability 2 months	.006	.002	2.46	.01	.35	.14	2.42	.02
Emotional Availability 12 months	-.006	.002	-2.52	.01	-.33	.13	-2.49	.01
Healthcare Provider Distress Promoting								
12-month cumulative distress	-.007	.006	-1.91	.23	-.14	.11	-1.31	.19
Parent worry	-.003	.001	-2.38	.02	-.13	.05	-2.53	.01
Child Worry								
12-month cumulative distress	.57	.24	2.40	.02	.23	.09	2.64	.008
Parent worry	.27	.09	2.97	.003	.23	.07	3.09	.002
Parent Worry								
2-month cumulative distress	.74	.43	1.71	.09	.23	.12	1.91	.06
12-month cumulative distress	.34	.21	1.66	.10	.16	.09	1.85	.07

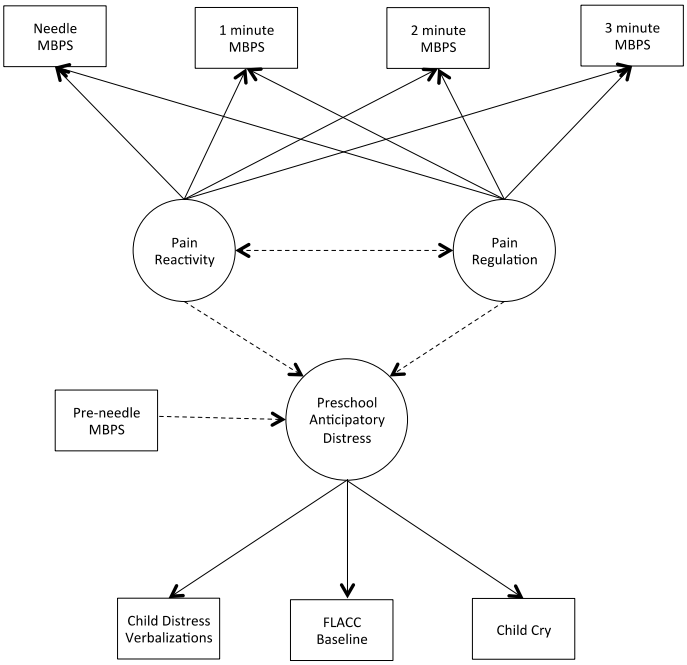

Figure 1. Child pain-related anticipatory distress at preschool conditioned on infant needle pain (intercept) and infant regulation (slope) across the vaccination appointment. Rectangles represent observed measures, whereas ovals represent latent factors. The same model was repeated at 2, 4, 6, and 12 months of age. Solid lines represent significant paths, whereas dotted lines represent non-significant paths. *Note*. N=202, *$p < .0125$.

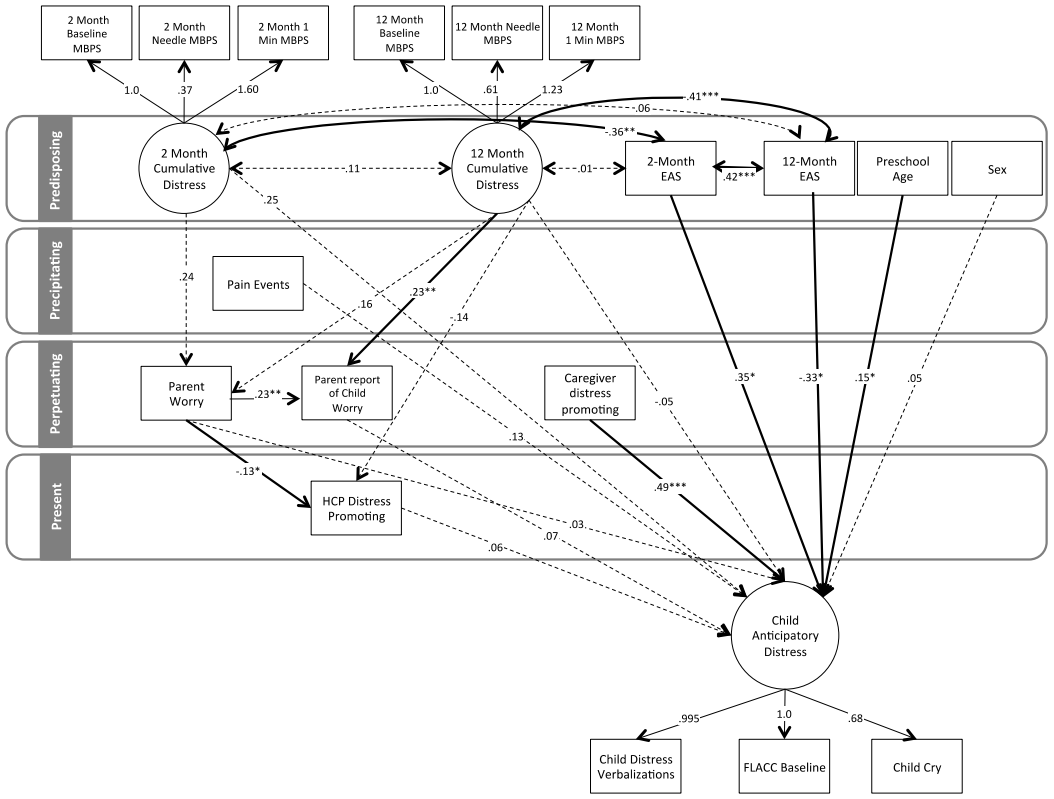

Figure 2. Anticipatory distress at preschool conditioned on 2-month cumulative distress, 12-month cumulative distress, 2-month emotional availability, 12-month emotional availability, preschool age, child sex, pain events, parent worry, parent report of child worry, caregiver distress promoting behaviours, and health-care distress promoting behaviours. Rectangles represent observed variables, whereas ovals represent latent variables. Single-headed arrows pointing away from latent variables towards observed measures (factor loadings) represent unstandardized parameter estimates. Double-headed arrows represent correlations. Single-headed arrows represent standardized estimates. Solid lines represent significant paths, whereas dotted lines represent non-significant paths. *Note.* N=202, *p < .05, **p < 0.01, ***p <.001; HCP: Healthcare provide

Chapter 5. Conclusion

This dissertation consisted of three studies to systematically create a coherent set of work that contributed to the conceptualization and understanding of factors that predict pain-related anticipatory distress at the preschool vaccination. Study 1 involved a systematic review of the factors predicting pain-related anticipatory distress to painful medical procedures in children using the developmental psychopathology framework. A narrative synthesis of the evidence indicated factors that predicted anticipatory distress, did not predict anticipatory distress, or factors that had inconclusive findings. Study 2 examined how well preschool pain-related anticipatory distress was predicted by infant pain responding at 2, 4, 6 and 12 months of age. In Study 3, using a developmental psychopathology framework, longitudinal analyses examined the predisposing, precipitating, perpetuating, and present factors that predicted anticipatory distress during routine preschool vaccinations. A brief summary of all the analyses and results over all three studies was prepared for the dissertation reader and can be found in Appendix A. The following discussion summarizes the findings from these three studies in greater detail, synthesizes their cumulative impact, and discusses limitations and future directions for research.

Study 1: Systematic Review of Predisposing, Precipitating, Perpetuating, and Present Factors Predicting Anticipatory Distress to Painful Medical Procedures

The overarching goal of Study 1 was to qualitatively synthesize the literature on factors that predict anticipatory distress to painful medical procedures using predisposing, precipitating, perpetuating, and present factors as a framework. Figure 2 from Chapter 2 highlights the key findings from the review, providing the overall findings, risk of bias, and the number of studies included in the synthesis. For the predisposing, perpetuating, precipitating, and present factors, where possible, child, parent, healthcare provider, and contextual factors were identified. The 31

factors that were included in the review were categorized by the two lead authors (NR and RPR) based on the outcome variables identified in the study. Although factors with two studies or more were included in Figure 2 for parsimony, all factors elucidated by the review were described. Given the narrative nature of the review, across factors when there was conflicting or inconsistent evidence within a category, an overall decision was made based on the majority of the evidence. When a clear majority of studies did not have a consistent finding, results were deemed to be inconclusive. Finally, with regards to risk of bias, since no tools for evaluating observational studies were available at the time of this systematic review, an abbreviated version of the Cochrane Collaboration risk of bias tool was used. Since the majority of the studies included in this review were observational in nature and did not randomize participants to groups, the abbreviated format of the tool was used so as not to disadvantage the observational studies. It should be noted that an observational study does inherently have a higher risk of bias than a randomized control-trial. Thus, determinations of low, moderate or high bias must ultimately be contextualized by the lack of experimental manipulation in observational studies.

Predisposing factors

In terms of predisposing factors that are hypothesized to increase the risk of the occurrence of pain-related anticipatory distress, the most substantial number of studies regarded child factors. Predisposing child factors that were positively associated with pain-related anticipatory distress were pre-existing child psychopathology (such as internalizing difficulties including anxiety and depression) and difficult child temperament. Both of these findings support previous theoretical work from the anxiety literature indicating that behaviour inhibition and an anxious temperament are associated with later development of anxiety (Vasey & Dadds, 2001). Yet, child sex, race, having siblings, and birth order were not associated with increased

likelihood of pain-related anticipatory distress in children in the review. Some past research on general anxiety has suggested girls are more susceptible to the development of anxiety than boys; however, this difference has not been reported in all studies (Vasey & Ollendick, 2000). Lastly, age and child attachment style had inconclusive results. The findings on age do not support broader literature indicating that younger children experience more anxiety than older children. Methodological factors may also have contributed to differences in results in that the majority of studies did not examine a discrete age range, but rather averaged over large age ranges of up to 15 years.

Regarding parent predisposing factors to pain-related anticipatory distress, parent anxious predisposition and parents' own experience and fear of painful medical procedures were positively associated with child pain-related anticipatory distress. These findings are consistent with the broader anxiety literature indicating that modeling and information transmission were the most common modes of acquisition reported by children (Rachman, 1977; Vasey & Ollendick, 2000). Previous literature has hypothesized that parents' anxiety is communicated to children via behaviour. This behaviour may leave children feeling unsupported and fearful in anxiety-provoking situations. Whether parent education predicts child anticipatory distress is unknown, which may be a product of how parent education was measured across studies.

In terms of contextual predisposing factors, our review did not find that previous hospitalizations were associated with increased pain-related anticipatory distress in children. It may be that hospital visits were too general to result in conditioning of a fear response. Very few studies focused on this area; thus, more work is needed.

Precipitating factors

The review identified two child factors as precipitating pain-related anticipatory distress. Specifically, previous pain events and previous pain behaviour were associated with an increased likelihood of pain-related anticipatory distress. This finding is consistent with anxiety literature purporting that direct conditioning is an important mechanism by which fear and anxiety develop (Rachman, 1977). This finding is also consistent with research conducted in infants and young children that has demonstrated that a higher number of repeated painful procedures is associated with higher pain at a subsequent procedure and distress in anticipation of pain (Taddio et al., 2002).

Perpetuating factors

There were both child and parent perpetuating factors that were associated with pain-related anticipatory distress. Child cognitions, including high threat appraisal, lower perceived control, and high aversion to the procedure were all associated with higher child anticipatory distress. Based on pathways of development of fear acquisition, it has been shown that cognitive distortions and biases about a procedure are associated with increased fear and anxiety (Vasey & Dadds, 2001). There were inconclusive results for child knowledge, child coping style, and other child behaviours. These inconclusive results highlight the need for additional research in these areas. Regarding parent perpetuating factors, parent distress-promoting behaviour, distress in the situation, and anticipation of distress were all associated with increased pain-related anticipatory distress in children. Similar to previous anxiety literature, parent distress-promoting behaviours that include criticism and reassurance are associated with higher fear and anxiety in children, whereby these behaviours are associated with onset and maintenance of child anxiety (Bogels & van Melick, 2004).

Present factors

Of the three present factors that were identified in the review as influencing pain-related anticipatory distress, parent presence and other environmental factors had inconclusive results. Furthermore, parent presence did not demonstrate consistent results. One study (Kain et al., 2006) suggested that one reason for this inconsistency may be that the parental impact depends on whether the parent is anxious themselves during the procedure. As noted previously, parents who are anxious are less available for their children and may even engage in behaviours which promote anxiety in the child. Regarding variables that positively influence child pain-related anticipatory distress, healthcare provider distress-promoting behaviour was associated with pain-related anticipatory distress. This finding again supports literature suggesting that behaviours such as criticism by adults directed towards children are associated with increased fear and anxiety (Bogels & van Melick, 2004).

Predicting Preschool Pain-Related Anticipatory Distress: Study 2 and 3 Contextualized by the Systematic Review

Relative contribution of pain responding from the first year of life (Study 2).

This was the first longitudinal study to use infant pain-related distress during vaccination from the first year of life to predict anticipatory distress about the preschool vaccination. A sample of 202 caregiver-child dyads (from the OUCH cohort) was observed during their infant and preschool vaccinations and was used in structural equation models examining whether pain reactivity (initial reactivity post-needle) and change in infant pain-related distress across the vaccination appointment (needle to 3-minutes post-needle) during each of four ages (2, 4, 6, and 12 months) predicted anticipatory distress at the preschool age. The baseline (i.e., pre-needle) pain-related distress score at each age was also used as a separate predictor. In each model, pain-

related distress regulation was operationalized as the change in pain scores over the course of the immunization appointment (from needle to 3 minutes post-needle). Pre-needle pain-related distress, pain reactivity, and pain regulation from any of the ages across the first year of life did not predict anticipatory distress at preschool. Results suggest that infant pre-needle pain-related distress, pain reactivity, and pain regulation are minimally related to anticipatory distress at the preschool age.

These results were in contrast to hypotheses which predicted that higher pre-needle distress and pain reactivity, as well as poor regulation during infancy, would be associated with higher levels of pain-related anticipatory distress at the preschool age. The basis for these hypotheses were two-fold. First, because previous literature has demonstrated a link between repeated pain experiences and subsequent increased anticipatory distress (Taddio et al., 2002), it was thought that infants, who experienced higher pain-reactivity in infancy, would have higher anticipatory distress at preschool. Regarding pain regulation, it was hypothesized that infants who had difficulty developing emotion regulation over the first year of life would continue to have difficulties with affect regulation into the preschool years (Bradley, 2003). These hypotheses were not supported by the current study. Perhaps the developmental stage of the first twelve months of life does not allow more permanent cognitive schemas to form that influence pre-needle distress at the preschool age, which is three to four years later. In studies that have demonstrated a link between previous painful procedures and anticipatory distress in infants and young children, the time window was much shorter (e.g., within the first 24 hours of life; Taddio et al., 2002). Furthermore, previous research has shown that there is extensive development in pain responses over the first year of life that likely limits the predictive validity of these pain behaviours for future pain behaviours (Pillai Riddell et al., 2013).

Relative contribution of factors from infancy and preschool (Study 3). In Study 3, using a developmental psychopathology framework, longitudinal analyses examined the predisposing, precipitating, perpetuating, and present factors that were associated with the development of anticipatory distress during routine preschool vaccinations. Anticipatory distress was established as the dependent latent variable. Subsequently, child age, cumulative pain-related distress from 2 months of age, cumulative distress from 12 months of age, pain events, parent emotional availability at 2 months of their child's age, parent emotional availability at 12 months of child age, child sex, caregiver distress-promoting behaviour, healthcare provider distress-promoting behaviour, parent report of child worry, and parent worry were all examined as predictors of pain-related anticipatory distress at the preschool age. Despite the findings from Study 2, for the sake of testing a comprehensive model, cumulative pain experiences at 2 and 12 months of age (a slightly different operationalization of pain was used from the infant appointments for the sake of model parsimony) and previous pain events would positively predict pain-related anticipatory distress at preschool. Based on results from the review, it was also hypothesized that caregiver emotional availability at 2 and 12 months of child age would negatively predict pain-related anticipatory distress. Child age was hypothesized to negatively predict pain-related anticipatory distress. Perpetuating factors such as parent worry, parent report of child worry, and parent distress-promoting behaviours were hypothesized to positively predict pain-related anticipatory distress. Finally, healthcare professional distress-promoting behaviour was hypothesized to positively predict pain-related anticipatory distress at preschool.

An explanatory model was developed whereby 40% of the variance in preschool anticipatory distress was explained. In partial support of hypotheses, parental behaviours from infancy and preschool accounted for the most variance in child anticipatory distress at preschool.

Parent behaviours from the infant and preschool vaccinations, as well as child age, were the only significant predictors of pain-related anticipatory distress at the preschool age. Parents' distress-promoting behaviours at the preschool appointment positively predicted child pain-related anticipatory distress and accounted for the most variance (19.3%) in pain-related anticipatory distress as compared to all other predictors entered in the model. This finding is consistent with the broader anxiety literature that has indicated that parent distress-promoting behaviour has been associated with increased anxiety in children (Bogels & van Melick, 2004). Caregiver emotional availability at 2 and 12 months of child age accounted for 6.4% and 6.1% of the variance of pain-related anticipatory distress at preschool, respectively, and were the only variables from the infant vaccinations that predicted pain-related anticipatory distress. The finding for 12-month EA is consistent with developmental and anxiety literature suggesting that caregiver sensitivity to distress is related to fewer behavioural problems, higher social competence, and better affect regulation (Bradley, 2003).

Somewhat contrary to hypotheses, higher emotional availability at 2 months predicted higher pain-related anticipatory distress at preschool. This result is despite concurrent relationships between 2-month pain scores and EA being in the expected direction (i.e. higher sensitivity is concurrently associated with lower pain responses). Past research by our lab has shown that the vast majority of infants at 2-months of age display high pain responses and regulate somewhat similarly (Pillai Riddell et al., 2013). We hypothesize that this lack of differentiation among infants suggests a less organized behavioural response pattern to regulating from noxious stimulation. Thus, it could be that parents who are less attuned to their infant's cues during the very early developmental period where infant behaviour is still organizing (i.e. parents displayed behaviours less contingent to their infant's behaviours) actually

show an adaptive early parental responding pattern because the infant's distress response may not simply be due to nociception but also due to immature abilities to inhibit high distress after a painful stimulus. Thus, at 2 months, lower parental EA results in lower anticipatory distress at preschool because these parents were able to discern context from child pain factors. This speculation must be contextualized by the fact that these were low risk dyads in our sample and while there was variability in EA, very few parents would be considered significantly suboptimal. This result may also be explained by Type I error.

Child psychopathology which was examined as a predisposing variable in the systematic review can to some extent be mapped on to child worry, which was examined as a perpetuating factor in Study 3. The results from the systematic review indicated that child psychopathology (e.g. anxiety, internalizing difficulties) positively predicted anticipatory distress to painful medical procedures. Results from Study 3 did not support this finding. Child worry, as reported by parents, did not significantly predict child anticipatory distress to vaccination. In the context of the review, child psychopathology was operationalized as pre-existing internalizing (e.g. anxiety) or behavioural problems that would predispose a child to anticipatory anxiety during a painful medical procedure (e.g. Ericsson, Wadsby, & Hultcrantz, 2006; Davidson et al., 2006; Fortier et al., 2011; Kiley & Polillio, 1997; Lumley et al., 1993). In Study 3, child worry was operationalized as parent report of the child's worry about the vaccination, which would only rarely be an indication of child psychopathology (i.e. phobic levels of worry). In Study 3, parent report of child worry was used due to the age of the children included and research that has suggested that children younger than 8 or 9 years of age have difficulty with self-report of distress and pain (von Baeyer & Spargud, 2007; Chan & von Baeyer 2016). Had the current

study examined children who were older than preschool age, we may have found results consistent with the systematic review.

One precipitating child factor from the systematic review that was examined in Study 3 is experience with previous pain events. In Study 1, experience with previous pain events positively predicted pain-related anticipatory distress; however, this same relationship was not found in Study 3. One possible explanation for this difference is that for several studies in the systematic review, the previous painful event constituted a surgery or a negative painful procedure. In Study 3, there were four potentially painful events that were included in the measure of cumulative previous pain events (circumcision, broken bones, hospitalization, and operations); however, the frequency of these behaviours was generally quite low as the mean occurrence was 0.17 with a possible range of 0 to 4. Children who have experienced more frequent or serious painful procedures may have an increased likelihood of experiencing pain-related anticipatory distress, as well as children who have had a recent negative experience (Jacobson et al., 2001).

The finding that child age positively predicted child anticipatory distress was not consistent with hypotheses that younger children would experience more anticipatory distress; however, the age range used in the current study was quite limited and this finding may be attributed to the measurement method for anticipatory distress. One of the variables that contributed to the latent factor of anticipatory distress was child distress verbalizations. It may be that older children were more verbal and had more developed vocabularies to be able to express their fear and anxiety than younger children.

Final Integrative Comments in the Context of the Developmental Psychopathology Model

The findings from Studies 2 and 3 have been discussed in relation to the general developmental and anxiety literatures. The goals of Study 2 and Study 3 were to systematically examine using a longitudinal cohort whether there was evidence to substantiate some of the associations outlined in the systematic review. Not all 31 factors identified in Study 1 were subsequently tested in Study 2 and Study 3. Ultimately, choices had to be made balancing inclusivity and parsimony when creating the models and not all factors were available for study. Of significant note is that although we measured child-self report of anxiety pre-needle as part of the larger longitudinal study, it was not used in the dissertation as we were unable to confirm that the obtained child self-report was reliable and valid, which is wholly in line with previous work on child self-reports (Bearden et al., 2012, Chan & von Baeyer, 2016). A discussion of these findings within a developmental psychopathology context follows.

The developmental psychopathology model emphasizes that no one predictor or risk factor accounts for the development of maladaptation, but rather there are numerous pathways to a certain outcome (Sroufe & Rutter, 1984). The theory also highlights the importance of examining the impact of risk, vulnerability, and protective factors on the development of maladaptation. The overarching goal of this dissertation was to systematically examine the risk and protective factors that predict anticipatory distress in a unified way that facilitates the understanding of the impact of a multitude of factors on the occurrence of anticipatory distress in early childhood. Early childhood is a particularly salient time to examine the factors that predict anticipatory distress, as most needle fears and phobias have been reported to have an onset between 5 and 10 years of age (McMurtry et al., 2015).

Based on the 31 factors elicited in the systematic review, most were child-specific factors but none of the articles in the review from the early childhood period were similar to the scope of the current study (longitudinal and multivariate modeling). One of the most important findings of our work, which culminated in the analyses of Study 3, was that parent factors predicted the most variance in preschool anticipatory distress. One possible explanation for this finding is that the developmental differences between the age of the children included in the review and the age of the children included in Study 3. The systematic review included children between 0 and 18 years of age, while Study 3 examined pain-related anticipatory distress in preschool-age children (i.e., ages 4 and 5). Older children are able to provide self-report of their feelings of affective states (Chan & von Baeyer, 2016) and are often considered more differentiated from their parents. The results from this series of studies converge to suggest that parent behaviours, both in infancy and at preschool, were the most important predictors of pain-related anticipatory distress.

Limitations

There are several limitations to note in the current studies. The inclusion criteria for Study 2 and Study 3 required caregivers to be fluent in English so that they could understand and complete consent forms and the demographic questionnaires. The caregivers included in this study were also highly educated, which indicates that our results may not generalize to less-educated caregivers and more high-risk populations. Additionally, although a broad age range was examined for the systematic review (children and adolescents from 0 to 18 years), a more restricted age range was examined in Study 2 and Study 3. Four and five years of age is on the lower end of the age range where needle fear and phobia are said to start to develop. Study 2 and Study 3 may have captured the precursors of early anticipatory distress, but not necessarily the precursors of distress at later developmental periods. Future longitudinal research should

examine predictive factors when children are older such as when they are receiving HPV immunizations in grades 7 and 8. This research is of particular importance because research has demonstrated that children under the age of 7 years are much less reliable in their reports of pain than older children (Tsze, von Baeyer, Bulloch, & Dayan, 2013), which we confirmed in this study.

Additionally, with regards to the systematic review, although risk of bias was evaluated for the outcome variables, arguable the risk of bias of predictor variables (i.e. predisposing, precipitating, perpetuating, and present) could also have been evaluated to have a more comprehensive assessment of risk of bias.

Lastly, in Study 3, previous pain events were reported by parents, rather than gathered from a medical chart, which means that we relied on parents to recall the painful medical procedures their child has undergone. Furthermore, there is some evidence that it may not in fact be the painful procedure itself that leads to anticipatory distress, but rather whether the experience was negative and what the child's memory of the experience was (Bijttebier & Vertommen, 1998). Future research should include a parent-report question about the child's affective experience of previous painful events as they happen (as retrospective autobiographical memory of preschoolers is still limited).

Clinical Implications and Future Directions

Given the association of parent behaviour with child anticipatory distress, the inclusion of parents in interventions to reduce needle fear is an important future direction. Until recently, limited attention had been paid to evidence-based intervention for needle fears and anxiety in children. Recently, a multidisciplinary team of Canadian researchers, Help Eliminate Pain in KIDS (HELPinKIDS), published a clinical practice guideline on exposure-based interventions

for the management of individuals with high levels of needle fear across the life span (McMurtry et al., 2016). Exposure-based therapy is a psychological and behavioural intervention that involves exposing an individual to a feared stimulus in a controlled way that eventually allows them to tolerate the stimulus while managing their distress. Exposure therapy is one of the most well supported evidence-based interventions for needle fear and anxiety. Based on the clinical practice guideline, exposure-based therapy was recommended for children older than 7 years with high levels of needle fear (McMurtry et al., 2016). Although the practice guideline did not report any randomized controlled trials that investigated the use of exposure-based interventions for children under 7 years, the authors did provide clinical recommendations for intervention for younger children. One key clinical recommendation for very young children was that it is important to include parents in the exposure-based therapy. The findings from Study 3 directly support this recommendation. Although parental presence alone has not uniformly been found to be helpful (Kain, Caldwell-Andrews, Maranets, Nelson, & Mayes, 2006; McMurtry et al., 2016; Pillai Riddell et al., 2015), coaching the parent as the mechanism for intervention may be useful. Furthermore, substantial evidence has shown that child fear and anxiety are maintained by parent behaviour and vicarious learning (Du et al., 2008). Providing education and coaching to counteract these effects may be essential for reducing pain-related distress in young children. For example, some previous research has indicated that parents who use verbal reassurance, were rated to be more fearful by their children when they were using reassurance (McMurtry, 2009). Identifying which parent behaviours should be avoided and which behaviours are helpful is important for guiding clinical interventions.

In addition to interventions that may include an exposure component, findings from the current research demonstrate just how critical caregiver behaviours during early infant

vaccinations are for predicting how a child approaches the preschool immunization. It is striking that the longitudinal relationships between caregiver emotional availability during infancy and preschool anticipatory distress are almost equal to the concurrent relationship between caregiver emotional availability and infant distress within the infant vaccination appointments. Future research should use the parent as a primary mechanism for intervention with regard to pain-related distress in children (Pillai Riddell, Gennis, Taddio, & Racine, 2016). Borrowing from the children's mental health literature, some of the most successful and evidence-based interventions for child emotional and behaviour difficulties have been interventions that place emphasis on improving the quality of the parent-child relationship and changing parent-child interaction patterns (Eyberg, Boggs, & Algina, 1995). It is important for future research to investigate interventions that involve parent coaching, reflection, and provide the opportunity for parents to change the way in which they interact with their children during potentially threatening and stressful situations.

The developmental psychopathology framework highlights the importance of understanding transactional relationships through the examination of mediating and moderating variables. Although the current analysis was one of the first to investigate multiple concurrent and longitudinal factors predicting pain-related anticipatory distress in children, future research should investigate the interactions among such variables. For example, research could investigate whether parent anxiety interacts with parent behaviour to impact anticipatory distress rather than having additive effects on anticipatory distress.

The systematic review in Study 1 identified a number of factors with inconclusive results, indicating that the literature in this area is mixed. Areas such as child attachment style, parent education, parent presence, child knowledge, and child coping style are factors that could be

further examined for their potential impact on anticipatory distress to painful medical procedures in children. Particularly relevant to clinical intervention would be the evaluation of psycho-education provided to parents and children prior to a painful medical procedure or the instruction of coping strategies. These cost-effective and time-limited interventions may be useful for reducing the risk of pain-related anticipatory distress in children. Another area that had a limited number of factors included from the review was healthcare provider factors. The behaviour and role of healthcare providers have been under-examined; yet, healthcare providers play an important role in interacting with children and their families during painful medical procedures. One potential future direction, involves a more in-depth analysis of certain research domains organized in the current systematic review. While beyond the score of the current project, for factors where there was a large amount of research that has been conducted (e.g. . age) but inconclusive results, a future direction would be to conduct more analyses of the individual articles. One could examine the effect sizes of studies, in the context of sample sizes, in order to formulate more conclusive findings.

Conclusions

Having examined predisposing, precipitating, perpetuating, and present factors across the individual child, parent, and healthcare provider, results from this series of studies indicate that parent behaviour was the strongest predictor of child pain-related anticipatory distress. Parent behaviour was the only factor that demonstrated consistent findings across Chapters 2 and 4, whereby parent behaviours that were distress-promoting were associated with increased anticipatory distress. Regarding caregiver emotional availability when the child is 12-months of age, more sensitive caregivers had children who had lower anticipatory distress at the preschool time point. Overall, these findings ultimately stress the importance of including parents in

intervention and prevention efforts for pain-related anticipatory distress, especially in infants and young children. Initiatives to reduce anticipatory distress in young children should include opportunities to guide parents in order for them to be optimally positioned to support their children prior to and during painful medical procedures.

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Appendix A

Summary of Analyses and Results

Study 1: (Racine, N., Pillai Riddell, R., Khan, M., Calic, M., Taddio, A. & Tablon, P. (2016). Systematic review: Predisposing, precipitating, perpetuating, and present factors predicting anticipatory distress to painful medical procedures in children. *Journal of Pediatric Psychology, 41*(2):159-181.)

Research Question: Which predisposing, precipitating, perpetuating, and present factors in the current literature predict child pain-related anticipatory distress?

Analysis: A search yielded 7088 studies, which were examined against inclusion criteria. 77 studies were included in the review.

Results: Narrative synthesis was used to apply a developmental psychopathology framework to the findings.

- 31 factors predicted child anticipatory distress to painful medical procedures.
- Factors associated with increased anticipatory distress:
    - Child psychopathology, difficult child temperament, parent distress-promoting behaviour, parent situational distress, previous pain events, parent anticipation of distress, parent anxious predisposition, previous parent experience of fear, healthcare provider behaviour, child cognitions, and child previous pain behaviour.
- Factors not associated with child anticipatory distress:
    - Child gender/sex, child race, having siblings, birth order, previous child hospitalization.
- Factors with inconclusive findings:
    - Child age, child attachment style, parent education, other contextual factors, parent presence, environmental factors, child knowledge prior to procedure, child coping style, and other child behaviours.

Study 2 and Study 3: Racine, N., Pillai Riddell, R., Flora, D., Taddio, A., Garfield, H., Greenberg, S. (in press). Predicting preschool pain-related anticipatory distress: The relative contribution of longitudinal and concurrent factors. *Pain*.

a) Part I (Study 2): Predicting preschool anticipatory distress to vaccination: Understanding the role of infant pain responding.

Research Question: Do pre-needle pain-related distress, pain reactivity, and pain regulation from 2, 4, 6, and 12 months of age during vaccination predict pain-related anticipatory distress prior to routine vaccination at the preschool age?

Analysis: Four latent growth models (LGM), one at each of the four time-points (2, 4, 6, and 12-months of age).

Results:

- Pre-needle pain-related distress at 2, 4, 6, or 12 months of age does not predict pain-related anticipatory distress at the preschool age.
- Pain reactivity, operationalized as needle pain, at 2, 4, 6, or 12 months of age does not predict pain-related anticipatory distress at the preschool age.
- Pain regulation, operationalized as the change in pain score from needle to 3-minutes post needle, at 2, 4, 6, or 12 months of age does not predict pain-related anticipatory distress at the preschool age.
- The four models accounted for between 3 and 10% of the variance in pain-related anticipatory distress at preschool.

b) Part II (Study 3): Predicting preschool anticipatory distress to vaccination using a developmental psychopathology framework.

Research Question: Examine longitudinal predisposing, precipitating, perpetuating, and present factors that predict pain-related anticipatory distress at the preschool age vaccination.

- Do child age, cumulative pain-related distress from 2-months of age, cumulative distress from 12-months of age, pain events, parent emotional availability at 2-months of age, parent emotional availability at 12-months of age, child sex, caregiver distress-promoting behaviour, healthcare provider distress-promoting behaviour, parent report of child worry, and parent worry predict pain-related anticipatory distress at the preschool time point?

Analysis: Structural equation modeling.

Results:

- The overall model explained 40% of the variance in pain-related anticipatory distress at the preschool time point.
- Factors that positively predicted child anticipatory distress:
    - Child age, parent emotional availability at 2-months of age, caregiver distress-promoting behaviour at the preschool time point.
- Factors that negatively predicted child anticipatory distress:
    - Parent emotional availability at 12-months of age.
- Factors that had no significant relation with anticipatory distress:
    - 2-month cumulative pain-related distress, 12-months cumulative pain-related distress, pain events, child sex, healthcare provider distress-promoting behaviour, parent report of child worry, parent reported worry.
- Cumulative pain-related distress at 12 months of age positively predicted parent report of child worry at the preschool time point.
- Parent worry negatively predicted healthcare provider distress-promoting behaviour at the preschool time point.
- Parent emotional availability at 2 months of age negatively predicted cumulative pain related distress at 2 months of age.
- Parent emotional availability at 12 months of age negatively predicted cumulative pain related distress at 12 months of age.
- Parent emotional availability at 2 and 12 months of age were positively related.

Appendix B

The searches for your topic were run using the OvidSP search platform in the following databases: MEDLINE, EMBASE, and EBM Reviews – Cochrane Central Register of Controlled Trials (CCTR) and PsycINFO to include articles indexed as of November 20, 2013.

The following tables record the search strategies and terms used in each of the databases. Search results were limited to evidence-based study design methodologies, publication years (2001+) and age group (children 0-18 years).

MEDLINE:

Set	History	Results	Comments
1	exp surgical procedures, operative/ or ambulatory surgical procedures/	2392734	Procedure Terms
2	exp infusion pumps/ or needles/	22422	Procedure Terms
3	administration, intravenous/ or infusions, intravenous/ or injections, intravenous/ or exp injections/	297882	Procedure Terms
4	catheterization/ or catheterization, central venous/ or catheterization, peripheral/ or catheterization, swan-ganz/ or cardiac catheterization/ or catheter ablation/ or urinary catheterization/ or intermittent urethral catheterization/	134789	Procedure Terms
5	blood specimen collection/ or phlebotomy/	12497	Procedure Terms
6	exp Vaccines/	178149	Procedure Terms
7	immunization programs/ or mass vaccination/ or Vaccination/ or ((immuniz* or immunis* or vaccinat*) adj2 (program* or campaign*)).ti,ab.	69256	Immunization program Terms
8	(venipuncture* or puncture* or aspirat* or insert* or catheter* or intravenous* or venous or cannula* or innoculation* or injection* or prick or pricked or pricks or jab or jabs or shot or shots).ti,ab.	1205457	Needle Procedure Terms
9	punctures/ or exp biopsy, needle/ or paracentesis/ or pericardiocentesis/ or spinal puncture/	70508	Procedure Terms
10	Or/1-9	3655227	Combined Procedure terms
11	pain/ or acute pain/ or nociceptive pain/	111949	Pain Terms

12	Pain Measurement/	62974	Pain terms
13	affect/ or anxiety/ or catastrophization/ or dental anxiety/ or fear/ or panic/	98940	Anxiety terms
14	anxiety disorders/ or phobic disorders/ or stress disorders, traumatic/ or stress disorders, post-traumatic/ or stress disorders, traumatic, acute/	51854	Anxiety disorder terms
15	crying/ or facial expression/	11408	Anxiety/distress terms
16	personality/ or temperament/	33905	Personality terms
17	(distress* or phobia* or scream* or scared or scare or scares or scaring or conditioning or somatization or somatisation or reactivity or "visual analog scale*" or "anxiety and pain scale*" or "fear scale*").ti,ab.	261826	Distress terms
18	or/11-17	559302	Outcomes results
19	(anticipator* or baseline* or "base-line*" or "base line" or "pre-operative*" or preoperative* or "pre-surgical*" or "pre-surger*" or "presurgical*" or "pre-surger*" or "pre-procedur*" or "preprocedur*").ti,ab. or pc.fs.	1532388	Anticipatory textword terms
20	10 and 18 and 19 and (pc or px).fs.	3721	Base Clinical Set 1
21	limit 20 to "all child (0 to 18 years)"	924	Base Clinical Set 1 limited to children
22	((anticipator* or baseline* or "base-line*" or "base line" or "pre-operative*" or preoperative* or "pre-surgical*" or "pre-surger*" or "presurgical*" or "pre-surger*" or "pre-procedur*" or "preprocedur*") adj2 (anxiety or anxious or distress* or fear* or sensitivity or phobia* or phobic*)).ti,ab.	2696	Base Clinical Set 2
23	limit 22 to "all child (0 to 18 years)"	704	Base Clinical Set 2 limited to children
24	21 or 23	1415	FINAL Results

EMBASE:

The search strategy for OvidSP Embase Classic+Embase <1947 to 2013 Week 46.

Set	History	Results	Comments

1	exp surgery/	3633665	Procedure Terms
2	infusion system/ or exp infusion pump/ or insulin pump/ or exp needle/	43608	Procedure Terms
3	exp infusion/ or exp injection/ or intravenous administration/ or drug administration/ or drug infusion/ or drug self administration/ or home intravenous therapy/ or drug administration route/ or intraarterial drug administration/ or intradermal drug administration/ or intramuscular drug administration/ or intraosseous drug administration/ or intravenous drug administration/ or parenteral drug administration/ or subcutaneous drug administration/	847626	Procedure Terms
4	catheterization/ or exp bladder catheterization/ or exp blood vessel catheterization/ or catheter ablation/ or heart catheterization/ or ureter catheterization/ or exp artery catheterization/ or exp vein catheterization/ or Swan Ganz catheter/	138973	Procedure Terms
5	blood sampling/ or phlebotomy/	128078	Procedure Terms
6	exp vaccine/	270513	Procedure Terms
7	mass immunization/ or exp vaccination/ or ((immuniz* or immunis* or vaccinat*) adj2 (program* or campaign*)).ti,ab.	136724	Immunization program Terms
8	(venipuncture* or puncture* or aspirat* or insert* or catheter* or intravenous* or venous or cannula* or innoculation* or injection* or prick or pricked or pricks or jab or jabs or shot or shots).ti,ab.	1708760	Needle Procedure Terms
9	puncture/ or paracentesis/ or pericardiocentesis/	30333	Procedure Terms
10	or/1-9	5735868	Combined Procedure terms Results
11	pain/ or application site pain/ or injection pain/ or injection site pain/ or postoperative pain/ or posttraumatic pain/ or pain assessment/ or nociceptive pain/	311079	Pain Terms
12	fear/ or anticipatory anxiety/ or exp anxiety/ or dental anxiety/	154388	Anxiety terms
13	anxiety disorder/ or catastrophizing/ or panic/ or exp phobia/ or posttraumatic stress disorder/ or acute stress disorder/	96631	Anxiety disorder terms
14	crying/ or facial expression/	17807	Anxiety/distress terms

15	personality/ or exp temperament/ or type a behavior/ or type b behavior/	107448	Personality terms
16	Or 11-15	631077	Outcomes results
17	anticipator* or baseline* or "base-line*" or "base line" or "pre-operative*" or preoperative* or "pre-surgical*" or "pre-surger*" or "presurgical*" or "pre-surger*" or "pre-procedur*" or "preprocedur*").ti,ab. or pc.fs.	1716486	Anticipatory textword terms
18	10 and 16 and 17	38140	Base Clinical Set 1
19	limit 18 to (infant <to one year> or child <unspecified age> or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	5179	Base Clinical Set 1 limited to children
20	((anticipator* or baseline* or "base-line*" or "base line" or "pre-operative*" or preoperative* or "pre-surgical*" or "pre-surger*" or "presurgical*" or "pre-surger*" or "pre-procedur*" or "preprocedur*") adj2 (anxiety or anxious or distress* or fear* or sensitivity or phobia* or phobic*)).ti,ab.	3587	Base Clinical Set 2
21	limit 20 to (infant <to one year> or child <unspecified age> or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>)	580	Base Clinical Set 2 limited to children
22	19 or 21	5506	FINAL Results

EBM Reviews - Cochrane Central Register of Controlled Trials

The search strategy for OvidSP EBM Reviews - Cochrane Central Register of Controlled Trials <October 2013> retrieved **1496** references of which **750** were unique and not duplicated in our other searches. This database consists exclusively of RCTs, no study design terms were used.

Set	History	Results	Comments
1	exp surgical procedures, operative/ or ambulatory surgical procedures/ or exp surgery/	77528	Procedure Terms
2	exp infusion pumps/ or needles/ or infusion system/ or exp infusion pump/ or insulin pump/ or	1472	Procedure Terms

	exp needle/		
3	administration, intravenous/ or infusions, intravenous/ or injections, intravenous/ or exp injections/ or exp infusion/ or exp injection/ or intravenous administration/ or drug administration/ or drug infusion/ or drug self administration/ or home intravenous therapy/ or drug administration route/ or intraarterial drug administration/ or intradermal drug administration/ or intramuscular drug administration/ or intraosseous drug administration/ or intravenous drug administration/ or parenteral drug administration/ or subcutaneous drug administration/	24371	Procedure Terms
4	catheterization/ or catheterization, central venous/ or catheterization, peripheral/ or catheterization, swan-ganz/ or cardiac catheterization/ or catheter ablation/ or urinary catheterization/ or intermittent urethral catheterization/ or exp bladder catheterization/ or exp blood vessel catheterization/ or catheter ablation/ or heart catheterization/ or ureter catheterization/ or exp artery catheterization/ or exp vein catheterization/ or Swan Ganz catheter/	4303	Procedure Terms
5	blood specimen collection/ or blood sampling/ or phlebotomy/	460	Procedure Terms
6	exp Vaccines/ or exp Vaccine	6067	Procedure Terms
7	immunization programs/ or mass vaccination/ or exp vaccination/ or ((immuniz* or immunis* or vaccinat*) adj2 (program* or campaign*)).ti,ab	1834	Immunization program Terms
8	(venipuncture* or puncture* or aspirat* or insert* or catheter* or intravenous* or venous or cannula* or innoculation* or injection* or prick or pricked or pricks or jab or jabs or shot or shots).ti,ab.	78211	Needle Procedure Terms
9	punctures/ or puncture/ or exp biopsy, needle/ or paracentesis/ or pericardiocentesis/ or spinal	1429	Procedure Terms

	puncture/		
10	Or/1-9	148550	Combined Procedure terms
11	pain/ or acute pain/ or nociceptive pain/ or pain/ or application site pain/ or injection pain/ or injection site pain/ or postoperative pain/ or posttraumatic pain/ or nociceptive pain/	16513	Pain Terms
12	Pain Measurement/ or Pain Assessment	12886	Pain terms
13	affect/ or anxiety/ or catastrophization/ or dental anxiety/ or fear/ or panic/ or fear/ or anticipatory anxiety/ or exp anxiety/	7815	Anxiety terms
14	anxiety disorders/ or phobic disorders/ or stress disorders, traumatic/ or stress disorders, post-traumatic/ or stress disorders, traumatic, acute/ or anxiety disorder/ or catastrophizing/ or panic/ or exp phobia/ or posttraumatic stress disorder/ or acute stress disorder/	3035	Anxiety disorder terms
15	crying/ or facial expression/	576	Anxiety/distress terms
16	personality/ or exp temperament/ or type a behavior/ or type b behavior/	571	Personality terms
17	(distress* or phobia* or scream* or scared or scare or scares or scaring or conditioning or somatization or somatisation or reactivity or "visual analog scale*" or "anxiety and pain scale*" or "fear scale*").ti,ab.	16208	Distress terms
18	or/11-17	44358	Outcomes results
19	(anticipator* or baseline* or "base-line*" or "base line" or "pre-operative*" or preoperative* or "pre-surgical*" or "pre-surger*" or "presurgical*" or "pre-surger*" or "pre-procedur*" or "preprocedur*").ti,ab.	89096	Anticipatory textword terms
20	10 and 18 and 19 and (pc or px).fs.	1406	Base Clinical Set 1
21	(infan* or neonat* or child* or adolescen* or teen* or girl* or boy* or youth* or tot or tots or toddler* or paediatric* or pediatric*).mp.	134052	Age group textword terms

22	20 and 21	408	Base Clinical Set 1 limited to children
23	((anticipator* or baseline* or "base-line*" or "base line" or "pre-operative*" or preoperative* or "pre-surgical*" or "pre-surger*" or "presurgical*" or "pre-surger*" or "pre-procedur*" or "preprocedur*") adj2 (anxiety or anxious or distress* or fear* or sensitivity or phobia* or phobic*)).ti,ab.	909	Base Clinical Set 2
24	23 and 24	245	Age group textword terms
25	22 or 24	1496	FINAL Results

PsycINFO

The search strategy for OvidSP PsycINFO <1806 to November Week 3 2013>.

Set	History	Results	Comments
1	exp surgery/ or surgical patients/	41505	Procedure Terms
2	((infusion adj2 pump*) or needle*).mp.	4133	Procedure Terms
3	drug administration methods/ or drug self administration/ or exp injections/	8736	Procedure Terms
4	catheterization/ or catheter*.mp.	1634	Procedure Terms
5	((blood adj2 (specimen* or work or collect* or sample*)) or phlebotomy).mp.	4639	Procedure Terms
6	immunization/ or vaccine*.mp. or ((immuniz* or immunis* or vaccinat*) adj2 (program* or campaign*)).ti,ab.	3454	Immunization program Terms
7	(venipuncture* or puncture* or aspirat* or insert* or catheter* or intravenous* or venous or cannula* or innoculation* or injection* or prick or pricked or pricks or jab or jabs or shot or shots).ti,ab.	64033	Needle Procedure Terms
8	(puncture* or paracentesis or pericardiocentesis or needle* or (spinal adj2 tap*)).mp.	5148	Procedure Terms
9	or/1-8	116056	Combined Procedure terms Results
10	pain/ or pain thresholds/ or nociceptors/	19940	Pain Terms

11	pain measurement/ or exp Pain Perception/	13829	Pain Terms
12	((dental adj2 anxiet*) or (affect or catastrophi*)).mp. or anxiety/ or exp fear/ or panic/ or panic attack/ or panic disorder/ or exp phobias/	195882	Anxiety terms
13	anxiety disorders/ or acute stress disorder/ or generalized anxiety disorder/ or panic disorder/ or exp phobias/ or posttraumatic stress disorder/ or anxiety management/	48082	Anxiety disorder terms
14	crying/ or facial expressions/ or grimaces/ or smiles/ or emotion recognition/	8975	Anxiety/distress terms
15	personality/ or temperment*.mp.	23522	Personality terms
16	distress/ or agitation/ or suffering/	18068	Distress terms
17	(distress* or phobia* or scream* or scared or scare or scares or scaring or conditioning or somatization or somatisation or reactivity or "visual analog scale*" or "anxiety and pain scale*" or "fear scale*").ti,ab.	101925	Distress textword terms
18	or/10-17	357721	Outcomes results
19	(anticipator* or baseline* or "base-line*" or "base line" or "pre-operative*" or preoperative* or "pre-surgical*" or "pre-surger*" or "presurgical*" or "pre-surger*" or "pre-procedur*" or "preprocedur*").ti,ab. or prevention/	96964	Anticipatory textword terms
20	9 and 18 and 19	1867	Base Clinical Set 1
21	limit 20 to (100 childhood <birth to age 12 yrs> or 120 neonatal <birth to age 1 mo> or 140 infancy <age 2 to 23 mo> or 160 preschool age <age 2 to 5 yrs> or 180 school age <age 6 to 12 yrs> or 200 adolescence <age 13 to 17 yrs>)	250	Base Clinical Set 1 limited to children
22	(infan* or neonat* or child* or adolescen* or teen* or girl* or boy* or youth* or tot or tots or toddler* or paediatric* or pediatric*).mp.	742401	Age group Textword search terms
23	21 or (20 and 22)	312	Base Clinical Set 1 final limited to children
24	((anticipator* or baseline* or "base-line*" or "base line" or "pre-operative*" or preoperative* or "pre-surgical*" or "pre-surger*" or "presurgical*" or "pre-surger*" or "pre-procedur*" or "preprocedur*") adj2	1532	Base Clinical Set 2

	(anxiety or anxious or distress* or fear* or sensitivity or phobia* or phobic*)).mp.		
25	limit 24 to (100 childhood <birth to age 12 yrs> or 120 neonatal <birth to age 1 mo> or 140 infancy <age 2 to 23 mo> or 160 preschool age <age 2 to 5 yrs> or 180 school age <age 6 to 12 yrs> or 200 adolescence <age 13 to 17 yrs>)	215	Base Clinical Set 2 limited to children
26	25 or (24 and 22)	268	Base Clinical Set 2 Final limited to children
27	23 or 26	519	FINAL Results

Appendix C

Table 8.5.a: The Cochrane Collaboration's tool for assessing risk of bias

Domain	Support for judgement	Review authors' judgement
Selection bias.		
Random sequence generation.	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.
Allocation concealment.	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
Performance bias.		
Blinding of participants and personnel *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Detection bias.		
Blinding of outcome assessment *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Detection bias due to knowledge of the allocated interventions by outcome assessors.
Attrition bias.		
Incomplete outcome data *Assessments should be made for each main outcome (or class of outcomes).*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Attrition bias due to amount, nature or handling of incomplete outcome data.
Reporting bias.		
Selective reporting.	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Reporting bias due to selective outcome reporting.
Other bias.		
Other sources of bias.	State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review's protocol, responses should be provided for each question/entry.	Bias due to problems not covered elsewhere in the table.

Appendix D

Who are we?

The Opportunities to Understand Childhood Hurt Laboratory, is located at York University. It opened in Summer 2004. Since then, under the leadership of Dr. Pillai Riddell, the lab has produced innovative research with infants and how they experience pain, particularly in the context of caregiver interactions.

Some of our previous participants.

YORK UNIVERSITÉ UNIVERSITY
redefine THE POSSIBLE.

Ouch Lab
Opportunities to Understand Childhood Hurt Laboratory

Opportunities to Understand Childhood Hurt Laboratory

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Here we grow... Again!

The O.U.C.H. Cohort

Next Steps

What we've done so far...

Since 2007, across the GTA, The O.U.C.H. Lab team has ambitiously followed over 750 babies during immunizations over their first year of life.

Almost 130 of these families also agreed to take part in another novel study to help us learn more about parent-infant attachment and pain behaviours.

Now our cohort babies have grown up! We are interested in looking at how they are developing at the end of early childhood. We need parents who participated in the first longitudinal study to contact us to register for the new study. The great thing for our cohort parents is that parents get the major benefit of getting a full preschool psychoeducational report on how their child learns best!

Final Steps...

The most innovative aspect of our research is yet to come. We would like to understand how your 4-6 year old functions in a variety of settings. This will tell us how infant behaviours during a stressful time relate to their functioning later in childhood, and what parent behaviours are important in optimizing this functioning.

Our new study involves videotaping their 4 to 6 year old immunization appointment, parent questionnaires, and a psycho-educational assessment at York University. We would also like to contact your child's teacher via telephone with a few questionnaires to learn more about how your child behaves in an educational setting.

Why participate?

1. This is a **once-in-a-lifetime opportunity** to be a part of the largest immunization cohort in the world examining pain in the context of parent behaviour.
2. The results of this longitudinal project are expected to provide novel insights into child development and we hope will **help improve outcomes** for children who struggle early.
3. Finally, after participating, you will receive **a summary psychoeducational report** (from a registered psychologist). These reports contain valid measures of your child's intelligence (IQ), academic achievement, and social and emotional functioning. Reports can be used to help your child optimize their learning potential.

Want to register?

Please email our Cohort Assessment Coordinator at **cohort@yorku.ca** or call at 416 736-2100, ext. 20177!

Appendix E

Participant ID: _____ **Date:** _____

PARTICIPANT INFORMATION SHEET - PARENT

PART 1: PARENT QUESTIONS – *These questions refer to the parent who will be most responsible for soothing child during needle.* (*If possible, all questions to be asked by Clinic RA)*

1. **Your birth date** (dd/mm/yyyy) _____

2. **Your relationship to child: Mother Father Other** _____

3. **Your current marital status** (circle one number):
   1. Married/Common Law
   2. Divorced/Separated
   3. Remarried
   4. Widowed
   5. Never Married
   6. Other _____

4. a) **Number of family members living in your household**: Adults _____ Children _____
   b) **For each child in your family, please list their age and sex**

   Age of child brought in today: _____ (years, months) **Male** **Female**

   Birth date of child (dd/mm/yyyy):_____

   Ages & genders of your other children

   Age: _____ Male Female

   Age: _____ Male Female

   Age: _____ Male Female

   Age: _____ Male Female

5. **a) Which caregivers are present at this immunization?** (circle one number):

1. Mom only
2. Dad only
3. Mom and Dad
4. Nanny
5. Grandparent(s)
6. Parent (s) and Nanny
7. Parent (s) and Grandparent(s)
8. Other _____
9. Parent(s) and Other _____

b) How many other children are present, if any? (do not include child getting immunized): _____

6. **Has your child been given EMLA or TYLENOL prior to appointment?:**
   EMLA TYLENOL NONE

7. Since your child turned one, have you taken any parenting classes/workshops? **Yes No**
   If yes, how many parenting classes/workshops? _____

8. Since your child turned one, have you read any infant parenting books or watched parenting videos?
   Yes No
   If yes, how many books or videos? _____

9. Since your child turned one, approximately how often do you visit parenting websites?:

Never	Once a day	Once a week	Once every few weeks	Once a month	Once a year

10. Since your child turned one, have you received any guidance from an organization or professional to help with parenting your children (e.g. health unit nurse, midwife, Early Years Centre, Healthy Babies Healthy Children, Hincks-Dellcrest, Jessie's Place)? **Yes No**
    If yes, from how many organizations/professionals? _____

11. Please estimate the amount of time in a typical day (in hours) that your infant **currently** spends under the primary responsibility of the following caregivers:

How many days do you currently work outside the home? _____

	Days When <u>you are working</u> at your job, how many hours in a typical day is infant under the primary care of….	Days When <u>you are NOT working</u> at your job, how many hours in a typical day is infant under the primary care of….
Mother		
Father		
Professional Daycare Facility		
School (JK, SK, Grade 1)		
Other (please describe)		
	TOTAL must equal 24 hours	**TOTAL must equal24 hours**

12. Who is currently the primary caregiver of your child?

Mother **Father** **Equally between Mother & Father** **Other** **_____**

13. Since one year of age, has your child been separated from his/her primary caregiver for longer than 24 hours (e.g. infant hospitalization, parent hospitalization, Children's Aid involvement, parent travel, family emergency)?

Circle: **YES** **NO**

***If you circled YES*:**

Approximately, how many separations longer than 24 hours have occurred? _____

How long was the longest period of separation? _____ (days)

14. **Child's Medical History:**

Please check next to any illness or condition that your child has had **since one year of age**. When you check an item, also note the approximate date of the illness or your child's age at illness.

Illness or Condition	Age(s)	Illness or Condition	Age(s)
☐ Measles	_____	☐ Visual problems	_____
☐ German Measles	_____	☐ Fainting spells	_____
☐ Mumps	_____	☐ Loss of consciousness	
☐ Chicken Pox	_____	*(please specify cause)*	_____
☐ Whooping Cough	_____	☐ Lead poisoning	_____
☐ Diphtheria	_____	☐ Ear problems	_____
☐ Scarlet Fever	_____	☐ TB	_____
☐ Meningitis	_____	☐ Bone or joint disease	_____
☐ Pneumonia	_____	☐ Anemia	_____
☐ Encephalitis	_____	☐ Jaundice/Hepatitis	_____
☐ High Fever		☐ Cancer	_____
(>41°C or 105.8°F)	_____	☐ Heart Disease	_____
☐ Seizure	_____	☐ Asthma	_____
☐ Allergy	_____	☐ Bleeding problems	_____

☐ Hay Fever	_____	☐ Eczema or hives	_____
☐ Injuries to head	_____	☐ Paralysis	_____
☐ Broken Bones	_____	☐ Stomach pumped	_____
☐ Hospitalization		☐ Thrush	_____
(please specify reason)	_____	☐ Circumcision	_____
☐ Operations			
(please specify)	_____		
☐ Otitis media	_____		

15. Has your child been diagnosed with any other chronic illnesses not listed above? **Yes** **No**

If yes, which chronic illness and at what age were they diagnosed? _____
_____

16. Has your child ever taken any medication long-term (i.e. longer than 2 weeks)? **Yes** **No**

If yes, please list. _____
_____

PART 2: PARENT RATINGS (PRE-IMMUNIZATION)

Pre-Immunization **Child Worry** Rating

On a scale from 0 to 10, how worried about the needle pain do you think your child is, right now, before the needle, where 0 is "no fear at all" and 10 is "the most worry possible"?

_____

Pre-Immunization **Self Worry** Rating

*On a scale from 0 to 10, how worried about the needle pain are **YOU**, right now, before the needle, where 0 is "no fear at all" and 10 is "the most fear possible"?*

_____

PART 3: PARENT RATINGS (POST-IMMUNIZATION)

To be done approximately 5 minutes after last needle!

Post-Immunization **Child Pain** Rating

On a scale from 0 to 10, how much pain do you think your child experienced from the needles they just received, where 0 is "no pain at all" and 10 is "the worst pain possible"?

_____

Post-Immunization **Child Worry** Rating

On a scale from 0 to 10, how worried about the needle pain do you think your child is, right now, after the needle, where 0 is "no fear at all" and 10 is "the worst fear possible"?

_____

Post-Immunization **Self Worry** Rating

*On a scale from 0 to 10, how worried about the needle pain are **YOU**, right now, after the needle, where 0 is "no fear at all" and 10 is "the most fear possible"?*

_____

Post-Immunization **Needle Awareness** Check

Did your child know they would receive a needle prior to coming to the doctor's office?

Yes **No**

How long after last needle were these ratings obtained?

_____ minutes

PART 4: VACCINES GIVEN BY IMMUNIZATION NEEDLE

RA to fill out (ask nurse or doctor for vaccine name and trade name)

		Company/Brand Name	Disease it Protects Against
☐	DTaP-IPV	_____	_____
☐	MMRV	_____	_____
☐	Varicella only	_____	_____
☐	MMR only	_____	_____
☐	Other _____	_____	_____

How many needles total?: _____

In order of administration:

1. Vaccines in needle #1: _____

Participant Information Sheet – CHILD CHILD RATINGS *(RA to fill out with child)*

**While parent is filling out Consent form/parent questions, please do Poker Chip Method with the child.

PRE-IMMUNIZATION

Note: The pre-immunization poker chip question will establish a baseline AND act as a "practice round" for this tool, i.e. to be sure the child understands how to answer when we ask again AFTER the needle.

Using the Poker Chip Method, begin with: "These chips represent how much ouchie you feel…

…where no chips means no ouchie, one chip means a little bit of ouchie, two chips means a little bit more ouchie, three chips means more ouchie, and four chips is the worst ouchie possible. How much ouchie do you feel right now?"

Rating (0-4): _____

Try to get the child to say "No chips." If child says anything but "No chips," probe to get them to "No chips" i.e. asking about why they feel hurt. If they respond with a genuinely painful experience (e.g. just fell down), please make note of that.

POST-IMMUNIZATION

Using the Poker Chip Method: "These chips represent how much ouchie you feel…

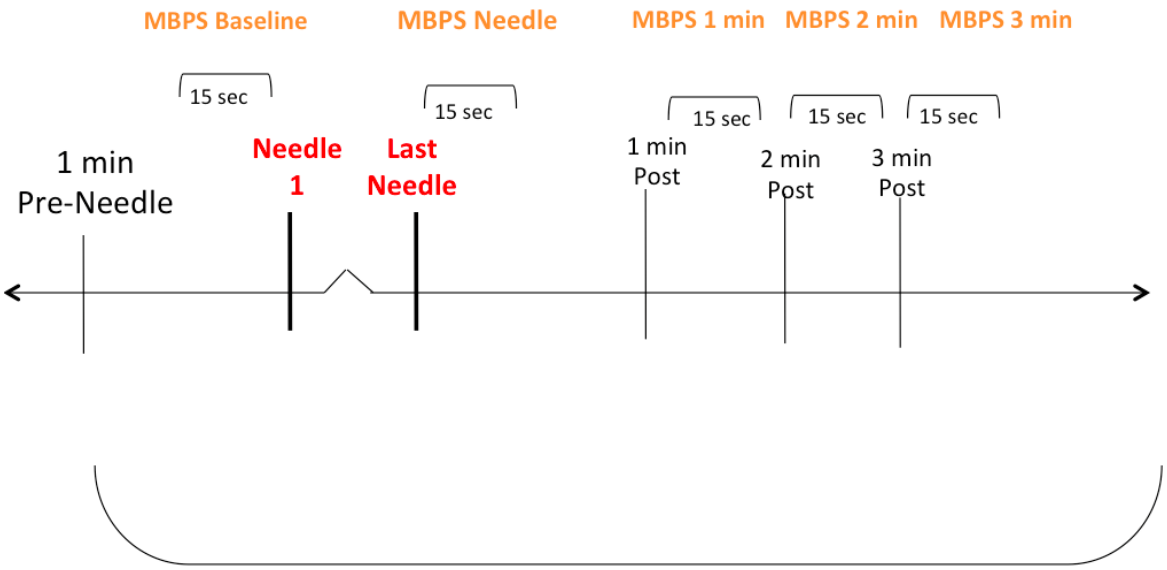
…where no chips means no ouchie, one chip means a little bit of ouchie, two chips means a little bit more ouchie, three chips means more ouchie, and four chips is the worst ouchie possible. How much ouchie do you feel right now?"

Rating (0-4): _____

How much did the needle hurt when it came out?

Rating (0-4): _____

Appendix F


MBPS Baseline
MBPS Needle
MBPS 1 min
MBPS 2 min
MBPS 3 min
15 sec
15 sec
15 sec
15 sec
15 sec
1 min
Pre-Needle
Needle
1
Last
Needle
1 min
Post
2 min
Post
3 min
Post
Emotional Availability Total

Appendix G

Modified Behaviour Pain Scale

Taddio, A., Nulman, I., Koren, B.S., Stevens, B., Koren, G (1995). A revised measure of acute pain in infants. *Journal of Pain Symptom Management*, *10*(6):456-463. doi:10.1016/0885-3924(95)00058-7.

Infant Position **during** Immunization
1 = Infant lying on doctor's table
2 = Infant Held in mother's arms - mother standing
3 = Infant Held in Mother's arms - mother sitting
4 = Infant standing in between mother's legs - mother sitting
5 = other: Specify_____

Modified Behavioral Pain Scale (Longitudinal Study)
Coder Name: _____ Coding Time: _____ to _____
Date: _____ Participant ID: _____
Clip Start: _____ Clip Finish: _____

Needle #1 Time: **Needle #2 Time:**	**BASLINE (15 sec. before Needle #1)** START:_____ FINISH:_____	**POST-NEEDLE (15 sec. after the last needle)** START:_____ FINISH:_____	**RECOVERY 1 (75 sec. after last needle for 15 sec. period)** START:_____ FINISH:_____	**RECOVERY 2 (135 sec. after last needle for 15 sec. period)** START:_____ FINISH:_____	**RECOVERY 3 (195 sec. after last needle for 15 sec. period)** START:_____ FINISH:_____
FACIAL EXPRESSION 0- *definite positive expression (smiling)* 1- *neutral expression* 2- *slightly negative expression (grimace; BB; NLF)* 3- *Definite neg. exp. (BB, NLF, EC, open lips, maybe RF)*					
CRY 0- *laughing or giggling* 1- not crying 2- *moaning, quiet vocalizing, gentle or whimpering cry* 3- *full lunged cry or sobbing* 4- *full lunged cry, more than baseline cry* ***(only if infant crying during baseline)***					
MOVEMENTS 0- *usual* movements/activity or resting /relaxed *2 – partial movement or attempt to avoid pain by withdrawing the limb from puncture (squirming, arching, limb tensing/clenching)* *3- Agitation with complex movements involving the head, torso OR the other limbs OR rigidity (generalized limb and/or body movements, or rigidity)*					

Appendix H

Emotional Availability Scale- 4th Edition

Biringen, Z. (2008). The Emotional Availability (EA) Scales Manual (4th ed.). Retrieved from www.emotionalavailability.com.

EAS Coding

Participant ID:

Date:

Rater:

Observation time:

Describe who is in the immunization room:

Clinical Screener

Clinical Screener Score	

EA Adult Sensitivity

#	Subscale	Range	Score
1	Affect	1-7	
2	Clarity of perceptions…	1-7	
3	Awareness of timing	1-3	
4	Flexibility, variety, and…	1-3	
5	Acceptance	1-3	
6	Amount of Interaction	1-3	
7	Conflict Situations	1-3	
-	Total	-	

EA Adult Structuring

#	Subscale	Range	Score
1	Provides appropriate guidance…	1-7	
2	Success of attempts	1-7	
3	Amount of Structure	1-3	
4	Limit setting, setting boundaries.	1-3	
5	Remaining firm in the face of	1-3	
6	Verbal vs. nonverbal structuring	1-3	
7	Peer vs. adult role	1-3	
-	Total	-	

EA Adult Nonintrusiveness

#	Subscale	Range	Score
1	Follow child's lead:	1-7	
2	Non-interruptive ports of entry	1-7	
3	Commands, directives:	1-3	
4	Adult talking:	1-3	
5	Didactic teaching:	1-3	
6	Physical vs. verbal interferences	1-3	
7	The adult is made to "feel" or	1-3	
-	Total	-	

EA Adult Nonhostility

#	Subscale	Range	Score

1	Adult lacks negativity in face or	1-7	
2	Lack of mocking, ridiculing, or	1-7	
3	Lack of threats of separation:	1-3	
4	Does not lose cool during low	1-3	
5	Frightening behavior/tendencies:	1-3	
6	Silence	1-3	
7	Themes or play themes hostile	1-3	
-	Total	-	

EA Child Responsiveness

#	Subscale	Range	Score
1	Affect/emotion regulation/	1-7	
2	Responsiveness:	1-7	
3	Age-appropriate autonomy-	1-3	
4	Positive physical positioning	1-3	
5	Lack of role reversal/over-	1-3	
6	Lack of avoidance	1-3	
7	Task oriented/concentrate	1-3	
-	Total	-	

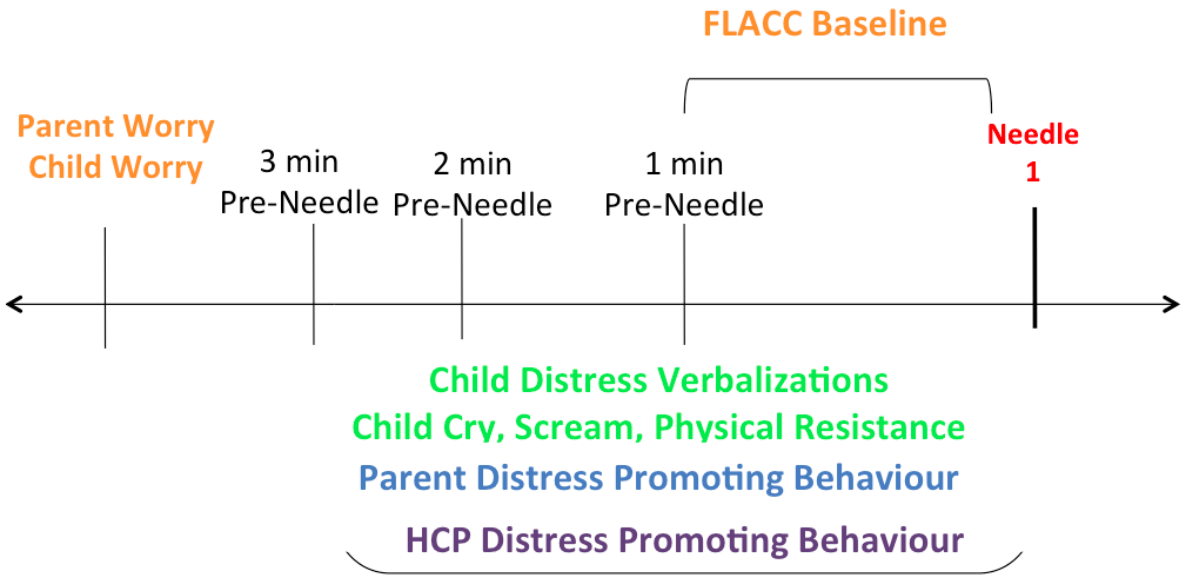
EA Child Involvement

#	Subscale	Range	Score
1	Simple Initiative:	1-7	
2	Elaborative initiative:	1-7	

3	Use of adult:	1-3	
4	Lack of over-involvement	1-3	
5	Eye contact, looking, postural	1-3	
6	Verbal involvement:	1-3	
7	Body positioning	1-3	
-	Total	-	

EA Dimensional sum:_____

Appendix I


FLACC Baseline
Parent Worry
Child Worry
3 min
Pre-Needle
2 min
Pre-Needle
1 min
Pre-Needle
Needle
1
Child Distress Verbalizations
Child Cry, Scream, Physical Resistance
Parent Distress Promoting Behaviour
HCP Distress Promoting Behaviour

Appendix J

FLACC SCALE

Merkel, S., Voepel-Lewis, T., Shayevitz, J.R., Malviya, S. (1997). The FLACC: A behavioral scale for scoring postoperative pain in young children. *Pediatric Nursing, 23*(3):293-297.

FLACC CODING SHEET

Date Coded: _____ Coder Name: _____ Participant ID: _____

Coding Time: _____ to _____ Clip Start: _____ Clip Finish: _____

Cleaning Time: **Needle #1 Time:** **Needle #2 Time:**	**BASELINE** **(1 min. before Needle 1)** START:_____ FINISH:_____				**POST NEEDLE 1** **(1 min. after last needle)** START:_____ FINISH:_____				**POST NEEDLE 2** **(2 min. after last needle)** START:_____ FINISH:_____				**POST NEEDLE 3** **(3 min. after the last needle)** START:_____ FINISH:_____			
Epoch Times (15 sec):																
FACE *0 - no expression or smile* *1 - occasional grimace, frown, withdrawn* *2 - frequent to constant frown, clenched jaw, quivering chin*																
LEGS *0 - normal position or relaxed* *1 - uneasy, restless, tense* *2 - kicking or legs drawn up*																
ACTIVITY *0 - Lying quietly, normal position, moves easily* *1 - squirming, shifting back and forth, tense* *2 - arched, rigid, or jerking*																
CRY *0 - no cry* *1 - moans or whimpers, occasional complaint* *2 - Crying steadily, screams or sobs, frequent complaints*																
CONSOLIBILITY *0 - content, relaxed* *1 - reassured by occasional touching, hugging, or being talked to, distractable* *2 - difficult to console or comfort*																

Appendix K

Child Anticipatory Distress to Immunization (CADI) Coding Manual

Additions and Modification of the Child-Adult Medical Procedure Interaction Scale- Revised (CAMPIS-R)

Blount, R.L., Cohen, L.L., Frank, N.C., Bachanas, P.J., Smith, A.J., Manimala, M.R., Pate, J.T. (1997) The Child-Adult Medical Procedure Interaction Scale–Revised: An Assessment of Validity. *Journal of Pediatric Psychology*, *22*(1):73-88.

Nicole Racine, M.A.

April 2014

General Coding Instructions

1. Being calm and focused is an important part of coding. Be sure to take regular breaks while coding.
2. Coding will be conducted using the Observer XT software. This software is loaded on all the coding computers in Sherman 2004.
3. Be sure to let Nicole know if there are any problems. If something seems unclear or confusing, it's always best to double-check.
4. You will need your coding manual for reference while coding. This will be kept in the cubby above the coding computers.
5. Reliability will be conducted on 20% of all cases. These cases will be assigned, will need to be transcribed and coded by both Maria and Nicole.
6. All tapes will be transcribed
7. All tapes will be coded for 3 minutes before needle and 2 minutes after needle.

ADULT VERBAL BEHAVIOUS (POINT)

ADULT TO ADULT

1. HMA Humor Directed to Adults
2. NPTA Nonprocedure-Related Talk to Adults
3. PTA Procedure-Related Talk to Adults
4. SMC Commands For Managing Child's Behavior

ADULT TO CHILD (or OTHER CHILD)

5. HMC Humor Directed to Child
6. NPTC Nonprocedure-Related Talk to Child
7. CCS Command to Use Coping Strategy
8. CPA Command to Engage In Procedural Activity
9. PRAS Praise
10. CRIT Criticism
11. NPC Notice of Procedure to Come
12. REASU Reassuring Comment
13. GCC Giving Control to the Child
14. APOL Apology
15. BCC Behavioral Commands to the Child
16. CST Checking Child's Status
17. NSC Negative Status Check*
18. EMP Empathy
19. NPE Notice of Procedure End*

20. PPT Positive/Neutral Procedural Talk*

21. NPT Negative Procedural Talk*

22. REF Reframing*

ADULT TO EITHER ADULT OR CHILD (or OTHER CHILD)

23. CGCT Child's General Condition Related Talk

24. CGSC Current General Status Comments

ADULT NON-VERBAL (STATE)

25. EMPT Empathic Touch*

26. FT Functional Touch*

27. REST Restraint*

CHILD VOCALIZATIONS (POINT)

28. VRES Verbal Resistance

29. EMSUP Emotional Support

30. VFEAR Verbal Fear

31. VPAIN Verbal Pain

32. VEMOT Verbal Emotion

33. INSEK Information Seeking

34. CIA Child Informs About Status

35. RRD Request Relief from Nonprocedural Discomfort

36. MCOP Making Coping Statement

37. NPTC Nonprocedural-Related Talk by the child

38. APV Assertive Procedural Verbalizations

39. CGCT Child's General Condition Related Talk

40. BRTH Audible Deep Breathing

41. HUM Humor by the Child

42. PTC Procedural Talk Child

CHILD NON-VERBAL (STATE)

43. CRY Cry

44. SCR Scream

45. PHY Physical Resistance*

*Behaviours that have been added in addition to the CAMPIS original codes.

Speaker Codes:

P- Parent/Primary Caregiver

C-Child

D-Doctor

S-Sibling

Needle Start Code

Needle Stop Code

Point Behaviours: Behaviours where the onset is noted

State Behaviours: Capture the start, stop, and duration of behaviours (e.g. cry).

Parent Present

0- Mom
1- Dad
2- Mom and Dad
3- Nanny
4- Grandparent

Sibling Present

0-no siblings

1- 1 sibling
2- 2 siblings
3- 3 siblings

Codes for Parent Verbal Behaviors (Point Behaviours)

CODE	DESCRIPTION	EXAMPLES
Humor directed to adults (HMA) Observer Codes:	Any statement that is clearly intended to be humorous and is primarily lighthearted in tone. Humor is often accompanied by laughter from the person making the statement may evoke laughter in the patient or in other staff members. Sarcasm may be coded as humor if it is accompanied by laughter on the part of the speaker or on the part of the listener. Sarcasm is not coded as humor if it is accompanied by an angry or harsh tone of voice.	1. Outright jokes of the "one-liner" variety. 2. Statements that suggest purely facetious, outlandish or outrageous ideas. 3. Statements that emphasize the humorous aspects of a situation or problem. 4. Statements which present lighthearted criticism of someone else in such a manner that would be lightly received (e.g. oh you sill duck) 5. "Sure, working on Sunday is my top priority" 6. Laugher (generally coded + for affect)
Humor directed to child (HMC) Observer Codes:	Any statement that is clearly intended to be humorous and is primarily lighthearted in tone. Humor is often accompanied by laughter from the person making the statement may evoke laughter in the patient or in other staff members. Sarcasm may be coded as humor if it is accompanied by laughter on the part of the speaker or on the part of the listener. Sarcasm is not coded as humor if it is accompanied by an angry or harsh tone of voice.	1. Outright jokes of the "one-liner" variety. 2. Statements that suggest purely facetious, outlandish or outrageous ideas. 3. Statements that emphasize the humorous aspects of a situation or problem. 4. Statements which present lighthearted criticism of someone else in such a manner that would be lightly received (e.g. oh you silly

		duck) 5. "Sure, working on Sunday is my top priority" 6. Laugher (generally coded + for affect)
<u>Non procedure-related talk directed toward child (NPTC)</u> Observer Code:	Talk that does not pertain to the treatment procedure or about the child's illness.	1. Conversation about the child's pet, siblings, parents, school, toys, etc. 2. Questions, unrelated to the child's illness or treatment, about the child's plans, wants, desires 3. Conversations about activities on the ward or about other children or staff members on the ward
<u>Non-procedure related talk directed toward other adults (NPTA)</u> Observer Code:	Talk that does not pertain to the treatment procedure or the child's medical well being.	1. "Did you drive in this morning" 2. "How is the new baby doing" 3. Questions about a parents other child, spouse, home, etc. 4. "Susie embarrassed me last night with her comment about the lady across the hall"
<u>Procedure-related talk-Adult to Adult (PTA)</u> Observer Code:	Any talk that directly pertains to the current needle procedures. Comments about past treatment procedures are included in this category only if they related to what is going on now. Commands included in this category may be related to actual physical manipulation of the child (ex. Help curl up in a ball), as this related to the ongoing procedures and is not issues as	1. "Hand me the swab, please" 2. "How many needles is she getting" 3. "When are the next needles?" 4. "How much spinal fluid do you need" 5. "Is it dripping? 6. "Are you using lidocaine today" 7. "It's not dripped

	a result of child distress behavior. Not included in this category are commands or suggestions related to managing the child's distress behavior during the procedures ("hold his legs"). The implication is that he is moving about and should be restrained- Code this as Commands or suggestions for Managing the Child's Behavior).	yet" 8. "I'm Dr. Smith. I will be doing the procedure today." 9. "You need to stand over " 10. "Would you had me some #7 gloves" 11. "How many of these tubes do we use?" 12. "This isn't the usual bone marrow procedure!" 13. "Is it dripping yet?" 14. "Roll him over" 15. "Curl him up in a ball"
<u>Child's general physical condition related talk (CGCT)</u> Observer Code:	Questions or comments about the child's history or future health care. For example, comments could refer to the BMA if that procedure is done and resident is currently conducting the LP. These comments must relate to the child's illness or treatment. This is other medical talk not pertaining to current needles.	1. Questions about the child's history 2. Parents request for information -how long does it take to get results back? -will she have to come back tomorrow? -She thought she was going to have to have this every week -How many visits do we have to make? -When does Dr. Gush believe her medication will change? -does Janie have to have chemo next time? 3. Child comments such as: -that time it took a long time -the other doctor washed too hard last time

Current general status comments (CGSC) Observer Code:	Comments by adults regarding the child's current physical, emotional and/or behavioral status. Merely an observation rather than a comment directed toward changing that which is observed would qualify for this category.	1. She seems to have labored breathing today 2. He has stiff muscles 3. Johnny, your muscles are tight 4. He is upset today 5. Boy is she out of it
Command to use coping strategy (CCS) Observer Code:	Any orders, suggestions, or statements of a rule, which direct the child to engage in a coping behavior. These strategies are generally issues immediately prior to a painful event, and may suggest one (but not exclusively one) of the following: relaxation, distraction, use of coping statements, or deep breathing. An example such as "Can you breath now" is coded CCS in spite of it giving the impression of control to the child (GCC)	1. Use your deep breathing now 2. Would you like to count backwards from 10 very slowly? 3. Imagine you are Superman and this is a test of your strength 4. Squeeze your mother's hand when you feel the bumble bee 5. Just relax, alright? 6. Count to three…
Command to engage in procedure-related activity (CPA) Observer Code:	Any orders, suggestions or statements of a rule, which directs the child to engage in some procedure-related activity. Common commands might include asking the child to prepare his/her pajamas for the wash, telling the child to curl up for the LP, asking a child to move a part of his/her body, or asking the child to tell them when something hurts.	1. It's time to roll up in a ball for the LP 2. Could you move your hand so that I can fix the IV 3. You need to turn over for the wash 4. Tell me when this hurts, ok?
Praising (PRAS) Observer Code:	Any statement referring to the child or the child's prior, ongoing, or future behavior that is positive in evaluation, shows approval or is	1. The positive behavior is specified (e.g. you used your deep breathing very well)

	rewarding	2. The positive behavior is not specified: e.g. "Great" or "there you go" 3. Descriptions of child's behavior denoting better-than average performance: e.g. "Tommy is doing so well!" or "you are really being braver than ever"
<u>Criticism (CRT)</u> Observer Code:	Any verbalization that finds fault or implies fault with a) activities, b) products, or c) attributes of the child. Criticism includes negatively evaluative adjectives or adverbs referring to the child, statements of disapproval, statements pointing out something wrong about the child or the child's behavior, and statements pointing out that the child is not doing something positive. Also included as Criticism are obvious sarcastic statements, if these are unaccompanied by laughter on the part of either the speaker or listeners. Usually criticism is accompanied by a harsh voice tone.	1. Timmy has not been going to school the way he should have 2. Boy, you are in a bad mood today 3. That was not a very nice thing to say 4. That was not very funny 5. You didn't use your breathing that time like I told you to 6. Boy, you really controlled yourself that time (after a big scream) 7. You're being a pain.
<u>Notification of procedure to come (NPC)</u> Observer Code:	Any statement denoting that a procedure is about to occur, including the wash, the stick, etc. If the same information is repeated by the parents or staff, either without the child's request for reassurance or emotional support, or with the	1. Okay here comes the wash 2. Now, it's just gonna be a little bee sting 3. One more stick 4. This is going to feel cold 5. Dr. Powell is going

	child asking for mere repetition of the information, code the subsequent notification as NPC.	to put on her gloves now, O.K. 6. It's that soap 7. I'm going to give you a little break.
Reassuring Comment (REASUR) Observer Code:	Procedures related comments that are directed toward the child with the intent of reassuring the child about his/her condition, or the course of the procedure. These may be volunteered by staff and/or parents and may be in response to questions by the child or may reflect the child's comments. If procedure related information is repeated in response to the child's request for reassurance or emotional support, code these procedural notifications as REASU	1. "A little bit of exercise will take care of that" 2. "You're okay" 3. "It's almost over" 4. "We're hurrying" 5. "Honey, it's just soap, okay?" 6. "I'm not doing anything" 7. "Just touching honey"
Giving control to child (GCC) Observer Code:	Any statement to child denoting that child has control over some event to occur with relation to the procedure. Generally this includes staff suggestions where the child is given a choice about the procedure. "Can you breath now?" is coded CCS even though it has the impression of giving control to the child.	1. "Let me know when you are ready to start." 2. "Which side would you like to lie one?" 3. Do you want a pillow for your head? 4. Do you like it better when we tell you or don't tell you? 5. Can you start now? 6. Are you ready?
Apologizes (APOL) Observer Code:	Any statement relating a sense of sorrow or a sense of responsibility for the pain the child is expressing. These statements may occur prior to, during, or after a painful event, and may occur in conjunction with other verbal	1. "Timmy, we don't like doing this either" 2. "I'm sorry this is taking so long" 3. "I wish I didn't have to hurt you"

	codes.	
Commands or suggestions for managing child's distress behavior (SMC) Observer Code:	Statements suggesting methods for controlling the child's behavior while in the treatment room. Suggestions may include direct demands to treat the child in a particular way, or stating alternatives for managing the child such as referring to methods that have or have not worked well in the past or "wondering aloud" whether different methods might result in less stress.	1. "I think she does better when she knows what is going to happen" 2. "When he gets too upset, if you'll just stop a few seconds he'll calm down" 3. He does best with Dr. Horne" 4. "Hold his legs"
Behavioral commands to the child (BCC) Observer Code:	Commands by adults toward the child which direct the child to change some aspect of his or her behavior. This category is designed to include the limits that parents typically set on their child's behavior and behavioral request/commands of the child. This category is distinguished from CRIT in that the focus of BBC is toward managing the child's behavior, whereas the focus of CRIT is to find fault with the child and/or has an evaluative nature to the verbalizations. BBC is distinguished from CPA in that CPA is directed toward some specific procedural activities	1. "No, don't hurt your mom" 2. " Don't slap me, you've not allowed to hit me" 3. "Shhhhh…" 4. "Wipe the tears" 5. "Ralph, you need to talk to us." 6. "Ralph, talk to your dad." 7. "Ralph, you have to behave" 8. "Sit down and be quiet"
Checking child's status (CST) Observer Code:	Any question directed toward child which asks for his or her opinion about his or her status. Inquiries may refer to how the child is feeling, whether the child is afraid, whether the pain is too bad, etc. Also included are reflections of the	1. "Did you feel that?" 2. "Do you think your sleepy medicine is wearing off?" 3. "Are you comfortable?" 4. "That didn't hurt, did it?"

	child's answers to adults' questions regarding his or her status. Examples such as "Can you breathe now?" even though they do in a sense inquire about the child's condition, are coded as CCS because they are suggesting to the child the use of a coping strategy.	5. Reflecting to the child, "Sore all back there" in response to the child's comment about being sore.
Negative Status Check Observer Code: Neg Stat Check	Inquiries about emotion or sensation that include negative words (yucky, sick, scared, bad) This code involves a suggestion of negative state. (Chorney, 2013)	"Does your stomach feel yucky?" "Do you feel sick?" "Are you scared?" "Is it bothering you?" "Does it hurt?" "Do you think it will hurt?"
Empathy (EMP). Observer Code:	Statements which show an appreciation for the frame of reference of the person being spoken to.	1. "I know this is hard" 2. "I know this is taking a long time" 3. "I know it hurts" 4. "This must be hard" 5. "You must be getting tired" 6. "You must be getting sick of this"
Other (OT) Observer Code:	Code other whenever verbal behavior does not fit any other categories. This includes verbalizations that are not clear enough for accurate recording, sentences that are cut off in mid-stream before the meaning can be ascertained. Use this as a last result when audible, complete sentences are issues. Excluded from this category are "yes",	1. "Can you…" 2. "ummmm" 3. Mumbling 4. "I think that you" 5. "Honey"

	"no", "shoot", "huh" "Aw-shoot", "what", etc. These should be coded according to the context of the conversation if possible.	

Notification of procedure end (NPE) Observer Code:	Verbal statement to let the child know that the procedure is over.	1. "It's over" 2. "It's finished" 3. "You're all done"
Positive/ Neutral Procedural; Talk by Adult Observer Code:	The parent engages in talk that is related to the current or past procedure to the child in a way that is neutral or positive. Does NOT include negative pain or fear words.	1. "It will be one poke here, and one poke here and be over very quickly" 2. "It will hurt, but only for a short time" 3. "It will be a poke just like a bumble bee or just like last time" 4. Talking about the needle 5. Talking about another child or adult having to get a needle 6. Talking about blood
Negative Procedural Talk by Adult Observer Code:	The parent engages in talk that is related to the current or past procedure to the child in a way that is negative.	1. It's really gonna hurt 2. It's going to be really scary 3. Remember how scared/hurt/how much you cried last time?
Reframing	When an adult reframes getting the experience in a positive way.	1. Look at that blood, isn't it cool? 2. You have two Band-Aids on your arms

	When an adult changes a procedural negative to a neutral or a positive. For example, if somehow the parent makes talking about blood a positive.	just like a super hero 3. You were so brave

Codes for Parent Non-Verbal Behaviors (State Behaviours)

Empathic Touch	momentary empathic touches (e.g., patting, rubbing a back) (Chorney, 2013)	
Functional Touch	Adults touching child in a way that was needed to get the procedure done (positioning them) (Chorney, 2013)	
Restraint	Adult has to hold down the child or hold them in a hug positive in order to keep them still because they are distressed. (Chorney, 2013)	

Codes for Child Verbal Behaviors (Point Behaviours)

CODE	DESCRIPTION	EXAMPLES
<u>Verbal Resístanse (VRES)</u> Observer Code:	Any verbal expression of delay, termination, or resistance. It must be intelligible.	1. "stop" 2. "no more" 3. "don't" 4. "let me rest" 5. "take the needle out" 6. "I don't want it"

		7. "Take me home" 8. "I have to go to the bathroom"
Emotional Support (EMSUP) Observer Code:	Verbal solicitation of hugs, hand holding, physical or verbal comfort by the child. Do not code EMSUP for "mommy" if part of statement requires another code. For example "Mommy, get me out of here" is coded as VRES.	1. "Hold me" 2. "mommy and daddy" 3. "momma please" 4. "Help me" 5. "I want my pacifier"
Verbal fear (VFEAR) Observer Code:	Statements of being apprehensive or in fear. The statement must be intelligible.	1. "I'm afraid" 2. "I'm scared"
Verbal pain (VPAIN) Observer Code:	Statement of pain, damage or being hurt. May be in any tense. Can be anticipatory as well as actual. Has to be a statement, not a question.	1. "That hurts" 2. "It stings" 3. "owwwwh" or "Owwhee" 4. "You're killing me" 5. "You are pinching me" 6. "Don't hurt me"
Verbal emotion (VEMOT) Observer Code:	Statements other than VFEAR or VRES which express the child's emotional state. Anger, self-pity, or resentment would be emotions conveyed here. This category is reserved for negative emotions only.	1. "Why does this have to happen to me" 2. "I hate you" 3. "I don't like doing this"
Information seeking (INSEK) Observer Code:	The child asks questions about medical procedures	1. "when will you stick me" 2. "when will you be finished" 3. "will you let me know when you're ready to start" 4. "will you tell me when you are going to do something" 5. "Is the needle in?" 6. "Is the drip coming?"

Child informs about status (CIA) Observer Code:	The child either volunteers or answers questions about his or her current status	1. "I'm sore back there" 2. "I'm sleepy" or "yes, a little" in response to the question "are you sleepy" 3. "yes" or "no" to the question "are you numb yet" or "can you still feel it"
Request relief from nonprocedural discomfort (RRD) Observer Code:	The child request relief from something that is clearly not procedurally related	1. "prop up my pillow" 2. "my elbow hurts" 3. "the lights too bright" 4. "You're squeezing my hand too hard" 5. "I can't move my foot"
Making coping statements (MCOP) Observer Code:	The child makes some statements which indicates courage or attempts to soothe himself or herself verbally	1. "I'll be okay" 2. "I'm superman/woman" 3. "I can take it" 4. "It won't hurt" 5. "It won't last long" 6. "Superman would not cry" 7. "I can get an ice cream afterward" 8. "I get a Band-Aid" 9. "I did good"
Nonprocedure related talk by child (NPTC) Observer Code:	The child engages in talk that is no way related to his or her current physical condition or the procedure	1. "That cat was a girl" 2. "I was watching He-man the other day" 3. "school is going okay" 4. "we exercise some at home"
Procedure Talk by Child (PTC)	The child engages in talk that is related to the current or past. Can be positive or negative.	1. That's weird that we have blood. 2. The last time I got a needle it was in this arm. 3. Even Julie had to get

Observer Code:		a needle. 4. I always see Dr. Greenberg for my needles
Assertive procedural verbalization (APV) Observer Code:	Commands, statements, or requests by the child which seek to direct the course of the procedure or some aspect of the adult's behavior as it related to the procedure, without attempting to terminate the procedure or some aspect of the procedure. The essence of what is being targeted here is the child exercising some aspect of control over the course of the procedure without trying to terminate the procedure.	1. "Don't mash too hard" 2. "Count to three then stick it in there, okay?" 3. "Push it in fast" 4. "Please tell me when you are ready" 5. "Can you hurry" 6. "go slow"
Child's general condition related talk (CGCT). Observer Code:	This is the same category as in the Codes for Staff/Parent behavior, but with the child doing the talking.	
Audible deep breathing (BRTH) Observer Code:	Deep breathing that is used to cope with the procedures. Breathing that is part of the child's distress does not count as B.	
Humor (HUM) Observer Code:	This is the same category as in the codes for staff/parent but with the child doing the talking.	

Procedure-Related Talk by	The child engages in talk that is no way related to his or her	1. Talking about the needle

Child (PTC) Observer Code:	current physical condition or the procedure	2. Talking about another child or adult having to get a needle 3. Talking about blood

Codes for Child Non-Verbal Behaviors (State Behaviours)

CODE	DESCRIPTION	EXAMPLES
Cry (CRY)- Observer Code:	Crying sounds-usually unintelligible but can be double coded with verbal categories. Sobbing, whimpering. Coded when crying is audible, child may be moaning or whining. Normally subject will be visibly distressed. Stop code when cry/moan is no longer audible (do not stop if child is taking a breath while crying). Verbalizations such as "No!", "I don't want to." that occur during crying/whining are coded simultaneously.	1. "Sobbing" 2. "Boohooohoo" 3. Crying sounds
Scream (SCRM)- Observer Code:	Vocal expression of pain at high pitch/intensity, usually unintelligible but can be coded with other verbal categories. Not included in this category is loud yelling at a low pitch.	1. Sharp, shrill, harsh, high tones 2. Shrieks 3. "owwwwwh"

	Must be higher pitch than crying. Normally subject will be visibly distressed. Stop code when scream is no longer audible (do not stop if child is taking a breath while screaming). Verbalizations such as "No!", "I don't want to." that occur during screaming are coded simultaneously.	
Physical Resistance	If the child moves around, will not stay in position or tries to climb off table (PBCL definition) Also coded if the child is guarding the area that is going to receive the needles. (PBCL, Zeltzer)	

Appendix L

CAMPIS Coding

ID: _____ Name: _____ Date of Coding: _____

Needle Time: _____

Coding start time (3 minutes before needle): _____

Coding end time (2 minutes after needle): _____

#	Verbalization	Child (C) or Parent (P), Doctor (D)	CAMPIS Code
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