Parents' Analgesic Decision Dilemmas:

Trading Children's Pain Relief for Risk Reduction

by

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Dedication

I dedicate this work to my daughters, Rebecca and Sarah, whose intelligence, commitment and compassion never cease to amaze and inspire me; to my parents, for teaching me all of the important things in life; and to Alan for his love, friendship, encouragement, and keen sense of humor that provided me the fortitude necessary to complete this process.

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Abstract

Background: Effective pain management requires analgesic decisions that balance the need to maximize pain relief and safety. However, reports of unrelieved childhood pain, analgesic misuse, and serious analgesic-related adverse drug effects (ADE) suggest that parental analgesic trade-off decisions are often inadequate. Based on decision theory, this dissertation examined parents' analgesic decisions and explored factors that influenced their responsiveness to varying pain and ADE signals.

Methods: Parents of children undergoing painful, short-stay surgery (N=468) completed surveys regarding their understanding of the possible opioid-related ADEs (gist knowledge), their perceptions of ADE seriousness, and their preferences for providing pain relief versus avoiding ADEs. Analyses compared both responses to hypothetical scenarios and real postoperative opioid decisions to see how parents responded to varying pain and ADE signals and to explore how gist analgesic understanding and preferences influenced their decisions to give opioids.

Results: Parents were more likely to give opioids (hypothetically and postoperatively) when faced with higher pain and to withhold opioids when presented with ADEs, suggesting a general recognition of pain and ADE signals. However, parents were more likely to withhold the prescribed opioid dose for symptoms of nausea/vomiting than oversedation (odds ratio 0.68; $p = 0.018$), suggesting that oversedation symptoms may be less salient than nausea/vomiting. Perceived seriousness, but not gist possibility knowledge, influenced the decision to withhold opioids for oversedation, demonstrating that gist awareness of ADEs in itself may be insufficient

to influence safe opioid use. Strong preference for pain relief over ADE avoidance weakened the effect of analgesic knowledge/perception on the decision to withhold opioids for oversedation, showing how preferences may interfere with knowledge when symptoms are less salient.

Conclusion: Many parents lack a critical understanding of serious analgesic-related ADEs, such as oversedation, placing them at risk for making unsafe or ineffective treatment decisions. Parents need a clearer understanding of possible ADEs, their potential seriousness and consequences in order to safely and effectively manage pain postoperatively. These findings should be used to guide the development of interventions to optimize parent decision-making and symptom surveillance regarding pain medications and, in turn, enhance children's comfort and safety.

Chapter I

Introduction

Nearly every child and adolescent will, at some time, experience pain that requires use of analgesics in the home setting. Recent studies show that 88% to 90% of healthy school-aged children and adolescents have reported having some sort of pain and up to 85% had taken non-opioid or opioid analgesics within several weeks of being surveyed (Fouladbakhsh, Vallerand, & Jenuwine, 2012; Huguet & Miro, 2008). Furthermore, half of high-school seniors who reported using non-prescribed opioids said that they did so to alleviate pain (McCabe & Cranford, 2012). Efforts to reduce childhood pain have led to a two-fold increase in opioid analgesic prescriptions for children over the last decade (Fortuna, Robbins, Caiola, Joynt, & Halterman, 2010). Although such efforts have likely reduced pain for many children, the potential for mismanagement and misuse in the home setting is of growing concern.

Indeed, reports suggest that pain relief remains suboptimal for many children following hospital discharge, resulting in delayed recovery, return to normal function, and, sometimes, prolonged pain (Fortier, MacLaren, Martin, Perret-Karimi, & Kain, 2009; Stewart, Ragg, Sheppard, & Chalkiadis, 2012). Unrelieved childhood pain interferes with routine activities and school attendance, often requires unplanned visits to providers and emergency departments, and sometimes, hospital readmission (Fortier, et al., 2009; Fouladbakhsh, et al., 2012; Roth-Isigkeit, Thyen, Stoven, Schwarzenberger, & Schmucker, 2005; Stewart, et al., 2012; Warnock & Lander, 1998). Pain, therefore, adds significant costs and burden to families and the healthcare system. These and other reports of the high prevalence of unrelieved pain, and ongoing or chronic pain

(Huguet & Miro, 2008; Perquin et al., 2000) suggest a significant gap between attempts to improve pain management and outcomes for children.

Since parents make the majority of pain management decisions in the home setting, they play a significant role in managing pain outcomes for children. Yet, little is known about how parents make these decisions or what factors influence them. This is critical given that ineffective treatment decisions can result in suboptimal pain relief or, unwittingly, jeopardize the safety of children. For instance, parents routinely administer analgesics for general everyday pains and after surgery (Jonas, 2003; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, & Halonen, 2003), but often give more than or less than the prescribed daily doses in a manner that correlates only poorly to moderately with their children's pain intensity (Hamers & Abu-Saad, 2002; Helgadottir & Wilson, 2004; Huth & Broome, 2007; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003; Rony, Fortier, Chorney, Perret, & Kain, 2010; Stewart, et al., 2012; Unsworth, Franck, & Choonara, 2007; Vincent et al., 2012; Warnock & Lander, 1998; Wiggins & Foster, 2007; Zisk, Grey, Medoff-Cooper, MacLaren, & Kain, 2008). Additionally, a large number discontinue analgesics even in the presence of ongoing pain (Hamers & Abu-Saad, 2002; Warnock & Lander, 1998), suggesting that parents are responding to or influenced by other situational or personal factors when making these decisions.

Various factors, including concerns about adverse drug effects (ADE), have been shown to influence adult patient's decisions to take analgesics (Older, Carr, & Layzell, 2010). However, it remains unknown how ADEs impact parents' decision-making despite reports of their common occurrence in adults and children who take opioids (Duedahl & Hansen, 2007; Gregorian, Gasik, Kwong, Voeller, & Kavanagh, 2010; L. E. Kelly et al., 2012; Kotiniemi et al., 1997; Sutters et al., 2012; Sutters et al., 2010). ADEs add complexity to medication decisions

since they introduce varying trade-off dilemmas wherein parents must choose between minimizing ADEs versus maximizing pain relief as the pain experience unfolds. Adults with pain have indicated a willingness to give up some pain relief in order to minimize ADEs, even to the point of analgesic discontinuation (Gan et al., 2004; Gregorian, et al., 2010). Yet, it is unknown whether parents make similar trade-off choices when treating their children's pain. Furthermore, while some analgesic decisions involve simple trade-offs between improved pain relief and minimizing non-serious side effects, others may, in fact, jeopardize safety. A growing number of children, for example, require emergency room visits or hospitalization for ADEs, many of which are related to analgesic use (Budnitz et al., 2006). Additionally, the potential for devastating consequences from analgesic use and misuse is underscored by the five-fold increase in opioid poisoning deaths among adolescents (Warner, Chen, & Makuc, 2009), reports of opioid-related deaths after surgery (L. E. Kelly, et al., 2012), and acetaminophen overdose and death (Nourjah, Ahmad, Karwoski, & Willy, 2006). Such grave outcomes may be, in part, related to ineffective trade-off decisions by parents or their children.

Making effective medication decisions requires a basic (gist) level of knowledge about the benefits and risks of prescribed or non-prescribed drugs (Shrank & Avorn, 2007). Such knowledge includes understanding the potential effectiveness of a drug to relieve the type of pain being experienced (i.e., its potency) as well as the possible ADEs and their potential seriousness. Additionally, an understanding of how to respond to ADEs while continuing to treat pain is necessary to ensure safe but effective pain management. Understanding the relative attributes of prescribed opioids and alternative treatments, including over-the-counter (OTC) non-opioids, is required so that parents can choose the most appropriate agent.

However, evidence suggests parental uncertainty about how to give analgesics safely, and a lack of awareness of common and serious ADEs (P. Kankkunen, K. Vehvilainen-Julkunen, A.-M. Pietila, & P. Halonen, 2003a; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003; Rony, et al., 2010; Tait, Voepel-Lewis, Snyder, & Malviya, 2008; Zisk, Grey, MacLaren, & Kain, 2007). Such knowledge deficits may contribute to poor decisions regarding analgesic administration (e.g., giving more or the same dose when they should give less or a different drug, or giving less or nothing when more is warranted) resulting in poor quality pain outcomes or even disaster. Indeed, a recent study showed how widespread confusion and errors contributed to analgesic-related injury and deaths in young children (Tzimenatos & Bond, 2009). Further, parental knowledge deficits may inadvertently promote risky medication practices and misuse among their children since adolescents who self-treat their pain with opioids and non-opioids may rely on their parents for information (Boyd, Esteban McCabe, & Teter, 2006; Fouladbakhsh, et al., 2012; Stoelben, Krappweis, Rossler, & Kirch, 2000). A recent review supports this possibility since data show that adolescent non-medical use of opioids often follows medical use, and is accompanied by misperceptions that these drugs are safe (Schepis, 2011).

Parents' preferences regarding pain treatment and outcomes may further affect their decisions in ways that impose risks or lessen analgesic effectiveness for children. Adults have expressed differing preferences for pain relief and side effects for their own treatment (Gan, et al., 2004; Gregorian, et al., 2010). However, whether or how these preferences translate into treatment decisions for their children is unknown. Since no studies have explored parents' preferences for their children's pain treatment, further study is required to better understand whether or how such preferences facilitate or impede effective analgesic decisions.

Significance of the Problem and Primary Aims

Effective pain management involves making decisions that balance the desired benefit of analgesics (i.e., pain relief) with their undesired risks (i.e., ADEs). It is, therefore, crucial to understand whether parents' analgesic decisions reflect effective trade-offs and to identify factors that potentially impede their effective decision-making. Such understanding is imperative to guide the development of meaningful interventions to optimize analgesic decision-making and outcomes.

This dissertation explored how parents' analgesic knowledge and preferences relate to their decisions to treat acute pain in children when faced with common, non-serious or potentially serious ADEs. The primary aims were to: 1) Examine the relationships between parents' baseline gist analgesic knowledge and perceptions and their hypothetical decisions to treat children in pain with or without the presence of ADEs, and 2) Explore the contribution of parents' preferences for analgesic treatment thresholds and outcomes toward their hypothetical decisions to treat the child in acute pain with or without ADEs. The secondary aim was to describe parents' actual use of analgesics to treat their children's pain after hospital discharge and how pain and the presence of ADEs influenced their actual treatment decisions.

Overview of the Chapters

Chapter II presents a review of the evidence and describes gaps in knowledge regarding parental pain management in the home setting. Chapter III describes the conceptual model that guided this work, and Chapter IV, the methods. Chapters V-VIII summarize the analyses and results, and Chapter IX discusses these findings and their important clinical implications. This dissertation was intended to close the significant gaps in knowledge regarding factors contributing to the safety and effectiveness of parents' analgesic decisions for their children.

Chapter II

Background

Unrelieved Pain in Children

Despite widespread efforts to improve pain management across populations, multiple cross-sectional studies have described a high incidence of pain in healthy children, as well as prolonged moderate to severe levels of pain in children following surgery. As many as 91% of children have reported such pain levels in the first days after surgery (Groenewald, Rabbitts, Schroeder, & Harrison, 2012; Hamers & Abu-Saad, 2002; Jonas, 2003; Wiggins & Foster, 2007), and despite differences in pain severity between surgical procedures, even children undergoing relatively minor procedures are not immune to severe pain (Hamers & Abu-Saad, 2002; Kotiniemi, et al., 1997; Stewart, et al., 2012; Vincent, et al., 2012). Perhaps most concerning is the high prevalence of chronic pain in children and adolescents (Huguet & Miro, 2008; Perquin, et al., 2000; Roth-Isigkeit, et al., 2005), and of prolonged pain after surgery that impairs recovery and return to normal function for many children (Fortier, Chou, Maurer, & Kain, 2011; Fortier, et al., 2009; Stewart, et al., 2012). Recently, 13% of children reported ongoing but intermittent pain and 2%, constant pain several months after surgery, and a majority stated that pain began immediately after surgery (Fortier, et al., 2011). While this study did not explore how pain was managed in the days to weeks after surgery, findings suggest that acute pain may have been inadequately managed.

By and large, research aimed at pediatric pain management has focused on in-hospital or provider management, even though a majority of analgesic decisions likely take place at home.

Recent trends toward ambulatory or short stay surgery for children (Cullen, Hall, & Golosinskiy, 2009) have, in fact, shifted much of the burden of pain management to parents. The existing evidence, albeit limited, suggests wide variability in treatment decisions by parents, with many giving more than or less than the number of prescribed daily analgesic doses. One survey of 315 parents whose young children (aged 1-6 years) had undergone a variety of painful outpatient procedures demonstrated that more than one third experienced moderate to severe pain, yet less than 25% were given the prescribed daily doses of non-opioid or opioid analgesics (Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003).

Other studies have found that while half of parents reported treating their children "regularly" in the first few days after otorhinolaryngologic surgery, many decreased or stopped giving opioid and non-opioid analgesics even as clinically significant pain persisted (Hamers & Abu-Saad, 2002; Warnock & Lander, 1998). In one study, more than a third of parents had sought help regarding pain management but had administered, on average, only half of the prescribed doses of opioid analgesics (Warnock & Lander, 1998). More recently, parents were found to give only half of the prescribed daily doses of acetaminophen with codeine to their children during the first three days after tonsillectomy despite evidence for limited pain relief (i.e., small changes in pain scores after dosing) (Wiggins & Foster, 2007).

Importantly, up to one third of parents have reported avoiding the use of analgesics in the family, though a much smaller number (5-10%) believed that analgesics are unnecessary or should only be used as a last resort (Hamers & Abu-Saad, 2002; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003; Kankkunen et al., 2008). In contrast, 11-31% have reported giving more analgesic doses than ordered, a stronger medication, or combinations of drugs that were not prescribed, suggesting attempts to manage or prevent pain independent of

provider orders (Hamers & Abu-Saad, 2002; Unsworth, et al., 2007). One parent even admitted to doubling the dose of analgesic for pain management rather than calling their child's provider for help (Warnock & Lander, 1998). Together, these findings suggest considerable variability in parents' analgesic decisions. Yet, to date, investigators have not explored reasons for such decisions, and have concluded, overall, that prescription medications are underutilized, and that parents require more skill and knowledge to better manage their children's pain after discharge from the hospital.

Pain Relief Importance

Evidence for the existence of ongoing moderate to severe pain in children after surgery has led some investigators to hypothesize a lack of parental knowledge regarding the importance of pain management. However, data from several studies refute this notion. An early qualitative study of 17 parents whose children had undergone surgery found that *all* expressed the need or desire to provide pain relief as well as pain prevention, and most employed a variety of medication and non-medication comfort measures to relieve their child's pain (Kankkunen, Vehvilainen-Julkunen, & Pietila, 2002). Additionally, a majority of parents whose children were undergoing surgery agreed with general statements that pain can cause psychological (89%) and physical (69%) injury, respectively (Zisk, Grey, MacLaren, et al., 2007), and more than 90% agreed that analgesics should be used to treat common aches and pains, or postoperative pain (Forward, Brown, & McGrath, 1996; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003; Kankkunen, et al., 2008). Furthermore, 78-90% of parents reported giving their children analgesics for either every-day or postoperative pain (Forward, et al., 1996; Jonas, 2003; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003). Together, these findings suggest

that most parents recognize the importance of pain relief and are willing to give analgesics. Variations in their treatment decisions may, therefore, reflect other factors.

Parental Pain Recognition

Some investigators have hypothesized that unrelieved pain reflects the parents' inability to assess or recognize their children's pain. However, qualitative interviews found that parents use a number of methods, not unlike those caregivers use, to determine whether their children are in pain (Kankkunen, et al., 2002). Using structured postoperative diaries, parents recently identified a number of pain behaviors in their children after surgery, including quiet and withdrawn behaviors, verbal cries or complaints, protection of an injury, and need for attention (Rony, et al., 2010). Furthermore, a recent study demonstrated very good sensitivity and specificity of parents' global pain impressions in detecting pain in their children following bone fracture (Zisk, Grey, Medoff-Cooper, & Kain, 2007). Others have found moderate to good correlations between parents' and children's pain ratings, despite some evidence for over- or underestimation by parents (Chambers, Giesbrecht, Craig, Bennett, & Huntsman, 1999; Chambers, Reid, Craig, McGrath, & Finley, 1998; Franck, Allen, & Oulton, 2007; Helgadottir & Wilson, 2004; A. M. Kelly, Powell, & Williams, 2002; Voepel-Lewis, Malviya, & Tait, 2005; von Baeyer, Chambers, & Eakins, 2011; Zisk, Grey, MacLaren, et al., 2007). These data provide evidence that parents are, indeed, reasonable judges of their children's pain.

Several studies have also found low to moderate, but significant correlations (r = 0.20 – 0.52) between children's pain scores and parents' administration of analgesia, suggesting that parents' decisions to treat pain are based, at least in part, on the child's pain severity (Helgadottir & Wilson, 2004; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003; Rony, et al., 2010; Vincent, et al., 2012; Zisk, et al., 2008). In one study, parents gave an additional 0.13

doses of analgesic for each one point increase in their child's Parent Postoperative Pain Measure (PPPM) score following fracture, while others gave 0.22 additional doses for each one point increase in pain score on the day after surgery (Rony, et al., 2010; Zisk, et al., 2008). In contrast, others found no relationship between PPPM rankings of mild, moderate, and severe pain and analgesic doses given by parents on days 2, 3, or over weeks 1 or 2 after tonsillectomy (Fortier, et al., 2009). Overall, the evidence suggests that parents are fair to good at recognizing pain in their children, and base their treatment decisions, in part, on pain intensity.

Parental Preferences for Treatment Thresholds

The differing relationships between parents' dosing and their children's pain scores may reflect, in part, differences in their beliefs about what pain intensity level warrants treatment. A growing body of literature has yielded average pain score thresholds or "cut-points" at which adults and children express the desire for analgesia (DeLoach, Higgins, Caplan, & Stiff, 1998; Dihle, Helseth, Paul, & Miaskowski, 2006; Gauthier, Finley, & McGrath, 1998; Mendoza et al., 2004; Voepel-Lewis, Burke, Jeffreys, Malviya, & Tait, 2011). Although these average cut-points are strikingly similar across studies despite a variety of settings (emergency room versus postoperative) and types of pain (i.e., chronic versus acute), data also show a great deal of individual variability (i.e., scores at which *individual* adults or children desire an analgesic). Furthermore, one study found that preferred cut-points varied depending on the postoperative day (Mendoza, et al., 2004), suggesting that personal threshold preferences may change with other expectations as the pain experience unfolds.

Parents' preferred treatment thresholds for their children has only been described in 2 studies, to date. In one of these, investigators found significant variability in the levels of pain at which parents would administer acetaminophen for common pains (e.g., mean severity of 4.4 ±

2.1 out of 10 to treat earache). Furthermore, these data exposed differing preferred treatment thresholds for different types of everyday pains (e.g., mean 4.4/10 for headache versus 5.9/10 for muscle/limb pain) (Forward, et al., 1996). Another study found wide variation in parents' estimates of their child's preferred treatment thresholds after surgery (i.e., range of 2 to 4.5 out of 6 on a Faces Pain Scale [FPS]) (Demyttenaere, Finley, Johnston, & McGrath, 2001). In this study, parents' own treatment thresholds were not explored, and parents' estimates agreed with their child's *stated* thresholds in only 24% of cases. Parents' estimates were higher than the child's in 56% of the cases, and lower in 32%. These data emphasize the potential variability in parents' and children's treatment thresholds. It remains unknown whether there is similar variability in the thresholds at which parents would prefer to give opioid or non-opioid analgesics for their children's postoperative pain. Furthermore, it is unknown whether treatment thresholds shift in the presence of other symptoms (i.e., ADEs), or whether such arbitrary thresholds affect the quality or safety of pain management.

Interventions to Improve Parents' Pain Recognition

Data from several studies suggest that parental assessments of their child's pain intensity may not be lacking, and even with explicit instructions to treat based on pain scores, parents' assessments insufficiently explain their treatment decisions. Attempts to improve parents' assessment of pain through education and the use of specific tools have failed to demonstrate significant improvements in parents' administration of analgesics (i.e., measured by increased doses of analgesics given) or in children's pain scores after surgery.

One study examined whether improved pain assessment would improve the concordance between parents' actual use of analgesics and a prescribed algorithm that acetaminophen should be given for mild pain, ibuprofen for moderate pain and codeine after ibuprofen for the severest

pain (Unsworth, et al., 2007). Parents were randomized to assess pain at their discretion (i.e., routine using whatever they would normally do to recognize pain) versus using a formal assessment (i.e., obtaining child's self-reported FPS), and were instructed regarding what scores represent mild or moderate to severe pain. There were no differences in the total number of analgesic doses given between groups, nor in the number of doses of ibuprofen or codeine given, but acetaminophen was given more often to children whose parents assessed their pain at their own discretion. Nearly two thirds of parents in both groups gave non-opioids when there was no pain (FPS = 0 or parents' perception), reflecting a widespread preference to prevent pain.

Unsworth et al. (2007) further found that parents who formally assessed their children followed the analgesic instructions for only 53% of doses they administered. They gave a lower-order drug than instructed for 6% (e.g., acetaminophen when ibuprofen should have been given) and a higher order or non-prescribed combination for 41% (e.g., ibuprofen plus acetaminophen, when only one of these should have been given). When parents formally assessed their child's pain as mild, they strayed from instructions for nearly one third of their treatments, giving nothing in 5% and a higher order drug in 31% of cases. Treatments were discordant with instructions for nearly one quarter of episodes of moderate to severe pain where parents gave codeine against orders in 10% of these cases, a combination of non-opioids in 34%, and under-treated in the majority (55%). These data suggest that, despite explicit instructions based on children's pain ratings, parents made many decisions that strayed from those advised. The reasons for such decisions were not explored, nor were the influence of the child's other signs or symptoms.

A more recent study randomized 50 parents from several settings to assess their child's pain using the PPPM and a global rating scale (none, mild, moderate, severe) versus the global

rating scale alone, and similarly found no differences between groups in the amount of pain reported nor in the number of analgesic doses administered following outpatient surgery (Kankkunen et al., 2009). Twelve and 13% of parents in the intervention group, however, gave the maximum daily recommended doses on days 1 and 2, respectively, although this was not significantly different from the controls. Pain management instructions were not standardized suggesting that decisions were left to the discretion of the parents.

Lastly, Franck et al. (2007) randomized 111 children aged 6-12 to have their pain assessed using either a paper version of a pain scale versus a tattooed version and found no differences in documented pain scores, number of analgesic doses given, nor in pain scores between groups at home. These findings suggested a limited effect of this new pain assessment method despite its excellent acceptance by children and their parents.

Parent Analgesic Knowledge

While a basic understanding of medications is important for effective and safe decision-making, relatively little is known about parents' analgesic knowledge. Despite familiarity with commonly used OTC analgesics, parents may lack knowledge regarding their safe use. Recent surveys found that most adults admitted to the emergency department with pain lacked knowledge about the acetaminophen (or paracetamol) content and recommended maximum daily doses of common OTC medications, and 18% reported taking more than the upper limit in order to achieve pain relief (Fosnocht, Taylor, & Caravati, 2008; Wood et al., 2010). Similarly, only 49% of surveyed parents who had given acetaminophen or ibuprofen for fever or pain within 24 hours of their child's emergency room admission gave a correct dose (Li, Lacher, & Crain, 2000). Furthermore, 47% of these parents gave their children doses that were too low, and 15% gave doses that were too high. Only half based their dosing on a physician's instructions, while

8% guessed, and surprisingly, 20% based their dosing on the "height of the fever." These studies suggest a widespread lack of knowledge that could potentially impact safety.

Knowledge deficits regarding more potent analgesics, such as those prescribed after surgery, may be even greater. Many parents have reported uncertainty about how to dose analgesics postoperatively and how to know when pain becomes too severe (Kankkunen, et al., 2002). Others have expressed a general concern and worry about being able to manage their children's postoperative pain at home (Vincent, et al., 2012). In structured surveys, up to half of parents agreed with or were uncertain about statements that analgesics work best when used infrequently or as little as possible (Forward, et al., 1996; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003; Kankkunen, et al., 2008; Rony, et al., 2010; Zisk, Grey, MacLaren, et al., 2007). Parents have also expressed surprise at how high the recommended analgesic doses were postoperatively and disbelief when provider instructions did not agree with package inserts (Kankkunen, Vehvilainen-Julkunen, et al., 2003a; Kankkunen, et al., 2002; Kankkunen, et al., 2008). Some of these ambivalent parents reported a greater reliance on friends, family, package inserts or pharmacists over healthcare providers when making analgesic decisions.

Other data suggest that many parents lack gist knowledge about analgesic ADEs. Thirty-seven percent have reported being uncertain as to whether "pain medication has many adverse effects" (Zisk, Grey, MacLaren, et al., 2007), and 25%-30% about whether children become dependent or whether pain medicines are addictive (Finley, McGrath, Forward, McNeill, & Fitzgerald, 1996; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003; Rony, et al., 2010; Zisk, Grey, MacLaren, et al., 2007). Importantly, a lack of specificity in these surveys regarding analgesic types and effects hinders the interpretation of findings regarding parent knowledge.

One recent study more specifically asked parents to indicate their knowledge of common opioid-related ADEs, and found that many had no understanding of the possibility of nausea and vomiting (23%), itching (28%), sedation (15%), constipation (31%), or respiratory depression (35%), and one quarter to half of parents were unaware of the serious nature of certain effects such as over-sedation and respiratory depression (Tait, et al., 2008). More than half of the parents in this study could not recall being given any information about the risks and benefits of the opioids prescribed to their children.

Hegarty et al. (2012) similarly found that while all parents were given analgesic information preoperatively in a mailed packet and by phone the day before surgery, less than half (48%) recalled receiving any information in the packet and 36%, in the phone call. Yet, the majority of these parents (85%) reported that analgesic instructions, given at any time, were clearly understood. Such findings add to the evidence suggesting that individuals perceive a greater understanding of medication information than they actually demonstrate when assessed (Sepucha et al., 2010). Together these studies suggest that a large number of parents lack critical knowledge regarding the analgesics ordered for their children. Yet, the relationship between specific knowledge deficits and parents' treatment decisions remains unknown.

Preferences, Perceptions and Treatment Decisions

Although no studies have directly examined parent preferences for their children's analgesic outcomes, related literature offers some insight into the relationship between preferences, perceptions and similar medical decisions. For instance, several studies have demonstrated differing preferences for different outcomes (e.g., pain relief, nausea, vomiting, etc.), as well as heterogeneity in adult patients' willingness to trade-off pain relief for ADE reduction when taking analgesics for acute or chronic pain (Gan, et al., 2004; Gregorian, et al.,

2010; Katic, Krause, Tepper, Hu, & Bigal, 2010; Older, et al., 2010). One of these found that most of the variance in analgesic preference was explained by ADEs and not analgesic ability to relieve pain (Gregorian, et al., 2010). Further, these preferences were stable from preoperatively to two weeks postoperatively, even as ADEs presented.

Whether parents make similar trade-off evaluations for their children's pain outcomes is unknown, however evidence suggests that parents do think differently about risks and may make more risk-averse decisions when their role as parent is made salient (Eibach & Mock, 2011). For example, a large sample of adults was asked to make hypothetical medical decisions either for themselves or in the role as parent of an at-risk child (Zikmund-Fisher, Sarr, Fagerlin, & Ubel, 2006). Subjects in the role of parent choosing for their children were more likely to choose treatments described as "survival maximizing" (i.e., flu immunization or cancer treatment) compared to those making decisions for themselves. Additionally, subjects in the parent-role exhibited higher "emotional activation" scores (e.g., composite of distress, concern, responsibility), suggesting a differing level of engagement when making decisions for their children. These findings suggest that parents may exhibit different trade-off perspectives and focus on different treatment attributes and outcomes when making decisions for their children.

The influence of emotion and tendency for risk-aversion has also been demonstrated in other studies of parents whose perceptions of risks and benefits predicted only a portion of variance in their immunization decisions, with a significant proportion attributed to anticipated feelings of regret of causing harm by action (i.e., immunizing) or inaction (i.e., not immunizing) (Wroe, Bhan, Salkovskis, & Bedford, 2005; Wroe, Turner, & Salkovskis, 2004). These findings suggest that parents' decisions reflect preferences to minimize harms to their children due to treatments themselves (i.e., commission), as well as harms from not treating (omission). The

trade-off conflicts posed by such choices and the preference to minimize harm may, indeed, be a source of the emotional activation and distress demonstrated above.

Parents' trade-off perceptions (i.e., relative treatment benefit/ risk understanding) have also been associated with their likelihood of initiating or ensuring their children's adherence to chronic medication regimens (Bussing et al., 2012; Conn et al., 2005; Conn, Halterman, Lynch, & Cabana, 2007). Lastly, Wroe (2002) showed that adult patients' *intentional* non-adherence to chronic medications was mostly explained by their perceptions of pros and cons of the treatment (i.e., decision balance), and concluded that intentional medication discontinuation may represent a rational, risk-related decision-making process. Together, these studies suggest a significant influence of preferences regarding the risk-benefit trade-off on patients' and parents' treatment decisions that may help to explain their medication decisions.

A few studies have examined parental analgesic "beliefs" or "attitudes" and the relationship between these general perceptions and analgesic administration. Several structured surveys expose variability in parents' perceptions regarding analgesic side effects with just over half agreeing that "as little pain medication as possible should be given due to side effects," and three quarters, that "analgesic side effects are something to worry about" (Zisk, Grey, MacLaren, et al., 2007). In contrast, in both Finnish and American samples of parents, only few agreed with statements that analgesics for home use have "dangerous" side effects (1 and14%, respectively) or, more generally "are dangerous for children" (8 and 21%) while a greater number (27 and 34%) agreed that doses at home should be smaller than in the hospital (Kankkunen, et al., 2008). Significant but weak relationships have been found between parent analgesic perceptions and their use of analgesics in several studies (Forward, et al., 1996; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003; Rony, et al., 2010). For instance, scores on a side effects

subscale, where higher scores reflected "positive analgesic attitudes," correlated positively but weakly (r = 0.11; p<0.001) with mothers' administration of acetaminophen to children in a healthy population-based sample of 298 (Forward, et al., 1996). Furthermore, scores correlated negatively with mothers' stated thresholds at which they would treat their children's earaches and headaches (r = -0.16 and -0.15, respectively, p < 0.001).

More specifically, Kankkunen et al. (2003) found that compared to parents who gave analgesics to their children postoperatively, those who did not were more likely to agree that "*analgesics for home use may have dangerous effects.*" Others recently found that scores in the highest quartile of a medication attitudes questionnaire (indicating "*attitudinal barriers toward providing children analgesia*") predicted lower doses given by parents (Rony, et al., 2010). Despite differences in phrasing or timing of questions and populations, these studies suggest, overall, that general attitudes regarding adverse effects – which may provide some indication of preferences – contribute, at least in small ways, to parent treatment decisions. None of these studies, however, examined the potential presence and influence of parents' trade-off preferences, that is, their desire to control pain as well as reduce risk.

Preferences for Treatment, Parent Role, and Child Characteristics

Whether fathers and mothers differ in their preferences for managing their child's pain and how such differences relate to treatment decisions is unknown. However, related data suggest that parent role, as well as the child's characteristics may influence analgesic use in the home. For instance, one study found that fathers rated their sons' experimental pain thresholds significantly higher compared to their daughters', while mothers' ratings for sons and daughters were similar (Moon et al., 2008). This study also showed that fathers' scores were more concordant with their children's scores compared to mothers' scores. Other studies of chronic

and laboratory-induced pain show positive relationships between mothers' attention to pain and their children's complaints and between either parents' past pain history and children's pain modeling (Evans, Lu, Tsao, & Zelter, 2008; Walker et al., 2006). Together, these data suggest a potential influence of parent role and their past pain experiences on children's pain experiences.

An influence of child sex on parents' decisions to treat is also plausible, given evidence of significant relationships between gender, pain behaviors and perceptions. For instance, in experimental settings, healthy boys, particularly those with higher masculinity ratings, were less willing to express pain compared to girls (Myers et al., 2006; Wise, Price, Myers, Heft, & Robinson, 2002). Compared to boys, girls have also associated perceptions of moderate to severe pain with lower pain scores (Gauthier, et al., 1998), but have also expressed satisfaction with pain and analgesia at higher scores (Voepel-Lewis, et al., 2011). Finally, some data suggest differences between girls' and boys' self-reported everyday pain, its triggers and imposed restrictions, as well as their medication use in response (Roth-Isigkeit, et al., 2005). These findings suggest, perhaps an influence of experience and possibly gender socialization toward pain and treatment perceptions. Lastly, there may be an influence of child age on parental decisions since older children have reported satisfaction with treatment at higher scores compared to younger children (Voepel-Lewis, et al., 2011). How parents respond to these differences, and whether their treatment preferences or decisions differ based on age and sex of the child remains unknown.

Parental Willingness to Give Non-opioids and Opioids

Familiarity and past experience with pain and analgesics were recently found to strongly influence adult patients' intentional decisions to take analgesics following outpatient surgery (Older, et al., 2010). Parents' willingness to give familiar, OTC non-opioids versus more potent

narcotic analgesics may be similarly related to familiarity and experience. For instance, a general population of mothers were found to have, on average, four different types of children's analgesics in their cupboards, although rarely (< 2%) prescription analgesics (Forward, et al., 1996). Almost all of these mothers kept acetaminophen at home (96%) and 75% had administered this drug to their children in the preceding month. Most of these and another group of parents reported not being worried about giving acetaminophen (80%) and that it is safe to give in recommended doses (90%) (Finley, et al., 1996; Forward, et al., 1996). Such findings show a general willingness to administer analgesics that are familiar.

Data from parents whose children had outpatient surgery similarly suggest a high level of comfort giving acetaminophen that may differ from comfort with giving opioids. In one study, parents who were not explicitly advised about when to administer the prescribed codeine versus non-opioids primarily gave paracetamol or ibuprofen (93% of doses) or a combination of these (7%), while none gave the prescribed opioid (Unsworth, et al., 2007). In another study, compared to 76% of parents who administered the prescribed opioid, more parents (86%) gave their children acetaminophen during the first 3 days after tonsillectomy and increasingly substituted this common analgesic for the opioid over time, despite ongoing moderate pain (Huth, Broome, Mussatto, & Morgan, 2003). A number of studies have also found that, often in lieu of analgesics, parents use a variety of non-pharmacologic comfort measures (e.g., cuddling, rest, distraction, ice packs), rating them as effective as analgesics in relieving their child's postoperative or fracture pain (Jonas, 2003; P. Kankkunen, K. Vehvilainen-Julkunen, A.-M. Pietila, & P. Halonen, 2003b; Kankkunen, et al., 2002; Zisk, et al., 2008).

Together, these data demonstrate variability in parents' pain treatment choices that are not well-explained by the level of pain intensity alone. Reasons for variable parent choices were

not explored, but may involve knowledge deficits or uncertainty, personal preferences, as well as degree of trust in providers – factors that are common themes in adult patients' reasons for using analgesics after surgery (Older, et al., 2010). Many adults who reported taking their prescribed analgesics after surgery stated they did so to follow the doctors' instructions since they trusted their opinion or wanted to do as they were told. Why parents choose to follow or veer from analgesic prescription instructions remains largely unknown.

Variable Effect of Interventions on Parent Decisions

Despite ongoing gaps in knowledge regarding parent analgesic decisions, several studies have attempted to "improve" parents' analgesic use at home by altering their perceptions, by giving more directive instructions or by ensuring the immediate availability of their child's prescription. These studies have focused on increasing parents' analgesic administration and have yielded mixed effects on parents' analgesic use and children's pain scores.

Huth, et al. (2003) randomized 51 parents to receive either routine information versus a pain booklet and individual instruction that included information about the importance of pain management, how to assess and manage children's pain with analgesics and non-pharmacologic approaches. Although parents in the intervention group demonstrated a significant increase in perceived analgesic benefits post-intervention, there were no differences in analgesic use or children's pain scores between groups.

In another study, parents were randomized to receive "take home" analgesics (i.e., dispensed to parents prior to discharge) versus "advised only" (i.e., parents required to purchase analgesics) in an attempt to increase their analgesic use (Hegarty et al., 2012). Instructions in both groups were to give ibuprofen every 8 hours for the first day, and paracetamol with codeine as needed for more painful procedures only. Parents in both groups gave the same number of

analgesic doses (drug type not reported) over the first 24 hours after surgery (mean 3 doses, range 1-12), and a similar proportion of children experienced moderate-severe pain (41% in the advised group vs. 38%, dispensed). The rates of nausea and vomiting were also similar between groups (21% and 16% for the advised and dispensed groups, respectively). Importantly, the study may have been confounded by the fact that majorities of parents in both groups reported having OTC analgesics at home prior to surgery.

Two studies have randomized parents to "around the clock" (i.e., ATC) versus as needed (PRN) dosing of codeine/acetaminophen (Sutters et al., 2004) or hydrocodone/acetaminophen in an attempt to overcome attitudinal barriers (Sutters, et al., 2010). Parents in both studies were educated using a dosing "skills lab" and instruction not to give anything other than the prescribed analgesic. Parents in the ATC groups were additionally given a digital timer for dosing notification. In both studies, there were no differences in analgesic dosing on the day of surgery, but higher dosing for the ATC groups on days 1 to 3. Dosing decreased significantly over the 3 days for the PRN groups, but not the ATC groups. There were no differences in pain scores between groups in the codeine study but significant decreases for some of the assessments on days 1 and 2 for the ATC group in the hydrocodone study.

Importantly, there was a high incidence of ADEs across groups in both of these studies by Sutters (2004 & 2010). For instance, the codeine study reported that 35 and 49% of children in the PRN and ATC groups, respectively, had nausea, 13 and 21% had vomiting, and 8 children with intolerable nausea and vomiting had been excluded (group membership not reported). In the hydrocodone study, there were no differences in events between groups on days 0-3 (small effect size), yet all events decreased over time for the PRN but not the ATC group, with the exception of constipation. Nausea remained the same over time for the ATC group (from 31%

on day one to 27% on day 3) and constipation increased (from 6 to 22%). There was a high incidence of "daytime sedation" across groups (Sutters, et al., 2010). Investigators did not explore whether or how parents whose children experienced ADEs altered analgesic dosing in response.

Of concern, investigators dismissed the high incidences of ADEs and concluded that "*fear of opioid-related side effects should not be used as a reason not to administer ATC therapeutic weight-based dosing to children at home after tonsillectomy*" (Sutters et al., 2010, p. 102). This suggestion is particularly alarming since it dismisses the potential impact of ADEs on the comfort and safety of children. Indeed, children undergoing tonsillectomy are at high risk for respiratory depression (Brown, 2011; Niesters, Overdyk, Smith, Aarts, & Dahan, 2013), and as many as 18% of children taking opioids at home have been found to have "heavy sedation" (Kotiniemi, et al., 1997), which is a known precursor to respiratory sedation (Eckstrand et al., 2009; Vila et al., 2005; Voepel-Lewis et al., 2012). Indeed, signs of oversedation were evident, but overlooked by parents of several children who died from opioid toxicity (L. E. Kelly, et al., 2012; Madadi et al., 2010). The notion that ADEs should be downplayed in prescriptive instructions, therefore, represents a concerning bias and potentially risky viewpoint.

Summary and Gaps in Evidence Regarding Parents' Analgesic Decision-Making

The evidence, to date, suggests that most parents administer analgesics for general everyday pains or after surgery, yet little is known about factors contributing to their decisions or whether these decisions are potentially effective or ineffective. Although optimal pain management often requires trading off analgesics or doses that promote more potent pain relief in order to minimize or lessen ADEs, studies, by and large, have exposed an underlying investigator bias that parents should give more analgesic doses rather than effectively balance

their decisions within the context of ADEs. The primary focus on pain relief and a paucity of attention to ADEs has left a significant gap in knowledge regarding the effectiveness and safety of parents' analgesic decisions.

The high prevalence of medication ADEs as well as clinically significant pain in children suggests that analgesic trade-off decisions are often sub-optimal and that knowledge may, indeed, be lacking. Furthermore, the potential for serious ADEs, such as over-sedation or respiratory depression, suggests the need for parents to recognize and respond to signs of opioid toxicity, including oversedation. Yet, it remains unknown whether specific knowledge deficits hamper parents' ability to recognize and respond to either common or serious events. A lack of critical knowledge regarding how to effectively manage such trade-off situations may lead parents to rely, instead, on their preferences for treatment outcomes.

To date, parents' preferences for their children's outcomes remain unknown, and it is unclear whether strong preferences influence their analgesic decisions in ways that potentially jeopardize safety or effective pain relief. Although it is clear that many parents and adult patients' analgesic use is highly variable, it is unknown what factors contribute to potentially sub-optimal treatment decisions. Limited evidence suggests stable patient preferences where some adults in pain prefer analgesic options that provide less pain relief to those with higher risks, while others prefer an option with greater pain relief despite known risks (Gan, et al., 2006). It remains unknown whether parents have similar preferences for their children or how such preferences impact the effectiveness and safety of their decisions.

Lastly, interpretation of evidence, to date, is hampered by the lack of specificity in surveys, particularly with regard to differentiating parent knowledge and perceptions regarding opioids and non-opioids. Given the importance and potentially serious consequences of analgesic

risk-benefit tradeoff situations, it is imperative to identify factors that contribute to ineffective or potentially harmful treatment decisions. Findings, to date, have left an important gap in our understanding of parental analgesic treatment decisions that must be addressed in order to develop appropriate strategies to improve analgesic decisions and ensure safety in the home setting.

Chapter III

The Analgesic Decision: A Conceptual Framework

The Analgesic Decision

Effective pain management in the home setting relies on analgesic decisions that balance the trade-off between maximizing pain relief and maximizing safety. Furthermore, analgesic decisions involve a dynamic and context-dependent process that is likely affected by multiple factors as the pain experience unfolds. Most central to this process is the *decision* itself, which is, like other decisions, a "*course of action. . .made to achieve goals . . . based on [parents' or provider's] beliefs about what outcomes will be achieved by the action*" (Baron, 2008c).

A high quality analgesic decision is regarded in the same vein as a good medical decision, that is, one that is likely to promote a better health outcome (Reyna, 2008a). Good decisions are, therefore, not only those associated with favorable outcomes (e.g., good pain relief), but those that potentially prevent or reduce risk (e.g., adverse drug effects), and that involve choosing among options for the one that promotes a better overall outcome (Yates, Veinott, & Patalano, 2003). A poor decision might, in contrast, include choosing an option or dose of analgesic that is less likely to promote pain relief in the presence of significant pain, or one that adds certain risk in the presence of serious adverse event symptoms (e.g., oversedation).

A good analgesic decision should also reflect an "*informed choice,*" that is, the individual's evaluation of treatment options within the context of their personal values (Woolf, 1997; Woolf et al., 2005). Informed decision-making requires understanding the options for treatment including their risks and benefits, the uncertainties associated with treatment, and

which treatment(s) promotes the outcomes that are best associated with personal values (Woolf, et al., 2005). Thus, informed choice of whether to give an analgesic or not, when to give it, whether to give the prescribed dose, a different dose, or perhaps, a different drug, relies on knowledge, understanding, personal values, and preferences.

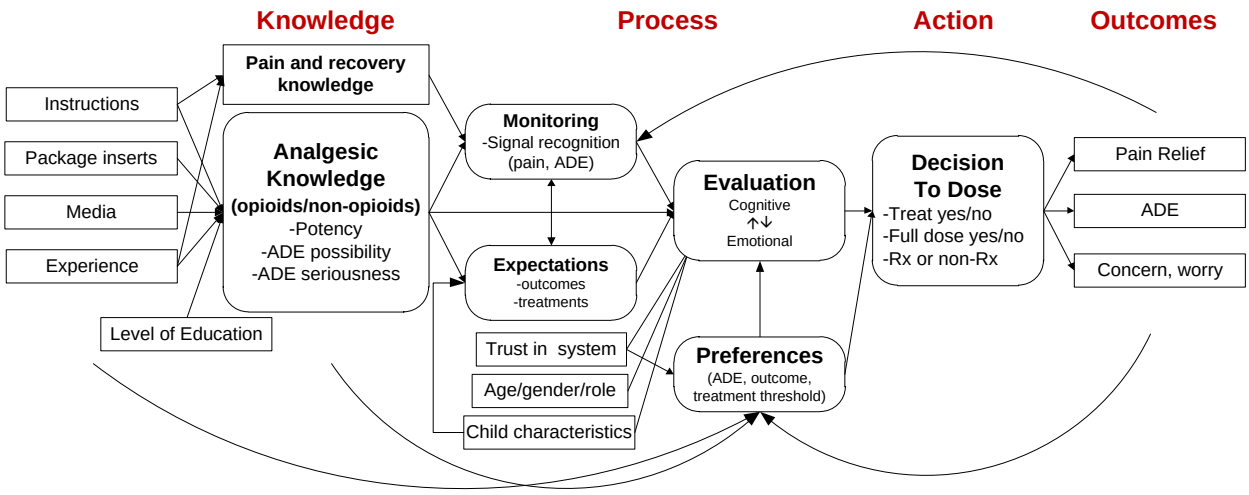
Analgesic Decision Process and Concepts

Evaluation. Parents' choice of administering an analgesic or withholding one is reliant on their *evaluation* or judgments of multiple factors that come into play during the decision process. This involves weighing up the options (i.e., alternative drugs or comfort measures) and possibilities (i.e., pain relief or adverse effects) within the context of the problem (i.e., the situation at hand). The process involves recognition of "*signals*" that arise from monitoring the situation, that is, whether or how much pain and other symptoms are occurring; interpretation and *understanding* of these signals, and; whether or how these signals fit with *expectations* of the situation and effects of treatment. Evaluations also involve parents' overall *preferences* for treatment and outcomes (i.e., when to treat and whether to maximize pain relief or minimize risk). Such preferences may manifest in different ways as the situational context unfolds (Elwyn & Miron-Shatz, 2010).

Simple evaluations require, at a minimum, the knowledge of what to look for, the potential treatment options, and their relevant attributes (Elwyn & Miron-Shatz, 2010). For the analgesic decision, the minimum level of knowledge necessary for effective evaluation is a recognition of important signals (i.e., pain level and important symptoms), the options (e.g., opioid, non-opioid, other comfort measure), their ability to relieve pain (i.e., potency), their possible adverse effects, and the potential seriousness of these effects. The theoretical model of

the analgesic decision process that guides this research is depicted in Figure 1. The concepts and decision theory from which this model was derived is described in detail below.

Figure 1. Conceptual Model of Analgesic Decisions



Pain and symptom (i.e., "signal") recognition. The variable responses of children to pain and medications mean that parents must recognize the potential seriousness of signs and symptoms, monitor them, and be able to respond appropriately. This ability has been referred to as signal detection which implies the recognition that a "signal" indicates something relevant to be attended to or acted on. This notion has been used to evaluate and explain clinician decision-making, particularly with regard to patient safety and medical diagnoses (Meyer & Lavin, 2005; Thompson & Yang, 2009). In the analgesic context, such signals include the level of pain or pain interference with function or recovery, and the nature of adverse drug events (ADE) and other symptoms. Parents expect pain after surgery, but must recognize when pain requires action. Parents may also expect or, conversely, be surprised by an ADE. Appropriate response to an ADE requires signal detection and the understanding that the signal is serious enough to warrant attention.

Signals usually occur within a background of "noise," or otherwise unimportant distractions or irrelevant information (Meyer & Lavin, 2005). The individual's ability to correctly respond to signals within the context of noise is related to their expectations and situational awareness, that is, their mental representation of situation-specific information and the possible implications (McGuinness, 2004). McGuinness (2004) more simply describes situational awareness as the individual's answers to questions such as; "*What is happening? Why is it happening? What will happen next? What does it mean in terms of my objectives? What can I do about it?*" (p.1). Good decision-making, thus demands an appropriate attachment of meaning (e.g., seriousness), and the distinction between actions that will appropriately address the relevant signals.

When faced with situations where the child has multiple signs (e.g., significant pain, over-sedation, nausea), parents must, therefore, have and retrieve knowledge that enables differentiation of important signals (e.g., over-sedation) and appropriate action (e.g., stop opioid). The ability to discriminate between valid and invalid situational descriptors reflects "signal sensitivity" (McGuinness, 2004). Importantly, individuals may demonstrate a cognitive strategy or "response bias" leaning conservatively toward rejecting an uncertain or ambiguous signal or, more liberally, toward accepting it. For instance, parents who are uncertain about ADEs may lean toward always ignoring them and treating the pain signal alone, or may always attend to ADEs, indiscriminately withholding analgesics. Such biases may inadvertently lead to ineffective or unsafe actions, or conversely, may be protective.

Analgesic knowledge and decision-making. Recognizing important signals and taking appropriate action in response to them requires an understanding and retrieval of relevant analgesic knowledge. Parents' analgesic knowledge is likely derived from multiple sources

including provider instructions, drug information inserts, past experiences, and the media (e.g., advertising and news). How parents integrate and reason with this knowledge is what influences their ultimate decision to treat. Their understanding and integration of information may be moderated to at least some degree by their educational level and background (Zisk, Grey, MacLaren, et al., 2007).

Gist knowledge, dual processing and reasoning. Analgesic knowledge and understanding is dependent on memory and the ability to retrieve these memories within context. Fuzzy trace theory (FTT) posits that information is rapidly encoded and ordered into working memory based on levels of precision ranging from verbatim knowledge (i.e., interval level data that preserve exact numerical representations) to "fuzzy" or vague *gist knowledge* (i.e., crude nominal or categorical representations, such as presence versus absence of an attribute/characteristic) (Reyna & Brainerd, 1995). Reasoning involves the use of verbatim and gist knowledge where verbatim provides a basis for a more cognitive or analytical type of problem solving and gist a more qualitative and intuitive approach. These two distinct types of reasoning or thinking have been described as System 1 and System 2, which involve fast, automatic or intuitive thinking (i.e., instinctive) versus slow, controlled or deliberative thinking (i.e., rational), respectively (Kahneman, 2011). Fast, intuitive thinking processes involve interpreting situations based largely on associative or gist memory.

A large body of evidence supports that the preferred method for reasoning is the lowest, least precise or more qualitative level in the "hierarchy of gist" and that this preference increases with experience or expertise (Djulbegovic, Hozo, Beckstead, Tsalatsanis, & Pauker, 2012; Reyna, 2004, 2008b). The knowledge that parents rely on when making analgesic decisions, then, is more likely to reflect a gist or qualitative understanding of a drug's characteristics (e.g.,

ability to relieve pain, the possibility of specific ADEs). Reliance on gist is, furthermore, likely to increase as parents become more experienced with treating their child's pain.

Gist knowledge and trade-offs. Importantly, individuals are cognitively flexible, drawing on different levels of knowledge (i.e., gist or verbatim) depending on the complexity of the task at hand (Reyna & Brainerd, 1995; Reyna, Lloyd, & Brainerd, 2003). As the pain experience becomes more complex (e.g., child in pain but also experiencing adverse symptoms or ADEs), parents may draw on different types of knowledge when evaluating options and making decisions. Less complex analgesic decisions may call only for retrieval of a simple risk categorization (i.e., risk, no risk), while complex decisions may call for retrieval of higher order knowledge such as ordinal (lower or higher risk) or, perhaps, higher verbatim (this risk probability versus that risk probability) (Reyna, 2008b).

Having a basic gist awareness of a particular risk or outcome reduces the possibility that someone will be surprised if and when that outcome occurs (Zikmund-Fisher, 2012). However, according to Zikmund-Fisher (2012), more complex trade-off situations demand a gist understanding of comparative possibility (i.e., which option provides greater benefit or fewer risks) in order to determine a dominant treatment option. He argues that higher levels of comparative probability understanding (i.e., verbatim) may be unnecessary in order to make effective tradeoffs *if* what is needed is only to understand that there is a higher or lower chance of an outcome (i.e., ordinal gist). Gist knowledge that one analgesic is more likely associated with a serious ADE while another is not may, therefore, be all that is needed for parents to make a good trade-off decision for their child, particularly as that ADE or signal presents itself. On the other hand, more precise information regarding numerical risk data may be required when individuals need to consider the degree of differential risk or benefit between treatments

(Zikmund-Fisher, 2012). Thus, more precise risk data may be important when two alternative analgesics carry different degrees of risk for a particular ADE (e.g., low vs. high risk of nausea).

Emotion in evaluation and judgment. Parents' evaluation and ultimate choice of an analgesic option involves not only gist knowledge, but also consideration of the preference for potentially competing goals (i.e., pain relief versus ADE avoidance or reduction). Such preferences may be largely influenced by the emotional meaning that the parent has attached to specific outcomes (e.g., pain) or attributes of an option (e.g., nausea). Whereas reasoning is considered to be the cognitive or "thinking" process behind rational judgment (Baron, 2008a), evidence from actual and simulated decision-making experiments suggests that judgment is largely influenced by an emotion-based process (Finucane, Peters, & Slovic, 2003; Loewenstein, Weber, Hsee, & Welch, 2001). This dual cognitive-emotional process of decision-making is a dominant theory to explain how people judge options and arrive at their decisions (Djulbegovic, et al., 2012; Reyna, 2008a, 2008b; Reyna & Brainerd, 1995; Reyna, et al., 2003).

This process involves anticipatory emotions which are "*immediate visceral reactions* (e.g., fear, anxiety, dread)" to particular stimuli (i.e., risks or uncertainty) that arise during a decision-making situation (Loewenstein, et al., 2001). Such reactions are generally rapid and intuitive (i.e., part of System 1 thinking) compared with cognitive evaluations, and they may actually protect against danger by refocusing cognitive processes on high priority issues (Loewenstein, et al., 2001). Reactions to risk involve an interaction between a person's cognitive and emotional evaluations, wherein the cognitive appraisal induces emotions and, likewise, those emotions influence the appraisal (Loewenstein, et al., 2001). When the choice of an option is difficult, such as when outcomes are uncertain or when goals are in conflict, the influence of emotion may be even greater (Elwyn & Miron-Shatz, 2010). Thus, the interplay

between cognition- and emotion-based reasoning may be particularly germane to the analgesic decision given the conflicting goals of maximizing pain relief and maximizing safety, as well as the uncertainty of particular risky outcomes (i.e., whether or not an ADE will occur).

Emotions may further sway judgments when risks are vivid or "affect rich," that is, they evoke strong emotions such as fear or disgust (Amsterlaw, Zikmund-Fisher, Fagerlin, & Ubel, 2006; Loewenstein, et al., 2001; Zikmund-Fisher, Fagerlin, & Ubel, 2010). In these situations, judgment may be influenced by a disproportionate weighting of attributes or options due to strong, intuitive feelings, good or bad, and, perhaps, the desire to avoid regret after a decision is made. Findings from a recent study by Amsterlaw, et al. (2006) demonstrated how the possibility of affectively salient complications (i.e., colostomy and intermittent diarrhea) led individuals to make decisions that were incongruent with their preferences (i.e., reduced mortality) and rational judgments (risk/benefit probabilities) in order to avert such risks.

For analgesic decisions, strong, negative emotions associated with one or more attributes, like severe pain or addiction or vomiting, may therefore strongly sway the parents' choice to give or withhold an opioid. Analgesic attributes that do not evoke emotional meaning for the individual (e.g., sedation) may be ignored during the analgesic decision process, since information that does not evoke positive or negative feelings is not readily evaluable or interpretable (Peters, Klein, Kaufman, & Meilleur, 2013). Affective processing may in some cases enhance analgesic decisions (e.g., withholding a medication associated with a severe ADE). Conversely, emotions can lead to suboptimal analgesic decisions that err on the side of preference principles rather than sound analgesic knowledge.

Preferences and reasoning. Depending on the complexity of the situation at hand, different attributes or signals may be more or less salient to the individual's deliberations,

leading to inconsistencies and potential "errors" in their decision-making (Schneider & Barnes, 2003). The influence of preferences during these evaluations may be related to whether or how emotional meaning has been encoded into memory in concert with gist knowledge representations. FTT suggests that emotional gist "principles" are framed from pre-existing values that are reflected in *preferences* (i.e., evaluative judgments) (Reyna, et al., 2003). These gist preference principles and their associated affect (positive or negative) are retrieved when the individual is faced with new decision problems. They help to define, guide, and sometimes, disrupt knowledge-based reasoning by introducing potential biases or inconsistencies that make decision-making appear to be irrational. Reyna et al. (2003) suggests that the positive principle reflects the preference that more of some attribute is better than less, or some of it is better than none, all other attributes being equal (e.g., more pain relief is better than less). Conversely, the negative preference principle reflects the notion that less of an attribute is better than more, or none of it is better than some (e.g., few or no ADEs are better than some).

These gist preference principles are readily retrieved together with gist knowledge about options and their attributes, thereby, influencing the individual's judgments about them. Some investigators argue that preferences are fluid and constructed as individuals gain more information (Elwyn & Miron-Shatz, 2010). In FTT, however, it is assumed that core values and preferences do not necessarily shift even though the individual's qualitative interpretation of options may change with changing contexts or situations (Reyna, 2008b).

Recognition and preferences. Integration of personal preferences and affect into the evaluation process can sometimes lead to a holistic representation of options, particularly when they are well-known (Svenson, 2003). Holistic representations reflect the overall "attractiveness" of the option and can influence decisions by an overall impression rather than a

consideration of specific attributes. For instance, since most parents are highly familiar and comfortable with the analgesic, acetaminophen, they may form a holistic positive representation about this option and choose to administer this drug over other less familiar options or those for which they have a negative impression (e.g., Vicodin®). This holistic representation may also lead to underestimation of negative characteristics of the option (e.g., acetaminophen-associated liver failure).

Competing gist knowledge, preferences and decision error. According to FTT, decision error results from failure to encode appropriate gist, competing gist interference, or failure to retrieve appropriate preference principles in context (Reyna, 2008b; Reyna, et al., 2003). Individuals may, for instance, encode facts correctly (e.g., Vicodin® carries the possibility of over-sedation) but not their qualitative significance (e.g., seriousness of over-sedation), leading to omissions of important principles in the decision process. Conversely, a person may have encoded appropriate gist knowledge but doesn't use it due to competing gist from other less relevant background "noise" or information (Reyna, 2008b). Analgesic decisions that involve various options with differing risks in changing contexts may be particularly error prone due to the presence of compelling gist knowledge or preferences for specific but perhaps less relevant attributes (e.g., possibility of addiction may be more compelling than the need to relieve pain).

Decision errors may be attributed, in part, to biases that result from "heuristics" (i.e., cognitive short-cuts) which is a processing strategy whereby some information or attributes are ignored in order to make decisions more efficiently (Gigerenzer & Gaissmaier, 2011; Gigerenzer & Selten, 1999). In this type of processing, evaluation of two or more alternatives involves a simple search for cues, stopping at the first option that meets an aim, and choosing the option that is favored by the most important or salient reason (Gigerenzer & Gaissmaier, 2011).

Recognition or fluency heuristics influence judgment by placing greater weight or value on attributes or options that are more readily recognized compared to others. For instance, some attributes of a medication (e.g., strong pain relief) or signals (e.g., nausea) may be more readily recognized compared to others (e.g., risky over-sedation), thereby earning greater weight in decisions. Contradictory but important attributes or signals that are unfamiliar may be ignored, potentially leading to poor decisions. Such heuristics may be associated with either failures of understanding or the influence of strong values, preferences, or emotions (Baron, 2008b). Biased decisions occur more often when outcomes are uncertain, ambiguous or risky, and when emotionally salient attributes lead to the neglect of other more relevant information.

Expectations, reference points, and decision-making. Parents' expectations for the pain experience and treatment effects may lead to arbitrary "reference points" on which to base their ongoing analgesic trade-off evaluations and decisions. Frame of reference provides a "*fundamental source of meaning*" to situations that help individuals to define the problem, identify options, and determine the relevant attributes and preferences (Schneider & Barnes, 2003) p. 420). Individuals may choose different options based on what they believe to be the status quo, or starting point. For analgesic decisions, the reference may be the prescription itself (i.e., analgesic dose and prescribed frequency), a starting level of pain (e.g., pre-operative, baseline, or some expected level), or a preferred treatment threshold (i.e., the level of pain that parents think should trigger treatment).

Such reference points and subsequent expectations are likely influenced by the parents' role, since mothers and fathers may have differing knowledge, preferences and expectations regarding the pain experience based on their own past experiences. Additionally, the child's characteristics (i.e., age, gender, previous pain experience) may influence or moderate parental

expectations and decisions. For instance, parents may expect younger children to be more vulnerable to drug effects, and therefore set a lower starting dose or higher treatment threshold. Differing expectations for boys versus girls may also influence reference treatment thresholds.

Lastly, when decision-makers are uncertain about how their goals (as determined by preferences and affect) should be mapped onto options, they may restructure the problem in a manner to provide more support for their status quo or initial choice (Svenson, 2003). In this manner, uncertainty or ambivalence regarding certain signals may lead parents to fall back on what they believe to be a safe and sure or status quo option (e.g., give the prescribed dose).

Conceptual Model for Analgesic Decisions

Conceptually, then, parents' decisions to treat their children's pain with analgesics are dependent on the retrieval and application of gist knowledge, their ability to recognize and interpret important signals, as well as their own preferences regarding pain relief and risk avoidance. In order to gain a better insight into parental analgesic decisions with an aim to ensure good decision-making, it is important to know how parents respond to various pain and analgesia related signals, and whether or how knowledge and preferences contribute to effective or ineffective decisions as the pain experience unfolds. Based on this model and dual processing theory, I hypothesized that the relationships between these factors and parents' decision to treat or withhold an analgesic would shift in relation to the changing context of the pain experience/situation as differing signals became more or less salient.

Chapter IV

Aims and Methods

This study explored parents' analgesic knowledge and preferences for treatment and outcomes, and examine the relationships between these factors and parents' decisions to administer analgesics to children who are experiencing acute postoperative pain. I was primarily interested in factors that may influence parents' decisional responses to situational signals including; the child's pain level, symptoms of a rare but potentially serious opioid-related adverse drug event ADE (i.e., over-sedation), or symptoms of a common, but less serious ADE (i.e., nausea, vomiting). My central hypothesis was that gist analgesic knowledge deficits would be associated with parents' ineffective (withhold the prescribed opioid to child in moderate-severe pain who is not experiencing an ADE) or unsafe (give the prescribed opioid to child experiencing ADEs) analgesic decisions.

In addition to describing parents' decisional responses to various signals (i.e., pain level and ADEs), the primary aims of this study were to; 1) Examine the relationships between parents' baseline gist analgesic knowledge and perceptions and their decisions to treat children in pain with or without the presence of ADEs, and 2) Explore the contribution of parents' preferences for analgesic treatment thresholds and outcomes toward their treatment decisions. The secondary aim was to describe parents' actual use of analgesics to treat their children's pain after hospital discharge and to identify factors associated with their real decisions. The specific research questions and hypotheses that were tested are shown in Table 1.

Table 1. Specific Aims, Hypotheses and Research Questions
Specific Aim (SA) 1: To examine the relationships between parents' baseline gist knowledge and their decisions to treat children in acute pain with or without the presence of ADEs.
Hypothesis (H) 1a: A lack of gist knowledge regarding the possibility and/or seriousness of opioid-related nausea and vomiting will be associated with a failure to lower the dose or discontinue opioids for children in pain where this ADE is present.
H1b: A lack of gist knowledge regarding the possibility and/or seriousness of opioid-related excessive sedation will be associated with a failure to discontinue opioids for children in pain where this ADE is present.
H1c: Parents' gist understanding of relative analgesic potency and risk will be associated with their decisions to substitute acetaminophen for the prescribed opioid for children in moderate-severe pain.
Research Question (RQ) 1: How do parents' gist understanding and perceptions of opioid ADEs relate to their decisions to administer opioids to children in pain with or without ADEs?
SA2: To explore the contribution of parents' preferences for analgesic treatment thresholds and outcomes toward their decisions to treat the child in acute pain.
RQ2a: How much of the variance in parents' opioid administration is explained by their preferences for pain relief versus ADE avoidance, when adjusted for gist understanding, situation (ADE presence), and parent/child characteristics?
RQ2b) How do parents' threshold preferences contribute to parents' treatment decisions?
RQ2c: How do parent and child characteristics relate to their treatment decisions?
SA3: To explore parents' use of analgesics to treat their children's pain after discharge and factors that affect their decisions.
RQ3a: How many doses and what type of analgesics (opioids and non-opioids) are administered by parents in the first 3 days following surgery?
RQ3b: Does gist analgesic knowledge and/or parent preferences correlate with parents' use of prescribed analgesics in the home setting?
RQ3c: How do the child's pain and ADE experiences relate to parents' decisions to administer prescribed analgesics?
RQ3d: Do parents describe any other factor (e.g., cost or availability of analgesic) that affect their decisions to give analgesics in the home setting?

Research Design

I used a prospective, exploratory, survey design to answer the research questions and test the proposed hypotheses. Specifically, I employed a descriptive, cross-sectional, within-subject hypothetical model of decision-making to test the first two hypotheses. For these, hypothetical

scenarios were manipulated in order to observe parents' decisions and to examine factors associated with them (Baron, 2008b). To explore the research questions in the third aim, I used a longitudinal approach, wherein factors were collected during the preoperative waiting period and the outcomes over the first three days after hospital discharge.

Ethical Review

The Institutional Review Board (IRB) University of Michigan Medical School approved the study with a waiver of consent to screen for potential subjects using the daily surgery schedule (HUM00070613; Appendix A). All subjects provided their written informed consent prior to inclusion (Appendix B). I piloted all survey instruments following exemption from the IRB (HUM00070550; Appendix C).

Setting

The primary study setting was the pediatric perioperative area of C. S. Mott Children's Hospital which is a dedicated pediatric hospital within the University of Michigan Health System, a tertiary care, academic institution in the Midwestern region of the United States.

Sample

Adult parents (i.e., > 18 yrs of age) of children (aged 3 to 17 years) who underwent an elective, non-cardiac surgical procedure known to be associated with moderate to severe pain that required treatment with a prescribed opioid following hospital discharge were recruited. Parents who understood written English, and were the legal guardian and caretaker residing in the home where the child recovered after surgery were included. Parents were excluded if they were participating in another pain study, if their child had a hematologic/oncologic or other condition requiring ongoing, chronic pain management, or if their child required more than an overnight hospital stay postoperatively.

Description of the Instruments

We developed the surveys using an iterative process following a review of the extant literature, and with expert input from pediatric pain providers in the Department of Anesthesiology and from decision researchers in the School of Public Health and Medical School. The Preoperative Survey consisted of three sections; 1) General Knowledge of Pain Medicines, 2) Preferences for Analgesic Outcomes, and 3) Hypothetical Pain Treatment Decisions. The general content of the survey is described in Table 2 below, and complete surveys are included in Appendix D. We piloted various iterations of the instrument in small samples of parents (n = 4-5 with each iteration, up to 30 in all) in the perioperative waiting areas to examine face validity and feasibility (i.e., that the instrument appears to measure general analgesic knowledge and preferences from the perspective of parents, and does so in an efficient manner). Following several revisions to wording, formatting, and structure, we piloted the final survey among 10 parents and asked them to verbalize in their words what the survey was meant to do. All parents readily stated that it was meant to see what they knew about analgesics, and how they preferred to treat their children's pain under different situations. Completion took approximately 15-20 minutes, and parents' responses were complete, supporting the face validity and feasibility of the survey.

General knowledge of pain medicines items. These items assessed parents' general or gist knowledge regarding the commonly used OTC analgesic, acetaminophen (i.e., Tylenol®), and the most commonly prescribed narcotic, hydrocodone/acetaminophen (i.e., Vicodin®). I adapted the items, in part, from a previous study that assessed parents' understanding of children's postoperative pain management (Tait, et al., 2008). Although not all children are

prescribed Vicodin® after surgery, all oral opioids are associated with the same types of ADEs. Thus, gist knowledge of these agents would have relevance for parents' real analgesic decisions.

Table 2. Description of the Preoperative and Postoperative Surveys

Preoperative Survey		
Component	**Description**	**Assessment**
General Knowledge of Pain Medicines	29 items (nominal or Likert responses) Assesses gist understanding of possible ADEs, seriousness of ADEs, and relative understanding of effectiveness or potency 18 items (nominal) assess familiarity with and recent use of common analgesics (OTC and prescribed)	Face validity
Trade-off Preferences for Analgesic Outcomes	6-Items (ordinal response) Assesses parents' preference for pain relief (PR) relative to ADE avoidance; scores range from -12 to +12 (higher scores indicate a preference for pain relief (PR), and lower scores, ADE avoidance) 2-Items (nominal response) assess parents' stated-choice for drug (e.g., high PR/high ADE vs. Lower PR/low ADE)	Internal consistency, structural validity & predictive validity
Preference for Treatment Thresholds	2-Items (likert response) assess preferred treatment thresholds (i.e., lowest level at which parents prefer to administer a drug to their child) using 0-10 Faces Pain Scale (FPS)	Face validity
Hypothetical Decision Scenarios	4 Scenarios wherein pain level and ADE presence are manipulated (nominal response) Assesses parent decisions under varying trade-off situations	Face validity
Postoperative Survey-Diary		
Pain Treatment Diary	21 structured and open-ended questions (nominal and string) Records parents' actual administration of pain drugs at home, the child's pre-treatment pain level, experienced ADEs, and management issues	Face validity

The gist knowledge deemed relevant for parents' analgesic decisions includes an understanding of whether an ADE is a possible drug effect and a general understanding or perception of the relative seriousness of specific ADEs. Relevant ADE items were adapted using information from drug package inserts, and lay literature including opioid warning cites (Leavitt,

2010). Items were not meant to provide an exhaustive set to measure understanding, but rather, a more specific assessment of parents' understanding of the possibility and seriousness of certain common and less common, but serious effects. Since gist perceptions regarding the relative potency (i.e., ability to relieve pain) and overall riskiness of analgesics may be important when deciding between treatment options, items were added to address these factors. Clinicians with expertise in pediatric pain management (2 nurses, 2 pain researchers and a pharmacist) reviewed the knowledge items and qualitatively judged the content to adequately assess the domain of interest, i.e., gist knowledge/perceptions needed to recognize ADEs and their relative importance.

An abbreviated list of common, as well as rare but potentially serious opioid adverse effects identified in the literature and drug inserts was included (Kotiniemi, et al., 1997; Sutters, et al., 2010; Tait, et al., 2008). The survey asked parents to indicate whether people ever experience each ADE using nominal responses (definitely not, probably not, probably do, definitely do). Likert responses were used to assess parents' gist understanding of ADE seriousness (not serious to extremely serious) and the relative strength and riskiness of opioid and non-opioid analgesics.

Trade-off preference items. This component assessed parents' relative preference for pain relief versus ADE avoidance (i.e., trade-off preferences). The items incorporated a risk-benefit ordinal ranking component and a simplified stated-choice method, similar to methods described in previous studies examining patient preferences for chronic medication treatment (Bridges, Onukwugha, Johnson, & Hauber, 2007; Johnson & Hauber, 2008; Johnson, Hauber, & Poulos, 2009; Phillips, Johnson, & Maddala, 2002). I used this method to simply elicit the relative value that parents place on general and specific treatment outcomes without burdening

them by a more complicated preference elicitation method (Ali & Ronaldson, 2012; Phillips, et al., 2002). The items were based on those from surveys that assessed patient perceptions of medication benefits and risks using a risk-benefit tradeoff framework (i.e., the perceived importance of benefits versus the concern for adverse effects) (Clifford, Barber, & Horne, 2008; Tibaldi et al., 2009), as well as from surveys using stated-choice analgesic preferences (Gan, et al., 2004; Gregorian, et al., 2010; Johnson & Hauber, 2008).

The final survey incorporated six statements to assess the relative importance of providing pain relief relative to the need to minimize ADEs. Parents ranked their agreement with each statement from strongly disagree (-2) to strongly agree (+2). Items reflecting a preference for risk avoidance (items 2 and 6) were recoded so that all could be summed to reflect the overall preference for pain relief (i.e., scores ranging from -12 to +12), where lower numbers indicate a preference for ADE avoidance, higher numbers, pain relief, and the middle range, indifference or ambivalence (Clifford, et al., 2008; Tibaldi, et al., 2009). We included two distinct stated-choice items depicting hypothetical trade-off attributes of analgesic options (i.e., one option with excellent pain relief but higher ADEs –either nausea or excessive sedation, and the other with fair pain relief but lower ADEs). The survey asked parents to choose their preferred drug option for each question in order to elicit trade-off preferences.

We piloted a preliminary 10-item preferences survey among 100 parents of children aged 3-17 years who agreed to complete the survey. One hundred surveys were distributed, and 91 complete surveys were returned. I conducted an exploratory factor analysis using the principle components method (assuming a common variance) and reliability analysis to examine the relationship between items on the scale and to reduce the number of items (Fabrigar, Wegener, MacCallum, & Strahan, 1999). The Kaiser-Meyer-Olkin (KMO) sampling adequacy (0.80) and

the Bartlett's test of sphericity (χ^2=319.14; p<0.001) supported the appropriateness of the analysis, and application of the Kaiser criterion (Eigenvalue>1) identified a 3 factor solution explaining 67% of the variance. The six items from two theoretically coherent factors were retained, and a repeated factor analysis demonstrated that 2 factors (i.e., fair pain relief versus complete pain relief) explained 67% of the variance in this abbreviated survey (KMO sampling adequacy 0.734; p < 0.001) (results depicted in Appendix E). Scores on the 6-item survey ranged from -10 to +9 (mean 2.17; confidence interval 1.39, 2.95) and were normally distributed. The internal consistency of the 6 item scale was supported with Cronbach's coefficient alpha 0.71 (confidence interval 0.61, 0.80; p < 0.001). Preference scores were compared between parents who chose Drug A versus Drug B for the two stated-choice items in order to assess predictive validity. Scores were higher (i.e., greater preference for pain relief) for Drug B in the first choice question (i.e., excellent pain relief but higher nausea/vomiting compared to Drug A; 4.05 ± 2.7 vs. 0.37 ± 3.44; p < 0.001), and higher for Drug A in the second (i.e., excellent pain relief but more sleepiness and excessive sedation compared to Drug B; 2.84 ± 0.27 vs. 0.27 ± 3.28; p<0.001). These findings support preliminary internal reliability and predictive validity of the scale.

Parents' analgesic threshold preferences. Two items required parents to indicate the lowest level of pain at which they would administer either Tylenol® or Vicodin® for their child's postoperative pain by circling the respective face on the commonly used FACES© pain scale (FPS) (Hockenberrry & Wilson, 2009). I chose this pain assessment method since it could be applied across the age groups of children whose parents were included.

Hypothetical pain scenarios. We developed these items to assess parents' treatment decisions when faced with varying levels of pain and differing ADEs. The survey provided

simple instructions regarding the hypothetical opioid prescription (Vicodin®) and an alternative over-the-counter non-opioid (Tylenol®), to mimic real information provided on printed prescriptions as well as common verbal instructions regarding use of Tylenol®. Immediately following these instructions, were four pain scenarios wherein the level of pain and the presence (or absence) of either a common ADE (i.e., nausea/vomiting) or potentially serious one (i.e., excessive sedation) were manipulated. In three of these, the child's pain level was held constant at a moderate to high level (i.e., FPS = 6) (Hockenberrry & Wilson, 2009). Data suggest that this pain intensity level is above the average level considered "treatable" by adults, children, and parents (Forward, et al., 1996; Voepel-Lewis, 2011; Voepel-Lewis, et al., 2011). These scenarios included one with no ADE symptoms, one describing the common ADE, nausea plus one episode of vomiting, and one describing symptoms of the potentially serious ADE, oversedation. In the fourth scenario, the child's pain level was lower (FPS = 4, or the average treatable pain score) and the child had the common ADE symptom, nausea.

For each situation, the survey asked parents to make a forced choice between five treatment options (i.e., the prescribed opioid dose, half of the prescribed dose, half the prescribed dose plus Tylenol®, Tylenol® alone, or another option (to be written in by parents). We later coded parents' choices coded for analysis as shown in Table 3. Responses of "other" were coded as appropriate (e.g., ibuprofen = non-opioid; comfort measure or homeopathy = no analgesic). A single, open-ended question asked the parents to explain why they made the choice they did for each scenario. This question was intended to elicit the primary signals that were used in decision-making. Two independent coders later coded these responses based on the primary scenario or prescription signals attended to by parents including; pain level or need for pain relief, ADE presence or concern, time for next dose of medicine, or doctor's order.

Parent and child characteristics. I included several items to elicit data regarding parent and child characteristics including; the parents' role, level of education, and race, as well as the child's age, sex, and surgical procedure. A 10-item Health-Systems Trust Scale assessed parents' trust in providers or the health system since this factor has been shown to be associated with medication adherence and analgesic use (Older, et al., 2010). The scale used here has good internal consistency (Cronbach's alpha 0.75) and construct and concurrent validity in measuring the trait, *trust in the healthcare system* (Armstrong et al., 2006; Older, et al., 2010; Rose, Peters, Shea, & Armstrong, 2004).

Postoperative pain treatment diary (Appendix F). This self-administered survey provided a simple method for parents to record the type and number of analgesic doses given postoperatively, and the child's pain level prior to dosing. The survey additionally asked parents to describe any ADEs that occurred (open ended) and whether they changed care in relation to the ADE(s). Parents were asked whether they sought help after discharge, from whom, and why, and also to add any comments regarding concerns or issues with the child's care at home. These open-ended descriptions were coded and analyzed in a descriptive manner. The number of doses of prescribed opioid and non-opioid analgesics was tallied, and the average pain score triggering treatment with either was calculated. Lastly, the percentage of morphine equivalents given per day out of the prescribed amount, and the difference between prescribed and actual doses administered were calculated.

Decisional Outcomes (i.e., Dependent Variables)

The primary outcomes of interest were the parents' decisions to administer analgesics as defined in Table 3. Decisions were dichotomized by grouping parents' nominal responses to the four hypothetical scenarios. The primary outcomes were 1) the parents' decision to administer

the prescribed opioid dose (Group A) and 2) the decision to administer any opioid dose (includes the prescribed dose, Group A, and the lower dose choices, Group B). Withholding opioids altogether included the choice of giving a non-opioid (Group C) or nothing (Group D). These outcomes were chosen based on generally accepted (i.e., normative) criteria for treating children with moderate to severe postoperative pain and for reducing or responding to an analgesic ADE. Parents' real analgesic decisions were measured using the number of postoperative doses given over the first 3 postoperative days, and the percentage of prescribed doses administered, as recorded using the postoperative diary.

Table 3. Description and Measurement of Decision Outcomes

Decisional Outcomes	**Measured by responses to hypothetical scenarios as coded below**	**Level of Measurement**
Gave prescribed opioid dose	*Prescribed dose (Group A) vs. other choice (includes lower opioid dose, non-opioid, or nothing, Groups B+C+D)*	Nominal
Gave any opioid dose	*Opioid (includes prescribed dose or lower dose, Groups A+B) vs. other choice (includes non-opioid or nothing, Groups C+D)*	Nominal
Overall analgesic decision	*Opioid (includes prescribed dose or lower dose, Groups A + B) vs. non-opioid (Group C) vs. nothing (Group D)*	Nominal
Postoperative Outcomes	**Measured by responses in postoperative diary**	
Postoperative analgesic doses administered	*Number of analgesic doses given* *Percentage of prescribed dose given*	Ratio Ratio

Factors of Interest (i.e., Independent Variables)

The primary factors of interest were the parents' analgesic gist knowledge of ADE possibility and perceived seriousness, and their preferences for analgesic outcomes (i.e., pain relief versus ADE avoidance) and treatment threshold (i.e., lowest level of pain at which they

would give an opioid). Of particular interest, was the parents' domain-specific knowledge of the possibility and perceived seriousness of the potentially dangerous ADE, oversedation, and the more common, less-serious ADEs of nausea and an episode of vomiting. Gist knowledge, analgesic perception, and preference items were coded and analyzed as defined in Table 4.

Table 4. Definition and Measurement of Independent Variables of Interest

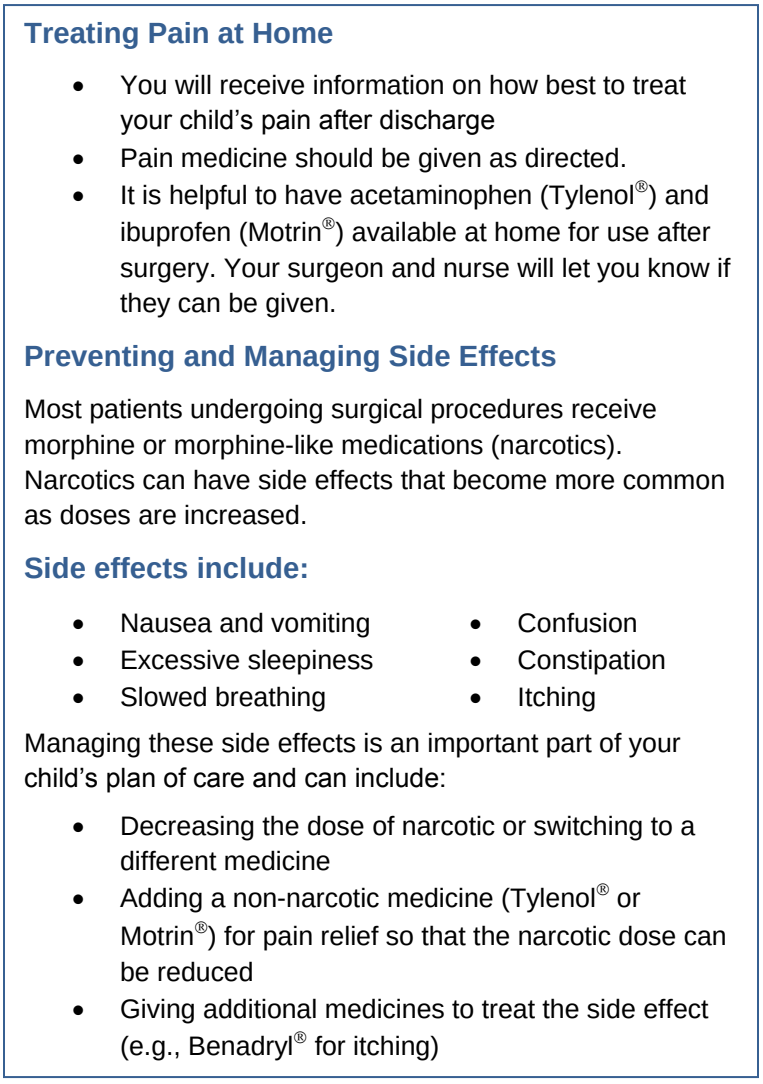
Variable	Measure (range)	Level of measurement
Gist analgesic knowledge and perceptions		
ADE Possibility Knowledge	*Effect possible (probably/definitely versus probably not/definitely not) (0/1)*	Nominal
ADE Seriousness Rating	*Likert rating of ADE seriousness (1 to 6)*	Interval
Knowledge/Perception Ratings	*Linear combination of ADE knowledge* seriousness perceptions*	Interval
Domain-specific knowledge/ perception (i.e., knowledge of a specific ADE *seriousness)	*Sedation awareness * seriousness (0 to 6)* *Nausea awareness *seriousness (0 to 6)*	
Aggregate opioid ADE knowledge/ perception	*Sum [individual ADE knowledge * seriousness scores] (0 to 48)*	
Comparative opioid potency difference	*Vicodin® potency rating minus Tylenol® potency rating (-4 to +4)*	Interval
Comparative opioid risk difference	*Vicodin® risk rating minus Tylenol® risk rating (-4 to +4)*	Interval
Analgesic Preferences		
Pain Relief (PR) (i.e., Trade-off) Preference (pain relief vs. ADE avoidance)	*Sum of preference items (higher score = prefer pain relief) (-12 to 12)*	Interval
Analgesic Threshold Preference	*FACES® scale rating (0-10, where 0 = no pain, and 10 = worst pain)*	Interval

Procedure

We reviewed the surgery schedule daily to identify children who were scheduled to undergo a painful surgery procedure requiring a post-discharge opioid prescription (e.g.,

orthopedic, urologic, and other common procedures). Eligible parents were approached consecutively as they arrived for surgery in the preoperative area. Consenting parents completed surveys during the waiting period while their children were in the operating room. In this manner, all parents had received standard verbal and written information from their healthcare provider regarding what to expect after surgery, and about their child's general postoperative pain management plan including use of prescribed opioids and non-opioids, and a description of their common side effects (excerpt shown in Figure 2). We briefly instructed parents on how to complete the preoperative survey, and the assistant was available to answer questions as they arose. Once the preoperative survey was complete, parents were given the postoperative survey/diary with a pre-stamped return envelope to be taken home and completed over the first three days following their child's discharge from the hospital setting. We instructed parents to keep this survey with the child's pain medications, and to record each medication at the time of administration. Parents were telephoned or emailed on the third post-discharge day to remind them to finish any incomplete portion and return the survey.

Figure 2. Excerpt from the University of Michigan's General Preoperative Pain Management Instructions



Treating Pain at Home

- You will receive information on how best to treat your child's pain after discharge
- Pain medicine should be given as directed.
- It is helpful to have acetaminophen (Tylenol®) and ibuprofen (Motrin®) available at home for use after surgery. Your surgeon and nurse will let you know if they can be given.

Preventing and Managing Side Effects

Most patients undergoing surgical procedures receive morphine or morphine-like medications (narcotics). Narcotics can have side effects that become more common as doses are increased.

Side effects include:

- Nausea and vomiting
- Excessive sleepiness
- Slowed breathing
- Confusion
- Constipation
- Itching

Managing these side effects is an important part of your child's plan of care and can include:

- Decreasing the dose of narcotic or switching to a different medicine
- Adding a non-narcotic medicine (Tylenol® or Motrin®) for pain relief so that the narcotic dose can be reduced
- Giving additional medicines to treat the side effect (e.g., Benadryl® for itching)

Statistical Analyses

All analyses were conducted using SPSS© (version 20, IBM Corporation, New York). Prior to testing the hypotheses of interest, I examined the sample characteristics and factors of interest using general descriptive statistics. Histograms, boxplots, and, as deemed necessary, tests of normality (e.g., Kolmogorov-Smirnov) assessed the variables for normality. Simple comparisons of group differences (e.g., child sex and procedure or child sex and parent threshold preferences) were made using chi-square with Fisher's exact tests or unpaired *t* tests, where

appropriate. All tests were two-sided and P values of < 0.05 were accepted as statistically significant.

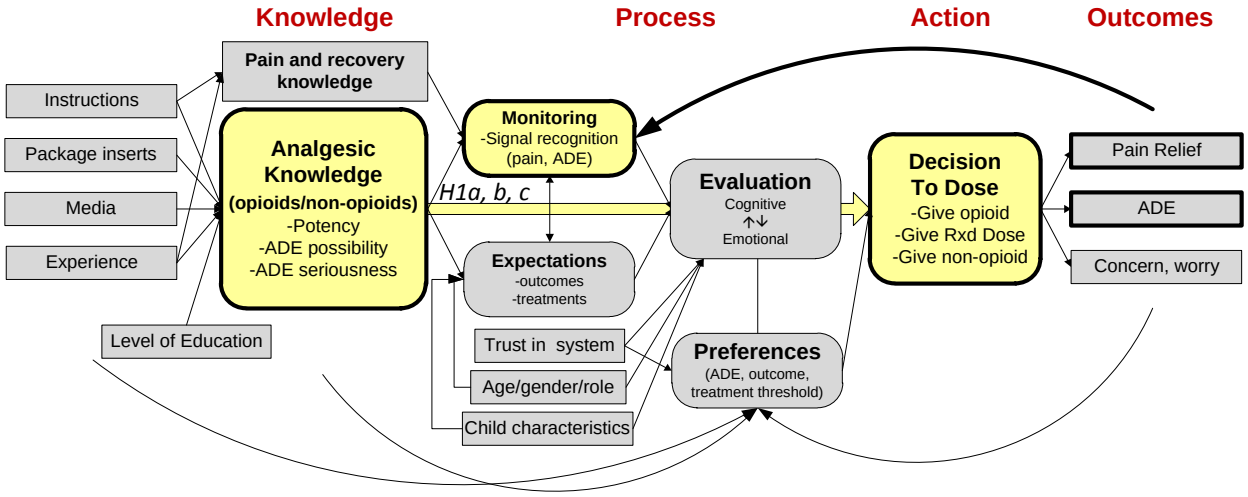
Next, I used the non-parametric analysis of variance for repeated measures (i.e., Friedman test) to examine parents' responses to the ADE and pain signals across scenarios (i.e., the change in parents' decisions to treat pain). We coded treatment decisions as in Table 3, above, to test the hypotheses, and analyses for each of these are described below.

Specific aim (SA) 1. ***Hypotheses (H) 1a and b: a) A lack of gist knowledge regarding the possibility and/or seriousness of opioid-related nausea and vomiting will be associated with a failure to lower the dose (i.e., to give something less than the prescribed dose) or discontinue opioids (i.e., give a non-opioid or nothing) for children in pain where this ADE is present. b) A lack of gist knowledge regarding the possibility and/or seriousness of opioid-related excessive sedation will be associated with a failure to discontinue opioids (i.e., give any dose opioid vs. withhold opioid) for children in pain where this ADE is present (Figure 3).*** I used separate chi-square tests to examine the relationship between parents' gist understanding of opioid-ADE (yes vs. no) and their dichotomized decisions to 1) give the prescribed opioid dose (Group A) versus lower the dose or withhold opioids (Groups B+C+D), and 2) give any opioid dose (i.e., the prescribed dose *or* lower dose, Groups A+B) versus withhold opioids (i.e., give non-opioid or nothing, Groups C+D). Unpaired *t* tests analyzed the relationship between parents' seriousness ratings as well as their aggregate opioid ADE knowledge/perception scores and these decisions.

SA1, H1c: ***Parents' gist understanding of relative analgesic potency and risk will be associated with their decisions to administer analgesics to children in moderate to severe pain.*** For this hypothesis, parents' comparative analgesic perceptions (i.e., comparative analgesic

potency, risk, and threshold differences– between Tylenol® and Vicodin®) were the relevant factors of interest. I used Kruskal-Wallis ANOVA to compare parents' comparative perceptions between those who gave any opioid dose (includes the prescribed dose or lower dose, Groups A+B), versus non-opioid (Group C), versus nothing (Group D) for children in the high pain scenarios. Associations between parents' dichotomized perceptions of the relative strength of half-dose Vicodin® versus full-dose Tylenol® and the decision to give any opioid dose (Groups A+B) vs. withhold opioids (Groups C+D) were examined using the Chi-square test.

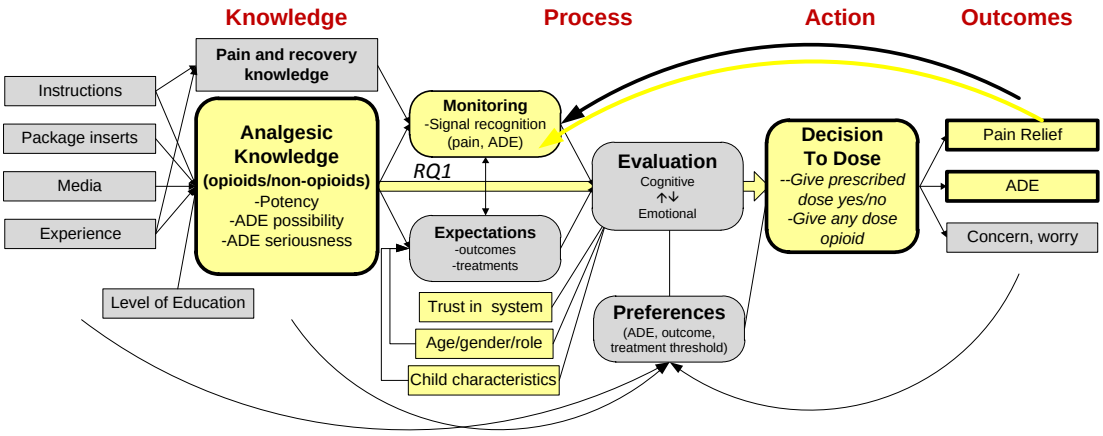
Figure 3. Hypothesized Relationship between Gist Analgesic Knowledge and Analgesic Decisions



SA 1, Research Question (RQ) 1: ***How do parents' gist understanding and perceptions of opioid ADEs relate to their decisions to administer opioids to children in pain with or without ADEs (Figure 4)?*** I used hierarchical, logistic regression (HLR) models to explore the relationships between the opioid ADE knowledge/perception factors and parents' individual hypothetical opioid decisions, controlling for parent and child factors. First, I explored the relationship between parent/child factors and decisions to ensure appropriate coding and inclusion of these variables in subsequent models. The parent/child factors were entered at the

first step and the opioid knowledge/perception (i.e., either domain specific or aggregate opioid knowledge/perception) and familiarity factors at the second. The decisional outcomes 1) *gave any opioid dose (i.e., dichotomized as give the prescribed dose/lower dose, Groups A+B vs. give non-opioid/nothing, Groups C+D)* and 2) *gave the prescribed opioid dose (i.e., dichotomized as give the prescribed dose, Group A vs. give lower dose/non-opioid/nothing, Groups B+C+D*) were regressed on the independent variables separately for each of the hypothetical scenario decisions. Models are described in more detail as the analyses are presented (Chapter VI).

Figure 4. Hypothesized Relationships between Knowledge, Parent/Child Factors and Analgesic Decisions



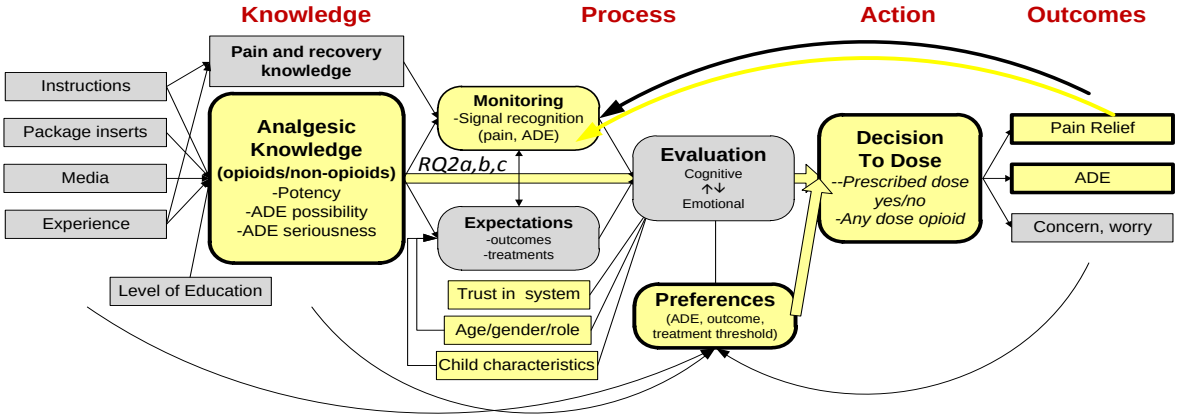
Specific Aim 2. ***RQ2a) How much of the variance in parents' opioid administration is explained by their preferences for pain relief versus ADE avoidance, when adjusted for gist understanding, situation (ADE presence), and parent/child characteristics (Figure 5)?***

RQ2b) How do parents' threshold preferences contribute to parents' treatment decisions?

I examined the effects of PR (trade-off) preference and opioid threshold preference on parents' decisions, by entering these factors into the HLR models in a third step, and evaluating the model coefficients and the effect on individual variable parameters and significance. Additionally, I used mixed effects logistic regression models to better explore the influence of

preferences on parents' repeated decisions to give any dose opioid (dichotomized as gave any opioid dose, Groups A+B vs. withhold opioids, Groups C+D). These models are described in more detail in the results section (Chapter VII).

Figure 5. Hypothesized Relationships between Knowledge, Preferences, and Analgesic Decisions



RQ 2c) How do parent and child characteristics relate to their treatment decisions?

To better explore the impact of parent/child factors, knowledge, preferences, and interactions, I restructured the data so that each decision represented a case with all other factors held constant. I then used mixed effects LR (generalized linear mixed models, or GLiMM) to examine the effect of the covariates on the non-independent, dichotomous decisions (n_4) of parents (N) (Hedeker, 2005). A random intercept for subject effects was added to the models to account for the potential correlation of the data between scenarios. The covariates in the models included the aggregate opioid ADE knowledge/perception factor, opioid familiarity, comparative opioid potency, PR Preference and opioid threshold preference factors, as well as the parent and child factors. I added variables for scenario pain level and ADE presence as covariates to assess the influence of these scenario signals on decision-making. The decision *give any opioid dose* (i.e., dichotomized as gave prescribed dose/lower dose, Group A+B vs. gave non-opioid/nothing, Groups C+D) was regressed on the independent variables.

To best explain the effect of these factors and their interactions on decisions, I calculated and examined estimated margins of the predicted probabilities for various levels of the factors of interest (e.g., ADE presence yes/no, procedure tonsillectomy vs. others, or mothers vs. fathers) when the covariates were set at average values, and when fixed at specified values (e.g., high versus low knowledge/perception). Specific analyses are described in Chapters VI and VII, below.

Specific Aim 3. ***RQ3a: How many doses and what type of analgesics (opioids and non-opioids) are administered by parents in the first 3 days after surgery?*** This exploratory question was answered using descriptive statistics. We tallied the number of doses of analgesics and opioids, and calculated the percentage of opioid given from the daily amount ordered.

RQ3b: Does gist analgesic knowledge and/or parent preferences correlate with parents' use of prescribed analgesics in the home setting? I used simple correlation coefficients to examine whether real opioid analgesic doses administered were related to either gist analgesic ADE knowledge/perception or parental preferences.

RQ3c: How do the child's pain and ADE experiences relate to parents' decisions to administer prescribed analgesics? I used univariate linear regression to explore the relationships between these factors (i.e., pain level and ADEs) and use of prescribed analgesics controlling for child factors as well as the use of over-the-counter analgesics.

RQ3d: Do parents describe any other factor (e.g., cost or availability of analgesic) that affect their decisions to give analgesics in the home setting? This final qualitative research question was summarized in descriptive form, only.

Sample Determination

Given the exploratory nature of this study and the lack of data regarding the relationships of interest, we calculated the sample size based, in part, on the feasibility of parent recruitment

during a six month study period, and on an effect size that would be considered to be clinically meaningful (Browner, Black, Newman, & Hulley, 2001). The resultant sample size ensured a sufficient number to test the main hypotheses (1a and 1b) and to allow testing for multiple correlations and individual predictors in the models used for RQ2a and b. Given a somewhat conservative estimate that less than half (~45%) of parents who lack gist knowledge regarding ADEs would fail to lower or discontinue the opioid compared to only 30% of those who are knowledgeable (i.e., 15% difference), 133 parents with and without adequate gist were required to demonstrate a difference in the outcome at least this large (α=.05, β = 0.20) (Browner, et al., 2001). In order to obtain at least 133 parents who lacked knowledge, a sample of at least 400 was required given an expected proportion of 30% (Browner, et al., 2001) who lack knowledge regarding possible opioid ADEs (Tait, et al., 2008). We deemed this sample to be sufficient to test the first hypotheses and to explore the relationships between (up to) 10 independent variables and outcomes in the regression models, given the rule of thumb that 40 to 1 cases-to-independent variables are required for stepwise regression modeling (Tabachnick & Fidell, 2007). While based on these estimates, 400 was considered the *minimum* sample needed, I continued recruitment for a six month period to obtain the largest sample possible (up to a maximum of 600) in order to ensure enough power to detect smaller effects.

Chapter V

Description of Parent Participants and their Baseline Preoperative Analgesic Knowledge, Perceptions, and Preferences

This chapter summarizes participant parents' baseline characteristics, including their analgesic knowledge and perceptions which were obtained from the preoperative survey completed as their children underwent surgery.

Sample and Setting

Over a six month study period, we consecutively recruited 505 parents/guardians in the preoperative area of C. S. Mott Children's hospital while their children underwent an elective, non-cardiac surgical procedure. Thirty-seven declined, leaving 468 parents in the analyses. Parent data were primarily analyzed using descriptive statistics and Table 5 describes the parent participants (<3% guardians or step-parents) and their children.

Parents' Analgesic Familiarity

Parents' yes/no responses to, "*Are you familiar with these pain drugs?,"* indicated 100% familiarity with at least one common, over-the-counter (OTC) non-opioid analgesics (all but one with acetaminophen and all but two with ibuprofen). Additionally, 411 parents (88%) claimed to be familiar with at least one of the listed opioids; 87% with Vicodin®, 65% with oxycodone, 44% with Lortab®, and 46% with Norco®. Nearly all parents (n=453, 97%) responded "yes" to having either Tylenol® (n=425, 91%) or ibuprofen (n=429, 92%) in the home before surgery and 412 (88%) recalled giving their child one of these agents within the previous six months (i.e., 74% acetaminophen and 76% ibuprofen). On the other hand, only 82 (18%) parents reported

having one of the listed opioids in the home and 41 (9%) had given one to their child in recent months. These data show greater familiarity or recognition and common use of OTC non-opioid analgesics in this sample.

Table 5. Characteristics of the Sample (N=468)

Parent Demographics		**Child's characteristics**	
Mothers	307 (66%)	Male	280 (60%)
Fathers	158 (34%)	Age (range 3-17 yrs)	8.2 ± 4.3
Age (range 19-66 yrs)	38.2 ± 8.0	Previous surgery	260 (56%)
Racial/cultural background			
White	387 (83%)		
Black	41 (9%)	**Child's Procedure**	
Hispanic	15 (3%)	Tonsillectomy	194 (42%)
Other	17 (4%)	Orthopedic	117 (25%)
Highest education		Urologic	57 (12%)
< High school	17 (4%)		
High school diploma	65 (14%)	General surgery	51 (11%)
Some college, trade school or associate's degree	181 (40%)	Other procedures	46 (10%)
Bachelor's degree	117 (25%)		
≥Graduate degree	76 (16%)		

Data presented as n (%) or mean ± standard deviation (SD)

Parents' Baseline Analgesic Knowledge and Perceptions

Parents' recognition (i.e., gist knowledge) of analgesic ADEs were summarized by their correct responses to, *"Do people ever have these side effects because they took Tylenol® or Vicodin®?"* Most parents (57-88%) correctly recognized the ADEs associated with Vicodin® (Table 6, column 2). Despite their greater familiarity, fewer (17-20%) identified the most common gastrointestinal (GI) effects of Tylenol® (Table 6, column 3), and only 51% identified liver damage as a possible adverse effect of Tylenol®. These findings demonstrate a general underestimation of ADEs associated with this common, OTC analgesic.

Table 6. Parent Knowledge Regarding Possible Analgesic Adverse Effects and their Seriousness

Adverse Drug Effect (ADE) – *in order of appearance on survey*	**Vicodin® Knowledge**	**Tylenol® Knowledge**	**Perceived Seriousness of Effect (*range 1-6*)***	**Opioid Domain-specific ADE knowledge (i.e., ADE correct X seriousness)**
	n (%) correctly identified as an ADE or not†		*mean ± SD*	*mean ± SD*
Nausea	382 (81.6%)	95 (20.3%)	2.52 ± 1.23	2.05 ± 1.48
Occasional Vomiting	336 (71.8%)	79 (16.9%)	2.95 ± 1.30	2.12 ± 1.72
Excessive sleepiness	388 (82.9%)	392 (83.8%)†	3.38 ± 1.44	2.85 ± 1.83
Constipation	343 (73.3%)	78 (16.7%)	3.22 ± 1.32	2.19 ± 1.82
Liver damage	339 (72.4%)	238 (50.9%)	5.33 ± 1.38	3.91 ± 2.65
Slowed breathing	307 (65.6%)	375 (80.1%)†	4.81 ± 1.46	3.18 ± 2.56
Itching	267 (57.1%)	102 (21.8%)	3.56 ± 1.44	2.05 ± 2.09
Habit/addiction	411 (87.8%)	404 (86.3%)†	5.31 ± 1.42	4.72 ± 2.17
Aggregate opioid ADE knowledge/perception (i.e., sum [individual ADE correct X seriousness) (range 0 to 48)				23.24 ± 11.61

**All ratings differed significantly from other ADE seriousness ratings ($p \leq 0.05$) with the exception of liver damage versus habit which were not significantly different from each other.*

†These items correct if parents identified them as "probably or definitely not" an effect with Tylenol®.

Parents rated ADE seriousness using a Likert-type scale from not serious (coded as 1) to extremely serious (coded as 6). These ratings varied significantly, with GI effects ranked less serious (e.g., nausea 2.52 ± 1.23) compared to excessive sleepiness (i.e., 3.38 ± 1.44), which was, in turn, ranked less serious compared to the other effects (e.g., habit/addiction 5.31 ± 1.42; see Table 6, column 4). A paired comparison demonstrated that parents perceived the seriousness of excessive sleepiness to be less than their average seriousness ratings (mean difference (MD) -0.50 [95% confidence interval (CI) -0.6, -0.4], $p < 0.001$). These findings suggest that while parents had a gist understanding of the relative seriousness of most ADEs, they may have lacked gist understanding related to excessive sleepiness, underestimating its importance.

Given the *mutual* importance of ADE awareness and perceived ADE seriousness, I created linear combinations of these variables. These linear combinations created individual, domain-specific ADE knowledge/percepton variables that factored in parents' perceived seriousness of the ADE (e.g., sedation knowledge*seriousness ranking). I then calculated the sum of each of these domain-specific knowledge/perception variables. This provided an aggregate knowledge/perception measure (i.e., opioid ADE knowledge/perception) that factored in the perceived seriousness only of effects parents knew (i.e., higher values reflecting greater knowledge * seriousness ratings). Parents' aggregate opioid ADE knowledge/perception ranged from 0 to 48 (mean 23.24 ± 11.61) and these scores were not normally distributed (Kolmogorov-Smirnov statistic < 0.001).

Relevant Group Knowledge Differences

I used simple bivariate comparisons, including chi-square, unpaired *t* tests, and analysis of variance, to examine relevant group differences. First, since previous studies suggested potential differences in pain experience and expectations based on parent role (Chapter II, pages 17-18), I examined potential differences between mothers' and fathers' analgesic knowledge that could potentially influence their analgesic decision-making. More mothers correctly identified most of the opioid ADEs compared to fathers, demonstrating greater gist knowledge (e.g., nausea 86% vs. 75%, vomiting 76% vs. 65%, excessive sleepiness 86% vs. 78%, constipation 78% vs. 65%, and itching 61% vs. 50%; see table 7 for further details). Parents' ADE seriousness ratings were, however, similar (table 7). Aggregate opioid ADE knowledge/perception scores were higher for mothers (24.28 ± 11.12) compared to fathers (21.69 ± 12.03; MD 2.59 [95% CI 0.038, 4.80], p = 0.022). These findings demonstrate greater opioid ADE knowledge/perception for mothers compared to fathers.

Table 7. Comparison between Mothers' and Fathers' Gist Opioid ADE Knowledge

	Gist Knowledge of ADEs n (%) Correctly Identified		Domain-specific ADE Knowledge/Perception *mean ± SD*	
	Mothers (n=307)	**Fathers (n=158)**	**Mothers (n=307)**	**Fathers (n=158)**
Nausea	264 (86%)*	118 (75%)	2.11 ± 1.44	2.0 ± 1.54
Vomiting	288 (76%)*	103 (65%)	2.19 ± 1.68	2.04 ± 1.82
Excessive sleepiness	265 (86%)*	123 (78%)	2.97 ± 1.80	2.66 ± 1.87
Constipation	240 (78%)*	103 (65%)	2.50 ± 1.76*	2.11 ± 1.88
Liver damage	231 (75%)	108 (68%)	4.04 ± 2.60	3.73 ± 2.75
Slowed breathing	212 (69%)	95 (60%)	3.39 ± 2.54*	2.80 ± 2.55
Itching	188 (61%)*	79 (50%)	2.19 ± 2.12*	1.78 ± 2.01
Habit/addiction	277 (90%)	134 (85%)	4.83 ± 2.08	4.57 ± 2.26

**p<0.05compared to fathers' gist ADE knowledge or aggregate knowledge ratings*

Since parents' analgesic knowledge may differ based on different baseline clinic-specific preparation, I compared the knowledge/perception factors between parents whose children were undergoing tonsillectomy, orthopedic or other procedures (collapsed to include genito-urinary, lower abdominal, and peripheral procedures combined). These analyses demonstrated similar ADE knowledge, seriousness ratings, and aggregate opioid knowledge/perception ratings between parents whose children were undergoing tonsillectomy (aggregate opioid ADE knowledge/perception mean 22.58 ± 11.09), orthopedic (23.73 ± 10.25), and other procedures combined (23.68 ± 13.12) ($F = 0.52$ ($df2$), $p=0.596$). These findings demonstrate that regardless of which surgical clinic they came from, parents had similar background opioid ADE knowledge/perception scores.

Comparative Analgesic Perceptions and Treatment Preferences

Next, a series of questions examined parents' comparative perceptions of opioid (i.e., the narcotic, Vicodin®) and non-opioid (i.e., Tylenol®) analgesics, as well as their treatment preferences, since decisions to give differing analgesics may depend on their relative understanding of the alternatives. First, for each of the drugs, Tylenol® and Vicodin®, parents

estimated "*how strong of a pain reliever [is the drug] when given in the recommended doses*" (rated from not strong [coded as 1] to very strong [coded as 5]). The difference in parents' ratings showed that the opioid was believed, in general, to provide stronger pain relief compared to the OTC analgesic (MD 1.81 [95% CI 1.7, 1.9], p< 0.001; see Table 8).

Table 8. Parents' overall Perceptions of Tylenol® and Vicodin®, and their Preferred Treatment Thresholds

Item (possible range)	Vicodin® *mean ± SD*	Tylenol® *mean ± SD*	Mean Difference *[95% confidence interval]; p value*
Perceived analgesic potency (1-5)	4.42 ± 0.86	2.62 ± 0.98	1.81 [1.7, 1.9]; 0.001
Perceived analgesic riskiness (1-5)	3.61 ± 1.10	1.64 ± 0.83	1.97 [1.89, 2.04]; 0.001
Preferred treatment threshold (Faces Pain Score from 0-10)	7.60 ± 2.3	4.77 ± 1.65	2.83 [2.67, 2.98]; 0.001

Next, parents indicated whether a half dose of Vicodin® provided equal to or greater pain relief compared to a full dose of Tylenol®. The majority (n = 316, 72%) believed that half a dose of the opioid provided stronger pain relief, 98 (22%) believed them to be equally strong, and 26 (6%) believed the full dose of Tylenol® to be stronger. These findings show that while parents, in general, believed the opioid (even at half a dose) to be a more effective or potent pain reliever, a fair number (28%) believed the full dose Tylenol to be an equal or better pain reliever than half a dose of the opioid.

Parents also rated "*how risky*" they believed these drugs to be when used to treat pain at home after surgery. Results demonstrated that parents believed the opioid to be significantly more risky than then non-opioid (MD 1.97 [95% CI 1.89, 2.04], p <0.001; see details Table 8). Lastly, parents indicated the lowest level of pain intensity at which they would they give these medications (Faces pain scale (FPS) 0-10, where 10 = hurts worst). These threshold preferences ranged from 0-10 for both drugs, with the average opioid threshold being significantly higher

than the non-opioid threshold (MD 2.83 [95% CI 2.67, 2.98], p < 0.001; see details Table 8). Together, these findings suggest that parents, in general, perceived the opioid to be a more effective, but riskier option that should be reserved for treating higher pain intensity.

Analgesic trade-off preferences. Parents' relative preference for pain relief over ADE avoidance was assessed using their aggregate score on the 6-item pain relief (PR) preference (i.e., tradeoff) scale (which was demonstrated to have adequate reliability; intraclass correlation coefficient 0.66 [95% CI 0.61, 0.71]). Parents' PR preference scores ranged from -10 to +12 (possible range -12 to +12) and were normally distributed with an interquartile range from -2 to +3 (mean = 0.81 [95% CI 0.49, 1.14]), suggesting a good distribution of parents who leaned toward ADE avoidance (negative values), tradeoff ambivalence (score 0) and preference for pain relief (positive values) (see Chapter IV, p. 44) (Clifford, et al., 2008; Tibaldi, et al., 2009). Importantly, PR preference scores correlated relatively weakly with parents' aggregate opioid knowledge/perception scores (r = -0.2; p<0.01), showing that parents' preferences were only marginally related to their opioid ADE knowledge/perception.

Parents' PR preference scores predicted their choice of analgesic for two "stated-choice" questions, where they were presented with drug options offering "excellent" pain relief with higher side effects (nausea/vomiting for decision 1 and over-sedation for decision 2) or "fair" pain relief with fewer side effects. Specifically, parents who chose the more effective, higher risk options had higher PR preference scores compared to those who chose the less effective, "safer" options for both decision 1 (MD 2.87 [95% CI 2.21, 3.52], p < 0.001) and 2 (MD 2.38 [95% CI 1.74, 3.01], p<0.001) . These data provided additional support for the predictive ability of PR preference scores for parents' analgesic trade-off decisions.

Relevant group differences in perception and preferences. Bivariate analyses compared mothers to fathers, parents of boys to girls, and parents of children undergoing tonsillectomy, orthopedic, or other procedures (combined) to assess whether there were differences in comparative analgesic perceptions and preferences that could affect analgesic decisions. Mothers had slightly higher PR preference scores than fathers (MD=0.86 [95% CI 0.18, 1.54], p=0.014), and lower thresholds for giving Tylenol® (MD= -0.39 [95% CI -0.71, -0.07], p = 0.017) and Vicodin® (MD= -0.60 [95% CI -1.05, -0.15], p=0.009. However, comparative opioid potency and risk differences were similar between parents ($p \geq 0.67$). These findings suggest a tendency for mothers to place a greater emphasis on pain relief, and for fathers to reserve treatment for higher pain intensity. Parents of boys and girls had similar opioid thresholds (MD = 0.34, [95% CI -0.13, 0.81], p=0.15).

Parents whose children were undergoing tonsillectomy, orthopedic, and all other procedures had significantly different PR preference scores (F 6.98 (*df*2), p = 0.001), opioid risk ratings (F 0.422 (*df*2), p = 0.015) and threshold preferences (F 3.81 (*df*2), p = 0.023). Specifically, parents of tonsillectomy patients had higher PR preference scores than those of other procedures (MD = 1.39 [95% CI 0.49, 2.31], p = 0.001), and lower opioid risk ratings compared to parents of orthopedic patients (MD = -0.32 [95% CI -0.63, -0.01], p = 0.044) and other procedures (MD = -0.029 [95% CI -0.58, -0.003], p = 0.047). Opioid thresholds of tonsillectomy parents were also lower compared to those undergoing other procedures (MD = -0.70 [95% CI -0.08, -1.32], p = 0.021), but not different compared to those undergoing orthopedic procedures (p = 0.359). Together, these findings suggest that compared to other parents, parents whose children were undergoing tonsillectomy, in general, placed a greater emphasis on pain relief over risk avoidance, and perceived opioids to be less risky.

Parents' Hypothetical Analgesic Decisions: Responses to Pain and Symptom Signals

To describe and evaluate parents' recognition and responses to various pain and symptoms (i.e., their signal detection and responses to these signals), I presented them with four hypothetical scenarios and asked them to imagine being faced with these decisions when taking their child home after surgery. Instructions stated that parents could give 2 mg Vicodin® every 4-6 hours as needed or may substitute Tylenol® to treat the child's pain. The scenarios (Scen) varied in the degree of pain and the presence or absence of adverse drug events (ADE). Specifically, participants considered a child with:

(1) higher pain level and no ADE (i.e., Scen Faces Pain Score (FPS)=6; no ADE)

(2) higher pain and with nausea and one episode of vomiting (Scen FPS=6; NV)

(3) higher pain and with signs of oversedation (Scen FPS=6, OS)

(4) lower pain level and nausea and one episode of vomiting (Scen FPS=4, NV)

For each decision, parents were asked to choose between giving the prescribed dose of opioid, a lower dose, a lower dose plus Tylenol®, Tylenol® alone, nothing or other choice (open ended). These decisions were coded into the nominal variables, *Gave Prescribed (i.e., full) Opioid Dose* (Group A), *Gave a lower opioid dose* (Group B), and *Withheld Opioids* (gave non-opioid or nothing, Groups C+D). To examine opioid decisions, these were dichotomized two ways;

1) *Gave Prescribed Opioid Dose vs. other decision* (Group A vs. Groups B+C+D) and

2) *Gave any Opioid Dose vs. Withheld* (Groups A+B vs. Groups C+D).

Variability in decision-making. Figure 6 depicts the opioid decisions made by parents for each of the scenarios (i.e., *gave any opioid dose* or *gave prescribed dose*). A non-parametric analysis of variance for repeated measures (i.e., Friedman test) demonstrated that parents' decisions to give opioids varied significantly across scenarios (Chi-square 331.3, $p < 0.001$),

where the prescribed opioid dose was chosen most often for Scen FPS=6, no ADE and least often for Scen FPS=4, NV. These findings demonstrated that a majority of parents changed their treatments based on the context and signals present in the situation.

Figure 6. Parents' Decisions to Give the Prescribed Dose or of Any Opioid Dose across Scenarios

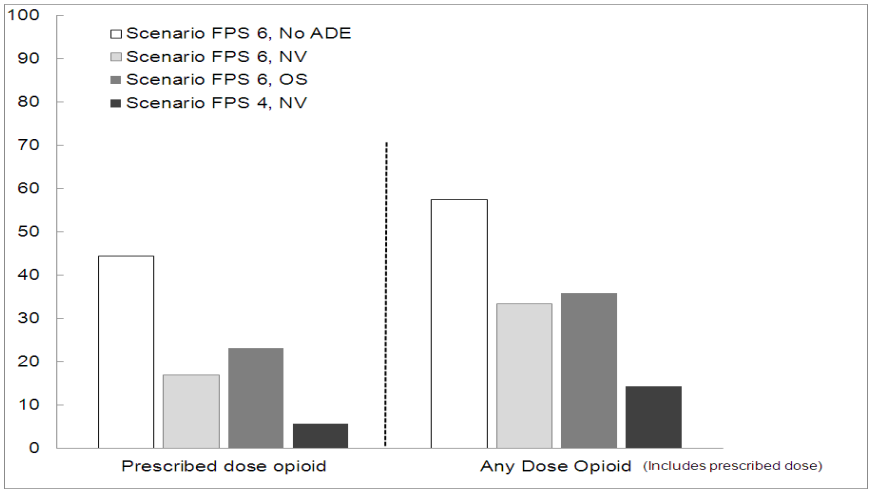


Figure Legend: *FPS=Faces Pain Score, ADE=Adverse Drug Events, NV=Nausea/Vomiting, OS=Oversedation. All comparisons within groupings significant at p<0.001 except for Scenarios FPS 6, NV vs. FPS 6, OS for the prescribed dose (p=0.018) and any dose (p>0.05) groups.*

Fifty-one percent of parents gave an analgesic (either an opioid or non-opioid) across all scenarios, while only 15 (3%) never gave one. Furthermore, nearly one third (n=144, 31%) acted conservatively, never choosing an opioid option while few parents (n=38, 8%) acted liberally by always choosing one. Lastly, only 14 (3%) always chose the prescribed opioid dose.

Parents' responses to the pain signal. Parents were more likely to give an analgesic (any opioid dose or non-opioid, Groups A+B+C vs. nothing, Group D) for the high pain scenarios compared to the low pain scenario (OR 2.30 [95% CI 1.80, 2.94], $p < 0.001$). There were even greater differences between the high and low pain scenarios in parents' decisions to give the prescribed opioid dose (Group A) versus other choice (Groups B+C+D) (OR = 6.66 [95% CI 4.41, 10.05], $p < 0.001$) and in the decision to give any opioid dose (Groups A+B)

versus withhold opioids (Groups C+D) (OR 4.37 [95% CI 3.3, 5.80], p <0.001). However, for the scenario where the child was in moderate pain (FPS=6) with no ADE symptoms, only 58% of parents gave *any* dose of an opioid and only 44% gave the prescribed dose. These findings suggest that while a majority of parents recognized and responded to the pain signal by giving an analgesic, the scenario signal (i.e., pain severity) was not important enough to motivate a large number of them to choose an opioid option – even in the absence of ADEs. For these parents, the pain signal may have needed to be stronger (i.e., a higher pain intensity score or, perhaps, other more relevant behavioral signs or symptoms).

Parents' responses to ADE signals. For the scenarios where there was both high pain (FPS = 6) and an ADE symptom (i.e., either nausea/vomiting or excessive sleepiness), parents were less likely to give the prescribed dose (Group A) than make another choice (Groups B+C+D) (OR 0.31 [95% CI 0.25, 0.40], p<0.001) or to give any dose of opioid (Groups A+B) than withhold opioids (Groups C+D) (OR 0.39 [95% CI 0.31, 0.49], p < 0.001). These findings demonstrate a general recognition of ADE signals by most parents. Importantly, fewer parents (n=79, 17%) chose to give the prescribed dose for the child in moderate pain with NV than for the more risky situation where the child was excessively sedated (n=108, 23%; OR 0.68 [95% CI 0.49, 0.94]; p = 0.018). These findings suggest that while most parents recognized and responded to ADE symptoms, the NV signal was more meaningful to parents than OS.

Parents' reasons for giving or withholding an opioid. Following each scenario, parents were asked to describe in an open ended manner why they made the choice they did. Parents' stated reasons for their decisions were reviewed and categorized based on their attention to the signals of interest (i.e., pain vs. ADE signal), attention to the prescription order (i.e.,

timing or doctor's order), and other prominent analgesic-related comments (e.g., "*don't like narcotics*," or "*prefer to give Tylenol®*." These results are summarized in Table 9.

Table 9. Summary of Parents' Primary Reasons for Analgesic Decisions across Scenarios

	Gave any Opioid Dose (Groups A+B)			Withheld the Opioid (Groups C+D)		
	Pain Relief/ Prevention	**Physician Order/Time for dose**	**No adverse effect or effect not bad**	**Concern for ADE**	**Pain not bad enough or "wait and see"**	**Don't like narcotics or prefer to rotate**
Scenario FPS=6, No ADE	133 (59%)	53 (24%)	93 (41%)	3 (2%)	84 (56%)	34 (23%)
Scenario FPS=6, Nausea/vomiting	71 (53%)	23 (17%)	14 (10%)	193 (73%)	80 (30%)	26 (10%)
Scenario FPS=6, Oversedation	84 (57%)	59 (40%)	17 (12%)	94 (35%)	65 (24%)	31 (11%)
Scenario FPS=4, Nausea/vomiting	22 (39%)	8 (14%)	7 (13%)	104 (32%)	222 (69%)	18 (6%)

FPS=Faces Pain Score. ADE = adverse drug event. Percentages calculated from n of reported comments for each item.

A majority who gave opioids across scenarios did so for pain relief or prevention, suggesting primary attention to the pain signal by these parents (see table 9, column 2). Notably, for the scenario FPS=6, No ADE, the primary reason for withholding an opioid was the belief that pain wasn't bad enough to give the opioid. In most of these cases, parents gave Tylenol and mentioned they would see how the child did without Vicodin®. This demonstrates recognition of pain, but its lack of importance (i.e., low intensity) for many parents.

Recognition or concern for the ADE was more often given as the primary reason by parents who withheld opioids for the NV scenarios compared to the OS scenario (OR 1.90 [95% CI 1.6, 2.25], $p<0.001$), suggesting greater attention to the NV signal compared to OS. Additionally, while 195 parents who withheld opioids after considering the OS scenario acknowledged "sleepiness" during their reasoning, 101 (52%) of these stated that "*sleep/rest is*

good" or that sleep meant that the child's pain wasn't bad enough to treat. This finding suggests that while most parents recognized the cue of excessive sleepiness, they did not understand its potential impact on safety.

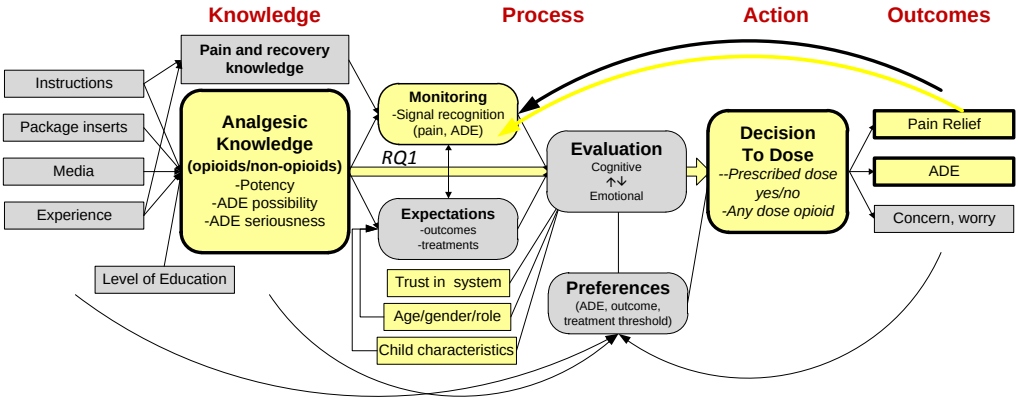
Parents who cited the need for pain relief/prevention as the primary reason for their decisions had higher pain relief (PR) preference scores to other parents (MD= 0.72 [95% CI 0.34, 1.10], $p<0.001$) while those noting concern for ADEs had lower scores (-0.39 [-0.77, -0.02]; $p=0.041$), suggesting that trade-off preference (i.e., leaning toward PR vs. risk avoidance) remained a primary motivation for decision-making.

Chapter VI

Analyses for Specific Aim 1: The Relationship between Parents' Analgesic Knowledge/Perceptions and their Treatment Decisions

This chapter explores findings regarding the relationships between parents' baseline analgesic knowledge/perceptions and their decisions to give opioids when faced with the child in pain with or without signs of an adverse drug event (ADE). I hypothesized that gist knowledge (i.e., the awareness that an ADE was a possible effect) and perceptions (i.e., their perceived seriousness of the effect or overall opioid effects) regarding opioid ADEs would significantly impact parents' analgesic decision-making in the presence of ADE symptoms (Figure 7). Description of the factors of interest, analyses and results of the specifically tested hypotheses are described in detail below.

Figure 7. Hypothesized Relationship between Gist Knowledge and Decisions to Give Opioids in the Presence of ADEs



To begin, I examined parents' decisions for the scenario with high pain (Faces Pain Score (FPS) =6) and no symptoms of an ADE to explore the potential impact of opioid ADE

knowledge/perceptions on opioid decisions in the *absence* of ADE symptoms. Parents' aggregate opioid ADE knowledge/perception ratings (i.e., the measure of parents' awareness [or lack thereof] of the full range of potential side effects and their perceived seriousness) were compared between parents who 1) gave the prescribed opioid dose (Group A) and those who chose a different option (i.e., lower dose opioid, non-opioid, or nothing, Groups B+C+D) and 2) parents who gave any opioid dose (Groups A+B) and those who withheld opioids (Groups C+D). Parents who *gave the prescribed dose* had similar opioid ADE knowledge/perceptions as parents who made another choice (mean difference (MD) = 1.49 [95% confidence interval (CI) -0.65, 3.63], p = 0.171). Furthermore, opioid ADE knowledge/perception was similar between parents who chose *any opioid dose* (i.e., Groups A+B) and those who withheld opioids altogether (Groups C+D) (MD = 0.24 [95% CI -2.10, 2.15], p = 0.982). These findings show that opioid ADE knowledge/perception had little effect on parents' decisions in the absence of an ADE.

H1a: ***A lack of gist knowledge regarding the possibility and/or seriousness of opioid-related nausea and vomiting (NV) will be associated with a failure to lower the dose or discontinue opioids for children in pain where this ADE is present.*** Next, chi-square tests were used to compare parents' opioid decisions between parents with and without gist nausea or vomiting knowledge (i.e., awareness of this possible opioid-related ADE) across *both* scenarios where NV were present. Compared to those who lacked knowledge, those with gist nausea knowledge were nearly 50% more likely to withhold any dose of opioid (i.e., give a non-opioid or nothing, Groups C+D) than to give an opioid (Groups A+B) (OR = 0.54 [95% CI 0.78, 0.37], $p < 0.001$). Similarly, those with gist opioid-related vomiting knowledge were more likely to withhold opioids (Groups C+D) than to give an opioid (Groups A+B) (OR=0.56 [95% CI 0.41, 0.77], $p \leq 0.001$). This gist knowledge was, however, not different between parents who chose

the prescribed dose (Group A) compared to another option (Groups B+C+D) (nausea knowledge - OR 0.98 [95% CI 0.59, 1.63] and vomiting knowledge - OR 0.95 [95% CI 0.54, 1.64]). Further details of parents' opioid decisions for each of the NV scenarios are presented in Table 10.

Table 10. Relationship between Analgesic Knowledge, Perceptions and Decisions to Give Opioids in the face of Nausea/Vomiting

	Gave Prescribed Opioid Dose (Group A vs. B+C+D)		**Gave Any Opioid Dose (Groups A+B vs. C+D)**	
Scenario FPS=6, NV	**n=79**		**n=154**	
	n (%); OR [95% CI] or MD [95% CI]	p	n (%); OR [95% CI] or MD [95% CI]	p
Those with gist nausea knowledge vs. those without knowledge	61 (16%) vs. 18 (21%) 0.72 [0.40, 1.29]	0.267	118 (31%) vs. 36 (44%) 0.56 [0.34, 0.92]	**0.019**
Those with gist vomiting knowledge vs. those without knowledge	21 (6%) vs. 5 (6%) 0.94 [0.35, 2.57]	0.91	47 (12%) vs. 19 (24%) 0.46 [0.25, 0.84]	**0.010**
MD† seriousness nausea	0.27 [-0.03, 0.57]	0.075	0.19 [-0.05, 0.43]	0.122
MD† seriousness vomiting	0.25 [-0.66, 0.57]	0.119	0.14 [-0.11, 0.40]	0.274
MD† nausea knowledge/perception	0.41 [0.05, 0.77]	**0.025**	0.35 [0.07, 0.63]	**0.015**
Scenario FPS = 4, NV	**N=26**		**N=66**	
Those with gist nausea knowledge vs those without knowledge	21 (6%) vs. 5 (6%) 0.94 [0.34, 2.56]	0.90	47 (13%) vs. 19 (24%)0.46 [0.25, 0.84]	**0.009**
Those with gist vomiting knowledge vs. those without knowledge	19 (6%) vs. 7 (5%) 1.06 [0.44, 2.58]	0.89	39 (12%) vs. 27 (22%) 0.48 [0.28, 0.83]	**0.008**
MD† seriousness nausea	0.12 [-0.62, 0.38]	0.635	-0.12 [-0.45, 0.21]	0.484
MD† seriousness vomiting	-0.14 [-0.66, 0.39]	0.615	-0.29 [-0.64, 0.06]	0.102
MD† nausea knowledge/perception score	0.02 [-0.58, 0.62]	0.944	0.19 [-0.20, 0.58]	0.333

†*Mean difference (MD) in score of those who gave the prescribed dose (Group A) vs. other choice (Groups B+C+D) or who gave any opioid dose (Groups A+B) vs. withheld opioids (Groups C+D)*

Parents' perceived seriousness of these effects was not significantly related to their decisions, however, compared to those who gave an opioid (Groups A+B), the aggregate nausea

knowledge*seriousness scores (i.e., domain-specific knowledge/perception scores) were higher for those who withheld opioids (Groups C+D) across the NV scenarios (MD= 0.28 [95% CI 0.05, 0.51], p = 0.014). Scores were not significantly different between those who gave the prescribed dose (Group A) and those who chose another option (Groups B+C+D) (MD=0.30 [95% CI -0.006, 0.60], p = 0.055). Together, these findings support, in part, the first hypothesis, showing that knowledge regarding these opioid-related ADEs influenced parents' decision-making when NV was present. In particular, knowledge regarding the possibility of opioid-related nausea or vomiting was sufficient to influence withholding opioids when these symptoms were present.

Similar analyses were conducted to test the next hypothesis; **H1b:** ***A lack of gist knowledge regarding the possibility and/or seriousness of opioid-related excessive sedation will be associated with a failure to discontinue opioids for children in pain where this ADE is present.*** Most parents (n=388, 83%) had a gist understanding that excessive sedation was a possible effect of Vicodin®, and this knowledge was not associated with parents' decisions to *give the prescribed dose (Group A vs. Groups B+C)* or to *give any opioid dose (Groups A+B vs. Group C)* (see Table 11, row 1). However, parents who gave any dose of opioid (Groups A+B) rated the seriousness of this ADE lower compared to those who those who withheld opioids (Group C) (MD = 0.40 [95% CI 0.12, 0.67], p = 0.005). This finding suggests that gist perceptions of seriousness facilitated a safer decision even if awareness of oversedation (OS) possibility did not. Hypothesis 1b was, therefore, partially supported. This result suggests that understanding the potential seriousness of certain adverse effects, such as OS, may be more important than gist knowledge of ADE possibility toward increasing their salience for safe decision-making.

Table 11. Relationship between Analgesic Knowledge, Perceptions and Decision to Give Opioids in the face of Oversedation

	Gave Prescribed Opioid Dose (Group A vs. B+C+D)		Gave any Opioid Dose (Groups A+B vs. C+D)	
Scenario FPS=6, Oversedation	**N=108**		**N=165**	
	n (%); OR [95% CI] Or MD [95% CI]	p	n (%); OR [95% CI] Or MD [95% CI]	**p**
Those with knowledge regarding opioid-related OS vs. those who lacked knowledge	92 (24%) vs. 16 (20%) 1.24 [0.69, 2.26]	0.473	135 (35%) vs. 30 (40%) 0.81 [0.49, 1.35]	0.415
MD† in OS Seriousness Ratings	0.30 [-0.02, 0.58]	0.064	**0.40 [0.12, 0.67]**	**0.005**
MD† in OS (domain-specific) knowledge/perceptoin Ratings	0.20 [-0.20, 0.60]	0.324	**0.48 [0.13, 0.83]**	**0.007**

†*Mean difference (MD) in score of those who gave the prescribed dose (Group A) vs. other choice (Groups B+C) or who gave any opioid dose (Groups A+B) vs. withheld opioids (Groups C+D)*

H1c: ***Parents' gist understanding of relative analgesic potency and risk will be associated with their decisions to substitute acetaminophen for the prescribed opioid for children in moderate-severe pain.*** Next, parents' decisions from the higher pain scenarios were explored using chi-square or Kruskal-Wallis ANOVA to examine the relationship between parents' analgesic perceptions of potency and risk and their decisions to substitute a non-opioid (Group C) or give nothing (Group D) in the event of opioid-related ADEs. Parents who believed a full dose of Tylenol® to be equal to or stronger than a half dose of Vicodin® were more likely to choose the non-opioid (Group C) vs. any dose of opioid (Groups A+B) during these decisions (OR = 1.34 [95% CI 1.05, 1.80], p = 0.02). Comparative opioid potency differences (i.e., the difference between their opioid and Tylenol® potency ratings, each rated 1-5, with larger numbers reflecting a bigger difference in the perception of drug effectiveness) were not different between parents who gave a non-opioid (Group C) versus any dose opioid (Groups A+B) across all high pain scenarios, but were lower for those who gave a non-opioid for Scenario FPS=6, no

ADE (MD = -0.28 [95% CI -0.53, -0.04], p = 0.03). This finding suggests that parents who believed the opioid and non-opioid to be closer in their ability to provide pain relief were more likely to choose the non-opioid in the absence of an ADE.

Comparative opioid risk differences (i.e., the difference between parents' perceived opioid and Tylenol® risk ratings, with high numbers reflecting a bigger difference the perceived risks of these drugs) were higher for those who substituted the non-opioid (Group C) for an opioid (Groups A+B) across the high pain scenarios (MD = 0.50 [95% CI 0.37, 0.63], p < 0.001). This demonstrates that the greater the difference in perceived analgesic risk the more likely parents were to choose the lower risk option.

Lastly, comparative opioid threshold preference difference (i.e., the difference between the level of pain at which parents would administer an opioid and that at which they would give Tylenol®, with higher numbers reflecting a bigger difference between the pain intensity scores at which parents prefer to give an opioid vs. non-opioid) was also greater between parents who chose the non-opioid option (Group C vs. Groups A+B: MD = 0.37 [95% CI 0.14, 0.60], p = 0.002). This finding demonstrates that when parents' analgesic thresholds were farther apart, they were more likely to give the non-opioid. Together, these findings show how comparative perceptions of effectiveness and risk, as well as preferred use, influenced parents' choices between the two analgesic options.

RQ1: ***How do parents' gist understanding and perceptions of opioid ADEs relate to their decisions to administer opioid analgesics to children in pain with or without ADEs?*** I used hierarchical, logistic regression (HLR) models to explore the relationships between the opioid knowledge factors and parents' individual hypothetical analgesic decisions when controlled for parent and child factors of interest.

First, I explored the relationships between parent factors (i.e., role, education, race, and trust in healthcare system), child factors (i.e., age, sex, previous surgery, and procedure) and opioid decisions to determine inclusion and coding of these variables in all subsequent models. Following several analyses showing no additional differences in model coefficients or main effects, the final independent factors of interest included: parent role (categorical), education (continuous), distrust score (continuous), child age (continuous), child sex (categorical), and procedure (categorical as tonsillectomy, orthopedic, all others). These were entered at the first step of every HLR analyses. The following variables were added at the second step; opioid knowledge/perception (i.e., either domain-specific [i.e., nausea-related or sedation-related knowledge/perception] or aggregate ADE knowledge/perception, where appropriate), recent opioid familiarity (i.e., have opioid in the home *or* gave one to the child within previous 6 months vs. not-familiar) and comparative opioid potency (i.e., difference between opioid and non-opioid potency ratings). The dichotomized outcomes *gave any dose opioid (Groups A+B) vs. withheld opioids (Groups C+D)* and *gave the prescribed dose (Group A) vs. other choice (Groups B+C+D)*, were regressed on these independent variables separately for each of the scenario decisions. (There was one exception: I could not perform this analysis for *gave prescribed dose* for Scenario FPS=4, NV, because too few parents chose the prescribed dose for this situation.) P values < 0.05 were considered significant. Hosmer & Lemeshow Tests demonstrated good model fits, and results are shown in Tables 12 through 18.

For Scenarios FPS=6, no ADE and FPS=4, NV, the addition of the knowledge/perception and familiarity factors did not significantly affect the model coefficients at Step 2, showing that these factors did not influence opioid decisions when a trade-off was either not apparent (i.e.,

high pain - no ADE) or, perhaps, less important (i.e., low pain - nausea) (see Tables 12-14, Step 2 summary data).

Table 12. Influence of the Knowledge, Perception and Familiarity Factors on Parents' Decisions to Give any Dose Opioid (Groups A+B) versus No Opioid (Groups C+D) for Scenario FPS=6, no Adverse Drug Event

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow Test for significance Step 1: χ^2= 15.237 (*df*7) p = **0.033**; NR^2 = 0.059; HL = 0.687 Step 2: χ^2= 2.292 (*df*3) p = 0.514 [Model χ^2= 17.529(*df*10) p = 0.063]; NR^2 = 0.067; HL = 0.561		
	Step 1	**Step 2**
Parent Female	0.984 [0.615, 1.577]	0.965 [0.598, 1.557]
Parent Education	0.998 [0.799, 1.248]	0.994 [0.795, 1.244]
Child Age	1.015 [0.956, 1.076]	1.009 [0.949, 1.072]
Child Male	0.667 [0.421, 1.055]	0.676 [0.426, 1.075]
Procedure Tonsillectomy	**2.17 [1.254, 3.757]**[b]	**2.206 [1.265, 3.846]**[b]
Procedure Orthopedic	**1.90 [1.049, 3.443]**[a]	**1.988 [1.080, 3.656]**[a]
Distrust Score	0.973 [0.928, 1.020]	0.973 [0.927, 1.020]
ADE Knowledge*Seriousness		1.002 [0.981, 1.023]
Relative Opioid Potency		1.168 [0.943, 1.447]
Recent Opioid Familiarity		0.877 [0.502, 1.531]

[a]*p < 0.05;* [b]*p < 0.01*

Table 13. Influence of the Knowledge, Perception and Familiarity Factors on Parents' Decisions to Give the Prescribed Dose of Opioid (Group A) vs. Other Choice (Groups B+C+D) for Scenario FPS6, no ADE

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow Test for significance Step 1: χ^2= 16.099 (*df*7) p = **0.024**; NR^2 = 0.061; HL = 0.216 Step 2: χ^2= 1.67 (*df*3) p = 0.644 [Model χ^2= 17.769(*df*10) p = 0.059]; NR^2 = 0.067; HL = 0.960		
	Step 1	**Step 2**
Parent Female	1.001 [0.629, 1.592]	0.964 [0.602, 1.544]
Parent Education	1.203 [0.966, 1.499]	1.204 [0.965, 1.501]
Child Age	0.993 [0.937, 1.051]	0.989 [0.933, 1.049]
Child Male	0.817 [0.524, 1.274]	0.832 [0.532, 1.302]
Procedure Tonsillectomy	**2.111 [1.223, 3.645]**[b]	**2.173 [1.252, 3.773]**[b]
Procedure Orthopedic	**2.089 [1.157, 3.771]**[a]	**2.060 [1.127, 3.764]**[a]
Distrust Score	0.970 [0.925, 1.017]	0.968 [0.923, 1.015]
Aggregate ADE Knowledge*Seriousness		1.005 [0.984, 1.026]
Relative Opioid Potency		1.128 [0.914, 1.392]
Recent Opioid Familiarity		1.124 [0.649, 1.944]

[a]*p < 0.05;* [b]*p < 0.01*

Table 14. Influence of the Opioid Knowledge, Perception and Familiarity Factors on Parents' Decisions to Give any Dose Opioid (Groups A+B) vs. No Opioid (Groups C+D) for Scenario FPS=4, Nausea/Vomiting

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow Test for significance Step 1: χ^2= 27.425 (*df*7) p**<0.001**; NR^2 = 0.132; HL = 0.670 Step 2: χ^2= 3.760 (*df*3) p = 0.289 [Model χ^2= 31.185(*df*10) p = 0.001]; NR^2 = 0.150; HL = 0.840		
	Step 1	**Step 2**
Parent Female	0.549 [0.289, 1.043]	0.539 [0.282, 1.031]
Parent Education	0.914 [0.676, 1.236]	0.954 [0.702, 1.296]
Child Age	**1.123 [1.035, 1.219]**[b]	**1.125 [1.035, 1.224]**[b]
Child Male	1.078 [0.573, 2.030]	1.061 [0.561, 2.007]
Procedure Tonsillectomy	**3.275 [1.480, 7.248]**[b]	**3.379 [1.501, 7.602]**[b]
Procedure Orthopedic	0.343 [0.116, 1.016]	**0.029 [0.096, 0.881]**[a]
Distrust Score	1.042 [0.977, 1.112]	1.039 [0.973, 1.110]
ADE Knowledge*Serious-Nausea		0.895 [0.718, 1.116]
Relative Opioid Potency		0.938 [0.694, 1.267]
Recent Opioid Familiarity		1.919 [0.906, 4.064]

[a]*p < 0.05;* [b]*p < 0.01*

Knowledge/perception and familiarity variables did, however, improve the model coefficients for the scenarios where both high pain (FPS=6) and ADE symptoms were present, helping to explain parents' opioid decisions in the presence of ADEs (Tables 15-17, Step 2 summary data). Specifically, when NV was present nausea-specific knowledge/perception predicted withholding opioids altogether (OR = 0.777 [95% CI 0.657, 0.918], Table 15) as well as withholding the prescribed dose (OR = 0.745 [95% CI 0.602, 0.923], Table 16).

Table 15. Influence of the Opioid Knowledge, Perception and Familiarity Factors on Parents' Decisions to Give any Dose Opioid (Groups A+B) versus No Opioid (Groups C+D) for Scenario FPS=6, Nausea/Vomiting

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow Test for significance Step 1: χ^2= 20.126 (*df*7) **0.005**; NR^2 = .077; HL = 0.102 Step 2: χ^2= 10.460 (*df*3) **0.015** [30.586(*df*10); p=0.001]; NR^2 = 0.115; HL = 0.742		
	Step 1	**Step 2**
Parent Female	**0.549 [0.339, 0.888]**[a]	**0.541 [0.331, 0.885]**[a]
Parent Education	0.895 [0.714, 1.123]	0.914 [0.727, 1.149]
Child Age	**1.067 [1.004, 1.134]**[a]	**1.065 [1.001, 1.134]**[a]
Child Male	0.730 [0.461, 1.158]	0.681 [0.425, 1.090]
Procedure Tonsillectomy	**2.404 [1.336, 4.327]**[a]	**2.341 [1.286, 4.260]**[b]
Procedure Orthopedic	1.198 [0.640, 2.245]	1.077 [0.563, 2.061]
Distrust Score	0.968 [0.921, 1.017]	0.964 [0.916, 1.014]
ADE knowledge*Serious-Nausea		**0.777 [0.657, 0.918]**[b]
Relative Opioid Potency		0.984 [0.787, 1.231]
Recent Opioid Familiarity		1.393 [0.792, 2.450]

[a] *p < 0.05;* [b] *p < 0.01*

Table 16. Influence of the Opioid Knowledge, Perception and Familiarity Factors on Parents' Decisions to Give the Prescribed Opioid Dose (Group A) vs. Other Choice (Groups B+C+D) for Scenario FPS=6, Nausea Vomiting

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow Test for significance Step 1: χ^2= 13.794 (*df*7) p = 0.055; NR^2 = 0.062; HL = 0.938 Step 2: χ^2= 13.231 (*df*3) p = **0.004** [Model χ^2= 27.025(*df*10) p = 0.003]; NR^2 = 0.119; HL = 0.459		
	Step 1	**Step 2**
Parent Female	0.612 [0.347, 1.080]	0.587 [0.328, 1.050]
Parent Education	1.110 [0.844, 1.460]	1.152 [0.872, 1.521]
Child Age	1.001 [0.928, 1.079]	0.991 [0.918, 1.070]
Child Male	1.235 [0.702, 2.172]	1.171 [0.657, 2.087]
Procedure Tonsillectomy	**3.104 [1.458, 6.606]**[b]	**3.208 [1.474, 6.982]**[b]
Procedure Orthopedic	1.831[0.803, 4.178]	1.562 [0.664, 3.674]
Distrust Score	1.008 [0.950, 1.069]	1.004 [0.945, 1.067]
ADE Knowledge*Serious-Nausea		**0.745 [0.602, 0.923]**[b]
Relative Opioid Potency		1.121 [0.846, 1.486]
Recent Opioid Familiarity		**1.997 [1.032, 3.864]**[a]

[a]*p < 0.05;* [b]*p < 0.01*

Sedation-specific knowledge/perception predicted withholding opioids altogether (OR 0.843 [95% CI 0.735, 0.967], Table 17), but did *not* predict giving/withholding the prescribed opioid dose (Table 18). Together, these findings demonstrate the important contribution of ADE knowledge/perception on decisions to withhold opioids when ADEs are present. Recent opioid familiarity was only significant in predicting the decision to give the prescribed dose for the high pain, NV scenario (Table 16). Thus, analgesic ADE knowledge/perception, and not familiarity was a more influential factor toward parents' analgesic decisions in this sample.

Table 17. Influence of the Opioid Knowledge, Perception and Familiarity Factors on Parents' Decisions to Give any Dose Opioid (Groups A+B) versus No Opioid (Groups C+D) for Scenario FPS=6, Oversedation

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow Test for significance		
Step 1: χ^2= 23.011 (*df*7) p = **0.002**; NR^2 = 0.088; HL = 0.702		
Step 2: χ^2= 8.984 (*df*3) p = 0**.030** [Model χ^2= 31.994(*df*10); p<0.001]; NR^2 = 0.121; HL = 0.803		
	Step 1	**Step 2**
Parent Female	0.908 [0.558, 1.480]	0.926 [0.562, 1.526]
Parent Education	0.887 [0.706, 1.115]	0.921 [0.730, 1.163]
Child Age	**1.081 [1.015, 1.150]**[a]	1.066 [1.000, 1.136]
Child Male	1.388 [0.865, 2.228]	1.302 [0.806, 2.104]
Procedure Tonsillectomy	**3.787 [2.042, 7.025]**[b]	**3.659 [1.952, 6.860]**[c]
Procedure Orthopedic	1.660 [0.871, 3.163]	1.465 [0.752, 2.854]
Distrust Score	0.999 [0.951, 1.048]	0.994 [0.946, 1.044]
ADE Knowledge*Serious-Sleepiness		**0.843 [0.735, 0.967]**[b]
Relative Opioid Potency		1.048 [0.836, 1.314]
Recent Opioid Familiarity		1.681 [0.952, 2.969]

[a]*p < 0.05;* [b]*p < 0.001*

Table 18. Influence of the Opioid Knowledge, Perception and Familiarity Factors on Parents' Decisions to Give the Prescribed Opioid Dose (Group A) vs. Other Choice (Groups B+C+D) for Scenario FPS=6, Oversedation

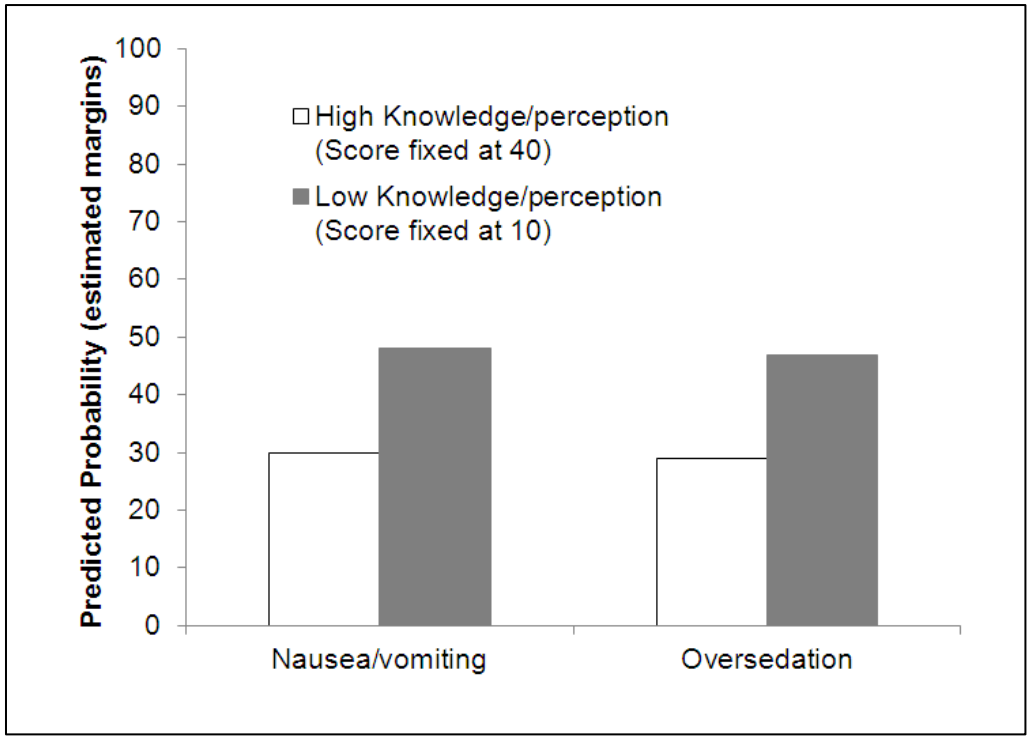
Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow Test for significance		
Step 1: χ^2= 16.754 (*df*7) p = **0.019**; NR^2 = 0.071; HL = 0.955		
Step 2: χ^2= 3.389 (*df*3) p = 0.335 [20.143 (*df*10) p = 0.028]; NR^2 = 0.085; HL = 0.588		
	Step 1	**Step 2**
Parent Female	0.947 [0.546, 1.641]	0.971 [0.556, 1.696]
Parent Education	0.973 [0.752, 1.258]	1.005 [0.774, 1.305]
Child Age	1.029 [0.959, 1.103]	1.032 [0.960, 1.109]
Child Male	1.442 [0.842, 2.471]	1.393 [0.808, 2.399]
Procedure Tonsillectomy	**3.136 [1.580, 6.227]**[a]	**3.106 [1.550, 6.225]**[a]
Procedure Orthopedic	1.151 [0.527, 2.518]	1.055 [0.473, 2.355]
Distrust Score	1.036 [0.981, 1.094]	1.034 [0.980, 1.092]
ADE Knowledge*Serious-Sleepiness		0.929 [0.797, 1.083]
Relative Opioid Potency		0.848 [0.668, 1.075]
Recent Opioid Familiarity		1.365 [0.719, 2.594]

[a]*p < 0.001*

Lastly, I used a generalized mixed effects logistic regression (GMLR) to better examine the effects of the covariates on parents' non-independent, dichotomous decisions to *give an opioid (Groups A+B vs. Group C).* These models are most useful to examine fixed effects of factors in the presence of repeated measures, such as the parent decisions in this study. Models included a random intercept for subject effects to account for the potential correlation of the data between scenarios. In addition to all other factors of interest (i.e., those included in the HLR models above), models included *Scenario ADE* and *Scenario High Pain* factors to account for and examine the effect of differing signals on decision-making.

I used these regressions to estimate marginal means for the predicted probabilities (PP) of administering opioids to a child in moderate pain (i.e., FPS=6) but with different levels of the ADE signal (i.e., no ADE, NV, OS) when the aggregate knowledge/perception factor was fixed at a high value (i.e., score 40 out of 48) and at a low value (score of 10). Findings from these models demonstrated that increased aggregate ADE knowledge/perception had a significant main effect on parents' decisions to withhold opioids ($F = 8.32$ ($df1$) $\beta = -0.03$, $p=0.004$). Figure 8 demonstrates, more specifically, how the PPs of giving an opioid when an ADE is present are affected when knowledge/perception was high compared to low. These analyses demonstrated that higher opioid ADE knowledge/perception led to withholding opioids when ADEs were present.

Figure 8. Effect of Aggregate Knowledge/Perception on the Predicted Probabilities of Giving an Opioid to a child experiencing an ADE

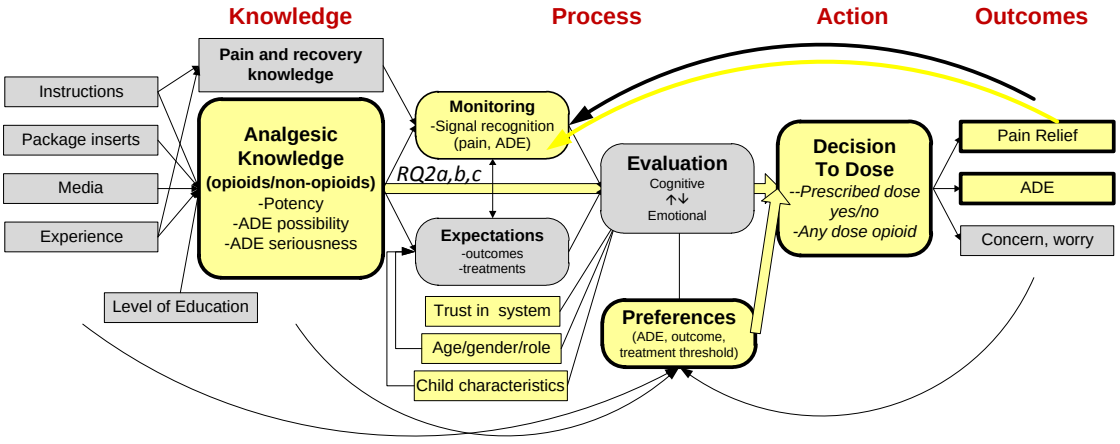


Chapter VII

Analyses for Specific Aim 2: The Influence of Parents' Preferences On their Analgesic Decisions

This chapter examines findings regarding how parents' trade-off preferences, that is, how they weigh the risks (adverse drug events [ADE]) and benefits (pain relief [PR]) of analgesics, contribute to their decisions to give analgesics. Additionally, these analyses examined the influence of preferred treatment thresholds (i.e., the lowest pain level warranting treatment with an opioid) on their decisions to treat. Figure 9 displays the relationships that were examined in these analyses, where the dichotomous decisions to *give the prescribed dose (Group A vs. B+C+D)* or *give any dose opioid (Groups A+B vs. C+D)* were the outcomes of interest. I hypothesized that parent preferences would largely influence their decisions to treat the child in acute pain, with or without the presence of ADE symptoms.

Figure 9. Hypothesized Relationships between Knowledge, Preferences, Parent/Child Factors and Decisions to Give Opioids



RQ2*a) How much of the variance in parents' opioid use is explained by their preferences for pain relief versus ADE avoidance when adjusted for gist understanding, situation (ADE presence), and parent/child characteristics? RQ2b) How do parents' threshold preferences contribute to parents' treatment decisions?* In Chapter VI (see tables 12-18), I used hierarchical logistical regression (HLR) models to examine the effects knowledge/perception (i.e., domain-specific (e.g., nausea knowledge) or aggregate ADE knowledge/perception (i.e., sum [ADE knowledge*seriousness ratings]), comparative opioid potency [difference in parents' perceptions of opioid vs. non-opioid effectiveness], and recent opioid familiarity [i.e., have opioid in home or gave one to child within 6 months vs. did not]) when controlled for parent/child characteristics (parent role, education, distrust, child age, sex, and procedure). To examine the effect of parents' preferences on decisions, I expanded these models in a new Step 3 that added pain relief (PR) preference scores (i.e., the measure of relative preference for PR over ADE avoidance derived from a set of six questions) and opioid threshold preferences (i.e., the pain intensity level at which parents' preferred to give an opioid). I evaluated model coefficients and the effects of these factors on individual variable parameters and their significance to determine the unique and moderating effects of preferences. As in Chapter VI, I repeated these analyses for parents' decisions to *give the prescribed dose (i.e., Group A vs. other choice, Groups B+C+D)* and to *give any opioid dose (i.e., Groups A+B vs. withhold opioids, Group C+D).*

Addition of the preference factors to the HLR analyses resulted in a good model fit and significantly improved all model coefficients, demonstrating that parents' preferences independently contributed to parents' opioid decisions (See Step 3 summary data in Tables 19-25). Specifically, higher preferences for pain relief (over risk avoidance) predicted both greater

use of opioids in any dose (Groups A+B) and of the prescribed opioid dose (Group A) for the scenarios describing high pain (FPS=6), nausea/vomiting (OR 1.151 [95% CI 1.070, 1.238] and OR 1.154 [95% CI 1.059, 1.256], respectively Tables 22 & 23) and with high pain, oversedation (OR 1.120 [95% CI 1.044, 1.201] and OR 1.107 [95% CI 1.024, 1.196], Tables 24 & 25). PR preference scores did not influence these decisions for the high pain, no ADE (Tables 19 & 20) or low pain, NV scenarios (Table 21). These findings demonstrate that this trade-off preference was important when parents were faced with obvious trade-off decisions involving consideration of both the need to maximize pain relief and maximize ADE avoidance, but not otherwise. This suggests that parents' risk-benefit preferences have a greater influence on decisions when risks are salient, but little influence when not.

Higher parental opioid threshold preferences (i.e., the lowest pain intensity level at which parents would prefer to administer an opioid to their child) predicted withholding opioids (Groups C+D) across all scenarios (OR ranged from 0.709 [95% CI 0.62, 0.81] to 0.897 [95% CI 0.808, 0.995], $p < 0.001$) as well as withholding the prescribed dose (Groups B+C+D; OR ranged from 0.807 [95% CI 0.726, 0.897] to 0.823 [95% CI 0.73, 0.97], $p<0.001$) for all but the high pain, oversedation scenario, showing the important influence that parents' treatment preference has on parents' decisions (see last row of Tables 19-24).

Although parents' ADE knowledge/perception significantly predicted parents' opioid decisions for the high pain, ADE scenarios at Step 2 in HLR analyses (Tables 22-24, columns 2), PR preference moderated this effect making it insignificant for the high pain, OS scenario (Table 24, column 3). For the high pain, NV scenarios, ADE knowledge/perception remained a significant predictor of parents' decisions to give the prescribed dose (Group A; OR 0.778 [95% CI 0.625, 0.969], $p < 0.05$, Table 23) or to give any opioid dose (Groups A+B; OR0.800 [95% CI

0.671, 0.953], p < 0.05, Table 23). These findings demonstrate that while gist knowledge/perception remained a significant predictor of analgesic decisions when cues such as NV were recognized and important, stronger preferences for pain relief outweighed the effect of knowledge/perception in situations where the cue was, perhaps, less salient (e.g., oversedation).

Table 19. Influence of Parents' Preferences on their Decisions to Give any Dose Opioid (Groups A+B) vs. No Opioid (Groups C+D) for Scenario FPS=6, No Adverse Drug Event

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow test for significance Step 2: χ^2= 2.292 (*df*3) p = 0.514 [Model χ^2= 17.529 (*df*10) 0.063]; NR^2 = 0.067; HL = 0.561 Step 3: χ^2= 24.498 (*df*1) p**<0.001** [Model χ^2= 43.181 (*df*12) p<0.001]; NR^2 = 0.160; HL = 0.338		
	Step 2 (repeated from table 12)	**Step 3**
Parent Female	0.965 [0.598, 1.557]	0.803 [0.486, 1.329]
Parent Education	0.994 [0.795, 1.244]	1.012 [0.802, 1.278]
Child Age	1.009 [0.949, 1.072]	0.999 [0.939, 1.063]
Child Male	0.676 [0.426, 1.075]	**0.572 [0.352, 0.929]**[a]
Procedure Tonsillectomy	**2.206 [1.265, 3.846]**[b]	1.682 [0.932, 3.036]
Procedure Orthopedic	**1.988 [1.080, 3.656]** [a]	1.850 [0.986, 3.471]
Distrust Score	0.973 [0.927, 1.020]	0.980 [0.932, 1.030]
Aggregate ADE Knowledge*Seriousness	1.002 [0.981, 1.023]	1.008 [0.985, 1.032]
Relative Opioid Potency	1.168 [0.943, 1.447]	1.192 [0.950, 1.496]
Recent Opioid Familiarity	0.877 [0.502, 1.531]	0.832 [0.467, 1.480]
Pain Relief Preference		1.033 [0.965, 1.105]
Threshold Preference-Opioid		**0.755 [0.668, 0.853]**[c]

[a]p < 0.05; [b]p < 0.01; [c]p<0.001

Table 20. Influence of Parents' Preferences on their Decisions to Give the Prescribed Dose (Group A) vs. Other Choice (Groups B+C+D) for FPS = 6, no Adverse Drug Event

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow test for significance
Step 2: χ^2= 1.67 (*df*3) p = 0.644 [Model χ^2= 17.769 (*df*10) p = 0.059]; NR^2 = 0.067; HL = 0.960
Step 3: χ^2= 17.327 (*df*1) p**<0.001** [Model χ^2= 36.518 (*df*12) p<0.001]; NR^2 = 0.134; HL = 0.231

	Step 2 (Repeated from table 13)	**Step 3**
Parent Female	0.964 [0.602, 1.544]	0.825 [0.506, 1.347]
Parent Education	1.204 [0.965, 1.501]	1.234 [0.982, 1.549]
Child Age	0.989 [0.933, 1.049]	0.985 [0.928, 1.046]
Child Male	0.832 [0.532, 1.302]	0.736 [0.463, 1.170]
Procedure Tonsillectomy	**2.173 [1.252, 3.773]**[b]	1.764 [0.989, 3.146]
Procedure Orthopedic	**2.060 [1.127, 3.764]**[a]	**1.949 [1.053, 3.608]**[a]
Distrust Score	0.968 [0.923, 1.015]	0.974 [0.928, 1.022]
Aggregate ADE Knowledge*Seriousness	1.005 [0.984, 1.026]	1.102 [0.989, 1.034]
Relative Opioid Potency	1.128 [0.914, 1.392]	1.130 [0.908, 1.406]
Recent Opioid Familiarity	1.124 [0.649, 1.944]	1.101 [0.629, 1.929]
Pain Relief Preference		1.038 [0.973, 1.108]
Threshold Preference-Opioid		**0.807 [0.726, 0.897]**[c]

[a]*p < 0.05;* [b]*p < 0.01;* [c]*p<0.001*

Table 21. Influence of Parents' Preferences on their Decisions to Give any Dose Opioid (Groups A+B) vs. No Opioid (Groups C+D) for Scenario FPS=4, Nausea Vomiting

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow test for significance
Step 2: χ^2= 3.760 (*df*3) p = 0.289 [Model χ^2= 31.185 (*df*10) p = 0.001]; NR^2 = 0.150; HL = 0.840
Step 3: χ^2= 26.806 (*df*1) p**<0.001** [Model χ^2= 58.929 (*df*12) p<0.001]; NR^2 = 0.272; HL = 0.704

	Step 2 (Repeated from table 14)	**Step 3**
Parent Female	0.539 [0.282, 1.031]	**0.399 [0.196, 0.811]**[a]
Parent Education	0.954 [0.702, 1.296]	0.961 [0.697, 1.326]
Child Age	**1.125 [1.035, 1.224]**[b]	**1.143 [1.043, 1.252]**[b]
Child Male	1.061 [0.561, 2.007]	0.843 [0.427, 1.663]
Procedure Tonsillectomy	**3.379 [1.501, 7.602]**[b]	**2.856 [1.180, 6.914]**[a]
Procedure Orthopedic	**0.029 [0.096, 0.881]**[a]	**0.246 [0.078, 0.778]**[a]
Distrust Score	1.039 [0.973, 1.110]	1.060 [0.989, 1.136]
ADE Knowledge*Serious-Nausea	0.895 [0.718, 1.116]	0.891 [0.702, 1.131]
Relative Opioid Potency	0.938 [0.694, 1.267]	0.942 [0.681, 1.304]
Recent Opioid Familiarity	1.919 [0.906, 4.064]	2.068 [0.936, 4.571]
Pain Relief Preference		1.045 [0.953, 1.146]
Threshold Preference-Opioid		**0.709 [0.620, 0.811]**[c]

[a]*p < 0.05;* [b]*p < 0.01;* [c]*p < 0.001*

Table 22. Influence of Parents' Preferences on their Decisions to Give any Dose Opioid (Groups A+B) vs. No Opioid (Groups C+D) for Scenario FPS=6, Nausea/Vomiting

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow test for significance		
Step 2: χ^2= 10.460 (3) p = **0.015** [Model χ^2= 30.586(*df*10); p=0.001]; NR^2 = 0.115; HL = 0.742		
Step 3: χ^2= 19.009 (1) **p<0.001** [Model χ^2= 65.506 (*df*12); p<0.001]; NR^2 = 0.235; HL = 0.350		
	Step 2 (Repeated from table 15)	**Step 3**
Parent Female	**0.541 [0.331, 0.885]**[a]	**0.399 [0.233, 0.681]**[c]
Parent Education	0.914 [0.727, 1.149]	0.914 [0.718, 1.163]
Child Age	**1.065 [1.001, 1.134]**[a]	1.061 [0.994, 1.133]
Child Male	0.681 [0.425, 1.090]	**0.550 [0.332, 0.911]**[a]
Procedure Tonsillectomy	**2.341[1.286, 4.260]**[b]	1.670 [0.879, 3.173]
Procedure Orthopedic	1.077 [0.563, 2.061]	0.943 [0.518, 2.029]
Distrust Score	0.964 [0.916, 1.014]	0.971 [0.921, 1.024]
ADE Knowledge*Serious-Nausea	**0.777 [0.657, 0.918]**[a]	**0.800 [0.671, 0.953]**[a]
Relative Opioid Potency	0.984 [0.787, 1.231]	0.949 [0.748, 1.205]
Recent Opioid Familiarity	1.393 [0.792, 2.450]	1.317 [0.729, 2.380]
Pain Relief Preference		**1.151 [1.070, 1.238]**[c]
Threshold Preference-Opioid		**0.790 [0.708, 0.881]**[c]

[a]*p < 0.05;* [b]*p < 0.01;* [c]*p<0.001*

Table 23. Influence of Parents' Preferences on their Decisions to Give the Prescribed Dose (Group A) vs. Other Choice (Groups B+C+D) for Scenario FPS=6, Nausea/Vomiting

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow test for significance		
Step 2: χ^2= 13.231 (*df*3) p = **0.004** [Model χ^2= 27.025 (*df*10) p = 0.003]; NR^2 = 0.119; HL = 0.459		
Step 3: χ^2= 9.901 (*df*1) p = **0.002** [Model χ^2= 48.172 (*df*12) p<0.001]; NR^2 = 0.206; HL = 0.244		
	Step 2 (Repeated from table 16)	**Step 3**
Parent Female	0.587 [0.328, 1.050]	**0.457 [0.246, 0.850]**[a]
Parent Education	1.152 [0.872, 1.521]	1.142 [0.858, 1.520]
Child Age	0.991 [0.918, 1.070]	0.976 [0.899, 1.060]
Child Male	1.171 [0.657, 2.087]	1.010 [0.553, 1.843]
Procedure Tonsillectomy	**3.208 [1.474, 6.982]**[b]	**2.325 [1.031, 5.241]a**
Procedure Orthopedic	1.562 [0.664, 3.674]	1.564 [0.646, 3.785]
Distrust Score	1.004 [0.945, 1.067]	1.020 [0.957, 1.086]
ADE Knowledge*Serious-Nausea	**0.745 [0.602, 0.923]**[b]	**0.778 [0.625, 0.969]**[a]
Relative Opioid Potency	1.121 [0.846, 1.486]	1.100 [0.823, 1.470]
Recent Opioid Familiarity	**1.997 [1.032, 3.864]**[a]	**2.047 [1.032, 4.060]**[a]
Pain Relief Preference		**1.154 [1.059, 1.256]**[c]
Threshold Preference-Opioid		**0.823 [0.730, 0.928]**[c]

[a]*p < 0.05;* [b]*p < 0.01;* [c]*p<0.001*

Table 24. Influence of Parents' Preferences on their Decisions to Give any Dose Opioid (Groups A+B) vs. No Opioid (Groups C+D) for Scenario FPS=6, Oversedation

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow test for significance		
Step 2: χ^2= 8.984 (*df*3) p = **0.030** [Model χ^2= 31.994(*df*10); p<0.001]; NR^2 = 0.121; HL = 0.803		
Step 3: χ^2= 4.209 (*df*1) p = **0.040** [Model χ^2= 46.704 (*df*12); p<0.001]; NR^2 = 0.712; HL = 0.388		
	Step 2 (Repeated from table 17)	**Step 3**
Parent Female	0.926 [0.562, 1.526]	0.778 [0.463, 1.309]
Parent Education	0.921 [0.730, 1.163]	0.905 [0.714, 1.147]
Child Age	1.066 [1.000, 1.136]	1.066 [0.998, 1.138]
Child Male	1.302 [0.806, 2.104]	1.232 [0.753, 2.018]
Procedure Tonsillectomy	**3.659 [1.952, 6.86]**[b]	**3.107 [1.631, 5.918]**[b]
Procedure Orthopedic	1.077 [0.563, 2.061]	1.461 [0.738, 2.891]
Distrust Score	0.994 [0.946, 1.044]	0.999 [0.950, 1.050]
ADE Knowledge*Serious-Sleepiness	**0.843 [0.735, 0.967]**[a]	0.900 [0.779, 1.041]
Relative Opioid Potency	1.048 [0.836, 1.314]	1.031 [0.817, 2.776]
Recent Opioid Familiarity	1.681 [0.952, 2.969]	1.551 [0.867, 2.776]
Pain Relief Preference		**1.120 [1.044, 1.201]**[b]
Threshold Preference-Opioid		**0.897 [0.808, 0.995]**[a]

[a]*p < 0.05;* [b]*p < 0.001*

Table 25. Influence of Parents' Preferences on their Decisions to Give the Prescribed Dose (Group A) vs. Other Choice (Groups B+C+D) for Scenario FPS=6, Oversedation

Omnibus Chi-Square(df) p value; Nagelkerke R^2; Hosmer & Lemeshow test for significance		
Step 2: χ^2= 3.389 (*df*3) p = 0.335 [Model χ^2= 20.143 (*df*10) p = 0.028]; NR^2 = 0.085; HL = 0.588		
Step 3: χ^2= 3.678 (*df*1) p = 0.055 [Model χ^2= 30.487 (*df*12) p = 0.002]: NR^2 = 0.127; HL = 0.595		
	Step 2 (Repeated from table 18)	**Step 3**
Parent Female	0.971 [0.556, 1.696]	0.829 [0.466, 1.475]
Parent Education	1.005 [0.774, 1.305]	0.978 [0.750, 1.275]
Child Age	1.032 [0.960, 1.109]	1.031 [0.957, 1.110]
Child Male	1.393 [0.808, 2.399]	1.303 [0.748, 2.270]
Procedure Tonsillectomy	**3.106 [1.550, 6.225]**[b]	**2.601 [1.280, 5.289]**[a]
Procedure Orthopedic	1.055 [0.473, 2.355]	1.011 [0.448, 2.282]
Distrust Score	1.034 [0.980, 1.092]	1.043 [0.986, 1.103]
ADE Knowledge*Serious-sleepiness	0.929 [0.797, 1.083]	0.999 [0.847, 1.178]
Relative Opioid Potency	0.848 [0.668, 1.075]	0.835 [0.656, 1.064]
Recent Opioid Familiarity	1.365 [0.719, 2.594]	1.284 [0.669, 2.466]
Pain Relief Preference		**1.107 [1.024, 1.196]** [a]
Threshold Preference-Opioid		0.894 [0.798, 1.001]

[a]*p < 0.01;* [b]*p < 0.001*

Mixed effect LR models, controlling for the random effect of parents on their repeated decisions, upheld the relationships between preferences and the decision to give an opioid. Specifically, higher PR preference predicted greater opioid use (F=18.57 (*df*1) β = 0.117, p<0.001), while higher threshold preference predicted lower use (F = 56.19 (*df*1) β = -0.336, p<0.001). To better clarify the impact of preferences, estimated margins of predicted probabilities (PP) of giving an opioid were calculated when trade-off preference (i.e., PR preference score) was fixed at high or low values (i.e., score 10 and -10 (possible score -12 to +12). Findings show that at high PR preference, the PP of giving an opioid was 49% [95% CI 38, 59%], while at a low value, the PP was only 14% [95% CI 9, 22%]. Similarly, when preferred threshold was fixed at a low value (FPS = 3) the PP of giving an opioid was 58% [95% CI 48, 69%], but when fixed at a high value (FPS = 10) was only 19% [95% CI 15, 24%]. These findings demonstrate the important influence of analgesic preferences on parents' decisions to give opioids to their children.

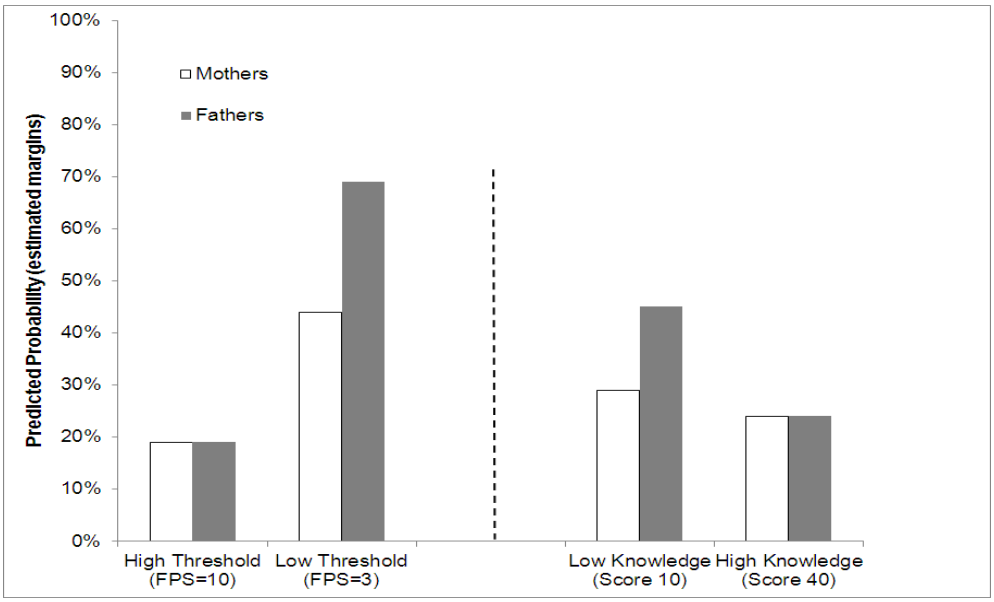
RQ2c How do parent or child characteristics relate to their treatment decisions?

Next, I used mixed effects LR models to explore the main and interaction effects of parent and child factors on parents' decisions to *give any dose opioid (Groups A+B vs. withhold opioids, Groups C+D)*. These models were used to better explain findings from the above HLR analyses suggesting potential differences between mothers and fathers, boys and girls, as well as between parents of children who were undergoing different procedures (see Tables 12-25). Specifically, I explored the interaction effects of child age, gender, and procedure (given potential interactions between these variables), and of parent role, PR preference, threshold preference, and knowledge. Estimated marginal means of predicted probabilities (PP) with 95% confidence

intervals are reported for various levels of the factors in order to clarify the effects of the coefficients (knowledge, PR preference, and threshold) on parents' decisions to give an opioid.

Parent role and decisions. There was a significant main effect for maternal role (F-13.32 (*df*1) $p < 0.001$), predicting lower administration of opioids overall ($\beta = -2.135$, $p<0.001$). This effect remained significant at low and high values of PR preference ($p \leq 0.006$). However, there were significant interactions for maternal role*threshold preference (F=6.38 (*df*1) $\beta = 0.163$, p=0.012) as well as for role*knowledge/perception (F=3.58(*df*1) p = 0.059), where mothers and fathers had similar probabilities of giving an opioid at high values of knowledge/perception and threshold, but significantly different probabilities at low values (Figure 10).

Figure 10. Predicted Probabilities of Mothers' and Fathers' Decisions to Give an Opioid at High/Low Values of Knowledge/Perception or Threshold Preferences



More specifically, mothers gave significantly less opioids than fathers in the presence of NV (F=10.0 (*df*1) p=0.002), but not OS or no ADEs ($p \geq 0.433$). For clarity, when knowledge

was fixed at a low value (score 10) the PP of mothers giving an opioid in the presence of NV was only 20% [95% CI 15, 26] compared to the probability of fathers which was 41% [95% CI 32, 51] p<0.001). These findings demonstrate that at high knowledge/perception levels, fathers were similarly responsive to the NV signal as mothers. On the other hand, mothers were more likely than fathers to respond to the NV signal at low knowledge, suggesting a greater sensitivity to this symptom.

At low threshold preferences, mothers were less likely to give opioids compared to fathers when there were no ADEs (F=4.8 (*df*1) p=0.03), in the presence of NV (F=17.0 (*df*1) p<0.001) and in the presence of OS (F=5.08 (*df*1) p=0.02). Together, these findings suggest that at lower knowledge/perception and lower treatment thresholds, mothers tended to make more conservative opioid decisions than fathers, while at high knowledge and pain thresholds, fathers and mothers made similarly conservative decisions.

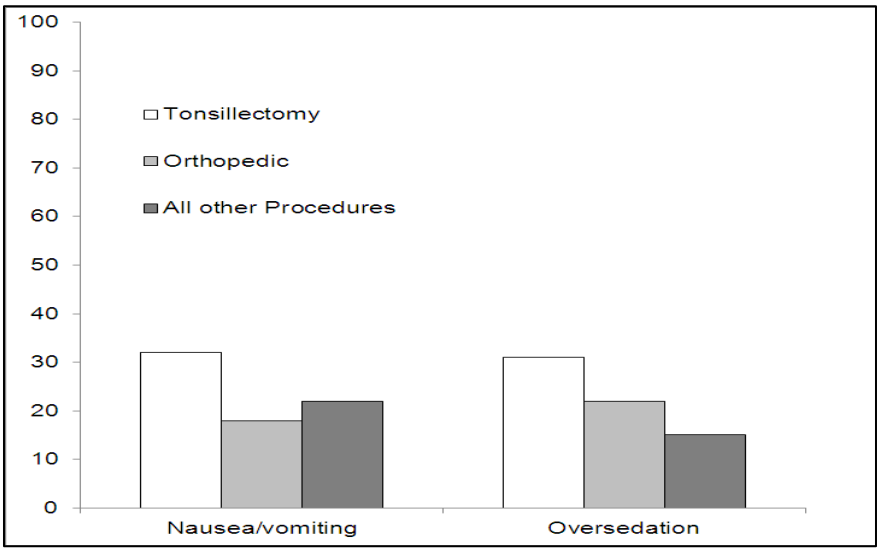
Child characteristics and opioid decisions. There was a significant main effect of child sex (F=6.647 (*df*1) β= -0.851, p = 0.010), and age on the decision to *give an opioid* (F=6.915 (*df*=1) β= -.005, p = 0.009), but not for procedure (F=2.69 (*df*2) β= 0.85, p = 0.07). Since children who undergo different procedures may differ in their age or gender, I explored the interaction of these variables, and found a significant interaction effect of the variable, sex*age*procedure (F=2.70 (df5) β= -0.718, p = 0.02). Specifically, girls were more likely to be given opioids (PP = 35% [95% CI 26, 46] compared to boys (PP = 18% [95% CI 13, 24] p = 0.001) only for the group "other procedures." This finding suggests a possible confounding effect of procedure on the relationship between sex and decisions, since the group "other procedures" consisted of a large subset of boys who underwent, perhaps, less invasive urologic procedures.

I further explored the effect of child age on decisions across procedures by examining PPs at fixed low (age=5yrs) and high (age=15yrs) values of age. Models demonstrated that the probability giving an opioid did not differ between procedures at high age (F=1.138 (*df*2), p = 0.321), but was significantly higher at low age for the tonsillectomy group (PP=39% [95% CI 33, 46]) compared to orthopedic (PP=28% [95% CI 21, 36], p = 0.01) and "other procedures" (PP=25% [95% CI 20, 32], p < 0.001). This finding shows that older children in pain were treated similarly with opioids across procedures, while younger children undergoing tonsillectomy were treated more liberally than others.

Child procedure and decisions to treat during ADEs. Lastly, I examined the effect of procedure on decision-making in the presence of ADEs by estimating PPs at high and low values of each of the coefficients aggregate opioid knowledge/perception, preferred opioid threshold, and PR preference. These analyses found that procedure was a significant predictor of giving opioids at high and low values of threshold preference, PR preference, and knowledge/perception ($p \leq 0.019$).

More specifically, in the absence of any ADE, there was no procedure effect on opioid decisions when knowledge/perception was fixed at high (F=2.04 (*df*2), p = 0.130) or low values (F=1.98 (*df*2), p = 0.139). There was, however, a higher probability of opioid use for tonsillectomy compared to the other groups in the presence of NV (F = 4.86 (*df*2), p = 0.008) and OS (F=4.47 (*df*2), p=0.012) (see Figure 11). These findings demonstrate that parents across procedures made similar decisions when faced with a high pain-no ADE situation, but when faced with a risk-benefit trade-off, parents whose children did not undergo tonsillectomy were more likely to withhold opioids, regardless of opioid ADE knowledge/perception. This suggests a lower sensitivity to ADEs among parents whose children were undergoing tonsillectomy.

Figure 11. Predicted Probabilities of Giving an Opioid in the Presence of an ADE based on Procedure



Chapter VIII

Analyses for Specific Aim 3: An Exploration of Parents' use of Analgesics to treat their Children's Pain after Discharge

To complement the data collected from parents in the preoperative setting, I also collected a more limited set of data regarding parents' real analgesic decisions in the home setting following their child's hospital discharge. These data are particularly valuable as they allowed me to examine whether children experienced variable pain and adverse drug events (ADE) similar to those described in the hypothetical scenarios, and how these experiences influenced parents' real analgesic decisions following surgery. These postoperative data were explored mostly with descriptive and bivariate analyses. I used a univariate linear regression model to examine the potential effects of the signals, pain level and presence of ADEs, on parents' opioid use at home controlling for child factors.

Sample Characteristics

Two-hundred nineteen out of 328 families who participated in the preoperative survey completed and returned their postoperative surveys (return rate 67% of families). However, 15 of these received only over-the-counter (OTC) analgesic prescriptions (ibuprofen or acetaminophen) due to less invasive surgery than planned and these were excluded from further analysis, leaving 204 for analysis. Data are presented as n (%) with percentages calculated from the number of complete responses for reported items.

Eighty-two (40%) of the respondents' children had undergone tonsillectomy procedures, 59 (29%) orthopedic, and 62 (31%) another surgical procedure (i.e., genito-urinary, lower

abdominal, or peripheral procedures). A majority of the children were male (n=120, 59%), and their mean age was 8.47 ± 4.33. The vast majority of survey respondents were mothers (n=186, 92%). The postoperative survey data were linked to the preoperative survey data by the respondent ID code.

Description of Analgesic Prescriptions

To facilitate a better understanding of how parents' analgesic use compared to their prescriptions and instructions, details of the postoperative prescriptions were recorded prior to the child's discharge and are presented in Table 26. The majority of prescriptions were for hydrocodone/acetaminophen (i.e., Vicodin®-type) agents, and all were written to be given "as needed for pain." Only a few prescriptions (13%) included a dose range (e.g., 1-1.5 ml) to be decided on by the parent, however, the majority (83%) were written with a frequency range (i.e., every 4-6 hours). As such, these prescriptions left much of the discretion for opioid administration to the parents' judgments.

Only 32 (16%) prescriptions included a written safety instruction such as; "*stop acetaminophen*," "*do not combine with additional acetaminophen*," "*do not exceed 4g acetaminophen/day*," "*do not give if appears sleepy*," "*give only while awake.*" Twenty-six (81%) of such instructions involved maximum acetaminophen dosages, 3 (9%) sedation warnings, and 3 (9%) were of another nature (e.g., "*do not give ibuprofen*"). Most of these additional instructions (n=21, 66%) were written for the tonsillectomy patients, and, of these, (86%) addressed acetaminophen safety. These findings suggest sparse written provider attention to potential analgesic safety issues, with most of these addressing the potential for acetaminophen overuse.

Few parents were given prescriptions or written instructions regarding laxative (n=21) or antiemetic (n=9) use, and most of these were provided by orthopedic (30%) or services other than otology (57%). This finding shows little preventive attention to these common ADEs.

Table 26. Description of Postoperative Analgesic and Other Prescriptions

	N (%)
Opioid Order	
Hydrocodone/acetaminophen (i.e., Lortab® or Norco®)	144 (71%)
Codeine/acetaminophen	24 (12%)
Oxycodone	36 (18%)
Ibuprofen or naproxen Order	28 (14%)
Acetaminophen Order	44 (22%)
Diazepam Order	22 (11%)
Antiemetic Order	9 (4%)
Laxative Order	20 (10%)
Total Number Analgesic Doses / Day Prescribed (median; range)	**6**; 4 to 6
Maximum prescribed opioid dose (i.e., morphine equivalents (mg/kg/day) (mean ± SD; median; range)	0.23 ± 0.10; 0.09; 0.07 to 0.87

Parents' Analgesic Decisions and Use Following Discharge

Decision-making at home. In order to better understand how analgesic decisions were made, I asked parents to record whether they filled their prescriptions, how they were instructed to give medications, and who made the decision to give (or take) medicines. Eighteen parents claimed to have not filled their prescriptions. Of these, 6 reported having the medication in the home before surgery, 8 stated that OTC medication was sufficient or that their child didn't want or need it, and 1 didn't have time to fill the prescription. Although all prescriptions were written to be given as needed, only half of the parents (n=93, 54%) recalled being told to give the medication in this manner, while one third (n=57, 33%) stated they were told to give the opioid around the clock (ATC) for the first few days after surgery. The majority of those told to give an

opioid ATC were parents of tonsillectomy patients (n=49, 86%). This finding suggests that parents of tonsillectomy patients may have been instructed differently from the written prescription. This may further help to explain the greater use of opioids among these parents during the hypothetical decision-making exercises above.

Respondents reported that most analgesic decisions were made by mothers (n=113, 57%) or by both parents equally (n=64, 33%), while fathers, alone, were described as having made the decisions in only 10 cases (5%). A majority of parents (n=147, 74%) reported that children took part in analgesic decisions (28% a little, 41% equal to large part, and 6% complete control). Additionally, 99 parents (46%) recorded that their children asked for medication, and that 76 (38%) refused at least some doses of medications. A considerable number of parents complained (using open-ended statements) that giving the prescribed analgesic (mostly Lortab®) was a struggle due to the repulsive taste. Some stated that they held their children down and forced the medication, while one concerned mom stated that her child refused all medication (even with attempts to substitute acetaminophen), despite having undergone a tonsillectomy. These findings demonstrate that analgesic decisions were made in a largely family participatory manner, with children's input sometimes conflicting with or hindering parental efforts to manage pain.

Prescribed opioid use at home. Most parents (n=145, 86%) recorded giving the prescribed dose for each individual dose they administered, while 19 (11%) gave at least one dose that was lower than the minimum and 5 (3%) gave at least one that was more than the maximum prescribed dose. Furthermore, 20 parents (13%) reported giving at least one dose earlier than the minimum interval prescribed, 61 (41%) gave all medications at the prescribed intervals, and 68 (46%) gave all doses less frequently than ordered. In order to compare parents' prescription opioid use, all opioids were converted to morphine equivalents (morphine

mg/kg/day) using standard equi-analgesic calculations. Given the variability in dosage ordered, analyses focused on the percentage of the maximum prescribed daily opioid doses administered. Most parents (n=165, 84%) recorded giving less than the maximum allowable morphine equivalents per day (Table 27), while 26 (13%) gave the amount ordered (within 10%) and 6 (3%) gave more than ordered. While these findings demonstrate a general tendency of parents to give less than the maximum prescribed daily doses during the first few postoperative days, there were instances of exceeding prescribed, individual doses as well as giving doses early in order to control pain.

Table 27. Parents' Analgesic Administration at Home after Surgery

	Range	**Median**; mean ± SD
Total number of analgesic doses given over three days	0 to 28	**9;** 8.8 ± 5.0
Total number opioid doses given	0 to 16	**5**; 5.3 ± 4.8
Total opioids given per day (morphine equivalents mg/kg/day)	0 to 0.45	**0.07**; 0.10 ± 0.09
Percentage of prescribed opioid given	-100 to 118%	**-58.7**; -54.29 ± 37.95
Non-opioid use		
Ibuprofen administered (mg/day)	0-3338	**0**; 180.13 ± 426.62
Additional acetaminophen administered (mg/day)	0-2680	**0**; 244.7 ± 465.8
Total acetaminophen (in combination drug + additional) (mg/day)	0-2680	**109.4;** 396.0 ± 617.6

Over-the-counter (OTC; i.e., non-opioid) use. Nearly two thirds of parents (n=132, 61%) reported giving a non-opioid separately from the prescribed opioid or opioid/non-opioid combination (Table 16). The total daily dose of acetaminophen did not exceed the maximum safe dose for any child. Although parents' recorded pain scores ranged from 0-10 regardless of which drug they administered, scores were significantly lower when they administered a non-opioid (mean FPS = 4.97 [95% CI 4.44, 5.41]) compared to an opioid (FPS = 5.99 [95% CI 5.46,

6.47], $p < 0.001$). These findings show that, in general, parents used non-opioids to treat lower pain levels and opioids for greater pain intensity.

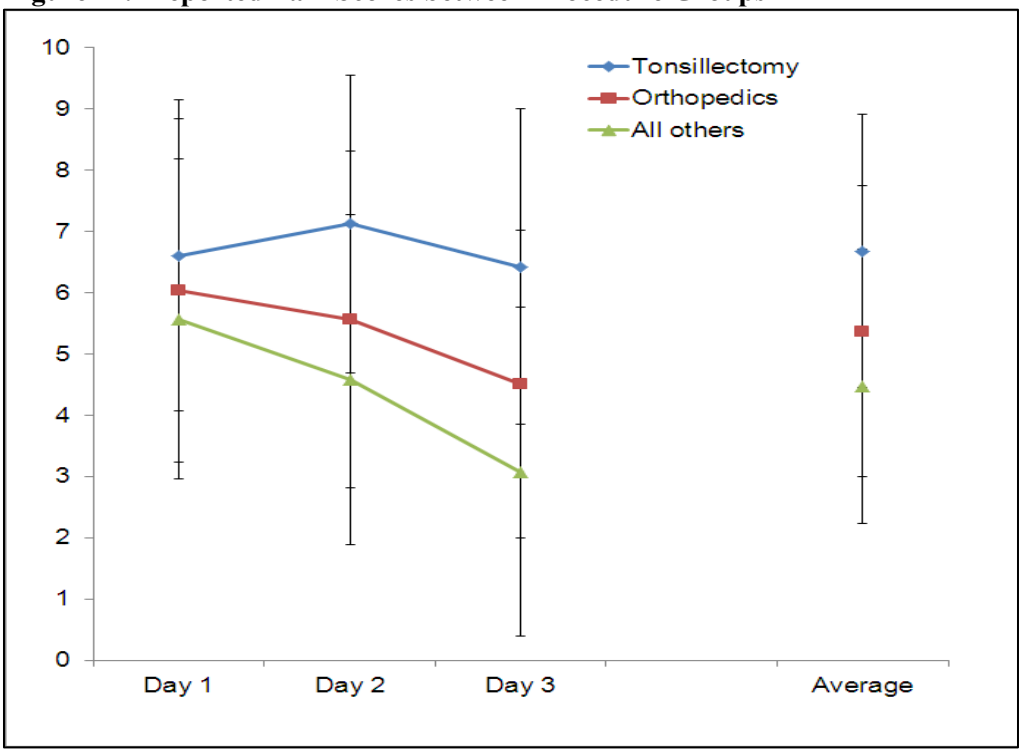
Differences in Analgesic Dosing and Pain Intensity by Child Procedure

Given differences in the hypothetical decisions of parents above, I compared analgesic use in the home setting between parents whose children had undergone tonsillectomy, orthopedic and other procedures. Parents whose children had tonsillectomies had similarly prescribed opioid amounts (mg/kg/day) compared to orthopedic procedures (mean difference (MD) = -0.02 [95% CI -0.05, 0.02], $p = 0.830$), and both of these groups had higher amounts prescribed compared to other procedures (MD = 0.054 [95% CI 0.002, 0.075], $p<0.001$; MD = 0.039 [95% CI 0.002, 0.075], $p = 0.033$, respectively). However, only the tonsillectomy group gave significantly more opioids (MD vs. orthopedic = 0.07 [95% CI 0.03, 0.10]; MD vs. all others = 0.09 [95% CI 0.06, 0.13], $p < 0.001$). A similar percentage of prescribed opioids was given to orthopedic and all other procedures ($p>0.05$).

Parents of children who underwent orthopedic and other procedures gave similar amounts of the OTC analgesics, ibuprofen and acetaminophen (MD 47.76 [95% CI -114.7, 210.2] and MD 126.9 [95% CI -124, 377.8], respectively, $p \geq 0.67$). And both groups gave significantly more ibuprofen and acetaminophen compared to the tonsillectomy group ($p<0.05$). These findings demonstrate that, parents whose children had tonsillectomy gave more opioids, while other parents were more likely to substitute non-opioids. This finding may reflect differences in analgesic instruction, with a greater emphasis on opioid use among the tonsillectomy parents and for non-opioid use among others. Conversely, differences in analgesic use may also reflect differences in the pain experience of children, given significantly higher average pain scores for those who had tonsillectomy (see figure 12, $F = 16.36(df2)$, $p < 0.001$). More specifically,

reported pain scores were not different between groups on the first postoperative day (F=2.63 (*df*2), p=0.075), but were higher for tonsillectomy patients compared to orthopedic and others on days 2 and 3 (p <0.01). Additionally, pain scores of orthopedic patients were not different from those of the other procedures group until day 3 (p = 0.013). Such pain score differences may further explain differences in opioid use at home.

Figure 12. Reported Pain Scores between Procedure Groups



Description of Adverse Drug Events (ADE) and Changes in Care

To examine the presence and potential influence of ADEs on parents' decisions, I asked parents to document, in an open-ended manner, whether their child experienced any possible ADEs. Ninety-seven parents (50%) reported that their child had an ADE either prior to hospital discharge (19%) or at home (42%), while 3% recorded that they were uncertain. These uncertain parents described effects and stated that they didn't know if the effect was related to analgesics or to surgery in general. Given the open-ended nature of this question, it remains possible that

ADEs were under-reported. This is particularly likely, given the large number of parents who were unaware of analgesic-related ADEs (range 12-43% for various opioid effects; see Chapter V, Table 6).

Table 28 describes the reported ADEs and parents' decision-making in response to events. Nearly half of the parents whose children purportedly experienced an ADE (n=45, 46%) stated that they changed their care due to the effect. Importantly, gastrointestinal ADEs (i.e., nausea/vomiting or constipation) were significantly more likely to motivate a change in care compared to other ADEs (61% vs. 31% changed care; Odds ratio 3.43 [95% CI 1.47, 7.99], $p < 0.001$). However, only one third of parents (n=11, 34%) whose children had excessive sleepiness or sedation changed their care, which was not significantly different from parents whose children had any other ADE (53%; OR = 0.46 [95% CI 0.19, 1.11], $p = 0.083$). Parents of tonsillectomy patients were similarly likely to have changed care in response to an ADE as other parents (OR = 1.27 [0.48, 3.38], $p = 0.628$). Together, these findings show that a substantial

Table 28. Adverse Drug Events after Discharge and Parents' Recorded Responses

	n (%)
Analgesic Adverse Effects at Home	83 (42%)
Nausea/Vomiting	32 (16%)
Sleepiness/Drowsiness	32 (16%)
Constipation	23 (12%)
Stomach Ache	9 (5%)
Rash/Allergy	7 (3%)
Personality Change	6 (3%)
Changed Care due to Side Effect	45 (23%)
Give Different Analgesic	29 (15%)
Gave Prescribed Analgesic Less Often	15 (8%)
Stopped Prescribed Dose	13 (7%)
Gave Different Dose of Prescribed Analgesic	9 (5%)

number of children experienced opioid-related ADEs after surgery, with gastrointestinal effects most likely to affect parents' decision-making regardless of procedure. And, similar to findings from the hypothetical decisions above, these data suggest that parents were more responsive to gastrointestinal side effects than to sedation.

Relationship between analgesic dosing and ADEs. Parents whose children had ADEs had been given greater amounts of opioid (mg/kg/day) compared to other parents (MD = 0.06 [95% CI 0.03, 0.08], $p < 0.001$) but similar amounts (mg/day) of ibuprofen (MD = 67.27 [95% CI 39.9, 174.5], $p = 0.217$) and acetaminophen (MD = 22.4 [95% CI -141.2, 186.1], $p = 0.789$). Additionally, children with ADEs were less likely to have undergone an orthopedic (OR = 0.40 [95% CI 0.20, 0.81], $p = 0.010$) or other procedure (OR = 0.17 [95% CI 0.08, 0.35], $p < 0.001$) compared to tonsillectomy. These findings are not surprising, since greater opioid use would be more likely to induce ADEs, and children who underwent tonsillectomy were given more opioids.

Description of Parents' Need for Help after Discharge

To examine potential pain and analgesic-related problems, I asked parents to record whether they sought help from anyone after discharge. One quarter of parents called a care provider or other person for advice, and the analgesic-related reasons for these calls are shown in Table 29. ADEs were the primary reason for calls for help, while unrelieved pain was the second most common reason. These findings reveal a significant amount of analgesic trade-off uncertainty in parents following hospital discharge. All parents who called for advice claimed that the person was helpful in resolving the problem.

Importantly, nine children returned to the emergency room or hospital within the first few days after surgery and 6 of these had undergone tonsillectomy (i.e., 7% of tonsillectomy parents

required unplanned return to hospital). Reasons for readmission included child's refusal to take oral medications and fluids, with concern for dehydration (n=5), allergic reaction to the analgesic and need for a new prescription (n=1), unrelieved pain with a need for a new prescription (n=2), and vomiting/possible aspiration (n=1). These findings expose the significant difficulty that parents, particularly those whose children undergo tonsillectomy, can experience in their attempts to manage pain after surgery.

Table 29. Parents' Need for Help Following Hospital Discharge

	n (%)
Called Provider for Help after Discharge	51 (26%)
Reason-analgesic-related adverse effect	25 (52.1)
Reason-pain control problem	14 (29.2)
Other (including surgical incision issues, etc.)	9 (18.8)
Who the Parent Called for Help	
Surgeon	24 (49%)
Nurse	18 (37%)
Pediatrician	4 (8%)
Friend/Family	2 (4%)
Other	1 (2%)

Relationships between Analgesic Knowledge/perception, Preferences, and Home Analgesic Use

Parents' diary data were linked to the preoperative survey data relative to the parent who completed the survey (i.e., mothers to mothers, primarily). Parents' aggregate preoperative opioid ADE knowledge/perception scores (i.e., sum [ADE knowledge*seriousness]) did not significantly correlate to the percentage of the prescribed opioid administered postoperatively (r = -0.05, p = 0.46). However, their pain relief (PR) preference scores (i.e., measure of their trade-off preference between pain relief and ADE avoidance) correlated significantly, albeit weakly, with opioid use (r = 0.247, p < 0.001) as did their preferred opioid thresholds (i.e., level of pain

at which they would give an opioid; $r = -0.26$, $p < 0.001$). These findings suggest that parental preference (primarily maternal) had a small but relatively minor relationship with postoperative dosing.

Predictors of Postoperative Opioid Use after Discharge

I used a univariate regression model to examine the main effects of parent and child factors on parents' opioid administration at home. I regressed the dependent variable, *Percent Opioid Dose Given* on the fixed factors (procedure [categorized as tonsillectomy vs. all others], presence of ADEs at home, and covariates (child age, parent opioid ADE knowledge/perception, PR preference, threshold preference, child's average pain scores at home, as well as OTC acetaminophen and ibuprofen use [i.e., total mg/day of these agents]).

One hundred sixty-two (162) surveys were included in the analysis (exclusions due to sporadic missing responses), and results are shown in Table 30. Results demonstrated that child age (older), tonsillectomy, and higher average pain scores predicted greater use of opioids, while greater OTC drug administration predicted lower opioid use. Furthermore, the child's average pain score explained a majority of the variance in parents' opioid use (partial eta squared = 0.11, or 11%), where every 1 point increase in the child's FPS score increased parents' prescribed opioid administration by 4.7% [95% CI 2.52, 6.88], $p<0.001$). OTC acetaminophen use explained nearly 9% of the variance in opioid use, while tonsillectomy explained only 5% of the variance in the percentage of opioid administered.

These findings show that pain intensity had the largest effect on parents' prescribed opioid administration after discharge. Substitution of non-opioids additionally had a significant, but smaller effect in reducing parents' opioid use. It is not surprising that parent opioid ADE knowledge/perception and preferences did not factor into real decisions since these factors had

variable influence on decisions based on scenario context (i.e., presence or absence of ADEs and pain intensity). Additionally, given the participatory nature of at home analgesic decisions, individual knowledge/perception and preferences were likely tempered by the knowledge and preferences of other family members, including those of the child. Lastly, the relationship between ADEs and at home opioid administration is confounded, since these effects occurred, not surprisingly, as a result of greater opioid use.

Table 30. Summary of the Relationships between Parent and Child Factors and Parent's Administration of the Prescribed Opioid After Surgery (% Prescribed Opioid Given)

Model Summary F=9.55 (*df*9) p <0.001; partial eta squared = 0.36 (36%)			
	β (95% CI)	**Sig.**	**Partial eta squared**
Child age	1.68 (0.36, 2.99)	**0.013**	0.04
Tonsillectomy procedure (vs. all others)	17.68 (5.43, 29.92)	**0.005**	0.051
Child's average pain score	4.70 (2.52, 6.88)	**<0.001**	0.107
ADE at home	-6.53 (-17.23, 4.16)	0.229	0.009
Parent's aggregate opioid knowledge	0.13 (-0.33, 0.58)	0.580	0.002
Parents' pain relief preference score	0.57 (-0.87, 2.00)	0.437	0.004
Parents' preferred opioid threshold	-1.67 (-3.91, 0.57)	0.144	0.01
OTC acetaminophen use (mg/day)	-0.021 (-0.03, -0.01)	**<0.001**	0.086
OTC ibuprofen use (mg/day)	-0.015 (-0.03, -0.002)	**0.027**	0.032

Chapter IX

Discussion

Summary

This dissertation examined parents' postoperative analgesic decisions when faced with various trade-off conditions between the child's level of pain and the presence of common or potentially serious adverse drug effects (ADE). This approach was particularly novel, since past studies have focused on parents' underutilization of analgesics when treating pain with a general disregard for their need to manage both the risks and benefits of these medications. The growing concern for analgesic mismanagement in the home setting highlights this actual risk-benefit trade-off. For instance, evidence suggests a significant prevalence of prolonged, unrelieved childhood pain that can lead to chronic pain and dysfunction (Fortier, et al., 2011; Fouladbakhsh, et al., 2012; Stewart, et al., 2012), as well as a worrisome number of analgesic adverse events and misuse that have resulted in death (Budnitz, et al., 2006; L. E. Kelly, et al., 2012; Nourjah, et al., 2006; Tzimenatos & Bond, 2009; Warner, et al., 2009). Such reports underscore the need to better understand parents' analgesic decisions and their implications for safety and effectiveness. This dissertation provides important data that examine the potential safety implications of parents' decisions to administer analgesics to their children and that explain how parents' analgesic knowledge and preferences influence these important decisions.

Main Findings

Signal detection and parental decisions. The ability of parents to make effective healthcare decisions for their children is likely related to their symptom recognition (i.e., signal detection) and overall situational awareness (i.e., their mental image of the signals as a whole,

their importance, and possible implications) (McGuinness, 2004). This means that for analgesic decisions, parents must recognize that the pain signal (i.e., pain level) warrants attention and treatment or, perhaps, that other concurrent symptoms (e.g., ADEs) take precedence. To examine parents' ability to recognize and respond to such signals, I first presented them several hypothetical postoperative scenarios wherein I manipulated the pain intensity level of the child and the presence or absence of ADEs. Of particular interest was how parents would differentiate and respond to the common but benign ADE, nausea and mild vomiting (NV), as well as the potentially serious ADE, oversedation (OS). Findings demonstrated that most parents changed their treatment decisions in response to these various situational signals, choosing the prescribed opioid analgesic most often for the child with higher pain and no ADE and least often for the child with low pain and mild NV. These findings showed how parents in this sample generally recognized and responded to variations in the situational signals.

Previous studies have demonstrated both the general ability of parents to recognize pain signals in their children, and to attach meaning to these signals by stating the importance of relieving pain (Kankkunen, et al., 2002; P. Kankkunen, K. M. Vehvilainen-Julkunen, A.-M. K. Pietila, & P. M. Halonen, 2003c; Kankkunen, et al., 2008; Rony, et al., 2010; Zisk, Grey, Medoff-Cooper, et al., 2007). Findings from the present study provide additional evidence for parents' overall recognition of the pain signal, since parents most often gave an analgesic, including the prescribed opioid dose, to children in the hypothetical high pain situations compared to the lower pain scenario.

However, pain in and of itself may be but one signal among many that require attention, particularly as the pain experience or situation unfolds. Thus, effective parental actions depend on their ability to differentiate and prioritize signals (McGuinness, 2004). This study

importantly demonstrates how parents respond to and prioritize potentially conflicting signals. Specifically, more parents withheld the prescribed opioid dose for the child with higher pain and NV compared to the more risky situation where the child had the same level of pain but was oversedated. These findings show that, while most parents responded to ADE signals in general, more were sensitive to the NV signal than to the OS signal. This difference in signal sensitivity may be the result of the meaning, or lack thereof, attached to the signals, making them more or less important to parents' evaluations of the situation. Since attributes that are less meaningful or recognizable may be ignored during decision-making (Gigerenzer & Gaissmaier, 2011), this could explain, in part, parents' lower response to the more serious OS signal.

To further explore how pain and ADE signals influenced parents' real decisions, participants were asked to record their child's early postoperative experience at home, including their analgesic decisions and use during this period. These data showed that the child's pain level explained most of the variability in parents' decisions to give prescribed opioids. Additionally, nearly half of the parents whose children had an ADE described changing their care in response to the effect, and, similar to their hypothetical decisions, parents were more likely to change care in response to gastrointestinal effects than to signs of sedation. These findings are similar to studies in adult patients with acute and chronic pain who placed a greater importance on reducing NV than sedation when choosing between pain relievers (Gregorian, et al., 2010). Together, such findings demonstrate the variability in the salience of pain and analgesic-related signs and symptoms that may affect patients' or parents' analgesic decisions.

Knowledge and analgesic decisions. Since appropriate signal recognition and differentiation requires a general understanding of relevant knowledge (Shrank & Avorn, 2007), I next explored the relationships between parents' analgesic knowledge (i.e., awareness of

analgesic ADEs and the relative seriousness of these effects) and their decisions. Higher opioid ADE knowledge/perception predicted parents' hypothetical decisions to withhold opioids when ADEs were present, but had no effect on their decisions in the absence of ADEs. Furthermore, general awareness (i.e., *gist* knowledge) of opioid-related NV was sufficient to influence parents' decisions to withhold opioids when these effects were present, but ADE awareness, alone, did not affect decisions when symptoms of oversedation (OS) were present. In this case, parents' understanding of the seriousness of the effect significantly influenced the decision to withhold opioids. These findings demonstrate that all knowledge is not equal in the ability to influence effective and safe analgesic decisions.

Previous studies have demonstrated general knowledge deficits and uncertainty regarding commonly administered over-the-counter (OTC) and prescribed analgesics (Fosnocht, et al., 2008; Kankkunen, Vehvilainen-Julkunen, Pietila, Kokki, et al., 2003; Kankkunen, et al., 2002; Kankkunen, et al., 2008; Li, et al., 2000; Rony, et al., 2010; Tait, et al., 2008; Wood, et al., 2010). Furthermore, reports of unintentional overdose and death from OTC and prescription analgesics expose a potential widespread lack of knowledge and its potentially grave implications (L.E. Kelly, et al., 2012; Nourjah, et al., 2006; Warner et al., 2009). Data from the present study, similarly, demonstrate significant parental analgesic knowledge deficits, even in a group of parents who had received preoperative analgesic preparation and were nearly prepared to make analgesic decisions following their child's surgery. These findings furthermore demonstrate the influence of specific deficits on parents' analgesic decisions, closing an important gap in evidence related to parents' opioid decisions. The finding that lower opioid-related sedation knowledge/perception was associated with parents' decisions to give the

prescribed opioid to the hypothetical child with symptoms of OS, has particular safety implications.

Individuals rely on different types of knowledge when faced with simple versus more complex decision-making tasks. During simple analgesic decisions parents likely draw on *gist* knowledge, that is, crude, categorical representations of information, such as presence or absence of an attribute such as ability to relieve pain (Djulbegovic, et al., 2012; Reyna, 2004, 2008b). More complex situations, such as trade-off situations where there are competing signals (e.g., high pain and an ADE), may require the use of higher level knowledge, such as ordinal or comparative ranking of various attributes (e.g., lower vs. higher risk, or seriousness) (Reyna, 2008b; Zikmund-Fisher, 2012). Findings from this study show that when faced with a less complex decision (i.e., higher pain and no ADEs), parents' gist ADE knowledge had no effect on the decision to administer opioids. However, their understanding of the pain relief potential (i.e., drug strength or potency) and riskiness of a prescribed opioid compared to OTC acetaminophen did influence their choice between drugs in this scenario. Specifically, parents who felt that the OTC choice provided close to or similar pain relief as the opioid, and who believed it to be much less risky were more likely to substitute the prescribed opioid with acetaminophen. Such findings suggest an influence of comparative analgesic rankings on analgesic choice. Ensuring that this type of knowledge is adequate, then, may be important to facilitate effective analgesic choices for parents.

Importantly, individuals may correctly encode facts into memory and therefore be able to demonstrate adequate gist understanding (e.g., awareness of a possible ADE), but may not have encoded its qualitative significance (e.g., seriousness or need for attention) (Reyna, 2008b; Reyna, et al., 2003). This incomplete coding of information may help to explain why simple gist

awareness knowledge was insufficient to influence parents' decisions to withhold the prescribed opioid for the child exhibiting symptoms of OS. Conversely, parents who gave the prescribed opioid in this situation may have been influenced by the more compelling gist knowledge regarding the need for pain relief (Reyna, 2008b). These findings demonstrate the importance of different types of knowledge toward effective and safe decision-making. Specifically, knowledge regarding the seriousness of certain effects may be more important than simple gist awareness of the effect in order to improve the salience of the ADE during decision-making. These data provide important guidance for the development of informational strategies to improve the safety and effectiveness of parents' analgesic decisions.

Parents' preferences and analgesic decisions. Since personal preferences regarding medications and outcomes have an important influence on decisions to use them (Gan, et al., 2004; Gregorian, et al., 2010; Katic, et al., 2010; Older, et al., 2010), I next examined how such preferences affected parents' decisions to give analgesics to their children. Specifically, I compared parents' pain relief (PR) trade-off preference scores (i.e., a measure of their relative preference to provide pain relief versus ADE avoidance) to their hypothetical and real decisions to give opioid analgesics. Trade-off preferences had a significant influence on parents' hypothetical decisions to give or withhold prescribed opioids for the child with high pain and symptoms of NV or OS, but no influence when a trade-off situation was not apparent (i.e., high pain but no ADE, or low pain and mild NV). Trade-off preference also correlated positively, though weakly, with at home administration of opioids. Lastly, parents' PR preference reduced the effect of knowledge on parents' hypothetical decisions to withhold opioids in the presence of OS, but not NV. These findings reveal the influence that trade-off preferences have on parents'

decisions, and how a strong preference to provide pain relief may interfere with the influence of knowledge in situations where a cue or signal (i.e., OS) is less salient.

It has been argued that the influence of preferences on an individual's evaluation of a situation is related to the emotional meaning that has been encoded together with knowledge, and that "errors" in decision-making may be related to interference from this emotional meaning (Reyna, et al., 2003; Schneider & Barnes, 2003). Such interference may help to explain factors at play in parents' responses to the child with conflicting signals of high pain and ADEs. For instance, it may be that the need to relieve a child's pain triggers an emotional response that has greater sway over certain decisions than the parent's analgesic ADE knowledge/perception. Such emotional interference may lead to inappropriate decisions in some cases, such as when the child exhibits potentially serious ADE symptoms. On the other hand, an emotional response to some attributes may work together with knowledge in facilitating a good decision (e.g., lower the opioid dose in presence of NV).

Since data from adult patients have suggested an influence of personal thresholds on their use of analgesics (Older, et al., 2010), I also explored the impact of their preferred treatment thresholds on their analgesic decisions. Specifically, I examined parents' indications regarding the minimal pain intensity level at which they would give an opioid or non-opioid analgesic and the influence of these thresholds on parents' decisions. Similar to previous reports (Demyttenaere, et al., 2001; Forward, et al., 1996), findings demonstrated significant variability in the levels of pain at which parents stated they would administer these analgesics for their child's pain. Parents' stated thresholds significant influenced their decisions across most of the hypothetical scenarios, and were negatively correlated with real opioid administration in the home setting. Additionally, parents' home analgesic use reflected the important influence of

pain threshold, given that opioids were used to treat higher pain intensity while non-opioids were used to treat less intense pain, and that pain intensity predicted higher daily opioid use. Together, these findings show how analgesic and treatment preferences can strongly influence and even interfere with knowledge during parents' decision-making processes.

Secondary Findings

In addition to my primary aims, I explored the potential effects of the parent's role, child's age, and their procedure on parents' hypothetical and real decisions to give analgesics. These analyses yielded several interesting findings. Firstly, while mothers were, in general, more conservative in their hypothetical decisions to administer opioids compared to fathers, this role difference was only significant under certain circumstances. For instance, in regression models where parental opioid ADE knowledge/perception was fixed at low values, mothers had a lower probability of giving opioids for scenarios depicting a child with NV symptoms, but not for other scenarios. Similarly, when preferred opioid thresholds were fixed at low values, mothers were less likely to give opioids, but across all scenarios. These findings show that at higher opioid knowledge/perception levels and threshold preferences, mothers and fathers made similar decisions, whereas at lower values, mothers tended to be more conservative. This may reflect differences in the emotional meaning that parents attach to various signals. Additionally, mothers may exhibit more risk-averse decisions due to the emotional activation evoked when asked to consider complex pain scenarios for their children. Indeed, higher composite distress, concern, and responsibility scores (i.e., emotional activation) have been found in individuals who made risk-averse decisions when making complex, hypothetical decisions for their child (Zikmund-Fisher, et al., 2006). It is quite possible, therefore, that mothers, in this study, had high emotional activation given that their children were undergoing surgery at the time of the

preoperative survey. This could have led to more risk-averse decisions, particularly when uncertain about the potential opioid-related ADEs. Given that fathers completed the surveys at the same time as mothers, and thus were likely under similar duress, these findings expose some underlying role or gender-based differences in analgesic decisions. Further study of this complicated relationship is therefore warranted.

This research also demonstrated that while parents of older children made similar hypothetical decisions to give opioids, those of younger children made different decisions based on the child's procedure. Parents whose children were undergoing non-tonsillectomy procedures gave fewer opioids to younger children, suggesting a more judicious approach to their care. Additionally, child age was a significant predictor of parents' actual administration of prescribed opioids in the home, with older children more likely to be given a larger percentage of their daily doses. These findings suggest that parents may tend to treat their younger children more conservatively.

Lastly, findings demonstrated that parents' hypothetical and real decisions were influenced by their child's procedure. Those whose children had tonsillectomy gave significantly more opioids compared to parents of other children. The procedure effect on hypothetical decisions was similar regardless of parental knowledge or preferences. However, in the absence of a trade-off condition (i.e., no ADE), there was no procedure effect, and parents were similarly likely to give an opioid across procedures. This finding suggests a similar approach among parents to treating higher pain (i.e., attention to the pain signal) in the absence of other symptoms. In contrast, compared to other parents, those of tonsillectomy patients were more likely to give an opioid in the presence of ADEs, suggesting a greater attention to the pain signal for parents of tonsillectomy patients, and a greater attention to the ADE signals for others.

It is not surprising that parents whose children were undergoing tonsillectomy were focused on pain relief, given a widespread emphasis in the literature on the need to better manage pain in this group (Sutters, et al., 2012; Sutters, et al., 2004; Sutters, et al., 2010). It is undeniable that tonsillectomy pain warrants attention given the importance of comfort and the related risk for dehydration that poses a serious threat to safety. The emphasis on the need to relieve pain by previous researchers and care providers likely influenced parents' decisions, since many recalled being informed to give their child the prescribed opioid analgesic around-the-clock (ATC) for the first few days. While ATC analgesic administration has been suggested as superior for managing tonsillectomy pain (Sutters, et al., 2012; Sutters, et al., 2010), this approach was recently criticized in an editorial given its potential safety implications (Sadhasivam & Myer, 2012). This editorial noted that nearly one quarter of death and hypoxic brain injury claims after tonsillectomy were attributed to opioids. They also highlighted evidence for the underestimation of risks due to explicit exclusion of subjects experiencing ADEs in at least one of the studies touting the benefits of ATC dosing. Others have similarly pointed out the significant risks associated with opioids in this high risk population (Subramanyam, Varughese, Willging, & Sadhasivam, 2013; Tunkel & Myer, 2013). Despite this more recent attention to the risks posed by opioids, the finding in the present study that parents of tonsillectomy children were less responsive to potentially serious ADEs may indicate ongoing knowledge deficits that should be of great concern for clinicians.

Clinical Implications

These results have several important implications for clinical practice. First and foremost is the exposed need for better analgesic education for parents. Most parents have the desire and understand the importance of managing pain in their children yet lack a basic gist understanding

of the common and potentially serious analgesic-associated ADEs. These knowledge deficits may place them at risk for making unsafe or ineffective treatment decisions for their children. Notably, information regarding the possible adverse effects of medications is not sufficient in and of itself to facilitate safe analgesic decisions. Rather, improved safety requires an understanding of the possibility of ADEs, their seriousness, and the potential consequences. Such information is necessary to improve the recognition and salience of certain ADE symptoms (e.g., OS) when they appear during medication use. Importantly, focused information regarding ADEs and their seriousness does not seem to influence parents' use of opioids in the absence of ADEs. Thus, specific ADE-risk information is not likely to dissuade parents from their attempts to manage pain but may serve to improve their decisions should ADEs occur.

Most parents are not averse to giving analgesics, including potent narcotics to manage their children's pain. However, they likely need better information regarding how to judiciously balance the use of opioids and non-opioids in the face of pain and ADEs when managing children's pain at home. Many parents already make analgesic trade-off decisions, giving opioids for higher pain and substituting non-opioids for lower pain. They seem to make these judgments based their own experiences and beliefs about the effectiveness and risks of these drugs. However, when faced with unfamiliar ADE symptoms parents may inadvertently give the wrong drug or dose in attempt to manage pain, failing to recognize or even ignoring relevant signs and symptoms.

Current practices of informing parents to administer analgesics "*prn*" (i.e., as needed), "*Give Lortab® for pain not controlled by Tylenol®*," or "*Do not give this medicine if your child is too sleepy*" are likely too vague to facilitate a safe and effective approach to treating pain. Likewise, instructing parents to give opioids ATC may lessen the importance of the need to

watch for and attend to potentially unsafe situations. Sadhasivam and Meyers (2012) addressed the potential safety implications of such advice, and have suggested genetic testing of children to determine their potential sensitivity to various opioids, including hydrocodone and codeine. However, since such testing is currently unfeasible and would not address the potential risks of medication misuse, an educational approach that better emphasizes the nature of poorly managed pain or signs of opioid toxicity, the potential seriousness and consequences of such conditions, is warranted. Such advice might include specific descriptions of symptom constellations (e.g., what does oversedation or poorly managed pain look like) that better prepare for parental signal recognition.

Sadhasivam & Meyers (2012) also suggest that postoperative tonsillectomy management should emphasize the use of safer, non-opioid analgesics, with less emphasis on opioids. Others have similarly pointed out that a primary emphasis on opioid use may be part of the reason why codeine-related deaths have all been from North America and are not found on other continents where postoperative management consists primarily of OTC non-opioids (Tremlett, 2013). Conversely, sole use of non-opioids may be insufficient to treat the severe pain that has been associated with tonsillectomy. Thus, a more balanced approach to pain management that includes both a broader use of non-opioids and a more targeted and judicious use of opioids may be warranted.

Although no parents in this study exceeded the maximum daily safe dose of acetaminophen, the data did identify deficient knowledge regarding acetaminophen-related ADEs that calls for improved clinician attention. These deficits are particularly concerning given press releases and published Food and Drug Administration (FDA) warnings calling for drug re-formulations, and "Black Box Warnings" labeling aimed at the pharmaceutical industry,

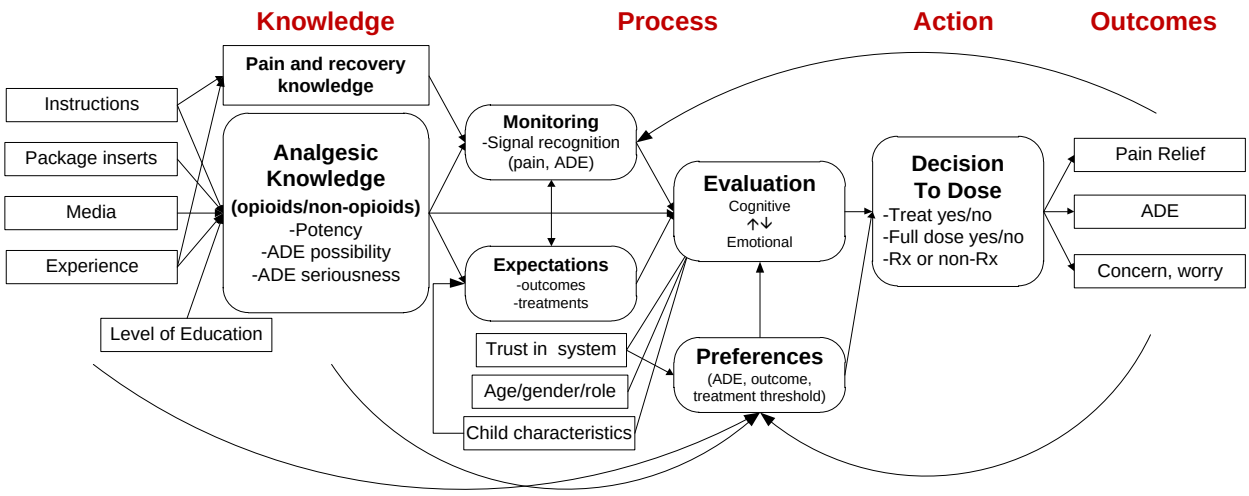
prescribers and patients (FDA, 2011). Clearly, this precautionary effort by the FDA has not yet reached most parents or providers who, in this setting, gave only sparse written attention to safe acetaminophen use. Mandated industry responses to the FDA warnings and recommendations will soon result in lower amounts of acetaminophen in tablets, capsules, and other dosage units (Parikh & Wilson, 2011). While this additional precautionary effort may reduce the amount of acetaminophen that can be given in one dose, it does not address the ongoing knowledge deficits of parents. Furthermore, this approach may have inadvertent negative consequences on parents' ability to manage pain safely at home, since it may increase the need for higher opioid dosage. Therefore, these findings, together with these upcoming changes in analgesic dosing availability, highlight an urgent need for improved instruction regarding acetaminophen use – particularly when prescribed together with another acetaminophen-containing analgesic. Lastly, since data suggest that half of OTC drug users rarely consult with a health-care provider when taking these medicines (Boudreau et al., 2013), there is an urgent need to better educate the public using a variety of media that reaches beyond parents seeking healthcare for their children.

Implications for Conceptual Model

The conceptual framework guiding this research provided a model depicting the complex relationships between parents' knowledge, preferences, and certain characteristics and their dynamic analgesic decisions. Results from this study support many of the proposed relationships, most notably those between analgesic ADE knowledge/perception, preferences and analgesic decisions. Importantly, this study did not examine the influence of parents' expectations on their signal evaluations and responses. However, parents' open-ended comments regarding their reasoning (e.g., "*I would expect this behavior after surgery*") provide partial confirmation of the influence of their expectations during their analgesic evaluative process.

Further study of the potential role of expectations and the relationship between knowledge, expectations and evaluation may be important, particularly for strategizing interventions aimed at modifying parents' signal recognition and responses.

Reproduction of Figure 1. Conceptual Model for Analgesic Decision-Making



Limitations

The nature of this research poses several limitations. First, despite the proposed usefulness of hypothetical scenarios to assess decision-making, parents may have responded differently to these than they would have to real situations, exhibiting, perhaps, a social desirability bias (Baron, 2008b). However, the use of hypothetical models facilitated the manipulation of important events (i.e., pain level and common and serious ADEs) that would have otherwise been difficult to study in the real world due to their relative rarity (e.g., oversedation) and the confounding influence of unmanageable factors (e.g., shared-decision making). Furthermore, evidence suggests that behaviors based on real and hypothetical situations are highly correlated (Robinson & Clore, 2001). The findings were also strengthened by the use of real decisions in conjunction with parents' hypothetical decisions, as these data upheld and lent external validity to many of the main findings.

Next, the hypothetical and real decisions explored in this study may have reflected several potential carry-over biases from completing the pre-decision knowledge and preference assessments, from the ordering of the hypothetical scenarios, and from taking part in the preoperative hypothetical study prior to reporting analgesic decisions at home. For instance, the preoperative assessment could have heightened parents' awareness or concerns for analgesic ADEs, thereby increasing their signal awareness during consideration of the hypotheticals as well as at home. Additionally, parents' evaluative process for the first scenario could have influenced their subsequent decisions, given a heightened awareness for specific signals such as pain. A future study randomizing the order of hypothetical scenarios, or examining postoperative decisions in the absence of a preoperative survey would be needed to explore this possibility.

It could be argued that the aggregate measure of opioid ADE knowledge/perception used in this study reflected parents' opioid risk perception more than knowledge. However, the findings that this factor correlated poorly with the parents' general rating of opioid risk (i.e., r = 0.190) and did not influence parents' decisions in the absence of ADEs provide some support that this variable measures a gist understanding that is different from risk perception.

Additionally, the use of pain intensity ratings to describe pain in the hypothetical scenarios may have provided an overly simplistic portrayal of postoperative pain, making parents' deliberation process more difficult. Inclusion of behavioral or functional pain interference symptoms may have given parents a broader perspective on which to base their analgesic decisions that may have also better reflected real life decision-making.

While every attempt was made to recruit all-comers who met inclusion criteria, the possibility of a selection bias cannot be over-looked, given that a small number of parents declined to take part (7% of those approached) and a larger proportion (33% of families) were

lost to postoperative follow-up. Given the general reasons provided by decliners, it is quite possible that they were even less knowledgeable about analgesics than participants. Reading literacy, and thus health literacy, may have been lower in these decliners. Although comparisons between families who returned surveys and those who didn't showed no significant differences in child or parent characteristics, knowledge, or preference variables, it remains unknown whether or how the experiences of these parents differed from those who completed the entire study.

Statistical analyses in this study focused on two decisional outcomes; i.e., parents' decision to give the prescribed dose (vs. another option) and their decision to give any opioid dose (vs. withhold opioids). Although it would be clinically important to understand factors related to parents' more nuanced decisions, such as give the prescribed dose versus a lower dose, the present study was underpowered to examine multiple comparisons within subgroups. Lack of power may also have been the reason for some of the negative findings for decisions to give the prescribed dose given the small number of parents who chose this option for some of the scenarios, as well as for some of the smaller group comparisons.

Finally, the lack of predictive influence of parents' opioid knowledge/perception, preferences on their real analgesic use in the home setting was likely confounded by the finding that a large proportion of decisions were made by *both* parents with input from the child. The potential effects of one parents' knowledge and preferences were, therefore, likely moderated by the knowledge/perception and preferences of others in the home.

Significance

To my knowledge, this study is the first to examine parents' analgesic treatment decisions using a conceptual framework that took into account the importance of trade-offs that occur over

the acute pain experience. The study provides new and generalizable knowledge regarding how parents' gist knowledge and preferences relate to their common and potentially serious trade-off decisions when managing acute pain after surgery in the home setting. Given the potential consequences of poorly controlled pain, misuse of analgesics, and mismanaged opioid-related ADEs, this information is essential to develop appropriate and successful strategies to improve decision-making. These data will be used to guide the development of interventions to optimize parent decision-making that will, in turn, enhance children's overall comfort and safety. Future research should be aimed at developing and testing strategies to improve parents' analgesic knowledge and decision-making.

Appendix A. IRB Approval Letter for Study

Medical School Institutional Review Board (IRBMED) • 2800 Plymouth Rd., Building 200, Room 2086, Ann Arbor, MI 48109-2800 • phone (734) 763 4768 • fax (734) 763 9603 • irbmed@umich.edu

To: Ms. Terri Voepel-Lewis

From:

Michael	Geisser
Alan	Sugar

Cc:

Terri	Voepel-Lewis
Brian	Zikmund-Fisher
Ellen	Smith

Subject: Initial Study Approval for [HUM00070613]

SUBMISSION INFORMATION:
Study Title: Parents' understanding and preferences regarding common pain relievers and treatment decisions
Full Study Title (if applicable):
Study eResearch ID: HUM00070613
Date of this Notification from IRB: 12/27/2012
Review: Expedited
Initial IRB Approval Date: 12/22/2012
Current IRB Approval Period: 12/22/2012 - 12/21/2013
Expiration Date: Approval for this expires at **11:59 p.m. on 12/21/2013**
UM Federalwide Assurance (FWA): FWA00004969 expiring on 6/13/2014
OHRP IRB Registration Number(s): IRB00001999

Approved Risk Level(s):

Name	**Risk Level**
HUM00070613	**No more than minimal risk**

NOTICE OF IRB APPROVAL AND CONDITIONS:
The IRBMED has reviewed and approved the study referenced above. The IRB determined that the proposed research conforms with applicable guidelines, State and federal regulations, and the University of Michigan's Federalwide Assurance (FWA) with the Department of Health and Human Services (HHS). You must conduct this study in accordance with the description and information provided in the approved application and associated documents.

APPROVAL PERIOD AND EXPIRATION:
The approval period for this study is listed above. Please note the expiration date. If the approval lapses,

Appendix B. Informed Consent

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

NAME OF STUDY AND RESEARCHERS

Title of Project: Parents' understanding and preferences regarding common pain relievers and treatment decisions

Principal Investigator: Terri Voepel-Lewis, MS, RN

GENERAL INFORMATION

We are conducting research to examine parents' understanding of common pain relievers, and their preferred ways for treating their children's pain at home using common pain relievers.

To gather information, we are asking 200 parents (mothers, fathers or both) to answer a survey about pain relievers.

The survey is voluntary. You do not have to complete it or answer questions you don't want to answer.

Your responses will help us find out parents' understanding of common pain relievers used to treat pain after surgery, and how parents prefer to manage their own children's pain after surgery, given some of the side effects of medicines.

It will take about 15-20 minutes to complete the questions. We would also like you to return one short portion of the survey 3-4 days after your child's discharge from the hospital to find out about your child's pain experience (their pain scores and side effects), how you managed their pain, and whether you had problems with any part of pain management. This will take an additional 5 minutes. You will be given a stamped envelope for returning this part. We will also ask if we can call to remind you to return the survey (or to do the survey by phone if you prefer). It is optional for you to give us your phone number for this purpose. If you do so, we assure that we will destroy your number once we call.

There is no charge to you or your health insurance for completing the survey. Some questions may cause you to feel uncomfortable, but may also prompt you to ask your nurse or doctor additional questions about treating your child's pain at home.

Your responses to these questions will remain confidential and your name and identifiers will not be recorded on the survey, and will be destroyed once we make the follow-up phone call.

There are no direct benefits to you for completing this survey.

What we learn from this survey will **help us develop strategies to help future parents** make good pain treatment decisions for their children after surgery.

If you have questions or concerns about this study or feel that the study has caused you any harm, contact:
Terri Voepel-Lewis
Department of Anesthesiology,
Box 4245, 1540 E. Hospital Drive,
University of Michigan Health System, Ann Arbor, Michigan 48109-4245
Telephone 734-936-0747 .

If you have any questions or concerns about your rights as a research subject, or any grievance, you may also contact the Institutional Review Board for Human Subject Research (IRBMED), University of Michigan, 2800 Plymouth Road, Building 200, Room 2086, Ann Arbor, MI 48109-2800; telephone 734 763-4768.

SIGNATURES

Research Subject:

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Name (print legal name): _____

Signature of Subject: _____

Date of signature: _____ *Date of Birth (mm/dd/yyyy):* _____

Principal Investigator (or Designee):

I have given this research subject (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____

Title: _____

Signature: _____ Date: _____

Appendix C. IRB Approval for Piloting Surveys

Medical School Institutional Review Board (IRBMED) • 2800 Plymouth Rd., Building 200, Room 2086, Ann Arbor, MI 48109-2800 • phone (734) 763 4768 • fax (734) 763 9603 • irbmed@umich.edu

To: Terri Voepel-Lewis

From:

Michael Geisser
Alan Sugar

Cc:

Terri Voepel-Lewis

Subject: Notice of Exemption for [HUM00070550]

SUBMISSION INFORMATION:
Title: Assessing Parent Preferences for Analgesic Outcomes and Analgesic Decisions: Instrument Development
Full Study Title (if applicable):
Study eResearch ID: HUM00070550
Date of this Notification from IRB: 11/19/2012
Date of IRB Exempt Determination: 11/19/2012
UM Federalwide Assurance: FWA00004969 expiring on 6/13/2014
OHRP IRB Registration Number(s):

IRB EXEMPTION STATUS:
The IRBMED has reviewed the study referenced above and determined that, as currently described, it is exempt from ongoing IRB review, per the following federal exemption category:

> **EXEMPTION #2 of the 45 CFR 46.101.(b):**
> Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless: (i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

Note that the study is considered exempt as long as any changes to the use of human subjects (including their data) remain within the scope of the exemption category above. Any proposed changes that may exceed the scope of this category, or the approval conditions of any other non-IRB reviewing committees, must be submitted as an amendment through eResearch.

Although an exemption determination eliminates the need for ongoing IRB review and approval, you still have an obligation to understand and abide by generally accepted principles of responsible and ethical conduct of research. Examples of these principles can be found in the Belmont Report as well as in guidance from professional societies and scientific organizations.

SUBMITTING AMENDMENTS VIA eRESEARCH:
You can access the online forms for amendments in the eResearch workspace for this exempt study, referenced above.

ACCESSING EXEMPT STUDIES IN eRESEARCH:
Click the "Exempt and Not Regulated" tab in your eResearch home workspace to access this exempt study.

Appendix D. Preoperative Survey

General Knowledge of and Preferences for Pain Medicines

This survey will explore your general knowledge of common pain medicines.

Pain Medicine Recognition

Are you familiar with these pain drugs?		Do you have the drug in your cabinet **at home**?	Have you **given** this drug to your child in the past **6 months**?
Tylenol (acetaminophen)	☐Yes ☐No	☐ Yes ☐ No ☐ Don't know	☐ Yes ☐ No ☐ Don't know
Ibuprofen (Motrin, Advil, Pediaprofen)	☐Yes ☐No	☐ Yes ☐ No ☐ Don't know	☐ Yes ☐ No ☐ Don't know
Vicodin (hydrocodone/acetaminophen)	☐Yes ☐No	☐ Yes ☐ No ☐ Don't know	☐ Yes ☐ No ☐ Don't know
Lortab (hydrocodone/acetaminophen)	☐Yes ☐No	☐ Yes ☐ No ☐ Don't know	☐ Yes ☐ No ☐ Don't know
Norco (hydrocodone/acetaminophen)	☐Yes ☐No	☐ Yes ☐ No ☐ Don't know	☐ Yes ☐ No ☐ Don't know
Oxycodone	☐Yes ☐No	☐ Yes ☐ No ☐ Don't know	☐ Yes ☐ No ☐ Don't know

People differ in how much they would prefer to get rid of pain over how much they want to avoid drug side effects.

Circle the response that tells how much you agree or disagree with each statement:

	Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
1) Pain relief is more important than the side effects of prescription pain drugs.	**SD**	**D**	**N**	**A**	**SA**
2) Avoiding nausea and vomiting is more important than my child's complete pain relief.	**SD**	**D**	**N**	**A**	**SA**
3) My child's pain relief is more important than making sure he is not too sleepy or sedated.	**SD**	**D**	**N**	**A**	**SA**
4) My child's pain relief is more important than making sure he does not feel sick or queasy from medicines.	**SD**	**D**	**N**	**A**	**SA**
5) Making my child comfortable is more important than reducing the possibility of side effects.	**SD**	**D**	**N**	**A**	**SA**
6) Avoiding excessive sleepiness or sedation is more important than getting rid of my child's pain.	**SD**	**D**	**N**	**A**	**SA**

Based on the descriptions below, **which drug would you prefer** to treat your child's pain **at home** after surgery?

Drug A	Drug B
• Most (75%) children get **fair** pain relief • **Few** (5%) children **feel a little sick** off & on • **No** (0) children **vomit** (throw up) • **No** (0) children get **constipated**	• Most (75%) children get **excellent** pain relief • **Many** (50%) children **feel a little sick** off & on • Few (5%) children **vomit** (throw up) • **Many** (50%) children get **constipated**
Would you **prefer to give** your child drug A or drug B to relieve pain at home? **Drug A** _____ **Drug B**_____	

Based on the descriptions below, **which drug would you prefer** to treat your child's pain **at home** after surgery?

Drug A	Drug B
• Most (75%) children get **excellent** pain relief • **Many** (50%) children get **sleepy** • **Few** (5%) children get **excessively sedated** *(is hard to wake up and can't stay awake for very long during the daytime)*	• Most (75%) children get **fair** pain relief • **No** (0) children get **sleepy** • No (0) children get **excessively sedated** *(is hard to wake up and can't stay awake for very long during the daytime)*

Would you **prefer to give** your child drug A or drug B to relieve pain at home?

Drug A _____ **Drug B**_____

TYLENOL

(acetaminophen - over the counter)

	"Do people **ever** have these side effects because they took Tylenol?" *(check one box per row)*			
Nausea (feeling sick)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Occasional vomiting (throwing up but able to keep some fluid down)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Excessive sleepiness (hard to wake up, can't stay awake during day time, snores a little when sleeping)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Constipation (No bowel movement for 2 days)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Liver damage	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Slowed breathing	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Itching (over arms or chest)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Habit (addiction)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**

List any other side effect you think might happen with Tylenol:

VICODIN

(hydrocodone/acetaminophen – Prescribed Narcotic Pain Reliever)

	"Do people **ever** have these side effects because they took Vicodin?" *(check one box per row)*			
Nausea (feeling sick)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Occasional vomiting (throwing up but able to keep some fluid down)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Excessive sleepiness (hard to wake up, can't stay awake during day time, snores a little when sleeping)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Constipation (No bowel movement for 2 days)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Liver damage	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Slowed breathing	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Itching (over arms or chest)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**
Habit (addiction)	☐ Definitely **Not**	☐ Probably **Not**	☐ Probably **Do**	☐ Definitely **Do**

List any other side effect you think might happen with Vicodin:

<u>If any of these side effects below happened to your child</u> at home after surgery, **<u>how serious</u> or dangerous** do you think it would be?

(check one box per row)

Nausea (feeling sick)	☐ Not Serious	☐	☐	☐	☐	☐ Extremely serious
Occasional vomiting (throwing up but able to keep some fluid down)	☐ Not Serious	☐	☐	☐	☐	☐ Extremely serious
Excessive sleepiness (hard to wake up and can't stay awake during day time)	☐ Not Serious	☐	☐	☐	☐	☐ Extremely serious
Constipation (No bowel movement for 2 days)	☐ Not Serious	☐	☐	☐	☐	☐ Extremely serious
Liver damage	☐ Not Serious	☐	☐	☐	☐	☐ Extremely serious
Slowed breathing	☐ Not Serious	☐	☐	☐	☐	☐ Extremely serious
Itching (over arms or chest)	☐ Not Serious	☐	☐	☐	☐	☐ Extremely serious
Habit (addiction)	☐ Not Serious	☐	☐	☐	☐	☐ Extremely serious

<u>List</u> any other side effect that make you worried about giving pain relievers to your child:

_____

_____

_____

Your general assessment of common pain medicines for treating a child's pain **at home after surgery**:

<table>
<tr><td rowspan="2">X the box that estimates how strong of a pain reliever each of these drugs are when given in the recommended doses:</td><td>Tylenol
(acetaminophen)</td><td>☐ ☐ ☐ ☐ ☐
Not Strong … Very Strong</td></tr>
<tr><td>Vicodin
(prescribed narcotic Hydrocodone/ acetaminophen)</td><td>☐ ☐ ☐ ☐ ☐
Not Strong … Very Strong</td></tr>
<tr><td>X the box that tells which of these doses gives stronger pain relief compared to the other:</td><td colspan="2">☐ Half dose Vicodin
☐ These doses are about equally strong
☐ Full dose Tylenol</td></tr>
<tr><td>X the face showing the lowest level of pain at which you would give your child Tylenol:</td><td colspan="2"> 
0 NO HURT · 2 HURTS LITTLE BIT · 4 HURTS LITTLE MORE · 6 HURTS EVEN MORE · 8 HURTS WHOLE LOT · 10 HURTS WORST</td></tr>
<tr><td>X the face showing the lowest level of pain at which you would give your child Vicodin:</td><td colspan="2"> 
0 NO HURT · 2 HURTS LITTLE BIT · 4 HURTS LITTLE MORE · 6 HURTS EVEN MORE · 8 HURTS WHOLE LOT · 10 HURTS WORST</td></tr>
<tr><td rowspan="2">How risky do you think these drugs are when used to treat children's pain at home after surgery?</td><td>Tylenol</td><td>☐ ☐ ☐ ☐ ☐
Not Risky … Very Risky</td></tr>
<tr><td>Vicodin</td><td>☐ ☐ ☐ ☐ ☐
Not Risky … Very Risky</td></tr>
</table>

Hypothetical Pain Treatment Decisions

On the next 4 pages, you will see 4 ***different and unrelated scenarios*** *that describe cases when parents need to decide if and how to treat a child's pain after surgery.*

Please think about each of these examples ***SEPARATELY****.*

Imagine that you are faced with these decisions.

For each scenario, pick ***one answer*** *that best tells what you think you would do.*

Imagine that you have brought your child home after surgery, and have been given the following prescription and orders:

(Note: These are ***NOT real drug doses****, but are examples only)*

Prescription:

Give **Vicodin** (hydrocodone/acetaminophen)
2 mL every 4-6 hours as needed for pain.

Other instruction:

You may give **Tylenol** (acetaminophen) 10 mL every 4-6 hours instead of but **not** in addition to vicodin (since vicodin contains acetaminophen)

Scenario 1)

Imagine your child got Vicodin 2ml <u>6 hours ago</u>, and nothing else since.

S/he has been <u>sleeping continuously</u>, has a little snoring off and on, and wakes up only when you shake his/her shoulder.

When awakened, your child complains of **<u>pain = 6</u>** out of 10, and then **<u>falls back to sleep</u>**.

How you would treat your child's pain (**X <u>one</u> box only**):

- ☐ Give 2 mL of vicodin (prescribed dose) ONLY
- ☐ Give 1 mL vicodin (a lower dose) ONLY
- ☐ Give 1 mL vicodin (lower dose) AND Tylenol
- ☐ Give Tylenol (acetaminophen) ONLY
- ☐ Give NOTHING at this time
- ☐ Give something else (describe)_____

Please describe why you made the choice you did:

_____

_____

_____

Now, please imagine that the previous scenarios did NOT happen.

INSTEAD, imagine the scenario below.

Scenario 2)

Imagine your child got Vicodin <u>6 hours ago</u>, and nothing else since.

S/he has been feeling sick and has vomited once, but has been able to keep down a little juice.

Your child is complaining of **<u>pain = 6</u>** out of 10.

How you would treat your child's pain (**X <u>one</u> box only**):

- ☐ Give 2 mL of vicodin (prescribed dose) ONLY
- ☐ Give 1 mL vicodin (a lower dose) ONLY
- ☐ Give 1 mL vicodin (lower dose) AND Tylenol
- ☐ Give Tylenol (acetaminophen) ONLY
- ☐ Give NOTHING at this time
- ☐ Give something else_____

Please describe why you made the choice you did:

_____

_____

_____

Now, please imagine that the previous scenarios did NOT happen.

INSTEAD, imagine the scenario below.

Scenario 3)

Imagine your child got Vicodin <u>6 hours ago</u>, and nothing else since.

S/he has been lying around, is tired but awake, and has not had any other problems since pain medicine was last given.

Your child is complaining of **<u>pain = 6</u>** out of 10**.**

How you would treat your child's pain (**X <u>one</u> box only**):

- ☐ Give 2 mL of vicodin (prescribed dose) ONLY
- ☐ Give 1 mL vicodin (a lower dose) ONLY
- ☐ Give 1 mL vicodin (lower dose) AND Tylenol
- ☐ Give Tylenol (acetaminophen) ONLY
- ☐ Give NOTHING at this time
- ☐ Give something else_____

Please describe why you made the choice you did:

_____

_____

_____

Now, please imagine that the previous scenarios did NOT happen.

INSTEAD, imagine the scenario below.

Scenario 4)

Imagine your child got Vicodin 6 hours ago, and nothing else since.

S/he has been feeling sick and has vomited once, but has been able to keep down a little juice.

Your child is complaining of **pain = 4** out of 10.

How you would treat your child's pain (**X one box only**):

- ☐ Give 2 mL of vicodin (prescribed dose) ONLY
- ☐ Give 1 mL vicodin (a lower dose) ONLY
- ☐ Give 1 mL vicodin (lower dose) AND Tylenol
- ☐ Give Tylenol (acetaminophen) ONLY
- ☐ Give NOTHING at this time
- ☐ Give something else_____

Please describe why you made the choice you did:

_____

_____

_____

General Information about You and Your Child

Your age: _____

Your gender:

☐ Male ☐ Female

Your relationship to the child:

☐ Mom

☐ Dad

☐ Guardian

☐ Other _____

Your race/culture:

☐ Black ☐ White ☐ Hispanic ☐ Asian

☐ Other_____

What is your highest level of education?

☐ Less than high school

☐ High school graduate

☐ Some college, associate degree or trade school

☐ Four year college graduate

☐ Graduate school

Your child's age: _____

Your child's gender:

☐ Male ☐ Female

Has your child had previous surgery?

☐ Yes ☐ No

Type of surgery your child is having today:

_____

Healthcare System Opinion Survey	Strongly Agree	Agree	Not Sure	Disagree	Strongly Disagree
The health care system puts my medical needs above all other considerations when treating my medical problems.	SA	A	NS	D	SD
Medical experiments can be done on me without my knowing about it.	SA	A	NS	D	SD
My medical records are kept private.	SA	A	NS	D	SD
People die every day because of mistakes by the health care system.	SA	A	NS	D	SD
When they take my blood, they do tests they don't tell me about.	SA	A	NS	D	SD
If a mistake were made in my health care, the health care system would try to hide it from me.	SA	A	NS	D	SD
People can get access to my medical records without my approval.	SA	A	NS	D	SD
The health care system cares more about holding costs down than it does about doing what is needed for my health.	SA	A	NS	D	SD
I receive high-quality medical care from the health care system.	SA	A	NS	D	SD
Some medicines have things in them that they don't tell you about.	SA	A	NS	D	SD

Appendix E. Factor Analysis of the Preferences Items

Correlation Matrix

		Q1	Q3	Q5	Q6	q2recode	q7recode
Correlation	Q1	1.000	.437	.235	.611	-.110	.256
	Q3	.437	1.000	.521	.535	.150	.427
	Q5	.235	.521	1.000	.285	.409	.369
	Q6	.611	.535	.285	1.000	-.085	.347
	q2recode	-.110	.150	.409	-.085	1.000	.171
	q7recode	.256	.427	.369	.347	.171	1.000

KMO and Bartlett's Test

Kaiser-Meyer-Olkin Measure of Sampling Adequacy.		.734
Bartlett's Test of Sphericity	Approx. Chi-Square	134.344
	df	15
	Sig.	.000

Communalities

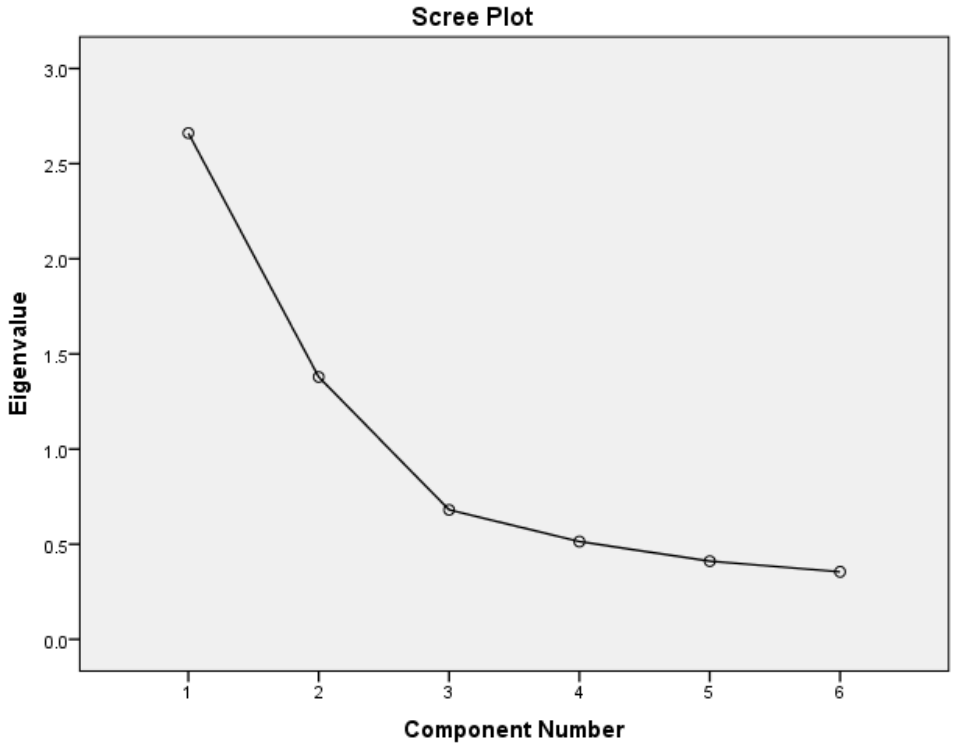
	Initial	Extraction
Q1	1.000	.696
Q3	1.000	.682
Q5	1.000	.703
Q6	1.000	.752
q2recode	1.000	.756
q7recode	1.000	.451

Extraction Method: Principal Component Analysis.

Total Variance Explained

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	2.661	44.344	44.344	2.661	44.344	44.344	2.290	38.175	38.175
2	1.379	22.983	67.327	1.379	22.983	67.327	1.749	29.152	67.327
3	.681	11.345	78.672						
4	.514	8.564	87.236						
5	.411	6.849	94.086						
6	.355	5.914	100.000						

Extraction Method: Principal Component Analysis.



Rotated Component Matrix[a]

	Component	
	1	2
Q6	**.866**	.051
Q1	**.833**	-.045
Q3	**.683**	.465
q2recode	-.260	**.830**
Q5	.318	**.776**
q7recode	.461	**.488**

Extraction Method: Principal Component Analysis. Rotation Method: Varimax with Kaiser Normalization. a. Rotation converged in 3 iterations.

Component Transformation Matrix

Component	1	2
1	.843	.537
2	-.537	.843

Extraction Method: Principal Component Analysis.

Rotation Method: Varimax with Kaiser Normalization.

Appendix F. Postoperative Parent Survey/Diary

Please complete this section over the first 3 days at home.

Record <u>all doses of pain medicines</u> given (e.g., Your child's prescribed dose (or change in dose), tylenol (acetaminophen), ibuprofen (motrin), etc.)

Day 1: Same day of discharge

Highest Pain Score 0-10:_____

Pain Medicine Given? ☐ yes ☐ no

If yes, record details of each dose below	**Name of drug given**	**Dose given**	**Pain score before drug given (*0-10*)**
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:

Day 2 (Day after discharge)

Highest Pain Score 0-10:_____

Pain Medicine Given? ☐ yes ☐ no

If yes, record details of each dose below	**Name of drug given**	**Dose given**	**Pain score before drug given (*0-10*)**
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:

Day 3 (2 days after discharge):

Highest Pain Score 0-10:_____

Pain Medicine Given? ☐ yes ☐ no

If yes, record details of each dose below	**Name of drug given**	**Dose given**	**Pain score before drug given (*0-10*)**
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:
Time:	Drug:	Dose:	Pain Score:

Please complete this section on day 3 after surgery

Did you get your child's prescription filled? ☐ yes ☐ no

If no, why (e.g., not available at your store, no time, cost, already in the house)?

How you were advised to give pain meds?

☐ as ordered ☐ as needed ☐ around the clock ☐ Other (describe):_____

Who made decisions to give pain medicine at home?

☐ Mostly me ☐ Mostly my spouse/partner ☐ Both of us equally ☐ Child only

Did your child take part in these decisions? ☐ yes ☐ no

If yes, how much of a part: ☐ a little part ☐ equal ☐ a large part ☐ complete control

Did your child **ever ask for medicine**? ☐ yes ☐ no

Did your child **ever refuse medicine**? ☐ yes ☐ no

Did your child have any **side effects** from pain medicines?

Before leaving the hospital? ☐ yes ☐ no ☐ don't know

At home? ☐ yes ☐ no ☐ don't know

If YES, what were the side effects? _____

Did you change anything about your child's pain treatment because of side effects?

☐ yes ☐ no

If YES, did you:

- ☐ give a different dose of prescribed medicine
- ☐ give the medicine less often
- ☐ stop the prescribed medicine
- ☐ give a different pain medicine (e.g., Tylenol)
- ☐ other (describe):_____

Did you call anyone about your child's condition in the first 3 days after discharge?

☐ yes ☐ no If yes, why?_____

If yes, who? ☐ Surgeon ☐ Nurse ☐ Pediatrician ☐ Pharmacist ☐ Friend/family member ☐ Other

In what ways was the person helpful or not helpful:

Please tell us anything else about your child's pain experience (what was hard, what could have made it easier to manage:

Appendix G. Permission to Use FACES Scale

Wong on Web Archive

FACES Permission Form

Online form

Please complete this form online, then print. Sign and fax the completed form to:

Natalie David
Rights Manager
Global Rights Department
Elsevier Ltd
PO Box 800
Oxford OX5 1DX
UK
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Fax: (+44) 1865 853333 (UK)
Email: permissions@elsevier.com or healthpermissions@elsevier.com

Permission is granted for use of the Wong-Baker FACES Pain Rating Scale subject to the stipulations listed below.

Borrowing author: Terri Voepel-Lewis, MS, RN
Intended use of scale: Survey of Parents' Pain Management Decisions
To be used/ published by: Instrument will be used in the survey, and published in a dissertation only.

Stipulations

1. Full credit shall be given on each reproduced copy of Wong-Baker FACES Pain Rating Scale in the following format and using the capitalized style of FACES in the title:
From Hockenberry MJ, Wilson D: *Wong's essentials of pediatric nursing*, ed. 8, St. Louis, 2009, Mosby. Used with permission. Copyright Mosby.
2. No changes in, additions to, or deletions from the drawings shall be made without prior written approval of the author. The exception is the use of a different coding number for each face, such as 0 to 10, using the numbers 0,2,4,6,8,10 only. The following brief word Instructions under each facial expression must accompany the scale: FACE 0: no hurt; FACE 1: hurts little bit; FACE 2: hurts little more; FACE 3: hurts even more; FACE 4: hurts whole lot; FACE 5: hurts worst. All translations must use the words from the source in Stipulation 1. Some exceptions may be granted but must be approved. The inclusion of the original, detailed instructions is optional. (See sample below).
3. Permission shall apply only to the work specified in this correspondence. New application shall be made for subsequent editions or for other uses of the material.
4. A copy of the page with the intended use of the FACES must be attached to this signed form.

NOTE: Due to the hundreds of requests we receive for the FACES scale, we are able to respond only to those requests that comply with the above stipulations.

Name: Terri Voepel-Lewis
Date: 12/6/2012
Signature:
Mailing Address: Rm 4917 Mott Hospital, Box 4245
1540 E. Hospital Drive
City: Ann Arbor
State/Province: MI
Postal Code/ZIP: 48109-4245

Country: US
Home Phone*: -
-OR-
Work Phone*: 734-936-0747
Fax: 734-763-6661
Email:

Permission granted on above terms by:
Signature:
Permissions Editor
Date: 14 December 2012

Create Printable Form

Wong-Baker FACES Pain Rating Scale

Alternate coding: 0 2 4 6 8 10

Brief word instructions: Point to each face using the words to describe the pain intensity. Ask the child to choose face that best describes own pain and record the appropriate number.

Original instructions: Explain to the person that each face is for a person who feels happy because he has no pain (hurt) or sad because he has some or a lot of pain. **Face 0** is very happy because he doesn't hurt at all. **Face 1** hurts just a little bit. **Face 2** hurts a little more. **Face 3** hurts even more. **Face 4** hurts a whole lot. **Face 5** hurts as much as you can imagine, although you don't have to be crying to feel this bad. Ask the person to choose the face that best desribes how he is feeling.

Rating scale is recommended for persons age 3 years and older.
Download FACES scale

::Last updated September 2008::

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