
by

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Abstract

It is estimated that 49-96% of adolescents with cancer will experience pain related to the disease and/or associated invasive procedures and treatments. Pain negatively impacts adolescent health-related quality of life (HRQL) and is associated with long-term morbidity. In response, a smartphone-based pain app, called Pain Squad+, capable of providing adolescents with real-time pain management support was developed and evaluated. Using user-centered methods, research aims were to utilize iterative cycles of usability testing with adolescents with cancer to refine the app (Study 1), to evaluate the ability to implement the Pain Squad+ app in a hypothesis-testing trial (Study 2), and to obtain estimates of treatment effects on adolescent health outcomes (Study 2).

In Study 1, iterative cycles of usability testing with 16 adolescents were used to refine the Pain Squad+ app to ensure it was easy to use, easy to understand, efficient, and acceptable to adolescents. In Study 2, 33 adolescents used the app for 28-days, receiving real-time self-management advice and clinical support from a nurse dependent on self-reported pain. Acceptability of the intervention assessed quantitatively and qualitatively was high. The study accrual percent was 75% and the withdrawal percent was 3%. Technical malfunctioning of the
app was rare. The nurse received pain-related emails from 39% adolescents with a mean time to follow-up of 62.5 hours (SD=55.5). Outcome assessment piloting was successful with a mean of 94.9% (SD=4.3) of baseline and 84.3% (SD=31.0) of post-study questions completed. Adherence to pain reporting was 69.0±40.8%. Significant trends in improvement in pain intensity and HRQL were observed (p<0.05). Small to moderate effect sizes were observed for the pain intensity items (0.20–0.69), pain interference (0.35), HRQL subscales (0.31–0.61), and pain care self-efficacy (0.27). Qualitative interviews revealed satisfaction with study participation, but also provided data that will be used to refine the Pain Squad+ intervention and study protocol.

In conclusion, a user-centered approach was implemented to develop and establish the testing procedures for the Pain Squad+ app. An adequately powered randomized controlled trial (RCT) should be undertaken to examine the impact of the app on health and health services outcomes in adolescents with cancer pain.
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CHAPTER ONE: INTRODUCTION AND PROBLEM STATEMENT

Cancer is the most common potentially fatal illness in Canadian children and adolescents (Canadian Cancer Society, 2012). Owing to advancements in therapies, the mortality rate of Canadian children and adolescents with cancer has fallen in the last 20 years (Canadian Cancer Society, 2012), resulting in an increase in the number of survivors. There are now approximately 1400 new diagnoses of cancer each year in Canada and the current 5-year survival rate averaged across all diagnoses is approximately 85% (Baxter et al., 2014; Canadian Cancer Society, 2012; Ellison, De, Mery, & Grundy, 2009). These improvements in survival rates have led to an increased appreciation and study of the psychological and physical impacts of cancer (Ellison et al., 2009); not only for survivors, but for young people undergoing active treatment as well (Erickson et al., 2013; Woodgate, 2005; 2008). Children and adolescents with cancer experience the symptoms of cancer and its associated intense protocols during treatment and for years following treatment (Armstrong et al., 2009; Boman, Lindblad, & Hjern, 2010; Kirchhoff et al., 2011; Kurt et al., 2012; Nathan et al., 2009). However, despite this knowledge, the management of symptoms has not kept pace with advancements in pediatric cancer treatment protocols (Woodgate, 2008). Symptom management can be complex, involving the patient, family and healthcare team and requiring dynamic combinations of interventions in order to provide the best possible health-related quality of life (HRQL) to young people with cancer. One cancer-related symptom known to be especially distressing to children and adolescents is pain (Collins et al., 2000; Hedén, Pöder, Essen, & Ljungman, 2013; Hedström, Haglund, Skolin, & Essen, 2003; Hockenberry & Hooke, 2007; Walker, Gedaly-Duff, Miaskowski, & Nail, 2010).
Adolescents with Cancer

Over the last 2 decades, adolescents (defined for this study as youths aged 12 – 18 years) with cancer have emerged from under the umbrella of childhood cancer as a subgroup with unique developmental characteristics and a unique cancer epidemiology (Baxter et al., 2014; Bleyer, 2002; Erickson et al., 2013; M. A. Smith et al., 2010; Sung et al., 2009). In addition, adolescent survival and self-reported HRQL ratings have lagged behind those of younger and older cancer patients (Barrera et al., 2003; Bleyer, 2005; Sung et al., 2009; Thomas, Albritton, & Ferrari, 2010; Varni, Burwinkle, Katz, Meeske, & Dickinson, 2002). With regards to HRQL, older age has been shown to significantly predict poorer scores on all aspects of function in children and adolescents with cancer (Sung et al., 2009). Several explanations for this observed phenomenon have been proposed, including inconsistent referral policies (i.e., cancer treatment at either adult or pediatric oncology centers), gaps in adolescent cancer research, limited health services and resources with an adolescent focus (Bleyer, 2005; Nathan, Hayes-Lattin, Sisler, & Hudson, 2011; Zebrack, Mathews-Bradshaw, Siegel, Livestrong Young Adult Alliance, 2010) and treatment non-adherence (Butow et al., 2010; Landier et al., 2011; Rosenberg, Macpherson, Kroon, & Johnson, 2013; Windebank & Spinetta, 2008). Unique characteristics related to developmental stage also may result in this population being especially susceptible to the emotional stresses of the cancer experience. Adolescence is a period of life fraught with role-changes, shifting expectations, and new and challenging social interactions. These developmental challenges, combined with a potentially underdeveloped ability to cope with cancer and its treatment sequelae, suggest that the cancer pain experience (i.e., clinical manifestation, emotional impact, management strategies and pain treatment outcomes) may be very different for adolescents compared to younger children and adults (Baggott et al., 2010; Erickson et al., 2013; Hinds et al., 2000). In spite of this observation, to date, the majority of
studies investigating cancer pain and pain management have grouped adolescents with either younger or older persons.

**Pain in Adolescents with Cancer**

**Sources of Pain**

Cancer pain may result from the disease itself or from the many associated invasive diagnostic and treatment procedures and can be either acute or chronic in nature. The quality of pain resulting from the disease can vary depending on the type of cancer and source of the pain (Collins, Stevens, & Berde, 2008). Malignancies involving bone and the central nervous system (CNS) are recognized as major sources of pain and most children and adolescents with these diagnoses initially present to their practitioners with complaints of pain (Collins et al., 2008; Shepherd, Woodgate, & Sawatzky, 2010; Wang et al., 2003). Leukemia and its treatment may also result in pain for children and adolescents as demonstrated in a study of 4 – 17 year olds with leukemia. In this study, children and adolescents participated in up to 7 interviews about pain over the course of the first year of cancer treatment and each participant reported pain on at least 1 of the interviews (Van Cleve et al., 2004).

Pain resulting from cancer treatment and procedures is also pervasive and problematic (Baggott et al., 2010; Friedrichsdorf, Finney, Bergin, Stevens, & Collins, 2007; Jacob, Hesselgrave, Sambuco, & Hockenberry, 2007; Neale, 2012). Children and adolescents, as well as their families and healthcare professionals, report that pain due to cancer treatment is more problematic than pain resulting from the malignancy itself or from procedures (Ljungman, Kreuger, Gordh, & Sörensen, 2006). Major sources of treatment-related pain in adolescents include mucositis (inflammation of the mucosal lining of the gastrointestinal tract; Green, Horn, & Erickson, 2010), postoperative pain, and phantom limb pain (related to limb amputations; Burgoyne et al., 2012). Pain is also a side-effect of pediatric chemotherapy
protocols (Gilchrist, 2012). For instance, a retrospective chart review of acute lymphoblastic leukemia (ALL) patients showed $37 \pm 6\%$ (M $\pm$ SD) of 11 – 15 year olds and $40 \pm 7\%$ of 16 – 20 year olds treated on a single protocol had vincristine-related neuropathic pain 3 years after treatment initiation (Anghelescu et al., 2011). Causes of cancer-related procedural pain include: lumbar punctures (LPs), bone marrow aspirations (BMAs), and venipunctures, as well as central venous catheter (CVC) insertion, access (in the case of subcutaneously implanted venous access devices [IVADs]) and removal (Collins et al., 2008; Hockenberry et al., 2011; Wint, Eshelman, Steele, & Guzzetta, 2002).

**Prevalence and Severity of Pain**

Pain in young people with cancer is common (Collins et al., 2000; Erickson et al., 2013; Hockenberry et al., 2011; Neale, 2012). Older children and adolescents (10-18 years) specifically have reported pain as the most commonly experienced symptom of cancer and its treatment (occurring in 49% of participants in the week previous to study). Furthermore, 81% of participants rated their pain from ‘moderate’ to ‘very severe’ using pain word descriptors on the Memorial Symptom Assessment Scale (Collins et al., 2000). Pain has also been reported to persist throughout cancer treatment, as demonstrated in a separate study involving 10 – 18 year olds with various cancer diagnoses receiving chemotherapy (Baggott et al., 2010). In this study, 62% of older children and adolescents experienced pain the week prior to chemotherapy administration with no significant decrease in the percentage of participants reporting pain in the 2-week period following chemotherapy (Baggott et al., 2010). Different childhood cancer diagnoses are associated with different risks of experiencing severe pain (Collins et al., 2008). The stage of the malignancy also affects the pain experience of children as pain is known to worsen and cause suffering in the terminal phase of cancer (Hooke, Hellsten, Stutzer, & Forte, 2002; Mercadante, 2004; Wolfe et al., 2008).
Impact of Pain

Pain from cancer is long lasting and has negative effects. Unrelieved pain in adolescents co-occurs with impaired sleep and daytime fatigue in 10 – 18 year olds (Baggott, Cooper, Marina, Matthay, & Miaskowski, 2012a) and has resulted in feelings of distress and fear (Hedén, Essen, Frykholm, & Ljungman, 2009b; Walker et al., 2010; Windich-Biermeier, Sjoberg, Dale, Eshelman, & Guzzetta, 2007). Cancer pain can also impede recovery from the disease (Shepherd et al., 2010), contribute to adolescent and family distress, (Collins, 2001; Hedén et al., 2013; E. Miller, Jacob, & Hockenberry, 2011; Walker et al., 2010) and is related to poorer overall HRQL (Calissendorff-Selder & Ljungman, 2006; Klassen et al., 2008; Sung et al., 2009). Pain related to cancers of childhood or adolescence may also negatively impact the quality of life during survivorship. A questionnaire-based descriptive study of over 10,000 adults who had completed treatment for childhood cancer and over 3,000 sibling controls revealed that adult survivors had an increased risk of reporting pain compared to siblings (Lu et al., 2011). Pain in the survivor group was relatively common, with 21% reporting a pain experience that they attributed to their history of cancer in the week preceding questionnaire completion (time since diagnosis: 16.5 ± 4.9 years [M ± SD]). Despite the increasing breadth of knowledge related to the etiology, prevalence, severity, and impact of pain; pain in adolescents with cancer continues to be poorly managed (Ameringer, 2010; Baggott et al., 2010; Jacob et al., 2007; Zernikow et al., 2012).

Apart from the abovementioned studies, little is known about the daily pain experience of adolescents with cancer in their everyday settings (e.g., home). To date, the majority of research into the cancer pain characteristics of adolescents has been cross-sectional and often retrospective. The few longitudinal studies that have been conducted have used infrequent sampling, collecting pain reports weeks to months apart (Van Cleve et al., 2004; Van Cleve,
Munoz, Rigg, Bava, & Savedra, 2012; Varni, Burwinkle, & Katz, 2004). As opposed to collecting momentary pain reports (i.e., asking adolescents to report current pain in real-time), these studies have relied on adolescents’ recall of pain over the preceding week or month; a practice known to be subject to inaccuracy due to recall bias (Gendreau, Hufford, & Stone, 2003). Pain research in adolescent cancer has also focused largely on sensory aspects of pain, namely pain severity. Multidimensional assessments of the emotional consequence of pain (i.e., affective dimension) and its impact on the lives of adolescents (i.e., evaluative dimension) are seldom conducted (Collins et al., 2000; Jacob, McCarthy, Sambuco, & Hockenberry, 2008).

**Smartphone-based Assessment of Adolescent Cancer Pain**

The lack of appropriate tools to support the longitudinal, momentary and multidimensional assessment of pain in adolescents with cancer likely contributes to the lack of a comprehensive knowledge base on the adolescent pain experience. However, a recent study using a smartphone-based multidimensional pain assessment application (app), known as Pain Squad™, has provided new information about pain in adolescents with cancer (Stinson et al., 2013).

The app uses twice daily pain questionnaires to longitudinally assess self-reported pain in adolescents. The pain assessment questions included in Pain Squad were modified from those in the validated e-Ouch electronic pain diary for adolescents with juvenile idiopathic arthritis (Stinson, 2009; Stinson et al., 2006b; 2008). Expert consensus developed through a meeting with 10-pediatric oncologists and 10-pediatric pain experts was used to modify the e-Ouch assessment to be cancer pain-specific. The question modifications were: (a) the pain body location-map was altered to include areas commonly painful in cancer; (b) a list of pain-associated symptoms (e.g., nausea) was added; (c) pain medication and other pain therapy lists
were made cancer-specific; and (d) a list of possible sources of pain (e.g., treatments or procedures) was included.

The complete pain diary questionnaire consists of 24 items on the multidimensional (i.e., sensory, affective, and evaluative) nature of pain, as well as questions related to pain management strategies used and their effectiveness. Diary questions are in the form of: (a) touchable visual analogue slider scales to rate dimensions of pain (pain intensity, pain unpleasantness, pain interference, control over pain) from 0 to 10; (b) a selectable body-map to identify pain locations; (c) multiple choice questions about pain characteristics (duration of pain, causes of pain, pain management strategies used, and their effectiveness); (d) lists of selectable words describing pain and associated symptoms; and (e) a free-text question to collect additional information that adolescents may wish to record. Questions cannot be ‘missed’ or ‘skipped’ as an adolescent cannot advance to the next screen before an answer is recorded. In the event that an adolescent did not experience pain since the preceding pain report, this can be indicated on the diary and subsequent questions about the nature of the pain experience are not asked.

In an effort to maximize engagement with the app, the process of completing pain assessments has been gamified, meaning gaming elements have been added to the app to motivate and engage users (King, Greaves, Exeter, & Darzi, 2013; Miller, Cafazzo, & Seto, 2014). Adolescents with cancer chose the law-enforcement theme from different thematic options that the research team presented them with during Pain Squad low-fidelity usability testing.

Data entered by adolescents are stored locally on the iPhone and then communicated to the server when the phone is online using an encrypted protocol. Pain data logged by an adolescent are not accessible via the phone. The server is hosted at the Hospital for Sick
Children (Toronto, Canada) and a user name and password are required to access data. The system also contains a password-protected Internet-interface, which will allow researchers to create studies, add study participants, and access results.

The Pain Squad app has been designed using user-centered methods and has undergone usability, content validity testing and clinical pilot testing with adolescents with cancer (Stinson et al., 2013), as well as psychometric evaluation (Stinson, Jibb, et al., 2015a). The 18 adolescents who participated in usability, content validity, and pilot testing were aged 8 – 17 years, with a variety of cancer diagnoses. Two iterative phases of usability testing allowed for Pain Squad to be revised, resulting in an app that is understandable and acceptable to adolescents with cancer. The importance of the Pain Squad diary questions was established by content validity analysis with 88% of questions being rated as “important” or “very important” by greater than 50% of adolescent participants. Piloting demonstrated the app to be likable, easy to use, and not bothersome to complete over the course of a 14-day trial. The construct validity of the pain assessment measure was demonstrated with significant ($p < 0.0001$) moderate to high (0.43 – 0.68) correlations between scores on the app and average weekly pain and negative or poor correlations with HRQL (-0.12 – -0.46) and pain coping (0.25 – 0.29) in a sample of 92 adolescents. Reliability of the tool was demonstrated as internal consistency (Cronbach coefficient alpha of 0.96; Stinson, Jibb, et al., 2015a).

In the study, 92 in- and out-patient adolescents with cancer used the Pain Squad app to complete twice-daily pain reports for 2 weeks (Stinson, Jibb, et al., 2015a). Using a longitudinal design with momentary pain assessments, 88 adolescent participants (95.7%) were shown to have pain during the 2-week period, with 12 adolescents (13.0%) reporting pain on every pain assessment completed. Average pain reported by adolescents across all pain assessments was 2.1 ± 2.9 (M ± SD)/10. However, when only assessments where pain was
reported > 0/10 were considered, pain intensity (4.2 ± 2.8/10), unpleasantness (5.6 ± 2.9/10), and interference (4.4 ± 2.7/10) were moderate on average. Data from this study are important as they demonstrate that pain is a daily and multidimensional problem for many adolescents with cancer. An understanding of the multidimensional experience of pain in real-time is needed to guide pain treatment decisions and support the timely management of adolescent cancer pain.

**Barriers to Adolescent Cancer Pain Management**

Advancements in treatment regimes and overarching changes to the healthcare system mean that adolescents with cancer spend less time hospitalized and more time in their home settings (Fortier, Sender, & Kain, 2011; Hendershot et al., 2005; Li et al., 2013). Patients and families are increasingly responsible for managing cancer-associated symptoms at home without direct supervision from healthcare professionals (Cowie et al., 2013). Although, the quality and consistency of pediatric cancer pain management at home is not well known, early research indicates that it may be poor (Fortier et al., 2012). For instance, it is known that despite on-going pain experiences during the first year following a cancer diagnosis, analgesic use in adolescents with cancer at home is infrequent (Van Cleve et al., 2004). Parents may be largely responsible for pain control in the home-setting and parental misconceptions about analgesic use and pain expression (e.g., children always express pain by crying) by children and adolescents with cancer have been demonstrated (Fortier et al., 2012). This finding is of particular importance because parental misconceptions about pain significantly predict \( p < 0.05 \) the under-management of children’s pain (Rony, Fortier, Chorney, Perret, & Kain, 2010).

Adolescent-reported barriers to cancer pain management have been specifically examined in a cohort of 60 adolescents (ages 12 – 17 years) with cancer who were either on- or off-treatment (Ameringer, 2010). Approximately 37% of adolescents reported moderate to
severe cancer-related pain in the last month ($6.55 \pm 2.77$ [M ± SD]/10). The primary barrier to effective pain management was the concern that parents would restrict social activities if pain were reported. This finding held true across adolescent age and sex and resulted in pain being undermanaged. Importantly, the concern related to impact of pain treatment on social activities is not a barrier that is cited by adults with cancer (Al-Atiyyat, 2008). This research underscores the need to think carefully and creatively when developing pain management strategies for adolescents with cancer.

**Self-management**

Self-management represents one strategy to improve cancer pain outcomes for adolescents, especially in the home-setting (Cowie et al., 2013). Self-management has been broadly defined as “the interaction of health behaviours and related processes that patients and families engage in to care for a chronic condition” (Modi et al., 2012). This definition has been extended to include non-chronic illnesses; namely cancer (Foster, Brown, Killen, & Brearley, 2007). Self-management involves a patient’s ability to monitor their condition and employ cognitive, behavioural, and emotional strategies to maintain a satisfactory quality of life (Barlow, Wright, Sheasby, Turner, & Hainsworth, 2002). In doing so, self-management is expected to enhance feelings of self-efficacy and empowerment to ultimately result in improved clinical outcomes (Bodenheimer, Lorig, Holman, & Grumbach, 2002). In a pediatric context, self-management behaviours are considered to be the product of 4 domains: individual, family, community, and healthcare system (Modi et al., 2012). Behaviours across these domains represent self-management in action and include: adherence with medication and treatment regimes, symptom monitoring, engagement in self-care activities (e.g., dressing changes), and healthcare utilization (e.g., attending clinic appointments, communicating with healthcare team).
At present, several studies have shown positive physical and emotional outcomes in adolescents engaged in self-management interventions when compared to adolescents receiving medical care alone (Breakey et al., 2014; Cafazzo, Casselman, Hamming, Katzman, & Palmert, 2012a; Rikkers-Mutsaerts et al., 2012; Ruotsalainen, Kyngäs, Tammelin, Heikkinen, & Kääriäinen, 2015; Stinson et al., 2010; Stinson, Wilson, Gill, Yamada, & Holt, 2009). However, despite these observed positive outcomes, the number of adolescents able to engage in these self-management programs is limited (Stinson et al., 2009). This deficiency is due to difficulties in accessing services (e.g., limited opportunity for engagement in self-management promoting programs) and costs associated with these therapies (Stinson et al., 2009). Harnessing the potential of mobile health (m-Health) technologies can help to overcome these barriers.

**Mobile Health Technology-based Symptom Management**

Mobile health management interventions (i.e., smartphone-based symptom management aids) offer a novel means to circumvent many of the barriers to accessing self-management therapies. No standard definition of the term ‘smartphone’ exists; however, it is generally accepted that a smartphone is a cellular phone with advanced connectivity and computing capabilities (Mosa, Yoo, & Sheets, 2012). The adolescent age group in particular is very amenable to the use of smartphone-technology and several recent survey studies have shown increasingly widespread adoption and use of mobile devices by this group. For instance, a 2015 report showed that 88% of American adolescents now own a cellular phone, with 73% of those adolescents owning or having access to a smartphone (Lenhart, 2015). Smartphone statistics are similarly high amongst Canadian adolescents, with a 2012 poll suggesting 62% now own a smartphone (comScore, 2013).
Smartphones may be especially useful in supporting homecare of patients, a rising trend in adolescent care management (Fortier et al., 2011; Hendershot et al., 2005), because of the ability of these devices to deliver real-time support. Healthcare-oriented real-time support refers to the provision of immediately accessible informational support to guide treatment decisions. Real-time support delivered through smartphones can provide patients with the ability to care for symptoms the moment the symptom occurs, which responds to the cited need of adolescent cancer patients to develop practical skills to manage their disease (Stinson, Sung, et al., 2012b). Studies into the remote monitoring and real-time management of symptoms, including pain, in adults with cancer have demonstrated the feasibility of these interventions and have begun to show an ability for these interventions to significantly improve patient (e.g., symptom severity) and system (e.g., healthcare utilization) outcomes (Aldiss et al., 2011; Chumbler, Kobb, et al., 2007a; Chumbler, Mkanta, et al., 2007b; Cleeland et al., 2011; Head et al., 2011; Kearney et al., 2009; Kroenke et al., 2010). Despite these successes, there has been no smartphone app developed and tested capable of supporting real-time pain management by adolescents with cancer.

**Problem Statement and Study Purpose**

Pain is a common and distressing problem for adolescents with cancer (Baggott et al., 2010; Collins et al., 2000) that is known to negatively impact HRQL (Calissendorff-Selder & Ljungman, 2006; Ruccione, Lu, & Meeske, 2013; Sung et al., 2009; Varni et al., 2004) and result in long-term morbidity (Hudson et al., 2003; Lu et al., 2011; Neale, 2012). Despite this knowledge, research into the development and evaluation of pain assessment and management interventions for this group is limited. To date, researchers who have conducted pain management studies have: (a) grouped adolescents with younger or older cancer patients, despite known developmental differences; (b) not assessed adolescent cancer pain in real-time
(i.e., using momentary reports) or conducted comprehensive multidimensional pain assessments; (c) rarely focused on the management of pain in environments other than acute care centers; and (d) not incorporated pain self-management techniques into interventions. Thus, the research aim was to use a user-centered approach to develop and pilot implementation of the *Pain Squad*+ app to aid adolescents with cancer in real-time pain management in their everyday settings, as well as to obtain preliminary estimates of intervention effect. The *Pain Squad*+ app uses the multidimensional pain assessment questionnaire and design of the successful *Pain Squad* assessment app described above, and in detail in Chapter 3, as a platform to provide pain management advice to adolescents with cancer.
CHAPTER TWO: LITERATURE REVIEW AND CONCEPTUAL FRAMEWORK

Internet and Other Communication-based Technology in Healthcare

The widespread use of the Internet and other communication technologies (e.g., telehealth, smartphone apps) has created new media for the delivery of health interventions (Ritterband, Thorndike, Cox, Kovatchev, & Gonder-Frederick, 2009). The Internet in particular is a major health information resource and mode of social communication, especially for adolescents and young adults. As such, Internet- and communication-associated technology is increasingly being integrated into the design and provision of healthcare services (Drotar et al., 2006; Gray, Klein, Noyce, Sesselberg, & Cantrill, 2005; Henderson, Keogh, Rosser, & Eccleston, 2013; Hieftje, Edelman, Camenga, & Fiellin, 2013). These technologies provide patients, families, and healthcare professionals with opportunities to: (a) learn, inform, and communicate; (b) receive meaningful social support; (c) rapidly access evidence-based health information; and (d) achieve greater involvement in healthcare decision-making (Ritterband et al., 2003).

Using technology to deliver health interventions can reduce access to care barriers including geographical, language and disability-related constraints. Technology-enabled immediate access to information has also been associated with diminished feelings of isolation and improved control over health on the part of patients (Hieftje et al., 2013; Mosa et al., 2012; Ritterband et al., 2009; Rosser & Eccleston, 2011).

Mobile Device Support of Self-management

Mobile devices, and smartphones in particular, represent an important modality for monitoring and managing health conditions (including cancer-related pain). The advantages of these devices in a healthcare context include their widespread use (Raine, 2010) and the tendency for people to carry them everywhere (Venta, Isomursu, Ahtinen, & Ramiah, 2008). These advantages mean that the number of people health interventions can reach, and the speed
with which they can be reached, has increased dramatically compared to decades ago. At present, several different mobile technology applications are being developed and tested for use in both pediatric and adult healthcare (Klasnja & Pratt, 2012; Mosa et al., 2012).

The most basic of the mobile technology interventions is text messaging (short messaging service or SMS), a service allowing messages of 160 characters to be sent between mobile phones. Because the vast majority of mobile phones are capable of sending and receiving SMS, this service does not suffer from the cost-associated drawback of more expensive devices (i.e., iPhones, BlackBerrys, devices with Android-based operating systems) (Klasnja & Pratt, 2012). Potential health intervention uses of SMS technology include: (a) the logging of symptom data; (b) communication with healthcare professionals; and (c) the ability for patients to receive remote reminders to engage in health behaviours (Klasnja & Pratt, 2012).

Despite any cost-associated shortcomings, the technological capabilities of smartphones make these devices superior candidates for symptom management interventions. Because of their advanced computing capabilities, smartphone operating systems are able to act as platforms for third-party apps (Mosa et al., 2012). The ability to run third-party apps, connect to the Internet and other devices, and use internal sensors such as cameras and microphones has made smartphones an especially promising avenue for healthcare intervention exploration.

To date, the published scientific literature related to smartphone-based healthcare apps has been summarized and classified in a single systematic review (Mosa et al., 2012). This review involved searching only 1 literature database (i.e., MEDLINE), but used a comprehensive search strategy (including hand-searching of reference lists) to review the entire database. Because of the broad search strategy used, 2,894 articles were identified and screened for relevance. All articles not describing the design, development, or evaluation of
smartphones apps were discarded. However, the procedure used to screen (e.g., number of screeners, discrepancy rate between screeners, how discrepancies were addressed) was not outlined.

The systematic review identified 55 studies describing 83 healthcare-associated apps. The apps described in the review were diverse and included those intended for healthcare professionals, medical or nursing students, and patients. None of the apps focused on cancer symptom or pain management. Apps created for use by healthcare professionals were the most numerous (57 apps from 43 studies). Healthcare professional apps included those designed to: (a) assist in disease diagnosis; (b) provide drug reference and medical education; (c) aid in literature searches; (d) enable communication between care providers; and (e) interface with patient medical records. Smartphone apps for medical or nursing students were primarily focused on supporting education through information provision. Finally, 15 apps from 14 studies were identified as intended for use by patients. Of these patient-focused apps, the majority focused on enabling at-home assessment or management of chronic conditions including diabetes, asthma, and unspecified cardiac or pulmonary conditions. Although this review was useful in identifying published research related to healthcare associated apps, the majority of studies identified described only app development and perceived utility by end-users. As such, app effectiveness was not described, leaving a knowledge gap related to how these apps might impact on patient, provider, or healthcare system outcomes. Still, the increasing breath of scientific research studies focused on smartphone apps highlights the perceived usefulness of the medium as a means to improve the healthcare process.

**Real-time Support via Internet and Other Communication-based Technology**

Real-time support in the context of healthcare describes the provision of rapidly accessible information to guide clinical decisions at the point of need (McGowan, Hogg,
Campbell, & Rowan, 2008). While the concept of clinical support for both healthcare professionals and patients alike is not new (Garg et al., 2005; Hochlehnert et al., 2006), the concept of providing this support the moment it is needed has not been well explored (McGowan et al., 2008). Telehealth, the Internet and smartphones, represent an important means to provide real-time healthcare support to patients, again because of their widespread availability and use.

The essence of technology-based real-time symptom management support for patients is the ability to track symptoms over time and provide clinical recommendations tailored to symptom reports, which may be based on standardized algorithms (Fortier et al., 2011; Gibson et al., 2010; Jacob, Duran, Stinson, Lewis, & Zeltzer, 2012; Kearney et al., 2009; Maheshwari, Chatterjee, & Drew, 2008). In addition, real-time support systems are advantageous because of their ability to promote clinician-patient communication and patient self-management (Gibson et al., 2010; Jacob et al., 2012; Kearney et al., 2009). An appealing quality of real-time support systems is the capacity they have to provide care support to patients in environments other than hospital settings, including home and work (Cowie et al., 2013). The capacity for ‘in the moment’ symptom management support in non-healthcare environments has great potential in the context of cancer care. For instance, adult patients with cancer spend considerable amounts of time outside of the hospital over the course of cancer treatment and report experiencing symptoms related to cancer and its treatment when not hospitalized (Cleeland et al., 2011; Cowie et al., 2013; Kroenke et al., 2010). Real-time support provided by technology may represent a means to continue to monitor cancer patients out of the hospital and improve symptom outcomes by providing timely management advice.
Real-time Support for Cancer Symptom Management

To date, a limited number of pilot and effectiveness investigations of real-time symptom management systems for patients with cancer have been conducted. These investigations have largely focused on adult cancer patients, with only 1 study including an adolescent patient population. A critical appraisal of the conceptualization, design, methods and results of these studies is presented in Appendix A. Below, the methods and results of each study are briefly summarized and the key elements from the critical appraisal are presented.

Chumbler et al. (Chumbler, Kobb, et al., 2007a) were the seminal group to examine the use of a real-time system in the context of cancer care. Specifically, a matched case-control study was used to investigate the use of a telehealth remote monitoring system on healthcare utilization by 125 adult American cancer patients. The telehealth system under investigation in this study enabled remote interactions between cancer patients and their care coordinators over a 6-month period. Patients answered daily questions related to chemotherapy-associated symptoms (i.e., pain, fatigue, nausea, worry, functional limitations) using a device plugged into their home telephone. The device used an evidence-based algorithm to probe patients about the nature of their reported symptom. Patient-entered data were then transferred to a remote care coordinator. If a research team-set threshold for symptom status was surpassed, the coordinator contacted the patient and used his or her own clinical judgment to provide symptom management advice. Telehealth patients used significantly fewer clinic visits (RR = 0.03; 95% CI = 0.00–0.24), bed days of care for all causes of hospitalization (RR = 0.50; 95% CI = 0.37–0.67), hospitalizations related to chemotherapy (RR = 0.43; 95% CI = 0.21–0.91) and bed days of care for chemotherapy hospitalizations (RR = 0.49; 95% CI = 0.34–0.71) than the control group. These results are tempered however by several study limitations. First, the non-randomized design of the study raises issue of selection bias on the part of the study authors.
Second, symptom prevalence and severity, which may have greatly impacted on healthcare utilization, were not assessed at baseline. The study conducted case matching for tumour-type only and did not match participants based on other possible confounding characteristics such as age or symptom type. Further, this study did not measure adherence to the program by patients or care coordinators, meaning intervention fidelity is not known. Finally, generalizability across patient groups was limited as participants were primarily male (94-95%) war veterans from a single center who were not living alone.

Chumbler et al. (2007b) conducted a second study to investigate the effectiveness of a real-time system for the remote assessment and management of symptoms on health outcomes in 34 adult patients with cancer. The intervention used in this case series pilot study was a home-based telehealth system that enabled interactions between patients at home and their cancer care coordinator. Specifically, patients answered questions related to chemotherapy-associated symptoms (i.e., pain, fatigue, nausea, worry, functional limitations) using the touchpad of their home telephone. Logged data were transmitted to a database daily for 6 months. Participants received self-care feedback relevant to the state of each symptom from a care coordinator. Results of this study included a high level of engagement with the system on the part of patients (mean [M] cooperation of 84%; range 4 – 100%) and a clinically meaningful improvement in HRQL following the intervention. However, several study limitations should be highlighted. For instance, despite effectiveness testing being a major aim of the study, a single-arm pre-test post-test design was used, precluding comparison of the intervention with a control group. The sample size of the study was also small and not supported by statistical rationale. The study did not include a description of the symptom management advice given to participants by care coordinators (e.g., content, response time) and the daily symptom assessment measure used was one-dimensional, assessing only the
prevalence of a symptom. In addition, statistical testing was not completed as intended. Specifically, results related to the study aim of assessing the impact of intervention engagement on HRQL were not presented. Last, the generalizability of results is limited by the participant group, which again consisted of American veterans from a single site who were predominately white (91%) and male (94%).

Studies following those by Chumbler et al. (2007a; 2007b) have used mobile- and Internet-based means (as opposed or as adjunct to touchtone landline telephones) to offer remote real-time cancer symptom management support to patients. The ASyMS project describes a group of studies involving the development and testing of a personal digital assistant (PDA)-based system for this purpose (Cowie et al., 2013; Kearney et al., 2009; 2006; Maguire, McCann, Miller, & Kearney, 2008). The system is intended to assist adults with cancer in the at-home management of chemotherapy-related toxicity during treatment. Outpatient adult chemotherapy patients complete twice-daily and ad hoc symptom questionnaires on a provided PDA. Data are then sent in real-time to a study server, which returned symptom management advice to the patient based on algorithms created by the research team. A 24-hour pager alerted a nurse to potentially dangerous symptom reports and the patient was then contacted and assisted with symptom management.

The 2009 study by Kearney and colleagues is the only study to report on results related to the impact of the ASyMS intervention on cancer symptom prevalence and severity. Specifically, the study describes a pilot randomized controlled trial (RCT) conducted in the United Kingdom to evaluate system feasibility and ascertain preliminary estimates of intervention effectiveness (Kearney et al., 2009). The study authors randomized 112 adult chemotherapy patients to either the ASyMS group or a usual-care group. The intervention group completed nausea, vomiting, fatigue, mucositis, diarrhea and hand-foot syndrome (tissue
inflammation of the palms of hands and soles of feet secondary to chemotherapy) assessments on the first 14 days of 5 chemotherapy cycles and received self-care advice from the system or a study nurse accordingly. Symptom assessments were completed using investigator-developed tools that were not tested for construct validity. Results showed moderate attrition rates (20-27%), which were not significantly different between study arms over time (demonstrated through survival analysis). More reports of fatigue (OR = 2.29; 95% CI = 1.04, 5.05; \( p = 0.040 \)), but less reports of hand-foot syndrome were seen in the control group (OR = 0.39; 95% CI = 0.17, 0.92; \( p = 0.031 \)). The severity of hand-foot syndrome (OR = -0.27; 95% CI = -0.52, -0.02; \( p = 0.033 \)) and distress related to the symptom (OR = -0.17; 95% CI = -0.33, -0.02; \( p = 0.028 \)) were higher in the intervention group. The authors postulated that this might have resulted from increased patient awareness of symptoms that are poorly assessed in routine clinical practice. The study results, however, should be interpreted with several method-related issues taken into account. First, the control group was not designed to control for the potential effect of attention (i.e., twice-daily assessments) on outcomes. Second, the outcome symptom assessment measure was the same as the ASyMS symptom assessment measure used throughout the study by the intervention group, making the assessment measure more familiar to the intervention group. Third, data regarding symptom advice, including the frequency, timing and content of nurse contact, were not presented. Without these data, results should be interpreted in light of unknown intervention fidelity. Last, despite recruitment at multiple sites and with a diverse population, data on recruitment rates and reasons for non-participation were not reported, negatively impacting study generalizability.

In 2010, a large multi-site RCT by Kroenke and colleagues examining the effectiveness of a telehealth collaborative monitoring and management intervention on pain and depression in 405 adults with cancer over a 12-month period was published. Patients were randomized to
receive either a telephone or Internet symptom survey with symptom management advice from a nurse or usual medical care. Contact by the nurse was made in response to patient reports of non-adherence to medications, poor symptom improvement over time, adverse effects, or on request. Validated and multidimensional assessment tools were used to measure pain and depression overtime. Adjustment to patient-care was made following team discussion and was based on standardized algorithms. Results showed the telehealth intervention significantly improved pain and depression scores compared to usual-care after the 12-month trial. Moderate effect sizes (0.39-0.67) for between-group differences in pain and depression were seen at both 3 and 12 months post-randomization. However, participant allocation to treatment group was also not stratified by site, which is needed to account for inter-site differences in factors such as clinical pain and depression management. Additionally, the control strategy did not account for the potential effects of attention and device-use in the intervention group. Engagement with the intervention, both on the part of patients and nurses, was not also reported. Finally, although this was a multisite study including both urban and rural centers, very specific inclusion criteria limit the generalizability of results.

Head and colleagues (2011) used a pilot RCT to examine the preliminary effectiveness of a telehealth intervention on symptom distress, HRQL, self-efficacy, and care satisfaction in patients with head and neck cancers. The study included 44 adult patients who were randomized to receive either evidence-based care advice via telephone in response to symptoms or usual medical care. Participants in the intervention group also received contact from a study nurse in the case of unrelieved or severe symptoms, however the threshold for this call was not presented. The intervention group completed daily assessments for the duration of an unspecified treatment and for 2 weeks following. Study authors did not report on the content or validity of symptom assessment questionnaires. A high level of engagement with the system
was demonstrated (assessment completed on 86 ± 15% [M ± SD] of days). Interestingly, unrelieved pain was the foremost reason for patients to require a symptom management support call from the nurse. Level of engagement with the system was positively correlated with the physical ($p = 0.048$) and emotional well being ($p = 0.042$) subscales of the HRQL measure. Results related to system effectiveness were presented as a descriptive summary of pre-test and post-test symptom, HRQL and self-efficacy scores for the intervention group. The same descriptive statistics were not presented for the control group and no inferential statistics regarding system effectiveness were included. Other limitations of this study include the lack of reporting on demographic and disease-related variables between groups. The content and timing of nurse calls to the intervention group was also not reported. Last, external validity was limited by participant recruitment from a single site and because participants were overwhelmingly male (90%).

Cleeland et al. (2011) have conducted an investigation into the effectiveness of a real-time remote symptom management system for patients with cancer. This study included 100 American patients with lung cancer or lung metastases undergoing thoracotomy. An interactive automated voice response system was used to contact patients twice weekly at home to assess pain, distress, disturbed sleep, shortness of breath, and constipation using a validated and multidimensional tool. If a patient reported a symptom above a clinician-set threshold, an email was sent to the surgical team’s advanced practice nurse. The nurse could then contact the patient with a symptom management recommendation. An attention control strategy was used such that the control group also completed symptom assessments, but did not receive management advice. Following the 4-week study, patients in the intervention group showed a greater reduction in symptoms exceeding set thresholds compared to the control group (19% versus 8%). A more rapid decline in symptom threshold events following thoracotomy was
also observed in the intervention group ($p = 0.003$). Limitations to be considered in interpreting these results include: (a) a small sample size that precluded the ability to assess intervention effectiveness on individual symptom severity; (b) lack of reporting on participant engagement with system; (c) recruitment rate and reasons for non-participation not being reported, affecting external validity; and (d) participant population from a single care center.

Aldiss et al. (2011) have conducted a 14-day pilot RCT intended to pilot and examine the preliminary effectiveness of a PDA-based symptom assessment and real-time management system for adolescents with cancer. The system that is the subject of the study is ASyMS-YG, which is aimed at managing chemotherapy-related toxicity in adolescents with cancer (Aldiss et al., 2011; Gibson et al., 2010; Gibson, Aldiss, Taylor, Maguire, & Kearney, 2009). The system assesses the presence and severity (measured as ‘mild’, ‘moderate’ or ‘severe’) of nausea, vomiting, fatigue, mucositis, diarrhea and pain. The ASyMS-YG pilot RCT randomized 4 adolescents to either receive symptom advice from ASyMS-YG based on symptom assessments or to receive usual medical care. Participants in the intervention group also received additional telephone-based advice from a nurse in the case of moderate to severe symptom reports. This advice was based on standardized algorithms created in consultation with adolescents and healthcare professionals. The study sample size precluded any meaningful quantitative analyses, but qualitative reports from adolescents indicated that the system was well-liked and 14 days was not considered a sufficiently long period of engagement with the system. Important shortcomings of this study include, the very small sample size and the lack of data regarding the fidelity of nurse responses to symptom reports. The generalizability of the results was also negatively impacted by the small sample of solely male participants, aged 13 – 15 years, treated at a single cancer care site.
With regards to the ASyMS-YG system in general, it is limited in several key ways. First, ASyMS-YG does not provide advice based on daily symptom assessment measures with established validity. Second, the ASyMS-YG system is intended to support the management of chemotherapy-related toxicity only and does not have the capacity to manage symptoms resulting from the disease of cancer and other treatment modalities (i.e. surgery, radiation). Third, intensity is the only aspect of pain assessed and the accepted multidimensional nature of the pain experience is largely ignored. Last, although adolescents and healthcare professionals have endorsed the use of ASyMS-YG for longer than 14 days, no means to enhance adolescent engagement with the system has been included in its design.

Sundberg et al. (2015) conducted a 1-arm pilot study with 9 men (mean age 69 years) receiving radiotherapy for prostate cancer across 2 sites with an aim of testing the implementation of a real-time symptom management intervention. The intervention collected daily symptom reports related to bladder and bowel function, sexual function, fatigue, pain, distress, and sleep. Symptom report data were sent to a study server that was monitored by a group of nurses. The nurses contacted patients to discuss severe symptom reports. Links to self-care advice were also provided to participants via the phone. After 14 days of use, 85% of participants had accessed self-care advice at least once, with a total of 20 viewing occasions across all participants. Qualitative interviews showed the system to be acceptable to participants who particularly endorsed the symptom questionnaire and the self-care advice as relevant, the application as user-friendly, and the nurse contact as valuable. No technical difficulties occurred. While the study did successfully examine several implementation outcomes, several methodological flaws existed. In particular, the very small sample size limits the generalizability of findings, the daily symptom assessments were not validated, the content and timing of nurse responses to patients was not reported, and no a priori criteria for
determining implementation success were set. In addition, the self-care advice provided to participants was not symptom-directed and algorithm-informed. Instead, participants were given access to a repository of standardized advice, placing the onus to access and interpret advice, when needed, on the patient.

Finally, a 1-arm pilot study of a pharmacist-run tele-oncology service using text messaging to monitor nausea and vomiting in ambulatory cancer patients has been conducted (Yap et al., 2013). The study sample included 68 male and female adults receiving chemotherapy (median age 49.5 years) at a single site. Post-chemotherapy, patients completed daily text message assessments of nausea and vomiting for 5 days. Self-care advice was provided according to an algorithm and a pharmacist contacted patients in response to uncontrolled symptoms. Results indicated that the intervention could be implemented for future testing. Specifically, adherence to reporting was 73.3%, most participants (90.0%) found the duration of monitoring acceptable, and the self-care advice was generally reported as useful (61.7%). The study accrual rate, however was poor (37.6%) with a large number of patients being uninterested in participation. Pharmacists made 22 calls across all participants in response to uncontrolled symptoms. The large, heterogeneous sample and the breadth of implementation outcomes measured (which, when possible were assessed in detail) enhanced study quality. However, no \textit{a priori} criteria for determining whether implementation into a future study would be possible were reported, limiting the ability to evaluate study success.

In summary, currently published research has begun to provide evidence for the effectiveness of real-time technology-assisted self-care (e.g., telehealth, the Internet) on patient and healthcare system outcomes in cancer patient populations. The acceptability and perceived helpfulness of these systems as reported by patients and healthcare professionals have also been demonstrated. However, only 3 published studies have provided evidence regarding the
methods used to develop the self-care advice algorithms, creating questions related to algorithm quality (Aldiss et al., 2011; Head et al., 2011; Yap et al., 2013). Furthermore, despite previously published qualitative evidence supporting the positive impact of real-time interventions on cancer patient’s feelings of self-efficacy (Kearney et al., 2006), this potentially important contributor to intervention effectiveness has generally not been well examined. Also, the generalizability of results for several of the published studies is limited by the narrow cancer patient populations included (Aldiss et al., 2011; Chumbler, Kobb, et al., 2007a; Chumbler, Mkanta, et al., 2007b; Head et al., 2009; Kroenke, Theobald, Wu, Tu, & Krebs, 2012; Sundberg et al., 2015). Finally, only 1 real-time self-care system has been specifically targeted at the unique developmental and pain experiences of adolescents with cancer (Aldiss et al., 2011). This adolescent-centered system, however, is based on one-dimensional and non-validated measures of pain, is targeted at pain in adolescents undergoing chemotherapy exclusively, and has not been shown to be effective.

**Pain-related Smartphone Apps Currently Available for Use**

A review of pain-related smartphone apps targeted at both pediatric and adult patients has been published (Rosser & Eccleston, 2011). This review included apps available for five of the major smartphone platforms (iPhone, Android, Blackberry, Nokia and Windows Mobile) between June and August 2010. The authors identified 111 smartphone apps for use in managing pain (Rosser & Eccleston, 2011). Apps were targeted at a range of health conditions known to cause pain, with the most common conditions targeted being headache or migraine (39%), followed by back pain (16%). The content of apps available at the time of the review varied, with 54% including education related to pain and its management, 24% including pain diary capabilities, and 17% including relaxation or meditation capabilities. Importantly, 86% of the apps did not report the use of scientific evidence or the involvement of healthcare
professionals in content development, and none had undergone effectiveness evaluations.

Several limitations of this review should be considered in interpreting its results. These limitations include the lack of: (a) a clear description of the search-strategies used by authors; (b) detail regarding the process of screening apps for inclusion (e.g., number of screeners, how discrepancies were addressed); and (c) detail related to how data on each app were abstracted. Still, the review provided a clear conceptual rationale for its conduct and presented important conclusions related to the dearth of high quality and rigorously evaluated pain management apps available.

Because the above review of publicly available apps was conducted in 2010 and the number of products available in the app stores has increased greatly since then, a more recent search was conducted (Lalloo, Jibb, Rivera, Agarwal, & Stinson, 2015). An electronic search was conducted between May and July 2014 of the official app stores for the 4 major smartphone operating systems: iOS (iTunes), Android (Google Play), BlackBerry OS (BlackBerry World), and Windows Phone (Windows Store). Entire stores were searched separately for the terms “pain” and “pain management” (i.e., no restrictions related to store subcategories such as “health and wellness” were imposed). Results of the search were not limited by language and no date of app publication was used to restrict search results.

Apps were included if the goal of the app was the treatment of pain and the primary intended user was a patient in pain. Apps were excluded if they focused only on the pain treatment features and resources offered by specific pain clinics or if their functionality did not extend beyond offering text-based information (i.e., e-books). Two authors performed app selection independently and all discrepancies regarding selection were resolved through discussion with a third party. There was greater than 75% agreement related to screening between authors prior to third party resolution. Following this screening process, 279 apps
were identified. Using the description of app purpose as stated on the app web page, each app was reviewed for its capacity to provide real-time pain management support to patients (pediatric or adult). The most common management function was pain self-care skill support (77.4%). Apps also provided pain education (45.9%), self-monitoring (19%), social support (3.6%), and goal setting (0.7%). No app was comprehensive in terms of pain self-management, with the majority of apps including only a single self-management function (58.5%). Finally, only 8.2% of apps included a healthcare professional in their development, no app provided a theoretical rationale for its design, and only 1 app underwent scientific evaluation.

**Conceptual Framework**

**Overview of Conceptual Frameworks**

Several conceptual frameworks have informed the development and evaluation of the *Pain Squad+* intervention. The first of these frameworks are the Expanded Health Belief Model (Rosenstock, Strecher, & Becker, 1988) and Connelly’s (1993) Model of Self-Care in Chronic Illness. These 2 models have been presented to provide conceptual context to the primary conceptual framework used to guide this research, Seto’s model (2011). Seto’s model details a mechanism by which self-management behaviour and health outcome change may occur in response to patient use of mobile real-time care interventions. In the present research, Seto’s model has been utilized to conceptualize how the key components of the *Pain Squad+* intervention may function to improve health outcomes for adolescents with cancer pain.

Finally, 2 additional conceptual frameworks are presented. First, Melzack’s (1999a) Neuromatrix Theory of Pain, which stemmed from his seminal theoretical work on the pain gate control theory, is reviewed as it pertains to the adolescent pain experience. This theory has been used presently to inform understanding of the subjective multidimensional nature of pain in adolescents with cancer. Understanding pain as both a subjective and multidimensional
phenomenon for adolescents has supported the inclusion of the *Pain Squad*+ intervention assessment questions and pain management advice. Last, a framework for the user-centered design of complex interventions, including electronic self-management interventions, is detailed. This final framework has provided a method to practically guide all phases of *Pain Squad*+ intervention development and preliminary testing in the present research.

**Expanded Health Belief Model**

**Health Belief Model origins.** Originally developed in the 1950s and revised more recently (Rosenstock et al., 1988), the Health Belief Model (HBM) provides a conceptual framework to explain changes and maintenance of health behaviours and to guide the development of interventions aiming to augment health behavior change (Champion & Sugg Skinner, 2008). The original model was developed by the United States Public Health Service to understand the widespread failure of people to participate in disease prevention programming, such as routine immunizations. Because behaviours such as accepting immunizations were considered generally simple to engage in, the original model did not include personal efficacy expectations as a predictor of engagement in health behaviours. The construct of self-efficacy was therefore later added to the model to improve the applicability of the HBM to the understanding of personal willingness to adhere to more complex health behaviours (Rosenstock et al., 1988). The model including the construct of self-efficacy is known as the Expanded Health Belief Model (Rosenstock et al., 1988).

**Description of the model and its key constructs.** The HBM hypothesizes that the likelihood of adhering to health behaviours depends on the occurrence of a catalogue of constructs, however the relationships between these constructs is not defined (Champion & Sugg Skinner, 2008; Rosenstock et al., 1988). The constructs predicting willingness to take action to prevent, screen for, or control illness conditions include: susceptibility, severity,
benefit, behavioural barriers, cues to action, and most recently, self-efficacy (Champion & Sugg Skinner, 2008). Other modifying factors related to socio-demographical, knowledge, and personality characteristics are also included in the model. These key constructs are presented below according to the conceptualization of Janz and Becker (1984), who have critically reviewed the use of the HBM in empirical research. Self-efficacy, a concept that was added to the model after Janz and Becker (1984), is also discussed.

**Individual perceptions.**

- **Perceived susceptibility:** Belief about the chance of experiencing a negative health outcome. The model posits that a person will not act to prevent a negative health outcome that is unlikely to afflict them (Carpenter, 2010).

- **Perceived severity:** Belief “about the seriousness of contracting an illness or of leaving it untreated, including evaluations of both medical and clinical consequences (for example, death, disability, and pain) and possible social consequences (such as effects of the conditions on work, family life, and social relations)” (Champion & Sugg Skinner, 2008). According to the expanded HBM, the more severe a person considers a negative health outcome, the more likely they are to act to prevent it.

- **Perceived self-efficacy:** Belief about one’s capabilities to organize and execute the course of action required to produce given attainments” (Bandura, 1997, p. 3). The model assumes a person who feels more competent to engage in health behaviours, is more likely to do so.

**Modifying factors.**

- **Demographic and sociopsychological variables:** Diverse factors including demographics (e.g., age, gender, ethnicity etc.), sociopsychological variables (e.g.,
personality, socioeconomic status, peer and reference group pressures etc.), and knowledge may influence perceptions (susceptibility, severity, threat) and self-efficacy and, in turn, the likelihood of engaging in a given health behaviour.

- **Perceived threat:** The product of susceptibility and severity is the perceived threat. Therefore, the dual beliefs that a person is susceptible to a negative health outcome and the negative outcome would be severe must be in place for a perceived threat to exist. The threat is also expected to have a cognitive component and is influenced by cues to action. According to the expanded HBM, the perceived threat and likelihood of engagement in a given health behaviour are positively correlated.

- **Cues to action:** Stimuli for a person to engage in health behaviour. Cues may be internal (e.g., experience of a worsening symptom) or external (e.g., media publicity, information from a healthcare professional).

**Likelihood of action.**

- **Perceived benefits:** The belief that engaging in a particular health behaviour will be beneficial in reducing the perceived threat. The greater the perceived benefit, the more likely a person is to engage in a behaviour.

- **Perceived barriers:** The belief that engaging in a particular health behaviour will result in a negative outcome. These barriers may be social, personal, economical, or environmental. The greater the perceived barrier, the less likely a person is to engage in a behaviour.

Using these constructs the expanded HBM therefore proposes that health-related action is more likely to occur if the following are simultaneously in place: (a) sufficient motivation making the health issue salient (i.e., cues to action); (b) belief in susceptibility to a health threat
(i.e., product of perceived susceptibility and perceived severity); (c) belief that a particular health behaviour would be beneficial in reducing the perceived threat (i.e., perceived benefit), and this benefit would outweigh any costs (i.e., perceived barriers) incurred; and (d) a feeling of sufficient competency to implement the health behaviour (i.e., self-efficacy).

Sociodemographic and knowledge characteristics are expected to modify individual perceptions and feelings of self-efficacy, which impacts the likelihood of engaging in a health behaviour (Champion & Sugg Skinner, 2008; Janz & Becker, 1984; Rosenstock et al., 1988).

**Connelly’s Model of Self-Care in Chronic Illness**

**Description of the model and its key constructs.** By modifying and extending the HBM, Connelly (1993) has developed a model to describe, explain, and relate the variables that influence self-care in chronic illness (Figure 1). Connelly defines self-care broadly as “behaviours to promote health, prevent illness, and treat and cope with health problems” (Connelly, 1993). Definitions of self-care vary widely in the literature (Omisakin & Ncama, 2011; Peeters, Wiegens, & Friele, 2013), but Connelly’s definition is aligned with Barlow’s definition of self-management presented in Chapter 1. As such, Connelly’s Model of Self-Care in Chronic Illness is useful in conceptualizing a means by which an intervention may influence engagement in self-management.

Importantly for this research, Connelly’s model enriches the explanatory power of the expanded HBM with regard to longer-term illness treated on an out-patient basis such as childhood cancer. Whereas the expanded HBM focused on willingness to adhere to health behaviours, Connelly’s Model focuses on the likelihood that a person with ambulatory longer-term illness will engage in the far more complex pattern of self-managing that condition and its symptoms. A second major difference from the expanded HBM involves the directionality of the relationships between model constructs. As discussed, the expanded HBM proposes that a
number of conceptual constructs influencing behaviour (e.g., perceptions, self-efficacy) must be in place for a behaviour to occur. The expanded HBM does not address possible reciprocal relationships between conducting the health behaviour (or not doing so) and the influencing constructs. Connelly’s model, however, includes the notion that the predisposing and enabling variables influencing a behaviour, as well as the actual health behaviour, interact in a circular fashion (Connelly, 1993).

![Figure 1. Connelly’s Model of Self-Care in Chronic Illness (Connelly, 1993)](image)

According to Connelly’s model, the likelihood that a person will engage in a particular behaviour is dependent on a series of predisposing and enabling variables. Predisposing variables are based on the same constructs outlined in the expanded HBM. Specifically, self-concept (not specifically described in the expanded HBM but related to the demographic and sociopsychological construct), health motivation (describing perceived benefits and barriers),
other individual perceptions, and self-efficacy are included as predisposing variables. Enabling
variables as they relate to the expanded HBM are patient characteristics, psychological status
and social support (describing the HBM’s demographic and sociopsychological variables);
regimen features and system characteristics; and cues to action. Finally, Connelly’s model
includes a dimension describing the general and therapeutic self-care behaviours in which a
person engages. According to Connelly’s conceptualization, general behaviours are those that
promote and maintain health and therapeutic behaviours are those undertaken specifically for
illness treatment. In Connelly’s model of self-care, the real-time pain self-management
intervention may be viewed as an enabling variable. In addition, Connelly’s conceptualization
of a reciprocal relationship between the predisposing variables and health behaviours is useful
in explaining how engaging in behaviours recommended to adolescents with cancer by the
Pain Squad+ app might further influence behaviour change. For example, an improved sense
of motivation may be observed in adolescents who successfully complete a given pain self-care
behaviour.

Seto’s Model of Mobile Real-Time Patient Care Support

Based on Connelly’s model, which incorporates the constructs of the expanded HBM, Seto (2011) has developed a model that guides how real-time pain self-management interventions, such as Pain Squad+, may assist patients in engaging in health behaviours (Figure 2). Seto’s model has been successfully used to provide conceptual direction to the development and effectiveness testing of a real-time mobile phone based system to support clinical management of heart failure by patients (Seto, 2011; Seto et al., 2012a; Seto et al., 2012b).

Seto has modified Connelly’s model in the following ways: (a) positioning a real-time intervention as the enabling variable for self-management behaviour change, (b) adding health
outcomes to the model to facilitate examination of the down-stream targets of self-management health behaviour change, (c) conceptualizing a feedback relationship between outcomes and predisposing behaviour change variables, and (d) proposing a direct relationship between the real-time intervention and health outcomes. Seto’s model proposes 7 interactions between the predisposing variables, enabling variables, self-management behaviour change, and outcomes. The utility of the model in explaining changes in health outcomes due to real-time patient monitoring and management has been demonstrated empirically. Specifically, the effect of a remote mobile phone-based self-care intervention for heart failure patients on HRQL, disease prognosis, and self-care has been examined using a RCT and post-study qualitative interviews (Seto et al., 2012b). The potential value of the model in predicting behaviour change and health outcome improvement was shown as study participants’ endorsement of the proposed model interactions during interviews.

![Seto's Conceptual Model](image)

*Figure 2.* Seto’s Conceptual Model of Behaviour and Health Outcome Change in Response to Remote Real-Time Patient Care Support.
Utilization of Seto’s self-management conceptual model. Interactions between health behaviour change constructs and health outcomes have been used in the present research to conceptualize the mechanism by which the Pain Squad+ intervention may function to improve pain for adolescents with cancer. These interactions are described below using the Pain Squad+ real-time self-management intervention for adolescents with cancer as a case study.

Interaction 1: Effect of enabling resource on self-management behaviour. According to Seto’s model, remote patient monitoring as an enabling resource will directly improve engagement in self-management. The enabling resource is expected to result in this improved engagement if it incorporates: alerts to engage in self-care, education related to self-care, recommendations to seek medical attention as needed, and individualized self-care regimens imparted by a patient’s healthcare professionals. For the purposes of this study, an intervention that is efficacious in terms of encouraging pain self-management should be one that includes: (a) automated adherence alerts to self-monitor pain; (b) the provision of real-time self-care advice in any environment in response to pain reports; and (c) individualized clinical support from a healthcare professional in response to sustained severe pain.

Interaction 2: Effect of predisposing characteristics on self-management behaviours. As the model proposes, those patients who are motivated, by perceiving the benefits of engaging in self-management as outweighing the barriers of doing so, will engage in self-management behaviours. The model also proposes that behaviours will be more likely to be carried out by patients who have greater self-efficacy expectations related to their self-management capacity. Those patients who are more aware of their personal health will also be more predisposed to self-manage their condition. In the case of the present research, those adolescents with cancer who are motivated, believe in their capacity to carry out the requisite behaviours, and demonstrate awareness of their health, and in particular pain, will presumably
engage in pain self-management, although in this study only self-efficacy was assessed at baseline. Internal health motivation to interact with *Pain Squad +* was also expected to be enhanced by the inclusion of the gamification mechanics of the app.

**Interaction 3: Effect of self-management behaviours on predisposing characteristics.**
The act of successfully engaging in self-management is expected to bolster patients’ motivation, senses of self-efficacy, and awareness of their condition. In the case of adolescents with cancer pain, health motivation will be enhanced should the benefits of self-management (i.e., improved health outcomes) outweigh the perceived barriers (e.g., nuisance of interacting with app). The gamification mechanics of *Pain Squad +*, which provides rewards scaled to the level of adolescent engagement with the app, is also expected to encourage motivation. Furthermore, those adolescents who engage in routine self-monitoring and management of their pain are expected to be more aware of the pain they experience and how it is best treated.

**Interaction 4: Effect of self-management behaviours on health outcomes.** The model draws a positive relationship between engaging in self-management (e.g., self-monitoring health, adhering to treatment regimes, seeking medical assistance as required) and improved health outcomes. Therefore, use of pain assessment, pain self-care strategies and communication with healthcare professionals should improve health outcomes for adolescents with cancer. The health outcomes of interest in Study 2 of this research project are: pain intensity, pain interference, and HRQL. Self-efficacy is also an outcome of study interest but is conceptualized as a predisposing characteristic as described above. All of these outcomes have been endorsed as important for pediatric pain management research by 2 scientific consensus groups: (a) the Pediatric Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (McGrath et al., 2008); and (b) the United States Food and Drug Administration Pain
Working Group (Berde et al., 2012). The operationalization of these outcomes and the measures to assess them are described in Chapter 4.

Interaction 5: Effect of health outcomes on predisposing characteristics. The model conceptualizes a direct effect of improvements in health outcomes on improved health motivation, self-efficacy, and health awareness. In the present study, health outcome improvements will motivate adolescents with cancer by improving their perception of pain self-management strategies as beneficial. Improved health outcomes are further expected to result in enhanced feelings of self-efficacy and awareness of the effectiveness of self-care strategies on pain.

Interaction 6: Effect of clinical management on outcomes. Seto’s model highlights that changes in health outcomes are likely due to a combination of improved self-care and clinical management by healthcare professionals who remotely monitor patients. Therefore, an intervention for adolescents with cancer should incorporate the capacity to individualize and optimize pain care, above that which is possible using self-management. In particular, remote monitoring of adolescent pain reports by a pediatric oncology registered nurses (RN) may improve health outcomes via: changes to medication regimes through consultation with the adolescent’s primary physician, instructions related to seeking medical care, and education to adolescents during pain episodes or “teachable moments”.

Interaction 7: Effect of clinical management on predisposing characteristics. Finally, Seto’s model proposes that clinical management by healthcare professionals directly impacts predisposing characteristics for self-management behaviours. In the case of adolescents with cancer pain, knowledge that the study nurse is monitoring pain reports is expected to improve adolescents’ motivation to engage in pain self-management and feelings of self-efficacy.
Furthermore, knowledge that the study nurse is monitoring incoming pain reports is expected to directly result in an improvement in adolescents’ symptom awareness.

**Additional Conceptual Frameworks Utilized**

**Melzack’s neuromatrix theory of pain.** Pain is a symptom commonly experienced by adolescents with cancer (Baggott et al., 2012b; Collins et al., 2000; Erickson et al., 2013). Pain is defined by the International Association for the Study of Pain (IASP) as an “unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” (1994). It has been further noted by IASP that the “inability to communicate in no way negates the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment” (2003).

**Origins of the neuromatrix theory.** The 3 components of the multidimensional conceptualization of pain were originally proposed in seminal pain research several decades ago (Melzack & Casey, 1968; Melzack & Wall, 1965). This early research by Melzack and colleagues proposed the gate control theory as a model to describe the nature of pain. Through the gate control theory, Melzack and colleagues recognized pain perception as being a complex physiological and psychological phenomenon. A major contribution of the gate control theory was its presentation of the CNS as an active system that filters, selects, and modulates inputs as opposed to a passive recipient and recorder of sensory information (Melzack, 1999b).

A central principle of the gate control theory is the existence of a gating mechanism, which modulates transmission of sensory information from primary afferent neurons to the spinal cord (Melzack & Wall, 1965; Moayedi & Davis, 2013). This gating mechanism is modulated by both: (a) peripheral input provided by pain and touch fibres and (b) cognitions, emotions and memories of prior experiences provided by the CNS. More specifically, the gate control theory proposes that descending fibres originating in supraspinal regions and extending
to the dorsal horn of the spinal cord can modulate nociceptive information. Brain centers responsible for cognitive and emotional processes may intensify pain perception by opening the “gate” in the dorsal horn or reduce pain by closing the “gate”.

**The neuromatrix theory.** Empirical evidence and advancements in neurobiological knowledge after the gate control theory was originally proposed have required its expansion (Melzack, 2005; Schiavenato & Craig, 2010). Specifically, a model relying on one-way signal transmission from afferent neurons does not explain the phenomenon of phantom limb pain (where pain is reported by a patient as occurring in an amputated limb; Trout, 2004). To account for this phenomenon, Melzack (2001) advanced the conceptualization in the original model and developed the *neuromatrix theory* of pain. The neuromatrix theory proposes that pain is actually the result of neural activity across several different structures in the brain that “diverge to permit parallel processing in different components of the neuromatrix and converge to permit interactions between the output products of processing” (1999a).

Because these brain structures function variously with respect to cognitive, affective and motor processes, the neuromatrix they form is capable of generating pain in the absence of a sensory stimulus, thereby offering an explanation for phantom limb pain. Melzack further noted that genetic variability across individuals combined with repeated processing of nerve impulses in the neuromatrix creates an individual “neurosignature” or neuronal assembly. This neurosignature is plastic overtime because neural connections can change, especially in adolescents (Fuhrmann, Knoll, & Blakemore, 2015), but it is important in explaining the subjective, individual nature of the pain experience. The complicated nature of central modulation of pain is exemplified in brain imaging studies demonstrating the existence of patterns of regional brain activity corresponding to painful events (Wager et al., 2013). Another important advancement of the neuromatrix theory involves its emphasis of pain
perception as occurring in the brain rather than the spinal cord, as in the earlier gate control theory. This advancement has initiated important considerations by clinicians and researchers related to social and cultural influences on pain (Trout, 2004). This advancement also provides rationale for the inclusion of physical and psychological pain management strategies in the Pain Squad+ intervention.

The multidimensional nature of pain. The conceptualization of pain as a multidimensional construct by Melzack and colleagues is an integral contribution of both the gate control and neuromatrix theories to modern pain knowledge. Pain as a construct, composed of sensory-discriminative, affective-motivational and cognitive-evaluative dimensions, is a concept widely accepted within contemporary clinical and research communities (Cervero, 2013; Moayedi & Davis, 2013). The sensory-discriminative dimension describes the sensory qualities of pain, including intensity and location, and the temporal and somatosensory properties of the sensation. The affective-motivational dimension describes emotional arousal related to the aversive aspects of pain. Specifically, it refers to the extent to which pain is perceived as unpleasant and distressing, as well as the possible subsequent flight response of the person in pain (Moayedi & Davis, 2013). Finally, the cognitive-evaluative dimension describes cognitions related to pain and refers to the degree to which it is seen as interfering with aspects of physical, psychological, and social functioning (Melzack, 2001; 2005; Melzack & Casey, 1968; Melzack & Wall, 1965).

An important justification for the assessment of pain as a multidimensional construct centers on the notion that the dimensions of pain are not mutually exclusive but rather interact in a complex manner. For instance, although the degree of pain unpleasantness is generally considered to be positively correlated with the intensity of the noxious stimulus (Duncan, Catherine Bushnell, & Lavigne, 1989), studies have shown that hypnosis may decrease pain
unpleasantness while having no effect on pain intensity (Rainville, 2002). This is an example of the impact of cognitive state on the affective-motivational dimension of pain. In this example, if only the sensory dimension of pain was assessed, the intervention would appear to be ineffective, despite its impact on pain unpleasantness. Importantly, this interplay between cognitions and affect is a cornerstone of cognitive behaviour therapies (Moayedi & Davis, 2013), which have been used in pain management of pediatric cancer pain (Landier & Tse, 2010).

Further, the ability for children and adolescents to appreciate the multidimensional nature of pain is now understood. Children and adolescents’ understanding of pain changes with age and progresses from a simple understanding of global pain severity towards an appreciation of the multidimensional nature of pain by older childhood (Craig, Grunau, & Branson, 1998; Walker, 2008). Specifically, children as young as 8 years have been shown to be able to differentiate between the dimensions of pain (Stinson, Jibb, et al., 2015a). However, despite this knowledge, research in adolescents with cancer pain has focused primarily on the sensory dimension, namely pain intensity, and largely ignored the other dimensions of pain (Collins et al., 2000; Erickson et al., 2013). The lack of focus on pain unpleasantness (i.e., affective dimension) and how pain interferes with the social, physical, and psychological realms of life (i.e., evaluative) is problematic because these dimensions are of particular importance to adolescents with cancer (Ameringer, 2010). *Pain Squad+* therefore will assess the multiple dimensions of pain in adolescents.

**Pain as a subjective phenomenon.** Pain is appreciated as a subjective phenomenon in the context of the neuromatrix theory. As such, general consensus in the field is that pain measurement by self-report, as opposed to observation or proxy-report, should be conducted whenever possible (vonBaeyer & Spagrud, 2007). Report by proxy is important in cases where
communication is limited by developmental stage, illness, cognitive impairment or communication difficulty. However, proxy-report is not always a reliable approximation of a person’s pain experience, and has been shown to be inaccurate in comparisons between proxy and adolescent reports of cancer pain (Gershon, Zimand, Pickering, Rothbaum, & Hodges, 2004).

Pain assessment has more recently been suggested as a social transaction occurring through the patient-clinician interaction and impacted by the biological, cultural, social, developmental and cognitive context surrounding both parties (Schiavenato & Craig, 2010). Through this social transaction model, one-dimensional measures are again considered an inappropriate means to assess pain and more holistic approaches are supported (Schiavenato & Craig, 2010; Voepel-Lewis, Piscotty, Annis, & Kalisch, 2012). The model also suggests that the contextual variables surrounding the assessment be considered when self-reports of pain to healthcare professionals are conducted (Schiavenato & Craig, 2010; Voepel-Lewis et al., 2012). Although the social transaction model advocates for considering context in assessing pain, it nonetheless continues to support the importance of considering pain a subjective phenomenon. The empirical literature also overwhelmingly endorses the feasibility and validity of self-report scales as a measure of pain in adolescents (including those with cancer) who possess the requisite cognitive development and acquisition of social communication skills (Baeyer, 2006; Huguet, Stinson, & McGrath, 2010; Stanford, Chambers, & Craig, 2005; Stinson, Kavanagh, Yamada, Gill, & Stevens, 2006a).

**Utilization of neuromatrix-related understanding of pain.** In the present research project, the complex and multidimensional nature of pain and the appreciation of the subjective quality of the pain experience were incorporated into adolescent cancer pain assessments. Specifically, the pain management intervention (i.e., *Pain Squad+* smartphone app) was
designed to facilitate multidimensional (i.e., sensory, affective and evaluative dimensions) adolescent-reported cancer pain assessments at least twice daily. The app allowed for the assessment of the intensity, unpleasantness, interference and location of pain. The duration, causes of pain and control over pain, as well as pain management strategies used, and their effectiveness, was also assessed. Capturing the multidimensional and subjective nature of pain provides a more holistic understanding of adolescent cancer pain (Wilson, 2014), which informs the pain management recommendations made by the Pain Squad+ app. For instance, the adolescent ratings of how pain interferes with activities of daily living (e.g., social relationships, physical activity) were used in addition to reports of pain sensory qualities (e.g., intensity) to guide pain management.

**User-centered design approach.** Although the Seto’s model has been used to conceptualize the overall pain management intervention under study in this research project (i.e., Pain Squad+ app), the design of the app will be conducted using user-centered methodology. User-centered design is an approach that grounds the process of product design in the needs and understandings of end-users (Arsand & Demiris, 2008; Mao, Vredenburg, Smith, & Carey, 2005; McCurdie et al., 2012). Further, highlighting the importance of the methodology, an international standard has been developed regarding best-practice user-centered design methods for the development of Internet and other communication technologies (Arsand & Demiris, 2008). The standard describes the planning, management and overview of the user-centered design process, but does not describe the specific methods that should be employed in the design of novel technology-based self-management solutions.

In response to this need, a framework based on international standards has been designed specifically to guide the user-centered development of self-management tools (Arsand & Demiris, 2008). This framework entails 4 main steps to user-centered design
(Figure 3). The first step is the identification of a need for a patient-centered system and includes assessment of the context of use and required system features with end-users (both patients and healthcare professionals as applicable). Techniques used to glean data for this phase include individual interviews, focus groups, and cultural observations (ethnographies; McCurdie et al., 2012). Based on data gathered in the initial step, a set of functional self-management system requirements and design guidelines are established and these drive system design decisions by researchers and developers (Arsand & Demiris, 2008; Cafazzo et al., 2012a; McCurdie et al., 2012; Seto, Leonard, Cafazzo, Barnsley, Masino, & Ross, 2012a). Following this phase, the system requirements as established by end-users, are used to develop a prototype self-management system or app.

![Diagram of Framework for Electronic Patient Self-Management Tool Design](arsand_demiris_2008)

**Figure 3.** Framework for Electronic Patient Self-Management Tool Design (Arsand & Demiris, 2008).

The next step involves the evaluation of the prototype using techniques such as walk-throughs and usability testing to identify flaws with the system as designed and receive suggestions from users on system improvements. Usability testing involves participant users working through the system while ‘thinking aloud’, during which an observer takes field notes on user behaviours and issues (McCurdie et al., 2012). Post-usability testing interviews with
participants may be used to obtain further understanding of the user experience. If no flaws are identified, the system is considered acceptable to users and may be deployed for further testing (Arsand & Demiris, 2008; McCurdie et al., 2012; Seto, Leonard, Cafazzo, Barnsley, Masino, & Ross, 2012a). If flaws are identified, additional iterations of the process are used to refine the system until it is ready for deployment (Arsand & Demiris, 2008; Mao et al., 2005).

The use of a user-centered design framework to guide the development of technology-based self-management tools has been advocated for repeatedly in the literature (Arsand & Demiris, 2008; Cafazzo & St-Cyr, 2012; Johnson, Johnson, & Zhang, 2005; McCurdie et al., 2012). Incorporating users in the design of these complex systems means that the resultant products are more likely to be used as intended, which in turn impacts on intervention effectiveness (Johnson et al., 2005; Mao et al., 2005). To date, several studies that have incorporated user-centered design in the development of technology-based health interventions have shown resulting interventions to be well-used and/or effective when tested (Cafazzo et al., 2012a; Seto, Leonard, Cafazzo, Barnsley, Masino, & Ross, 2012b; Stinson et al., 2013). The preliminary research conducted to date (detailed in Chapter 3) and this research project combine to describe a method to the development of the Pain Squad+ app that has, and will continue to, utilize a user-centered design approach (detailed in Chapter 4).

Research Objectives

Study 1 Objective

The objective is to refine the Pain Squad+ smartphone-based real-time pain management app intervention through usability testing such that it is easy to use, easy to understand, efficient to complete and acceptable to adolescents with cancer.

Study 2 Objectives
The primary objective is to evaluate the implementation of the *Pain Squad*+ app for study in adolescents with cancer. Determination of implementation outcomes will: (a) provide an estimate of the accrual rate for participants entering the study and reasons for non-participation; (b) provide an estimate of participant retention in the study; (c) determine the fidelity of the intervention; (d) pilot the outcome measures, (e) determine participant adherence to the study protocol; and (f) determine the acceptability of the intervention to adolescents with cancer.

A secondary objective is to obtain preliminary estimates of treatment effects on pain intensity, pain interference, HRQL, and self-efficacy in adolescents with cancer to inform the calculation of an appropriate sample size for a future RCT.
CHAPTER THREE: PRELIMINARY RESEARCH

Overview

This chapter is presented as 2 sections describing research conducted that provides the basis for the present study. The following are discussed: (a) the methods used to develop the *Pain Squad+* app; and (b) the algorithm and system features for the *Pain Squad+* app. Figure 4 shows the phased development of the *Pain Squad+* app and details of the completed research to date, as well as the main research studies of this dissertation.

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*Figure 4. Phased Development of the Pain Squad+ Real-Time Pain Management App.*

**Development of the *Pain Squad+* Pain Management App**

*Pain Squad+* uses the previously discussed multidimensional pain assessment questionnaire from *Pain Squad* in its design (Appendix B). In addition, it provides adolescents with pain management advice in response to their multidimensional pain reports in real-time. This pain management advice is based on a standardized pain management algorithm (development described below) and tailored to the preferences of individual adolescents.
Healthcare professionals additionally support adolescent pain management via the Pain Squad+ app. Specifically, adolescent-recorded pain that is moderate to severe (≥3/10) and sustained (i.e., 3 consecutive moderate to severe pain reports) results in an email alert being sent to a study oncology-trained registered nurse. The study nurse then contacts the adolescent’s primary medical care team to alert them to the report, initiating provider-driven pain management. Adolescents using the Pain Squad+ play the role of law-enforcement officers investigating pain cases. A taxonomy of gamification features or mechanics has been proposed in the literature (Miller et al., 2014). Those gamification mechanics incorporated into Pain Squad+ are: (a) ‘badges’ attained by meeting achievement goals (e.g., completing 5 consecutive scheduled pain assessments) and (b) a ‘point and levelling system’ used to inform the user of their level of familiarity with the app and reward continued expertise (i.e., advancement through law-enforcement ranks and receipt of videotaped acknowledgements related to app interaction).

Adhering to the Medical Research Council Framework (M. Campbell et al., 2000; N. C. Campbell et al., 2007) for the development of complex interventions, a systematic and user-centered approach to development of Pain Squad+ and its standardized algorithm have been utilized. First, a systematic review of the published peer-reviewed scientific literature focused on pain management in pediatric oncology was undertaken (Jibb et al., 2015). Second, a consensus conference with clinical and research experts was conducted to develop the Pain Squad+ system requirements (Jibb et al., 2014). Last, the developed pain management algorithm was vetted with adolescents and oncology care providers for its clinical utility (Jibb et al., 2014). All 3 stages of development are described below.
Systematic Review of Pediatric Cancer Pain Literature

Non-pharmacological interventions were targeted in this review as, apart from adherence to pain medication regimes, they are a primary mode for patients to engage in cancer pain self-management (Koller, Miaskowski, De Geest, Opitz, & Spichiger, 2012). Healthcare professional assistance (as described above) regarding pain management will be the vehicle by which the Pain Squad+ system can provide pharmacological pain management support.

To conduct this review, Medline, Embase, Web of Science, CINHAL (Cumulative Index to Nursing & Allied Health Literature), and PsycINFO databases were searched from database inception to June 17, 2013. Queries for each database were developed and carried out in consultation with a reference and information services librarian working at a pediatric academic tertiary care center and familiar with the field. Reference lists from secondary data sources identified by the search strategy above were also scanned for additionally relevant articles.

Methods. To conduct this review, MEDLINE, EMBASE, CINAHL, PsycINFO, and Web of Science databases were searched from the date the database was established until June 17, 2013. Database queries were developed in consultation with a reference and information services librarian who was familiar with the field. The titles and full abstracts of studies identified through the search were managed using EndNote Web software (Thompson Reuters, 2013) and screened. Studies were eligible for inclusion if they met the following criteria: (a) English language; (b) clinical study of any design; (c) patient population of children and adolescents (0 – 21 years) receiving care in pediatric hematology/oncology programs; (d) pain examined as a primary or secondary outcome; and (e) examining the effectiveness of a pain intervention that was not solely pharmacological in nature. Duplicate studies returned by the search were discarded and the remaining abstracts were assessed for
All search-identified titles and abstracts were assessed for inclusion. Full-text articles of abstracts that were potentially relevant to this review were obtained, read and assessed. A systematic approach to the data abstraction process was utilized to describe the characteristics of the identified studies in detail. Study data related to patient population, cancer, painful procedure, intervention, pain measure, results and study design were abstracted as appropriate. All abstracted data were categorized using a standardized table. A research assistant then reviewed the extraction and categorization of all data for accuracy.

The U.S. Preventative Services Task Force has presented a hierarchy of evidence to assess the benefits and harms of various clinical interventions (2008). This schema was used to categorize the studies identified in the present review. According to the schema, Level I evidence describes RCTs, systematic reviews or meta-analyses of homogeneous RCTs; Level II-1 evidence describes controlled trials not employing randomization; Level II-2 evidence describes well-designed cohort or case-control studies; Level II-3 evidence describes multiple time series or uncontrolled trials; and Level III evidence describes descriptive studies or case reports and the opinions of respected clinical experts. Because of the subjective nature of pain (von Baeyer & Spagrud, 2007), for the purpose of this study, children and adolescents were considered clinical experts in pain they experienced. Only primary data sources were included in this review; therefore, systematic reviews and meta-analyses on the topic were not presented. All studies were assessed for internal and external validity according to the study design-specific criteria outlined by the U.S. Preventative Services Task Force (2008).

**Search results.** The search strategy resulted in the identification of 8,278 titles and abstracts for review. Of these, 710 were duplicate studies and 7,410 did not meet the inclusion criteria. The full-text articles for the remaining studies were retrieved and reviewed. Following detailed review of these full-text articles, an additional 126 studies did not meet the inclusion
criteria. The remaining 32 studies were subjected to data abstraction, evaluated for quality and included in this review.

**Study characteristics.** A total of 1,171 children and young adults participated across the 32 studies identified by the authors. The number of participants in each study ranged from 8 – 124 (M = 37; SD = 24). Participants ranged in age from 1 – 21 years and had a variety of cancer diagnoses. Twenty-five studies were conducted within oncology programs at pediatric tertiary care centers, 1 study was conducted both at a pediatric tertiary care center and a community hospital, and six studies did not specify the study setting. Fifteen studies (47%) included pharmacologic pain management in at least 1 of the treatment arms. Of note, eight studies (25%) did not report the use of a validated pain assessment tool. Details of study characteristics are presented in Appendix C. Identified studies were categorized on the basis of the non-pharmacological pain management intervention under investigation. Specifically, the studies are categorized as investigations into the pain management effectiveness of aromatherapy, art therapy, distraction, hypnosis, physical activity, physical positioning, touch therapy, or multi-modal cognitive behavioural therapy. Several of interventions studied in each of these categories also included pharmacological pain management (e.g., topical lidocaine).

**Aromatherapy.** One small RCT (37 children and adolescents randomized) evaluated the impact of administering bergamot essential oil aromatherapy during stem cell transplantation (Ndao et al., 2012). As a secondary outcome, this study evaluated whether there was any difference in pain prevalence pre-transplantation and post-transplantation between participants administered aromatherapy and those receiving a placebo treatment. Pain prevalence decreased over time in both groups (not statistically significant) and there was no between-group difference noted.

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

**Distraction.** Six studies examined the impact of distraction on pain in children with cancer, with generally positive results. Virtual reality distraction, where a child is immersed in a virtual world through the use of visual and auditory stimuli, was compared to non-virtual reality distraction and standard medical treatment in a study of patients undergoing subcutaneous port access (Gershon et al., 2004). Less nurse-reported pain, behavioural indicators of pain, and heart rate were observed in the distraction groups compared to control, with no difference in youth or parent pain reports. Active distraction (i.e., bubble blowing) compared to attention control (i.e., heated pillow) during subcutaneous port access has been investigated in a sample of younger children (Hedén, Essen, & Ljungman, 2009a) without observed between-group difference in pain. A study of musical distraction on pain during LP in school-age children with cancer showed reduced child-reported pain, heart rate, and respiratory rate in the musical distraction group compared to control (Nguyen, Nilsson, Hellström, & Bengtson, 2010). An additional study of the effectiveness of youth-selected distraction (e.g., book) during subcutaneous access or venipuncture showed no between-group difference in youth-rated pain compared to control (Windich-Biermeier et al., 2007). However, participants in the distraction group rated the procedure more positively than those in the control group.

The effect of virtual reality compared to standard care in decreasing LP-related pain has also been investigated with no differences noted (Wint et al., 2002). However, youth in the distraction group qualitatively reported use of the system to be a positive experience. Finally, the impact of virtual reality distraction on procedural pain in patients undergoing subcutaneous
access showed observer-rated pain and heart rate to be lower in the virtual reality group compared to standard care (Wolitzky, Fivush, Zimand, Hodges, & Rothbaum, 2005).

**Hypnosis.** Nine identified studies examined the effect of hypnosis on pain in children and young adults with cancer. First, the effectiveness of direct versus indirect hypnosis on LP-related pain in children and young adults was compared (Hawkins, Liossi, Ewart, Hatira, & Kosmidis, 1998). Direct hypnosis refers to suggestions provided by a hypnotist that are immediately related to anesthesia. In contrast, indirect hypnosis evokes thoughts of colors, aromas, and/or temperatures that can be discussed as a proxy for anesthesia (Liossi & Hatira, 1999). Hawkins and colleagues (1998) found no difference in pain between indirect and direct hypnosis groups. In addition, no between-groups differences were observed in a study comparing hypnosis to quiet play during BMA; however, pain decreased in both groups when compared to a baseline BMA (Katz, Kellerman, & Ellenberg, 1987). A study of the effect of hypnosis, distraction, and standard care on pain related to BMA showed observer-rated pain for older children (i.e., 7–10 years) to be less in the hypnosis and distraction groups compared to control (Kuttner, Bowman, & Teasdale, 1988). In a comparison of direct hypnosis, cognitive behavioural therapies (CBTs) (i.e., relaxation training, deep-breathing, and positive reframing), and lidocaine injection during BMA, pain change scores from baseline were significantly greater than control in the hypnosis and CBT groups (Liossi & Hatira, 1999). A second study comparing direct hypnosis, indirect hypnosis, play, and education alone on youth-reported LP-related pain showed both hypnosis groups to report decreased pain compared to baseline (Liossi & Hatira, 2003). Direct hypnosis also was compared to play and education alone during LP with the addition of topical anesthetic (i.e., eutectic mixture of local anesthetics) at the procedure site for all patients (Liossi, White, & Hatira, 2006). Youth-reported pain was less in the hypnosis group compared to control. Self-directed hypnosis was then compared to play and
a no-treatment control with respect to effectiveness in decreasing venipuncture-related pain (Liossi, White, & Hatira, 2009). Participants in the hypnosis group reported less pain than those in the control groups.

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

**Physical activity.** One study has examined the effectiveness of 3 30-minute sessions of physical activity per week, with pain assessed as the bodily pain subscale of a HRQL measure (Speyer, Herbinet, Vuillemin, Briançon, & Chastagner, 2010). Results showed the intervention decreased parent-rated bodily pain compared to control, with no differences in youth-reported pain being observed.

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

**Touch therapy.** Four studies have evaluated the effect of healing touch, massage, or acupressure on pain in children and young adults with cancer and have demonstrated mixed results. A study of massage and acupressure on pain during the course of cancer treatment showed parents to qualitatively report that their child experienced pain relief as a result of the therapy (Ackerman et al., 2012). The effectiveness of massage compared to quiet play on pain
related to cancer and its treatment has also been examined (Post-White et al., 2008). Results showed no difference in observer- or youth-reported pain; however, heart rate was lower following massage compared to play, and qualitative interviews with children indicated that the massage intervention lessened pain. Another interview-based study with patients undergoing various painful procedures showed that holding hands with either their mother or nurse was perceived as lessening pain (Weekes, Kagan, James, & Seboni, 1993). Wong and colleagues (2013), the effect of touch by a trained practitioner on pain during the course of cancer therapy has been compared to attention control in a study of patients aged 3–18 years. Children and young adults in the intervention group had 1 30-minute healing touch session each day while receiving in-patient cancer therapy and at each out-patient clinic visit. The authors reported that pain in the intervention group decreased after each 30-minute session compared to immediately prior according to youth, parent, and nurse reports. This trend was not observed in the attention control group. Pain also decreased more in the healing touch group compared with control.

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

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

Additional research has examined the impact of distraction, deep-breathing exercises, and positive reinforcement compared to parent-initiated intervention on pain related to serial procedures (Manne et al., 1990). Results indicated a difference in parent-rated pain over time in the intervention group only. In addition, 2 CBT treatment arms (practice plus education prior to only the first of 3 procedures and the same prior to each of 3 procedures) were compared to standard care in a study showing no between-group difference in youth-rated pain (Månsson, Björkhem, & Wiebe, 1993). A study investigating the impact of preparation, relaxation, and distraction with lidocaine to lidocaine alone demonstrated no difference in between-group procedural pain (Pederson, 1996).

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

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

**Consensus Conference**

Following scientific review and Research Ethics Board approval at the Hospital for Sick Children, results of the conducted systematic review were disseminated to 15 national and international experts. These experts were pediatric pain clinicians (n = 4; 27%), pediatric oncology clinicians (n = 7; 57%), mHealth design and research scientists (n = 3; 20%), and an adult consumer living with pain (n = 1; 7%). All experts participated in a 2-day consensus conference in Toronto, Canada funded by a 2012 Planning Grant awarded by the Canadian Institutes of Health Research. Participants were selected based on their areas of clinical and research expertise. The experts were provided with the systematic review results to help inform their decision-making during the conference proceedings.
The conference used nominal group technique with the goal of developing expert consensus on: (a) pain assessment inputs by adolescents that should trigger the delivery of pain advice; (b) pain management advice; and (c) system feature requirements. Nominal group technique is a method used to pool judgement from a group of people with varied skills and knowledge bases to answer questions (Dunham, 1998). It has been previously used successfully to establish consensus on pediatric healthcare questions (Stinson, Connelly, et al., 2012a). Synthesizing the data generated at this conference, a prototype algorithm and catalogue of system features was developed.

**Pain Management Algorithm and System Feature Development**

The final step to the development of the pain management algorithm and system feature catalogue was qualitative interviewing with adolescents with cancer and pediatric oncology and pain healthcare professionals. This step was conducted to maximize the clinical utility and effectiveness of this new pain management app by exploring the perceptions and suggestions of adolescents and healthcare professionals as they related to *Pain Squad*+ and its care algorithm. Iterations of testing were used whereby algorithm and system feature issues identified in early interviews informed revisions to the algorithm before further interviewing was conducted.

Participants were recruited over a 3-month period in 2013 following Research Ethics Board approval at the Hospital for Sick Children. Adolescents who were English-speaking, 12 – 18 years, actively undergoing cancer treatment (being at least 3 months from diagnosis) were eligible to participate. The adolescent exclusion criterion was severe cognitive impairment as identified by a member of their healthcare team. Healthcare professionals were included in the study if they were English-speaking, had worked for at least 1 year, and specialized in either pediatric oncology or pain. Healthcare professionals were excluded if they were in training and
had not achieved full licensure. A convenience sampling strategy, augmented with purposive sampling was utilized to attempt to achieve maximum sample variation in age, sex and diagnosis for adolescents. Maximum variation in profession was sought from healthcare professionals.

Ten adolescents participated. Adolescents were 14.9 ± 2.0 years (M ± SD) and diagnosed with lymphoma (40%), ALL (30%), Ewing’s sarcoma (10%), osteosarcoma (10%) or Wilm’s tumour (10%). Seven adolescents were male and 3 were female. Nine healthcare professionals participated. Healthcare professionals were physicians (56%), a nurse (11%), a nurse practitioner (11%), a physical therapist (11%) and a psychologist (11%). Seven healthcare professionals specialized in pediatric oncology (78%) and 2 specialized in pediatric pain (22%).

Interview questions moved from general to specific and focused on eliciting adolescent and healthcare professional perceptions and suggestions on the system and algorithm (Sandelowski, 2010). The interviewer recorded field notes on participant comfort with the interview process and other non-verbal communication. All audio-recorded interviews were transcribed. Field notes were coded alongside transcripts.

The qualitative data analysis process began as soon as the first interview was conducted. Two people conducted data analyses and discussed themes that emerged from the interviews. Discrepancies in opinion were resolved using group discussion with a third party. A conventional qualitative content analysis approach was used to code data (Hsieh & Shannon, 2005). Changes to the catalogue of system requirements and the algorithm were made following individual interviews. Further interviews were conducted until neither adolescent nor healthcare professional had further suggestions for changes. All descriptive quantitative data were analyzed using SAS 9.1.3 software® (SAS Institute, 2006). Healthcare professionals
provided feedback on both the algorithm and its system features, while adolescents provided feedback on the system features as early interviews indicated adolescents were not proficient at or comfortable with vetting the algorithm. Each interview lasted between 20 and 45 minutes. Following this testing, a prototype Pain Squad+ real-time smartphone pain management app was created by a software development team (Appendix D shows app screenshots).

**Pain Squad+ Pain Management App: Algorithm and System Features**

Based on the systematic review, consensus conference and iterative algorithm and system vetting process, a pain care algorithm and the core features of the Pain Squad+ smartphone app were established. The vetted pain care algorithm is presented in Appendix E and the table of pain self-management advice provided by Pain Squad+ is presented in Appendix F. The required Pain Squad+ system features are described in Table 1 and are: (a) truncated ad hoc pain assessments (see Appendix G for questions used in truncated survey); (b) delivery of multiple pieces of pain management advice, especially in the context of pain self-management; (c) app-based access to a adolescent-selected piece of pain management advice; (d) pain reassessment; (e) capacity for individualized pain management recommendations, (f) capacity to prevent or mitigate procedural pain; and (g) clinical support from a nurse (recommended by healthcare professionals specifically).

\Table 1

**System Design Features of the Pain Squad+ Cancer Pain Management App**

<table>
<thead>
<tr>
<th>Design feature</th>
<th>Feature details</th>
<th>Rationale for feature, based on consensus conference results</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Truncated ad hoc pain assessment</td>
<td>In addition to scheduled long-form morning and evening pain assessments, adolescents will have the ability to complete a truncated (short-form) pain assessment on an ad hoc</td>
<td>The ad hoc assessment will provide the ability to complete a pain assessment and receive timely, ‘in-the-moment’ pain management advice during pain episodes. A truncated assessment for</td>
</tr>
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</table>
### b. Delivery of multiple different pain management recommendations

Adolescent-logged pain data will drive the app’s provision of a list of several user-selectable pain management recommendations. The pain management algorithm will determine the generated list. The provision of several different pain management recommendations will minimize the chance that an adolescent is provided with undesirable or inconvenient advice.

*Note:* The system will recognize ‘pain emergencies’ (e.g., sustained severe pain based on historically saved survey records) and recommend emergency action.

### c. Access to a selected pain management recommendation

Upon selection of a pain management recommendation, adolescents will be able to access this pain management strategy *via* the app (e.g., if ‘listen to music’ is selected, the app will link available music on the phone).

Direct access to the pain management strategy will minimize time-to-intervention and will maximize automation of tasks to improve the user-experience.

*Note:* Direct access will not be available for all recommendations (e.g., talk to your parent).

### d. Pain reassessment

Pain will be re-assessed 1 hour following a pain management recommendation. At this time, adolescents disclose if the previous management recommendation was used and liked. The combination of their current pain report and use and likeability of the recommendation are fed back into the algorithm and a new pain recommendation will be made (if pain is reported on re-assessment).

A follow-up assessment should be conducted to assess pain after the management recommendation. If an adolescent remains in pain, another recommendation should be made.

### e. Capacity for

Adolescent ratings of

To improve the user-
<table>
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<tr>
<th><strong>individualized pain management recommendations</strong></th>
<th>management recommendation likability will be translated into a 5-point ‘star-rating’. When future pain management advice is given to users, most-liked recommendations will be offered first.</th>
<th>experience, the system should attempt to personalize recommendations to individual pain management preferences.</th>
</tr>
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<tr>
<td><strong>f. Capacity to prevent or mitigate procedural pain</strong></td>
<td>Adolescents will have the ability to inform the system of upcoming procedures (e.g., venipuncture, subcutaneous <em>port-a-catheter</em>-access) and receive advice on pain prevention or mitigation strategies (e.g., ‘remember to listen to a favourite song’).</td>
<td>To be as comprehensive as possible in managing adolescent cancer-related pain, the app should endeavour to prevent and mitigate (as well as treat) pain.</td>
</tr>
<tr>
<td><strong>g. Clinical support from the study nurse</strong></td>
<td>A risk-assessment tool included in the software design will alert a study nurse <em>via</em> email of clinically important adolescent pain reports. The nurse will then contact the adolescent’s primary care team to assist in further clinical decision-making.</td>
<td>To improve the effectiveness and safety of the system, a trained specialist healthcare professional should monitor adolescents and support their pain care as needed.</td>
</tr>
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CHAPTER FOUR: METHODS

Research Questions

Study 1: Usability Testing

1. How can the smartphone-based real-time pain management app intervention (i.e., *Pain Squad*+) be refined using iterative cycles of usability testing so that is easy to use, easy to understand, efficient to complete, and acceptable to adolescents with cancer?

Study 2: Pilot Testing

Primary Questions (related to *Pain Squad*+ implementation outcomes).

1. Can testing of the *Pain Squad*+ pain management intervention for adolescents with cancer (aged 12 to 18 years) be implemented as planned in a future intervention effectiveness trial? Specifically:
   a. What is the percent participant accrual into the study?
   b. What is the percent participant retention in the study?
   c. Can the intervention be completed as planned (‘fidelity’)?
   d. What is the percent outcome measures completion?
   e. What is participant adherence to the intervention?
   f. What is the acceptability of the intervention to adolescents with cancer?

Secondary Question (related to *Pain Squad*+ effectiveness outcomes).

1. What is the effect of the *Pain Squad*+ real-time pain management intervention on pain intensity, pain interference, health-related quality of life, and self-efficacy after 28 days of use, compared to pre-intervention scores on each variable in adolescents with cancer (aged 12 to 18 years)?
Study 1: Usability Testing

Study Design

Based on the preliminary research described in the previous chapter, a prototype smartphone interface was created by a software development firm in Toronto, Canada. Governed by a user-centered design approach, Study 1 used iterative cycles of usability testing and interviews with adolescents with cancer to refine the app prototype.

Study Objective

The objective of Study 1 was to refine a smartphone-based real-time pain management app intervention (i.e., Pain Squad+) through usability testing such that it would be shown to be easy to use, easy to understand, efficient to complete and acceptable to adolescents with cancer.

Sample

Inclusion criteria. Participants meeting the following criteria were eligible for this study:

- Between the ages of 12 and 18 years.
- Able to speak and read English.
- Actively undergoing cancer treatment on an in- or out-patient basis.
- Being at least 3 months from diagnosis.
- Having self-reported pain of any intensity in the week immediately prior to recruitment.

Exclusion criteria. Participants were ineligible for this study if they:

- Had 1 or more major co-morbid (medical or psychiatric) conditions that would preclude involvement in the study, as per their healthcare professional.
- Were receiving palliative end-of-life care, as per their healthcare professional.
Setting and Sample Size

This study was conducted in a single haematology/oncology division of a metropolitan and university-affiliated pediatric tertiary care center (i.e., Hospital for Sick Children, Toronto, Canada). This site hosts one of the largest cancer programs in North America, with approximately 350 new diagnoses each year. Two previously published studies (Jibb et al., 2014; Stinson et al., 2013) with adolescents with pain have been conducted in the haematology/oncology division at this site. These studies have demonstrated that 72 ± 4% (M ± SD; range = 67 – 75%) of eligible individuals agreed to participate in similar research projects (unpublished data).

As this study employed an iterative testing approach to app development, the final sample size was determined by: (a) the number of testing cycles needed to sufficiently refine the app prototype and (b) the number of participants per testing cycle needed to reach data saturation (Cafazzo et al., 2012a; Seto, Leonard, Cafazzo, Barnsley, Masino, & Ross, 2012a; Stinson et al., 2006b; 2013). Review of the literature and previously conducted usability testing studies has indicated that prototype refinement is typically achieved within 2-3 cycles of testing (Macefield, 2009; Molich, 2010; Stinson et al., 2006b; 2013). Additionally, it has been demonstrated that data saturation can usually be reached with samples as small as 5-7 participants per iterative usability cycle (Kushniruk & Patel, 2004). Therefore, across 2-3 cycles, we aimed to recruit 10-21 adolescents for usability testing of the app prototype.

Sampling

Purposive sampling, where eligible individuals were approached for participation based on participant characteristics (Florczak, 2011), was employed for this study. A maximum variation sampling approach was used in an endeavour to produce a study sample that varied in terms of age, sex, and diagnosis. The testing procedures commenced after eligibility was
assessed, informed consent was obtained, and demographic and baseline outcome data were collected.

**Procedure**

Prior to participant recruitment, a scientific peer review for Studies 1 and 2 was conducted within the haematology/oncology division at the Hospital for Sick Children. Ethics approval for Study 1 was then obtained from the Research Ethics Boards at the Hospital for Sick Children and University of Toronto. A letter of information about the study was emailed to the heads of each of the cancer sections in the haematology/oncology division (Appendix H) and informal educational presentations about the study were made to the nurses who assisted with participant recruitment.

Adolescents who were eligible for participation based on their demographic- and disease-related characteristics were initially approached by a staff nurse and asked if they were interested in learning more about the study. If an adolescent agreed, the researcher approached the adolescent to ascertain whether they had experienced pain in the previous week. Any adolescent pain rating of > 0/10 met the inclusion criterion. This was the terminal step in determining eligibility. If the adolescent was deemed eligible, the researcher provided a verbal and written explanation of the study (including rights, safeguards to preserve anonymity, and risks and benefits of participation) and obtained consent from the adolescent (including consent to audio-record the proceedings). Parent consenting and adolescent assenting procedures were not used, as all adolescents understood the study protocol and its risks and benefits. Appendix I contains all research consent forms. Demographic and disease information (Appendix J), as well as information on comfort level with smartphone devices (Appendix K) was collected from each participant. All data were entered directly onto a secure password-protected Internet site (i.e., Research Electronic Data Capture site or REDCap site; www.project-redcap.org). The
researcher supervised and assisted adolescents with data entry as necessary. The usability testing session then began and the remainder of the study procedure was digitally audio-recorded. Whenever possible, a trained observer was present for usability testing sessions, providing the ability for a peer debrief after the session and enhancing the credibility of study results (Morrow, 2005).

Adolescents were asked to complete the app, documenting the pain of an adolescent with cancer presented to them using a vignette (Appendix L). The vignette was sex-specific (i.e., female- and male-specific versions) and was based on a similar vignette used in a previous adolescent with cancer usability study (Stinson et al., 2013). The appropriate vignette based on adolescent sex was provided to each participant. Adolescents were asked to “think aloud” about their perceptions related to the app and any difficulties encountered. Specifically, adolescents completed the same pain questionnaire used in the precursor app, Pain Squad (e.g., questions on pain intensity, pain unpleasantness, pain interference, control over pain etc.). The observer recorded the time taken for adolescents to complete a standardized app task, the documentation of pain described in the standardized vignette. Adolescents also received pain management advice from the app based the standardized pain assessment they imputed and were asked to provide feedback on the ease of use and understanding of the app’s management component, as well as feedback on the adherence-based rewards system (i.e., gamification mechanics of the app). Time to complete review of the management component and rewards system was not collected as variation in timing was expected to be due in part to user-level choices (e.g., the type and number of pain management strategies a user selected).

Once the adolescent had worked through the app, a brief interview with the researcher was conducted. The adolescent was asked a series of standardized open-ended questions according to a semi-structured interview guide (Appendix M). Questions were related to how
easy the app was to use, how understandable it was, adolescent-specific likes and dislikes related to the app, and perceived benefits of using the app. This interview guide was adapted from that used successfully in usability testing sessions of the original *Pain Squad* app with adolescents with cancer. The interview guide was piloted for ease of understanding with 3 adolescents who met the inclusion criteria before formal testing was conducted and no modifications to the guide were required following piloting. The researcher and the trained observer also took field notes during the usability testing session to record any observed technical difficulties encountered, as well as ease of use and learning.

To address biases or assumptions on the part of the researcher and the trained observer, a bracketing procedure was used throughout data collection and analysis. Bracketing involved the researcher and observer consciously developing awareness of implicit assumptions and predispositions and setting these aside to the greatest degree possible during interviews and analysis (Morrow, 2005). Peer debriefing between the researcher, observer and third parties (other members of the research team and software developers) also helped to minimize the impact of research subjectivity on results (Finlay, 2002; Morrow, 2005). Participants received an honorarium ($10 movie card) as compensation for time and effort donated to the study.

The above-described interview procedure was repeated until data saturation was reached. Saturation was defined as the point when new interview data collected were redundant with those previously categorized (Bowen, 2008). Saturation is a widely used qualitative indicator of dataset completeness and provides validation of coding categories used (Bowen, 2008). A software developer made revisions to the *Pain Squad*+ app based on issues identified during testing cycles and additional cycles were be conducted until no new issues were discovered. Further detail on Study 1 data management and analyses procedures are below.

**Study Instruments**
**Baseline participant information.** Each adolescent completed a brief demographic form and a questionnaire related to his or her comfort with using smartphones (Appendices J and K). The following demographic data were collected: age, sex, and ethnicity. Comfort with smartphones was ascertained using a researcher-developed questionnaire about smartphone ownership, level of usage, and likeability. Completion time of each questionnaire by adolescents was less than 5 minutes, as demonstrated previously (Jibb et al., 2014; Stinson et al., 2013). The researcher collected the following disease-related data from the adolescent’s electronic medical record: cancer diagnosis, cancer stage/risk, relapse-status, type of cancer treatment (e.g., chemotherapy, surgery), and date of cancer diagnosis. All of these questionnaires were unmodified or minimally modified versions of questionnaires that have been used successfully in previous studies of adolescents with cancer (Jibb et al., 2014; Stinson et al., 2013; Stinson, Sung, et al., 2012b).

**Data Management**

Participants entered baseline demographic data directly onto a secure study data management site (i.e., REDCap) via a study laptop computer at the time of recruitment. Data were exported directly from REDCap to Microsoft Excel software on the secure Hospital for Sick Children server. Logic and range checks were used to verify data accuracy. The researcher was previously trained on the use of this software. Data (including audio-recordings from sessions) stored on all study computers were backed-up onto the hospital server according to the hospital’s routine data storage protocol.

**Data Security**

In order to protect anonymity, upon enrolment in the study, each participant was assigned a unique numerical identifier, which was associated with his or her documentation. The code was isolated from the study data and stored in a database on the hospital’s secure
server. Any hardcopy documentation (e.g., consent forms, field notes) was stored in a locked cabinet in a locked office and was accessible only to the researcher. Digital recordings of the usability testing sessions were also stored on the hospital’s server.

**Data Analysis**

Demographic data were analysed using Microsoft Excel software. The characteristics of the study participants were summarized. Frequencies and percentages were calculated for discrete variables, and M and SD were calculated for continuous variables. Qualitative data analysis began once the first usability session was conducted so that issues identified in early sessions could inform later sessions using constant comparative analyses (Bowen, 2008; Lingard, Albert, & Levinson, 2008).

Qualitative analysis of usability testing data and post-test interviews is typically completed using a rapid-analysis approach (Arsand & Demiris, 2008; Kushniruk, 2002). Practicality is the rationale underlying this rapid approach. In particular, rapidly analyzing data from usability testing sessions and interviews can facilitate the timely identification of system issues, which may then be presented to software developers for revision. Importantly, this rapid-analysis approach, when used within the context of usability testing, is an appropriate means to efficiently and informatively analyze data (Beuscart-Zéphir, Watbled, Carpentier, Degroisse, & Alao, 2002). As such, rapid usability testing analysis methods were used in this study to improve the efficiency of app refinement.

Two individuals (the researcher and the trained observer) conducted data analyses. Immediately after each session, these individuals discussed themes that emerged during the each session with reference to field note data. Audio-recorded data were referred to as necessary. Discrepancies in opinion regarding themes were to be resolved using group discussion with a third party once the third party had reviewed the session audio-recording,
however no discrepancies occurred. A conventional qualitative content analysis approach was
used to code data (Hsieh & Shannon, 2005). Specifically, the researcher and the observer
independently made notes of impressions and thoughts on usability issues that arose during a
given testing session based on the study objectives. These impressions and thoughts were
considered as codes. The researcher and research assistant then grouped codes into meaningful
categories based on the relationships between codes. Categories were generated until all data
from the usability session are catalogued under existing categories (Patton, 2002; Sandelowski,
2000; 2010). Categories were grouped into themes and relationships among themes will be
determined (if applicable). Usability testing sessions continued until no data were generated
that had not already been categorized (i.e., data saturation). At this point, the entire range of
usability issues identified during a single iterative cycle were considered to have been
identified (Macefield, 2009; Molich, 2010). Software developers made revisions to the app
according to instructions from the research team that were based on usability-related themes.

Study 2: Pilot Testing

Study Design

Study 2 of this research project was a quasi-experimental study using a one-group
baseline versus post-study design (including mixed methods analyses) to examine ability to
implementing the Pain Squad+ app for future effectiveness testing and to preliminarily assess
effectiveness. This design was selected over an experimental design (i.e., a pilot RCT) because
a pilot trial would not have included a sample size large enough to observe a statistically
important difference between groups with regards to Pain Squad+ effectiveness. Therefore, all
participants received the intervention to improve the precision of estimating study
implementation outcomes (Eccles et al., 2002; Harris et al., 2006; Kirk, 2009). Preliminary
estimates of effectiveness (i.e., Pain Squad+ effectiveness outcomes) were assessed using baseline vs. post-study change scores, without a control group.

**Study Objectives**

**Primary objective.** The primary objective of Study 2 was to evaluate the implementation of the Pain Squad+ app for adolescents with cancer. In particular, the following Pain Squad+ implementation outcomes were determined: (a) the percent accrual for study participants and reasons for non-participation; (b) participant retention in the study; (c) the fidelity of the intervention; (d) percent outcome assessment completion; (e) adolescent adherence to the intervention; and (f) the acceptability of the intervention and study to adolescents with cancer.

**Secondary objective.** The secondary objective of Study 2 was to obtain estimates of treatment effects (effectiveness outcomes) on adolescent health outcomes, which has provided data that may be used to inform an appropriate sample size calculation for a future hypothesis-testing trial.

**Sample**

**Inclusion and exclusion criteria.** Adolescents met the same inclusion criteria as in Study 1, with the exception that any incidence of pain in the previous week had to have been self-reported as >3/10 and diagnosis should have occurred at least 2 months before study enrolment. The Study 1 exclusion criteria were applied.

**Setting and Sample Size**

Recruitment for this study was conducted in the haematology/oncology divisions of the Hospital for Sick Children and the Children’s Hospital of Eastern Ontario (Ottawa, Canada). As described in the Study 1 Setting and Sample Size Section, adolescents with cancer recruitment rates for similar studies at the Toronto site have been high. These high recruitment
rates have also been observed for cancer app pilot testing at the Ottawa site, which sees approximately 75 new cancer diagnoses each year (unpublished data). The patient populations at both of these sites are heterogeneous with respect to adolescent demographic- and disease-characteristics.

As this was a pilot study, and not a hypothesis-testing trial, no formal sample size calculations were conducted (Lancaster, Dodd, & Williamson, 2004; Leon, Davis, & Kraemer, 2011). Instead, the needed sample size was based on recommendations for pilot studies made by Hertzog (2008), which have been used successfully to determine likely implementation success before a large-scale RCT (Stinson et al., 2010). Specifically, a recruitment goal of 40 participants across these 2 sites was set.

**Sampling Strategy**

This study employed convenience sampling where eligible individuals were approached for participation based on relative ease of access (Florczak, 2011). As in Study 1, testing procedures commenced after eligibility was assessed, informed consent was obtained, and demographic and baseline outcome data were collected.

**Procedure**

**Recruitment procedure.** Ethics approval was obtained from the Research Ethics Boards at the Hospital for Sick Children, the Children’s Hospital of Eastern Ontario and the University of Toronto. A similar strategy to that used in Study 1 was employed to inform clinicians about the pilot study (i.e., email alert/explanation of study as shown in Appendix H, informal presentations to staff nurses). The researcher or research assistant liaised with the healthcare team as frequently as possible to determine the availability of adolescents eligible for participation. The number of healthcare team-assessed adolescents eligible for participation \(\text{per recruitment day per site}\) was recorded on the Cancer Pain Management App Recruitment
Log (Appendix N). If an adolescent was eligible for study participation, a staff nurse briefly described the study and asked the adolescent for permission to allow a more detailed study explanation from the researcher. Once permission to make initial contact was obtained, the researcher approached the adolescent to ascertain whether they have experienced pain >3/10 in the previous week and these data were recorded on the Cancer Pain Management App Recruitment Log. As in Study 1, this was the terminal step in determining eligibility. If an eligible adolescent declined to participate, their reason for refusal was recorded.

**Pre-test procedure.** Consent was obtained from interested and eligible adolescents. All participating adolescents then completed the same questionnaires on demographic information and comfort with smartphone devices used in Study 1 (Appendices J and K). Disease-related data were collected from the adolescent’s electronic health record by the researcher. Adolescents also completed baseline measures for all preliminary effectiveness outcomes (described below). The researcher and adolescents (assisted by the researcher) entered data directly into a secure password-protected Internet site (i.e., REDCap). Each participant was issued an Apple iPhone 6 loaded with the *Pain Squad*+ app. All participants were trained on app functionality with the standardized pain vignette used in Study 1 (Appendix L) and questions related to the study protocol were answered.

**Experimental procedure.** Adolescents completed a valid and reliable long-form, comprehensive pain assessment twice daily in the morning and evening for 28 days (Appendix B). In response to assessments positive for pain, adolescents received real-time pain management support from the *Pain Squad*+ app (either *via* recommendations for self-management techniques or *via* a study oncology-trained nurse depending on the developed algorithm). Audible iPhone notifications signalled adolescents to complete the assessment. The timing of the morning and evening assessments was customized to the individual participant by
the researcher when the study was initiated depending on participant preference. If an adolescent chose, assessment times were also customized according to day of week. An automated 30-minute window within which each assessment must be completed was set. An assessment not completed within the 30-minute window was registered on the server as “missed”. Three notifications for each assessment occurred: (a) an initial notification at the participant-requested time; (b) a notification 15 minutes after the initial alert; and (c) a notification 25 minutes after the initial alert.

Adolescents additionally had the option of completing ad hoc pain assessments using the truncated pain questionnaire (Appendix G) anytime between the automated notification times. The same algorithm-driven pain management recommendations as provided with the long-form assessments were issued in response to truncated assessments positive for pain. This feature provided participants with real-time advice. In all cases, if a pain recommendation was made, the app reassessed pain 1-hour later and offered additional advice as appropriate. Adolescents also received recommendations from the app on the prevention or mitigation of procedural pain, which may be sought prior to a painful medical procedure (e.g., venipuncture). All pain assessment data logged by adolescents and management recommendations given by the app were wirelessly transferred to the secure Hospital for Sick Children server. In addition to pain self-management advice being offered in response to all assessments positive for pain, email alerts related to clinically important incoming pain reports (i.e., 3 consecutive moderate to severe pain reports) were sent to a study nurse. The study nurse contacted the adolescent and/or their primary care team to discuss the pain reports and initiate intervention. The Pain Squad+ pain management algorithm dictated when an email alert would be sent to the study nurse (Appendix E). All participants involved in Study 2 received a $10 movie card as compensation for time and effort donated to the study.
Post-test procedure.

**Questionnaire data collection procedure.** On Day 29, the study team contacted each participant to remind him or her to complete follow-up questionnaires. To do so, each participant logged into the secure password-protected REDCap site with a unique identifier to complete questionnaires online. Email or telephone call reminders from the researcher to complete outcome measures were sent if the questionnaires were not completed promptly. The researcher also telephoned participants to thank them for their participation and to review instructions related to returning the phone to the research team. Telephone assistance from 09:00-17:00 Monday to Friday during the study was available to participants in the case of technical problems. The researcher routinely reviewed a computer summary of each participant’s pain report daily as additional insurance that patient safety issues were identified and resolved. Any safety issues that arose were to be tracked on the Cancer Pain Management App Activity Log (Appendix O).

**Semi-structured interview procedure.** When the researcher telephoned participants with instructions regarding how to return the study iPhone, a sample of participants were also asked to complete a post-study semi-structured interview. This interview provided additional in-depth data related to *Pain Squad*+ acceptability, perceived helpfulness related to health outcomes (e.g., pain, self-efficacy) and suggestions for improvement. Questions related to satisfaction with study procedures (e.g., length of study) were also asked. The number of participants to be interviewed was determined by the number of interviews needed to reach data saturation (Bowen, 2008) as described in Study 1.

A semi-structured interview guide was used (Appendix P). This guide was based on one previously used successfully with adolescents with cancer (Stinson et al., 2013). In addition, before formal testing, the interview guide was piloted for ease of understanding with
3 adolescents who met the inclusion criteria and no modifications were required. A purposive maximum variation sampling strategy was used to interview adolescents who varied in terms of age, sex, and diagnosis, as well as perceived *Pain Squad*+ acceptability, interaction with the system (as assessed *via* number of routine morning and evening assessments logged to the system, number of *ad hoc* assessments completed and number of healthcare professional contacts to participant), and baseline to post-study change scores on health-related study outcome measures. The interviewer was not blinded to participant characteristics or *Pain Squad*+ outcomes. The bracketing procedure and peer debriefing procedure described in Study 1 was used to minimize the impact of researcher subjectivity during both data collection and data analysis (Morrow, 2005). All interviews were audio-recorded with consent obtained from the adolescent.

**Rationale for using a telephone interview procedure.** Enhancing the practicality of collecting qualitative acceptability data from out-patient adolescents was the primary reason for selecting a telephone interview over a face-to-face interview. Telephone interviewing has been suggested as a useful means to discuss sensitive topics because it provides a degree of anonymity to participants (Holt, 2010; Sturges & Hanrahan, 2004). In the present study, this added sense of anonymity was considered useful in eliciting honest opinions, especially negative opinions, related to the app and study. Telephone interviewing has been used successfully with adolescents (Shannon, Mathias, Marsh, Dougherty, & Liguori, 2007) and has been shown to provide the same nature and depth of responses as face-to-face interviews (Sturges & Hanrahan, 2004). Telephone interviewing is also a well-liked mode of interviewing for participants (Holt, 2010).
Study Instruments

Details on each study instrument used, according to time of administration, are provided below (Table 2). As shown previously (Hinds et al., 2000; Roizen et al., 2008; Stinson et al., 2013), the time to complete each measure was less than 5 minutes.

Table 2

Study Instruments and Timing of Administration

<table>
<thead>
<tr>
<th>Time</th>
<th>Outcome measure</th>
<th>Instrument</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Adolescent characteristics</td>
<td>Adolescent Demographic Form&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Comfort with smartphone devices</td>
<td>Smartphone Comfort Form&lt;sup&gt;a&lt;/sup&gt;</td>
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<tr>
<td></td>
<td>Pain intensity</td>
<td>BPI (worst, least, average, current pain)</td>
</tr>
<tr>
<td></td>
<td>Pain interference</td>
<td>PROMIS PPI-SF</td>
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<tr>
<td></td>
<td>Health-related quality of life</td>
<td>PedsQL 4.0</td>
</tr>
<tr>
<td></td>
<td>Self-efficacy</td>
<td>GSE-Sherer Scale + pain-care self-efficacy item</td>
</tr>
<tr>
<td>Day 29+</td>
<td>Adherence</td>
<td>Cancer Pain Management App Activity Log&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Acceptability</td>
<td>Modified AES</td>
</tr>
<tr>
<td></td>
<td>Pain intensity</td>
<td>BPI (worst, least, average, current pain)</td>
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<td></td>
<td>Pain interference</td>
<td>PROMIS PPI-SF</td>
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<td></td>
<td>Health-related quality of life</td>
<td>PedsQL 4.0</td>
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<tr>
<td></td>
<td>Self-efficacy</td>
<td>GSE-Sherer Scale + pain-care self-efficacy item</td>
</tr>
<tr>
<td>Post-study</td>
<td>Acceptability and perceived Pain Squad+ usefulness</td>
<td>Telephone interview&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ongoing</td>
<td>Technical difficulties, attrition</td>
<td>Cancer Pain Management App Activity Log&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> researcher-developed tool.

Notes. BPI = Brief Pain Inventory. PROMIS PPI-SF = Patient Reported Outcomes Measurement Information System Pediatric Pain Interference Scale Short Form. PedsQL 4.0 = Pediatric Quality of Life Inventory 4.0. GSE-Sherer Scale = General Self-Efficacy – Sherer Scale.

**Baseline demographic information.** Questionnaires assessing demographic and disease-related characteristics, and comfort with smartphones were administered to adolescents at baseline, prior to study commencement. Demographic data collected were those related to
age, sex, and ethnicity. Disease-related data were related to cancer diagnosis, cancer stage/risk, relapse-status, type of cancer treatment (e.g., chemotherapy, surgery), and date of cancer diagnosis. A questionnaire about smartphone ownership, level of usage, and likeability was used to learn about comfort with smartphones. As in the Study 1, these questionnaires were developed for this study and are similar to those that have been used successfully in previous studies of adolescents with cancer (Stinson et al., 2013; Stinson, Sung, et al., 2012b).

**Primary outcome: Pain Squad+ implementation outcomes.** Implementation outcomes described the ability to implement the study protocol as designed. Proctor and colleagues (2011) have proposed a set of implementation outcomes for study when an intervention is being piloted. Proctor’s implementation outcomes have directed the selection of outcomes described in detail below.

**Study accrual and retention.** The Cancer Pain Management App Recruitment Log (Appendix N) was designed to record data related to: (a) number of eligible adolescents *per* recruitment day; (b) reasons for ineligibility; and (c) reasons for nonparticipation. The Cancer Pain Management App Activity Log (Appendix O) was used to record data related to attrition (i.e., occurrence and reasons for attrition).

**Intervention fidelity.** Fidelity refers to “the extent to which the core components of interventions are delivered as intended by the protocol” (p. 79; Gearing et al., 2011). To assess intervention fidelity, technical problems (i.e., occurrence, description, and resolution of technical problems), number and details of calls from the study nurse to the adolescent when needed, and time to call (expected to be within 12 hours of email alert) from study nurse were recorded on the Cancer Pain Activity Log and the Healthcare Professional Cancer Pain Intervention Log (Appendix Q).
**Outcome measure assessment piloting.** Outcome measure assessment piloting referred to the degree to which all outcome measures were completed as intended. Outcome measure completion was defined as 100% for a given adolescent when all outcome measure questions were completed at baseline and post-study. Questions where answers were optional (e.g., “If you answered ‘yes’, tell us why”) were not included in the analysis. Data were recorded on the Cancer Pain Management App Activity Log.

**Adherence.** Adherence was defined as 100% for a given adolescent when 56 reports (2 reports per day during the intervention) were completed. Twice-daily reporting using similar pain assessment apps has previously been used to measure adherence in similar interventions (Stinson, Jibb, et al., 2015a; Stinson et al., 2014). Engagement with the management recommendation features of the system and ad hoc pain reporting were not used to define adherence because usage of these features was expected to vary across participants. The researcher signed onto the server after Day 28 to extract data logged by adolescents and calculate percentage adherence. These data were recorded on the Cancer Pain Management App Activity Log.

**Acceptability.** Acceptability describes the degree to which the intervention is considered satisfactory to participants; in terms of how difficult, helpful, enjoyable and understandable it is to use, and how tolerable the amount of time required to complete it is (Wu, Johnson, Schepp, & Berry, 2011). The Acceptability E-Scale (AES) is a 6-item scale developed to specifically examine the acceptability of an electronic self-report assessment for patients with cancer (Tariman, Berry, Halpenny, Wolpin, & Schepp, 2011). The AES ascertains perceptions related to how helpful, difficult, and enjoyable the computer program was to use, how understandable the questions were, and how acceptable the time invested in reporting was (Tariman et al., 2011; Wu et al., 2011). The readability level for questions on the
scale is fifth-grade. Each question is answered using a 5-point Likert scale from 1 (not at all) to 5 (very much), giving a total possible score range of 6 to 30. A mean score of 3 on any item indicates a neutral response, with scores greater than 3 indicating acceptability (Tariman et al., 2011). An item mean score of 4 or greater indicates high acceptability (Wu et al., 2011).

Using Cohen’s criteria for measure establishment (Appendix R) in the adolescent with cancer population, the AES is considered “promising” (Cohen et al., 2008). The scale has undergone reliability and validity testing in adult cancer patients (18 – 80 years). Internal consistency reliability was demonstrated as a Cronbach coefficient alpha of 0.76. Construct validity was assessed as structural validity and factor analysis showed the scale to be one-dimensional (Tariman et al., 2011). The AES has also been shown to be feasible for use with adolescent and young adults with cancer (13 – 20 years; W.W. Wu et al., 2011).

For the purpose of the present research, the wording of the AES was modified to make it applicable to the study intervention (Appendix S). Specifically, the words “this computer program” were changed to “Pain Squad+” and the words “your symptoms and quality of life” were changed to “your pain”. Adolescents also answered an additional question related to how useful the app was in treating pain. Scores for this question were not included in the total AES score. These data were collected after Day 28. The semi-structured interview described above was also used to obtain acceptability-related data from adolescents.

**Secondary outcome: Pain Squad+ effectiveness outcomes.** The measures used to determine the secondary study outcome are described in detail below.

**Pain intensity.** Pain intensity refers to “how much pain hurts” (Huguet et al., 2010). Pain intensity has been suggested as a core outcome for measure in pediatric pain experimentation by the PedIMMPACT consensus group (McGrath et al., 2008). Pain was measured using the Brief Pain Inventory (BPI) items assessing the pain intensity. The BPI is a
comprehensive pain assessment measure originally designed to measure cancer pain (Cleeland & Ryan, 1994) and is considered the standard in clinical and research use in adult cancer patients (Mathias et al., 2011). The BPI uses 4 items to assess current pain intensity and worst, average, and least pain intensity in the previous week. Each item is rated numerically on a 0-10 scale with verbal anchors ‘no pain’ at 0 and ‘pain as bad as you can imagine’ at 10. The individual scores on each of the 4 items may be summed and averaged to provide a composite pain intensity score (Kroenke et al., 2012).

The BPI has been validated and used extensively in cancer pain assessment, making it a well-established measure for this purpose according to the Cohen criteria (Cohen et al., 2008). Internal consistency has been demonstrated for the 4 pain intensity items with Cronbach coefficient alpha values of 0.80 to 0.87. Test-retest reliability has also been examined (Cleeland, 2009). Short-term test-retest coefficients (1-day to 1-week) for the ‘worst’ pain item (0.93) and ‘average’ pain item (0.78) were high. As expected, lower test-retest coefficients were demonstrated for the ‘current’ pain item (0.59). Additionally, the intensity scale questions of the BPI have been used successfully in adolescents with cancer and those with other health conditions (Ameringer, 2010; Stinson et al., 2013). Further, the numerical rating scale used to assess each BPI item is a valid means to assess pain intensity in children as young as 8 years (Pagé et al., 2012). All participants completed this measure at baseline and after Day 28 (Appendix T).

**Pain interference.** Pain interference describes how pain restricts daily activities related to physical, psychological, and social functioning, as well as sleep, school, and enjoyment of life (Ameringer, 2009; McGrath et al., 2008; Varni et al., 2010). The Patient Reported Outcomes Measurement Information System Pediatric Pain Interference Short-form Scale (PROMIS PPI-SF) is a self-report 8-item scale developed using a systematic approach, which
included both qualitative (focus groups and cognitive interviews) and quantitative (item response theory analysis) methods (DeWalt, Rothrock, Yount, Stone, PROMIS Cooperative Group, 2007; Hinds et al., 2013; Irwin et al., 2010; Varni et al., 2010). The scale does not include subscales, but assesses the affective and evaluative (impact of pain on activities of daily living) dimensions of pain. The PROMIS PPI-SF is intended for use by 8 – 17 year olds with a variety of health conditions and has been explicitly evaluated in children and adolescents with cancer (Hinds et al., 2013), nephrotic syndrome, (Gipson et al., 2013) and cerebral palsy (Kratz et al., 2013).

Based on Cohen’s criteria for measure establishment, the PROMIS PPI-SF scale meets the criteria for an “approaching well-established” measure in the adolescent with cancer population (Cohen et al., 2008). Regarding measure scoring, each item is scored on a 5-point Likert response scale from ‘0’ (never) to ‘4’ (almost always) and totalling the scores for each item generates a summary score. Total scores are then converted to a T-score with a M of 50 and SD of 10 (based on a reference sample). The PROMIS PPI-SF is scored negatively so that a score of 60 is 1 SD worse than the mean.

Hinds et al. (2013) conducted psychometric testing of the PROMIS PPI-SF as part of an evaluation of all of the PROMIS pediatric measures in 8 – 17 year olds with cancer. This study demonstrated construct validity through hypothesis testing using ‘known-groups’ methods. Specifically, cancer survivors were shown to report significantly lower standardized pain interference scores than the children and adolescents in active treatment (Hinds et al., 2013). Simultaneous multiple regression showed that this significance held irrespective of age, sex, race, guardian’s education, tumour type, and the presence of other health problems. The PROMIS PPI-SF has also been shown to be feasible to administer (researcher determined time to administer measure was satisfactory and number of missed responses was minimal) and
acceptable to 8 – 17 year olds with cancer. The PROMIS PPI-SF will be administered to adolescents at baseline and after Day 28 (Appendix U).

**Health-related quality of life.** Wilson and Cleary’s (1995) conceptualization of HRQL was used to define this variable. Wilson and Cleary (1995) have described general quality of life as how happy or satisfied a person is with their life as a whole. Health-related quality of life then describes quality of life that is associated with a person’s health. Health-related quality of life is multidimensional and describes a person’s perceptions of their physical functioning, role functioning, social functioning, mental health, and general health (Katz, Burwinkle, Varni, & Barr, 2007; Varni et al., 2002; Wilson & Cleary, 1995) and is not specific to pain.

The Pediatric Quality of Life Inventory (PedsQL) 4.0 is a 23-item generic HRQL scale not specific to pain. It is comprised of 4 subscales (i.e., physical functioning, emotional functioning, social functioning and school functioning) with each subscale containing 5 to 8 items. The PedsQL 4.0 has been widely studied, translated into several different languages (Limbers, Newman, & Varni, 2009) and used in HRQL assessments in children and adolescents with cancer (Varni et al., 2002; 2004; Varni, Limbers, & Burwinkle, 2007), arthritis (Lundberg, Lindh, & Eriksson, 2012), sickle cell anemia, (Panepinto, Pajewski, Foerster, Sabnis, & Hoffmann, 2009) and asthma (Roncada, Mattiello, Pitrez, & Sarria, 2013), among other disease groups. The PedsQL 4.0 has been developed for 2 – 18 year olds (self-report forms for children 5 – 18 years and parent-proxy report forms for children and adolescents 2 – 18 years). Age-appropriate versions of the PedsQL 4.0 self-report have been developed such that 5 – 7 year olds complete a young child form, 8 – 12 year olds complete a child form and 13 – 18 year olds complete an adolescent form. In scoring the PedsQL 4.0, each item is scored on a 5-point Likert response scale from ‘0’ (never) to ‘4’ (almost always). Each
item is reverse-scored and then linearly transformed to a 0-100 scale (e.g., 0 = 100, 4 = 0).

Totalling the scores for each item and dividing by the number of items answered will generate a summary score. Subscale scores may also be generated in the same manner as the summary score.

Using Cohen’s criteria (Cohen et al., 2008), the PedsQL 4.0 scale is a well-established measure shown to be valid and reliable (Solans et al., 2010), and has been used in several studies of adolescents with cancer (Ameringer, 2010; Ruccione et al., 2013; Sung et al., 2009; Varni et al., 2004). The reliability and validity of the PedsQL 4.0 have been examined in adolescents with cancer (Varni et al., 2002). The reliability of the measure has been assessed as internal consistency (determined using Cronbach coefficient alpha). In the adolescent with cancer group (13 – 18 year olds), Cronbach coefficients of at least 0.75-0.93 are reported for each subscale of both PedsQL measures, indicating good internal consistency and low redundancy of items (Lohr et al., 1996; Terwee et al., 2007). Construct validity of the PedsQL 4.0 has been demonstrated using hypothesis-testing methods (Varni et al., 2002). Specifically, the known groups method was used to compare total scores and subscale scores for both measures. Using this method, children and adolescents with cancer were shown to have lower total and subscale HRQL scores than those without cancer ($p < 0.001$). Age-appropriate versions of the PedsQL 4.0 were administered to adolescents at baseline and after Day 28 (Appendix V).

**Self-efficacy.** Self-efficacy was defined using Bandura’s Theory of Behavioural Change as “belief in one’s capabilities to organize and execute the course of action required to produce given attainments” (Bandura, 1997, p. 3). Self-efficacy was measured with the Modified General Self-Efficacy – Sherer Scale (GSE-Sherer Scale). The GSE-Sherer Scale is a 12-item psychological scale that measures general belief in personal competence. The original
GSE-Sherer Scale consisted of 17 items, which was modified to a 12-item version due to low item-total correlations for 5 questions (Bosscher & Smit, 1998). The scale has been used in children as young as 10 years (Hinds, 1990). Each item is scored on a 5-point Likert scale with the anchors ‘agree strongly’ and ‘disagree strongly’. Item scores are summed to provide an overall self-efficacy score.

According to Cohen’s criteria, GSE-Sherer Scale is an established measure for assessing self-efficacy in adolescents with cancer. Psychometric testing of the measure has shown internal consistency to be good in adolescents (including those with cancer) as demonstrated by a Cronbach alpha value of 0.87 and moderate stability (Cramm, Strating, Roebroeck, & Nieboer, 2012; Hinds et al., 2000). The GSE-Sherer Scale also has strong evidence of validity, demonstrated as predictive validity (predicting past success in work and school tasks) and construct validity (positively correlated with the Rosenberg Self-Efficacy Scale; (Hinds et al., 2000; Sherer & Adams, 1983; Sherer et al., 1982). The GSE-Sherer Scale assesses the construct of self-efficacy in a general manner and therefore a researcher-developed pain care-specific item was added to the self-efficacy questionnaire. This additional item was scored in the same manner as the GSE-Sherer Scale. The entire self-efficacy questionnaire was administered to adolescents at baseline and after Day 28 (Appendix W).

**Data Management**

Baseline data were entered directly onto a secure study data management site (i.e., REDCap) via a study laptop computer at the site of recruitment. Quantitative outcome data were entered by participants directly into the same data management site at study completion, wherever possible. On a few occasions, adolescents who were in-patients at the time of study completion completed paper versions of the questionnaires and data were transcribed to the REDCap site by the RA. The researcher checked the accuracy of data transcription. The
researcher accessed data on the secure Hospital for Sick Children server. Quantitative data were exported directly from REDCap to SAS 9.1.3 software® (SAS Institute, 2006). Logic and range checks were used to verify data accuracy. Qualitative interview audio-recordings were also stored on the server and imported directly into QSR International NVivo 10.0 software (QSR International, 2012).

**Data Security**

The same data security measures described in Study 1 were used.

**Data Analysis**

**Quantitative data analyses.** All quantitative data related to the primary and secondary outcomes were analysed using SAS 9.1.3 software® (SAS Institute, 2006). Descriptive statistics were used to describe sample characteristics at baseline, momentary pain characteristics, and pain management strategies reported on the app during the study. Descriptive statistics were also used to analyse data related to accrual and retention rates, the fidelity of the intervention, outcome measure piloting, adherence, and acceptability. Frequencies and percentages were calculated for discrete variables, and M, SD, and ranges were calculated for continuous variables.

With regard to the *Pain Squad*+ effectiveness outcomes, M and SD calculations provided an estimation of the magnitude of treatment effects (i.e., effect sizes). Within-group effect sizes were estimated using the Cohen’s *d* statistic. Cohen’s *d* was computed by dividing the difference in mean effectiveness outcome scores between baseline and post-study, by the standard deviation of the individual differences. Effect size was interpreted as described by Cohen, namely as: 0.00-0.19 negligible, 0.20-0.49 small, 0.50-0.79 moderate, and >0.80 large (Cohen, 1988). These estimations were tempered by the small sample size used in the present study and the lack of control group (Kraemer, Mintz, Noda, Tinklenberg, & Yesavage, 2006;
Leon et al., 2011), but have provided preliminary data that may be used to inform sample size calculations for a future RCT.

Additionally, exploratory inferential testing was conducted to examine trends in the effect of Pain Squad+ on pain intensity, pain interference, HRQL, and self-efficacy from baseline to post-study. These analyses were exploratory as this was a pilot study and an *a priori* power analysis was not conducted. Paired *t* tests were used to compare mean baseline and post-study scores for each of the effectiveness outcomes. The assumptions for *t* tests (i.e., random sampling, homogeneity of variance, and normality) were met and no data transformations were required. A level of 0.05 was used as the criterion for statistical significance.

**Criteria for determining implementation success.** Implementation success criteria were based on pilot studies previously conducted with similar study populations and interventions (Stinson et al., 2010; 2013). These criteria were: accrual of >70%, attrition of <15%, minimal technical difficulties (i.e., reported by <10% of participants), high acceptability (item mean score of 4 on AES and positive endorsement for system determined using qualitative analyses of interviews), adherence of >80%, minimal missed responses on outcome measures (i.e., <10%), and >80% of study nurse contact with patients completed within 12 hours of the email alert.

**Qualitative data analyses.** A trained transcriptionist transcribed interview audio-recordings verbatim. Data analyses began once the first interview had been transcribed so that issues identified in early interviews could inform later interviews using constant comparative analyses (Lingard et al., 2008). The transcribed data were managed using NVivo 10.0 software (QSR International, 2012), which allowed for coding and annotation of text. All data were read several times by 2 people (the researcher and a research assistant) to obtain an overall
understanding, identify data codes, and ensure that all comments were carefully considered and included. The researcher and research assistant then independently coded the data using a line-by-line technique based on the study objectives. Codes were grouped into meaningful categories based on the relationships between codes. Categories continued to be generated until all study data were classified under the existing categories (Patton, 2002; Sandelowski, 2000; 2010). Categories were grouped into themes and relationships among themes will be determined (if applicable). Discrepancies in opinion regarding themes were to be resolved using group discussion with a third party once the third party had reviewed the transcripts, however no discrepancies occurred. An audit trail consisting of a detailed chronology of data collection and analytical decisions related to emerging categories and themes was kept as a means to enhance validity (Morrow, 2005).

**Ethical Considerations for Both Studies**

**Risks**

There were no foreseeable risks of an appreciable quality related to participating in either Study 1 or Study 2. Research Ethics Board approval at the Hospital for Sick Children, the Children’s Hospital of Eastern Ontario, and the University of Toronto was obtained before study commencement. Participation in the study was completely voluntary and adolescents could have withdrawn themselves at any time. All personal information was securely stored. Cancer-related symptoms (i.e., pain) may be a sensitive issue for some adolescents and some may have experienced emotional upset while discussing this or interacting with the app. Participants were alerted to this risk during the informed consent process and were informed to alert their healthcare team, a family member, and/or the researcher to any problems as needed. The researcher was not informed of any adverse events, however had any occurred, the safety protocol dictated that the event was to be reported to the adolescent’s primary physician as
soon as possible. Additionally, participants may have experienced some inconvenience related to the time required to complete the study (i.e., time to complete baseline questionnaires, interview time, time to complete the outcome questionnaires, and time to interact with the apps).

Pain assessments logged by adolescents were monitored by the study nurse (via email reports of clinically significant pain) and by the researcher (via monitoring of assessments sent to the study server). Safety issues that were monitored for by the researcher included reports of sustained pain and other physical or psychological adverse effects. No reports of unaddressed sustained pain occurred during the study. The protocol should these incidents have occurred involved the researcher contacting the study nurse or participant’s primary care team, who would then have contacted the participant. This monitoring was intended to provide a safeguard against safety issues that arose during the study.

**Benefits**

Participants did not directly benefit from participating in this study. However, participants were engaged in the user-centered usability testing of the *Pain Squad*+ app and contributed to improved understanding of how the app may be implemented for effectiveness testing. If shown to be effective in a future RCT, this app could serve to improve pain management for other adolescents with cancer.
CHAPTER FIVE: RESULTS

Study 1: Usability Testing

Sample Selection and Participant Characteristics

In total, 18 eligible adolescents with cancer were approached to participate from September 29, 2014, to January 30, 2015. Two adolescents (11%) declined to participate due to feeling ill and being preoccupied with another activity. Thus, the percent acceptance for usability testing participation was 89%. Sixteen adolescents with cancer participated across 3 iterative cycles of usability testing. Adolescents in all cycles ranged in age from 12 – 18 years (M = 14.8; SD = 2.1), and 9 (56%) were female. Adolescents were most commonly diagnosed with lymphoma (4; 25%). The frequencies, percentages, means and SDs for demographic and disease-related characteristics are shown in Table 3.

The majority of participants (11; 81%) reported owning a smartphone and 15 participants (94%) reported using a smartphone (either their own phone or that of a friend or family member) at least once per day. Participants were either comfortable (3; 18%) or very comfortable (16; 81%) using smartphones. Details related to adolescent smartphone use are shown in Table 4.

Usability Testing of the Pain Squad+ App

Three iterative cycles of usability testing were conducted to refine the Pain Squad+ app. The time from the completion of a single usability testing cycle to the implementation of needed app revisions by the software developers was 19 days for each of cycle 1 and 2 changes. Below, the data from all cycles of app testing have been categorized according to the study objectives: ease of use, ease of understanding, efficiency, and acceptability.
Table 3

**Characteristics of study participants**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cycle 1 (n = 4)</th>
<th>Cycle 2 (n = 6)</th>
<th>Cycle 3 (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years (SD)</td>
<td>15.3 (2.6)</td>
<td>15.5 (1.6)</td>
<td>13.7 (1.9)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>3 (75)</td>
<td>4 (67)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Male</td>
<td>1 (25)</td>
<td>2 (33)</td>
<td>4 (67)</td>
</tr>
<tr>
<td>Race/ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>0</td>
<td>1 (17)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Latin American</td>
<td>0</td>
<td>1 (17)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>South Asian</td>
<td>0</td>
<td>1 (17)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>South East Asian</td>
<td>1 (25)</td>
<td>1 (17)</td>
<td>0</td>
</tr>
<tr>
<td>White</td>
<td>3 (75)</td>
<td>2 (33)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Cancer diagnosis, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td></td>
<td></td>
<td>2 (33)</td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td></td>
<td>1 (17)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Adrenocortical carcinoma</td>
<td>1 (25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td></td>
<td>2 (33)</td>
<td></td>
</tr>
<tr>
<td>Ewing sarcoma</td>
<td>1 (25)</td>
<td>1 (17)</td>
<td></td>
</tr>
<tr>
<td>Lymphoma</td>
<td>1 (25)</td>
<td>2 (33)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>1 (25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-transplant lymphoproliferative disorder</td>
<td></td>
<td>1 (17)</td>
<td></td>
</tr>
<tr>
<td>Triton tumour</td>
<td></td>
<td>1 (17)</td>
<td></td>
</tr>
<tr>
<td>Mean duration of illness in years (SD)</td>
<td>0.4 (0.3)</td>
<td>0.4 (0.3)</td>
<td>1.0 (1.8)</td>
</tr>
<tr>
<td>Diagnosed with relapsed cancer, n (%)</td>
<td>1 (25)</td>
<td>0</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Treatment modality, n (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0</td>
<td>0</td>
<td>1 (17)</td>
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<tr>
<td>Chemotherapy</td>
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<td>6 (100)</td>
<td>6 (100)</td>
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<tr>
<td>Radiation</td>
<td>3 (75)</td>
<td>0</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Surgery</td>
<td>1 (25)</td>
<td>2 (33)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Stem cell transplant</td>
<td>0</td>
<td>0</td>
<td>1 (17)</td>
</tr>
</tbody>
</table>

<sup>a</sup> More than 1 response option possible per participant.
### Table 4

*Smartphone-associated information for study participants*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cycle 1 (n = 4)</th>
<th>Cycle 2 (n = 6)</th>
<th>Cycle 3 (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smartphone ownership, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>0</td>
<td>3 (50)</td>
</tr>
<tr>
<td>Yes</td>
<td>4 (100)</td>
<td>6 (100)</td>
<td>3 (50)</td>
</tr>
<tr>
<td>Times smartphone used <em>per day</em>, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>0</td>
<td>0</td>
<td>1 (17)</td>
</tr>
<tr>
<td>1-3 times</td>
<td>1 (25)</td>
<td>0</td>
<td>2 (33)</td>
</tr>
<tr>
<td>4-6 times</td>
<td>1 (25)</td>
<td>1 (17)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>7-10 times</td>
<td>0</td>
<td>1 (17)</td>
<td>0</td>
</tr>
<tr>
<td>&gt; 10 times</td>
<td>2 (50)</td>
<td>4 (67)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Purpose of smartphone use, n (%)a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>App use</td>
<td>3 (75)</td>
<td>5 (83)</td>
<td>3 (50)</td>
</tr>
<tr>
<td>Calling</td>
<td>1 (25)</td>
<td>4 (67)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Emailing</td>
<td>1 (25)</td>
<td>2 (33)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Game playing</td>
<td>3 (75)</td>
<td>4 (67)</td>
<td>5 (83)</td>
</tr>
<tr>
<td>Music listening</td>
<td>2 (50)</td>
<td>4 (67)</td>
<td>2 (33)</td>
</tr>
<tr>
<td>Texting</td>
<td>4 (100)</td>
<td>5 (83)</td>
<td>4 (67)</td>
</tr>
<tr>
<td>Not applicable</td>
<td>0</td>
<td>0</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Comfort using smartphone, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>A little</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Comfortable</td>
<td>2 (25)</td>
<td>1 (17)</td>
<td>1 (17)</td>
</tr>
<tr>
<td>Very comfortable</td>
<td>3 (75)</td>
<td>5 (83)</td>
<td>5 (83)</td>
</tr>
</tbody>
</table>

*a* More than 1 response option possible *per* participant.

### Ease of Use

All participants but 1 were able to complete testing of the pain assessment, pain management, and gamification mechanics (i.e., badge acquisition, point, and leveling system) of *Pain Squad+* app in a single session. Minimal assistance was required from the researcher. A technical issue with the app software causing the app to crash during the first usability testing iteration was the reason for the 1 participant’s inability to complete the session.

Participants across all testing cycles stated that *Pain Squad+* was easy to use. All participants
intuitively knew how to launch the app and begin a pain assessment. One adolescent stated, “Well, I felt it was easy enough. Easy to read. Very straightforward, which is what most people are looking for” (male, 16 years).

Ease of use was negatively impacted in the first testing cycle by technical malfunctioning of the app. Three out of 4 participants experienced difficulties completing the *Pain Squad+* pain assessment due to the app unexpectedly re-launching the assessment from midway through the questionnaire. Highlighting this issue, 1 participant stated, “Oh ok! I got to like the 5th question and it shot me back to number 2” (female, 13 years). Due to participant frustration related to having to repeatedly re-start the pain assessment, cycle 1 was stopped after 4 usability testing sessions. In response to this issue the software development team reprogrammed the app and tested it internally to ensure all pain assessment questions could be answered in sequence.

In cycle 2, half of the participants were observed to have difficulties with the responsiveness of the app. For example, an adolescent stated after the session that, “The only thing I can possibly think of, and it’s not actually a really big thing, but, is that the buttons are annoying. Like they don’t seem to want to work” (female, 18 years). To correct the issue, software developers increased the ‘clickable’ surface area corresponding to the app’s buttons and cursors.

Following the implementation of these changes, there were no issues related to *Pain Squad+* ease of use identified in cycle 3. Participants commented that, “It was really a very simple process. So the basics, all the instructions, helps you just…go” (male, 13 years) and “It was pretty easy, because everything's explained. Like, it's there and it tells you where to go for advice and stuff and you don't have to like look around” (female, 16 years).
Ease of Understanding

All adolescents endorsed the *Pain Squad+* app as simple to comprehend: “All the questions in the app were easy to understand and it was very helpful” (female, 15 years). However, some difficulties with understanding certain text-based aspects of the app were noted. In cycle 1, confusion associated with the question related to how much control an adolescent feels they have over their pain was noted. One participant noted, “When I use medicine and it takes away my pain, I feel like I have control. But when it comes back, that's when I don't [feel I can control my pain]. So I don't know [how to answer this question]” (female, 13 years). Three of the 4 adolescents in cycle 1 did not understand the meaning of the phrase “pharmacological pain management”, included as a selectable option in the pain management advice module of the app. To correct these misunderstandings, the wording of the ‘pain control’ question was changed to “How well do you think you were able to manage your pain since your last case?” and the descriptor for the pharmacological pain management modalities were set as “medicines to treat pain”. Following these revisions, no usability issues related to ease of understanding were uncovered in cycles 2 or 3.

Efficiency

The time to complete the pain assessment component of the app across all iterative cycles was 4.3 ± 3.5 minutes (M ± SD; range = 1.9 – 14.3 minutes), excluding the single adolescent that did not complete testing due to technical difficulties with the app. All participants except for 1 were able to complete the assessment in 6.4 minutes or less. The participant who required 14.3 minutes was very emotional during the testing process due to reasons unrelated to *Pain Squad+* use. This participant paused testing several times, but was keen to complete the assessment. Regarding the time required to complete the assessment and review pain management strategies plus allotted rewards, participants reported, “It was fine”
(female, 13 years) and "If I timed [the app notifications] for the right times [in my day], it would be ok" (male, 12 years).

**Acceptability**

Data related to *Pain Squad*+ acceptability were categorized as ‘likes’ and ‘dislikes’ related to the app design, content, navigation, utility, and customizability. All participants across the 3 cycles were satisfied with the *Pain Squad*+ app, with adolescents referring to app as a whole as “pretty neat” (male, 12 years) and “cool” (female, 17 years).

**Design and engagement enhancing features.** All adolescents across the testing cycles liked the design as well as the badge acquisition and point and leveling system of the app. Adolescents remarked that they found the app visually appealing, several times stating specifically that they liked the colour scheme. Adolescents also liked the use of the detective theme in the app: “It was cute how you have the whole rookie thing added to it. So at the same time as someone is trying to get rid of their pain, they're also enjoying themself” (female, 17 years). The videotaped acknowledgements of adherence to pain reporting were also an appreciated feature:

> I like that it had the little videos. It tells a story. Like telling [adolescents] that they are leveling up and stuff. I think that was cool. [The app] would stop what it was doing and like show me this video, and I was like, ‘Ok cool, I leveled up’. (male, 18 years)

Because no negative feedback about aesthetics was received during usability testing, no changes to the overall design or the gamification mechanics of the app were implemented.

**Content.** Participants provided generally positive feedback regarding the pain assessment and management content in the app. Participants particularly liked having multiple options to describe and manage their pain and the detail provided with regards to pain management advice:
It has so many options for [describing] the pain. Like they say, ‘How is it feeling?’ and they have so many options you can choose [affective elements and descriptors of pain]. You can choose so many of them instead of being like, ‘Oh it's this one’. (male, 13 years)

Yeah, I like them [pieces of pain management advice]. I liked when it gave step-by-step instructions on how to do it. Because just saying, ‘Relax’ doesn't help you relax.

(female, 16 years)

In cycle 2, 3 participants (50%) mentioned that the content of the different pain assessment questions seemed similar. For instance, an adolescent stated:

Well I thought some of the questions were just repetitive. I don't know…because it said, ‘from your last case how was your worst, average, least amount of pain’. It was asking the same thing but with a different wording. That's what I felt. (male, 16 years)

In response to this issue, 1 adolescent suggested: “Maybe you could put the words in different colours” (female, 15 years). To allow adolescents to clearly and quickly distinguish the meaning of the various pain assessment questions, key words were bolded and underlined. No further modifications to app content were required in cycle 3.

**Navigation.** Participants valued the ability to easily operate the Pain Squad+ app. This finding was apparent in cycle 1, when 1 adolescent (25%) stated:

I like how underneath the questions the app was asking, they gave a description of what they meant, so you didn't get confused or anything. So it said, ‘Tap here’ and told you when you could click multiple choices. That was a good idea. (female, 17 years)

The same participant also made a recommendation to streamline navigation through the app by minimizing the number of steps and time required to move from 1 app module to the next: “It kind of takes a few clicks to go back [out of the pain management section] though. If
someone’s in pain and they want advice, they’ll probably just want to get to it. They'll be impatient” (female, 17 years). This recommended change was made and no additional changes were needed in cycles 2 or 3.

**Utility.** Participants across all 3 cycles endorsed the utility of *Pain Squad*. The app was considered a useful adjuvant to the usual pain care adolescents with cancer received, especially because of its ability to provide real-time support. For instance, related to a question on perceived utility of the app an adolescent responded:

Yeah because it just gave you stuff you could do on the spot and advice you could do anywhere. When I was in pain, I was looking for everything to help it go away. Like I looked at everything. All night. I'd look at every website and I couldn't really find anything, so I feel like this would be really helpful. (female, 17 years)

Participants specifically noted the utility of the app as it pertained to providing access to pain management “at night or when someone wasn't around” (male, 18 years) as well as “at home…because I can't get advice from the nurses and stuff” (female, 16 years).

Adolescents in all cycles also stated that they would be likely to use the app daily for a sustained period of time because of its perceived value in guiding pain self-management. This finding is highlighted in the following quotation: “I think they’ll use it as long as they need it. If they’re in pain and they need something, pretty sure they'll go on it” (female, 17 years).

**Customizability.** Adolescents in all usability testing cycles described liking the ability to customize the app to their preferences. To do so, adolescents could select pieces of pain management advice that they enjoyed and thought were effective and these items were programmed by the app to be preferentially offered to adolescents on future pain reports.
**Study 2: Pilot Testing**

**Primary Outcome: Pain Squad+ Implementation Outcomes**

The primary research question for this study explored the ability to implement *Pain Squad+* in a future effectiveness trial as determined by: (a) percent participant accrual; (b) percent participant retention; (c) fidelity of the intervention; (d) percent outcome measures completion; (e) participant adherence to the intervention; and (e) intervention acceptability.

**Study accrual and retention.** In total, 130 adolescents with cancer were considered for study participation between April 6, 2015 and Jan 15, 2016. Eighty-six adolescents (66%) met the demographic and diagnosis-related criteria but, when asked, reported not experiencing pain greater than 3/10 in the preceding week and were thus excluded. Of the 44 eligible participants reporting pain, 11 (25%) refused to participate. The most common reasons for non-participation were not being interested in committing to the study (5, 45%) and considering caring for the study smartphone in addition to their own smartphone to be a hassle (3, 27%). Therefore, 33 adolescents were recruited into the pilot study over the ~9 month recruitment period and the percent accrual was 75%. Figure 5 shows participant flow through the entire study, pooled across both sites. Table 5 shows accrual and retention on a per site basis.

Regarding attrition, of the 33 adolescents with cancer recruited across 2 sites, 1 adolescent (3%) withdrew participation. This adolescent contacted the researcher 1 week after commencing the study to indicate that, although the idea of the *Pain Squad+* app was appealing, he worried about damaging the phone and was therefore withdrawing.

**Sample characteristics.** Adolescents ranged in age from 12 – 17 years (\(M = 14.0; \ SD = 1.6\)), and 13 (39%) were female. Adolescents were most commonly diagnosed with acute lymphoblastic leukemia (15; 45%). The frequencies, percentages, mean, and standard deviations for demographic and disease-related characteristics are shown in Table 6.
Figure 5. Adolescent Flow Through the Pain Squad+ Pilot Study.
Table 5. Participant accrual and retention across study sites

<table>
<thead>
<tr>
<th>Study site</th>
<th>Method</th>
<th>Period</th>
<th>Adolescents meeting demographic and diagnosis criteria, n</th>
<th>Adolescents self-reporting pain in previous week, n</th>
<th>Eligible adolescents recruited, n (%)</th>
<th>Adolescents withdrawing participation, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toronto (~350 new diagnoses each year)</td>
<td>Approached by a study team member</td>
<td>Apr 6, 2015 – Dec 30, 2015</td>
<td>117</td>
<td>41</td>
<td>31 (76)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Ottawa (~75 new diagnoses each year)</td>
<td>Approached by a study team member</td>
<td>Jun 8, 2015 – Jan 15, 2016</td>
<td>13</td>
<td>3</td>
<td>2 (67)</td>
<td>0</td>
</tr>
</tbody>
</table>
Table 6

*Characteristics of study participants*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age in years (SD)</td>
<td>14.0 (1.6)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>13 (39)</td>
</tr>
<tr>
<td>Male</td>
<td>20 (61)</td>
</tr>
<tr>
<td>Race/ethnicity, n (%)</td>
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</tr>
<tr>
<td>Aboriginal</td>
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</tr>
<tr>
<td>Arab/West Asian</td>
<td>1 (3)</td>
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<tr>
<td>Black</td>
<td>1 (3)</td>
</tr>
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<td>Filipino</td>
<td>3 (9)</td>
</tr>
<tr>
<td>Latin American</td>
<td>1 (3)</td>
</tr>
<tr>
<td>South Asian</td>
<td>8 (24)</td>
</tr>
<tr>
<td>South East Asian</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Trinidadian</td>
<td>1 (3)</td>
</tr>
<tr>
<td>White</td>
<td>10 (30)</td>
</tr>
<tr>
<td>Multiracial</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Cancer diagnosis, n (%)</td>
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</tr>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td>15 (45)</td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Colon</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Ewing sarcoma</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Germ cell</td>
<td>2 (6)</td>
</tr>
<tr>
<td>Langerhans cell histiocytosis</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Lung</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>7 (21)</td>
</tr>
<tr>
<td>Mixed-lineage leukemia</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Soft tissue sarcoma</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Mean duration of illness in years (SD)</td>
<td>1.7 (2.0)</td>
</tr>
<tr>
<td>Diagnosed with relapsed cancer, n (%)</td>
<td>9 (27)</td>
</tr>
<tr>
<td>Treatment modality, n (%)a</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>33 (100)</td>
</tr>
<tr>
<td>Radiation</td>
<td>6 (18)</td>
</tr>
<tr>
<td>Surgery</td>
<td>11 (33)</td>
</tr>
<tr>
<td>Stem cell transplant</td>
<td>4 (12)</td>
</tr>
</tbody>
</table>

* More than 1 response option possible per participant.
Most adolescents (29; 88%) owned a smartphone and used the device at least 4 times per day (28; 97%). Participants owning a smartphone most commonly used the device to text (26, 90%), listen to music (23, 79%), and use apps (23, 79%). Participants who owned a smartphone were either comfortable (2; 7%) or very comfortable (27; 93%) using the device. Details related to adolescent smartphone use are shown in Table 7.

Table 7. Smartphone-associated information for study participants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smartphone ownership, n (%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4 (12)</td>
</tr>
<tr>
<td>Yes</td>
<td>29 (88)</td>
</tr>
<tr>
<td>Times smartphone used per day, n (%)</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1 (3)</td>
</tr>
<tr>
<td>1-3 times</td>
<td>0</td>
</tr>
<tr>
<td>4-6 times</td>
<td>9 (31)</td>
</tr>
<tr>
<td>7-10 times</td>
<td>5 (17)</td>
</tr>
<tr>
<td>10 times</td>
<td>14 (48)</td>
</tr>
<tr>
<td>Purpose of smartphone use, n (%)</td>
<td></td>
</tr>
<tr>
<td>App use</td>
<td>23 (79)</td>
</tr>
<tr>
<td>Calling</td>
<td>12 (41)</td>
</tr>
<tr>
<td>Emailing</td>
<td>11 (38)</td>
</tr>
<tr>
<td>Game playing</td>
<td>17 (59)</td>
</tr>
<tr>
<td>Music listening</td>
<td>23 (79)</td>
</tr>
<tr>
<td>Texting</td>
<td>26 (90)</td>
</tr>
<tr>
<td>Comfort using smartphone, n (%)</td>
<td></td>
</tr>
<tr>
<td>Not at all</td>
<td>0</td>
</tr>
<tr>
<td>A little</td>
<td>0</td>
</tr>
<tr>
<td>Comfortable</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Very comfortable</td>
<td>27 (93)</td>
</tr>
</tbody>
</table>

a Percentages calculated using the 29 participants who reported owning a smartphone.
b More than 1 response option possible per participant.

Pain characteristics. A total of 1,172 pain reports (both scheduled morning or evening long-form and truncated ad hoc versions) were collected from the 33 study participants. Of these reports, 487 (42%) involved the adolescent self-reporting the occurrence of pain. Momentary current pain intensity was reported as mild (1.8 ± 2.7/10 [M ± SD/10]) on the Pain
Squad+ app. Thirty-one of the 32 participants who completed the study (97%) reported pain at least once during the 28-day Pain Squad+ testing period. Averaged over the period of data collection, pain interfered most with participant’s activities of daily living (2.0 ± 2.9/10) and had the least impact on schoolwork (0.3 ± 1.3/10). Table 8 shows details of the Pain Squad+ app entries where pain was reported as present (i.e., pain > 0). Under these circumstances, pain intensity (4.4 ± 2.6/10), unpleasantness (5.5 ± 2.2/10), and interference (4.0 ± 2.3/10) were moderate on average. Mean ‘worst’, ‘least’, and ‘average’ pain since the last pain report were 6.3 ± 2.1/10, 3.3 ± 1.7/10, and 4.8 ± 1.8/10, respectively.

**Pain management characteristics.** With regards to the intensity of the intervention in terms of pieces of pain management advice used, at least 1 pain management strategy was used in response to 28.3% (n = 138) of reports were adolescents experienced having pain. When treating pain, multiple pain management strategies were used, with a total of 1,070 strategies used over the course of the study. The modalities of pain management strategies used were: pharmacological (n = 456; 42.6%), psychological (n = 387; 36.2%), and physical (n = 227; 21.2%). On average, participants perceived themselves to have a moderate capacity to control experienced pain (6.4 ± 2.2/10).

Table 8

*Momentary pain characteristics of adolescents with cancer when experiencing pain*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean pain intensity (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current pain (range: 0 – 10)</td>
<td>4.4 (2.6)</td>
</tr>
<tr>
<td>Worst pain since last report (range: 0 – 10)</td>
<td>6.0 (2.5)</td>
</tr>
<tr>
<td>Least pain since last report (range: 0 – 10)</td>
<td>2.9 (2.0)</td>
</tr>
<tr>
<td>Average pain since last report (range: 0 – 10)</td>
<td>4.6 (2.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pain duration n (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Just a few minutes</td>
<td>50 (21.8)</td>
</tr>
<tr>
<td>About an hour</td>
<td>38 (16.6)</td>
</tr>
<tr>
<td>1 – 3 hours</td>
<td>90 (39.3)</td>
</tr>
</tbody>
</table>
4 – 6 hours 24 (10.5)
7 – 9 hours 20 (8.7)
10 – 12 hours 7 (3.1)

Cause of pain, n (%)\textsuperscript{a}
\begin{itemize}
  \item Disease 58 (18.1)
  \item Chemotherapy, surgery, radiation 101 (31.6)
  \item Medical procedures 49 (15.3)
  \item Other medical conditions 60 (18.8)
  \item Everyday pain 52 (16.3)
\end{itemize}

Mean pain unpleasantness (SD) 5.5 (2.2)

Mean pain interference (SD)
\begin{itemize}
  \item Sleep 3.8 (2.9)
  \item Daily activities 4.7 (2.7)
  \item Emotions 5.0 (2.4)
  \item Walking 4.3 (2.9)
  \item Relationships 2.3 (2.0)
  \item School 1.7 (2.6)
  \item Enjoying life 4.7 (2.6)
  \item Summary score 4.0 (2.3)
\end{itemize}

Mean control over pain (SD) 6.4 (2.2)

\textsuperscript{a} More than one response per pain report possible.

Note. Values pertain to those collected from both scheduled long-form and truncated ad hoc reports.

\textbf{Intervention fidelity.} Technical malfunctioning of the app, either due to \textit{Pain Squad+} software, hardware, or server issues, occurred for 6 participants (18\%). Specific technical problems were: (a) hospital server maintenance resulting in a participant being logged out of app (n = 1); (b) hospital server not sending notifications to participants to complete pain assessments (n = 4); and (c) participant receiving treatment out-of-country without a cellular data roaming option (n = 1). These issues were uncovered by contacting the participant regarding decreased compliance (first and third issue) or being alerted to server malfunction by the hospital information technology team (second issue). Contacting the adolescent and providing instruction on logging into the app easily resolved the first issue. Contacting the
adolescents and asking that they set the internal alarm on their phone as a reminder to complete scheduled pain assessments resolved the second issue. The third issue could not be resolved.

Regarding interaction between the study nurse and participants, the nurse received a total of 49 incoming email alerts regarding sustained pain from 13 participants. Therefore, 4% of all participant reports generated an email alert to the nurse. The number of alerts from a single adolescent ranged from 0 – 17 (M = 1.4; SD = 3.3).

The nurse successfully contacted adolescents who triggered email alerts 28 times (contact in response to 57% of incoming alerts) with a mean time to contact of 62.5 hours (SD = 55.5; range: 0.2 – 186.3). Most of the contacts reinforced adolescents’ current symptom management strategies, including adherence to prescribed medications, or provided education. Regarding the ability to meet the a priori criterion for implementation success, the number of contacts with an adolescent within 12 hours of an alert being received was 10 (20%). The a priori criterion was set at >80% of contact within 12 hours and therefore was not achieved. The primary reason for the length of time to contact was adolescents not answering repeated telephone calls or emails, often due to adolescents not having their study phone in close proximity.

The nurse contacted the participants’ primary care team 4 times in response to pain-related alerts. Reasons to not contact the care team were: (a) adolescent being admitted and under in-patient medical care; (b) adolescent satisfied with current pain care regime and declined offer to contact team; and (c) adolescent having no pain at the time of telephone or email contact. Overall, the nurse found the process of receiving alerts and initiating contact with participants or their primary care team to be manageable and not overly onerous.

**Outcome measure assessment piloting.** Each participant who completed the intervention, including those who were considered loss to follow-up post-study, answered an
average of 94.9% (SD = 4.3; range = 86.5 – 100) of the 74 baseline and 84.3% (SD = 31.0; range = 0 – 100) of the 82 post-study measure outcome questions. Outcome measure assessment questions most frequently omitted by participants were those related to functioning at school and school attendance. Four participants (13%) did not complete any post-study measures. Reasons for non-completion of measures were: loss to follow-up (n = 2), acute illness (n = 1), and receiving out-of-country treatment without Internet access (n = 1).

**Adherence.** Participants who completed the 28-day study protocol without experiencing technical problems interacted with *Pain Squad*+ (i.e., completed at least 1 pain report) for an average of 27.1 days (SD = 6.3 days). Although asked to complete pain assessments and recommended pain management advice for 28 days, the range of days of app interaction was 14.6 – 43.2 days. Fifteen (45%) participants completed more than the requested amount of days of app interaction. Overall adherence to twice-daily pain assessment completion for adolescents who did not experience technical problems was 69.4 ± 40.1%. Adherence decreased over time in the study with adherence to pain assessments in week 1 (77.2 ± 51.2%) being greater than that observed in week 2 (61.8 ± 46.0%), week 3 (67.0 ± 58.0%), or week 4 (38.5 ± 39.4%).

**Acceptability.** Table 9 presents adolescent acceptability scores as they relate to the *Pain Squad*+ app. Scores showed use of *Pain Squad*+ to be overall satisfactory to adolescents, with a total mean AES score of 24.1 (SD = 3.3) out of a possible 30 points. All items achieved a mean score of greater than 3, indicating acceptability on the scale item. Highly acceptable items, those achieving a mean score of 4 or greater, included those related to *Pain Squad*+ ease of use (M = 4.7; SD = 0.6), ease of understanding (M = 4.4; SD = 0.7), helpfulness of *Pain Squad*+ in describing pain (M = 4.0; SD = 0.8), and overall satisfaction with the intervention (M = 4.0; SD = 0.7). Items rated as acceptable but not highly acceptable were those related to
enjoyment in using *Pain Squad*+ (M = 3.2; SD = 1.0), the time associated with using the app (M = 3.9; SD = 1.0), and the investigator-developed item concerning the helpfulness of *Pain Squad*+ in treating pain (M = 3.2; SD = 1.0).

Table 9

*Summary of acceptability scores for Pain Squad*+

<table>
<thead>
<tr>
<th>Item</th>
<th>Possible response range</th>
<th>n</th>
<th>Actual response range</th>
<th>M  (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptability E-Scale (AES)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How easy was <em>Pain Squad</em>+ for you to use?</td>
<td>1 – 5</td>
<td>29</td>
<td>3 – 5</td>
<td>4.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.6)</td>
</tr>
<tr>
<td>How understandable were the questions?</td>
<td>1 – 5</td>
<td>29</td>
<td>3 – 5</td>
<td>4.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.7)</td>
</tr>
<tr>
<td>How much did you enjoy using <em>Pain Squad</em>+?</td>
<td>1 – 5</td>
<td>29</td>
<td>1 – 5</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(1.0)</td>
</tr>
<tr>
<td>How helpful was <em>Pain Squad</em>+ in describing your pain?</td>
<td>1 – 5</td>
<td>29</td>
<td>2 – 5</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.8)</td>
</tr>
<tr>
<td>Was the amount of time it took to complete <em>Pain Squad</em>+ acceptable?</td>
<td>1 – 5</td>
<td>29</td>
<td>1 – 5</td>
<td>3.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(1.0)</td>
</tr>
<tr>
<td>How would you rate your overall satisfaction with <em>Pain Squad</em>+?</td>
<td>1 – 5</td>
<td>28</td>
<td>2 – 5</td>
<td>4.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.7)</td>
</tr>
<tr>
<td><strong>Summary score</strong></td>
<td>6 – 30</td>
<td>28</td>
<td>12 – 29</td>
<td>24.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(3.3)</td>
</tr>
<tr>
<td>Additional investigator-developed item</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>How helpful was <em>Pain Squad</em>+ in treating your pain?</td>
<td>1 – 5</td>
<td>29</td>
<td>1 – 5</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(1.0)</td>
</tr>
</tbody>
</table>

**Qualitative Examination of Adolescent Perceptions of Pain Squad**+

Most study participants (n = 30; 91%) agreed in advance to participate in telephone-based post-study qualitative interviews. A strategic selection was made among these participants using the purposive technique to cover as broad a range of intervention and study perspectives as possible. In particular, both male and female adolescent who varied in age and gender were selected. Variance in AES ratings of *Pain Squad*+, adolescent adherence to the pain reporting, and health outcome change scores was also achieved. In total, 20 adolescents
drawn from the pool of all Study 2 participants were interviewed. Adolescents who were interviewed ranged in age from 12 – 17 years (M =14.4; SD =1.6), and 9 (45%) were female. Adolescents were most commonly diagnosed with acute lymphoblastic leukemia (7; 35%) and lymphoma (5; 25%). Nineteen (95%) adolescents who were interviewed completed the entire study and 1 (5%) withdrew participation after completing 5 days of the intervention. Table 10 presents the demographic and disease-related data of the adolescents who were interviewed, quantitatively reported Pain Squad+ acceptability (AES score), interaction with the Pain Squad+ system, and change scores (from baseline to post-study) on health-related study outcome measures. Interview length ranged from 7 to 20 minutes (M = 11; SD = 3). Interview data were categorized into 5 main themes: acceptability of the intervention, potential active ingredients of the intervention, suitability of the intervention, recommendations for improvement, and acceptability of the study. Each theme was comprised of several categories and codes as shown in Table 11.

Acceptability of the intervention.

**General impressions.** All adolescents who were interviewed enjoyed using the Pain Squad+ app. These adolescents were pleased with the app stating that is was “fun” (female, 12 years), “really neat” (female, 15 years), engaging, and perceived as useful. As stated by 1 participant in particular:

It’s really appealing to the eye. The colour, theme is good. The font. And it’s not really that hard to understand. The vocabulary is really straightforward and all of the things on it, like you know, the multiple-choice questions and the [visual analogue scale] sliders are really easy to use. And for cons? Don’t really think I can really think of any. (male, 16 years)
Table 10 Characteristics of interviewed Pain Squad+ participants

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Sex</th>
<th>Cancer diagnosis</th>
<th>AES score</th>
<th>Adherence (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Change scores</th>
<th>Scale range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BPI</td>
<td>PROMIS PPI-SF</td>
</tr>
<tr>
<td>15</td>
<td>F</td>
<td>ALL</td>
<td>22</td>
<td>28.5</td>
<td>0.3</td>
<td>-0.1</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>ALL</td>
<td>23</td>
<td>83.9</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>Ovarian</td>
<td>23</td>
<td>108.9</td>
<td>-1</td>
<td>-2.2</td>
</tr>
<tr>
<td>13</td>
<td>M</td>
<td>LCH</td>
<td>missing</td>
<td>withdrew</td>
<td>missing</td>
<td>missing</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>ALL</td>
<td>24</td>
<td>58.9</td>
<td>4.5</td>
<td>13.6</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>Colon</td>
<td>27</td>
<td>37.5</td>
<td>0.8</td>
<td>31.4</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>Lymphoma</td>
<td>29</td>
<td>71.4</td>
<td>1</td>
<td>6.3</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>Lymphoma</td>
<td>25</td>
<td>92.9</td>
<td>-1.5</td>
<td>-4.9</td>
</tr>
<tr>
<td>12</td>
<td>M</td>
<td>ALL</td>
<td>28</td>
<td>51.8</td>
<td>1.5</td>
<td>2.1</td>
</tr>
<tr>
<td>16</td>
<td>F</td>
<td>AML</td>
<td>25</td>
<td>155.3</td>
<td>-1.5</td>
<td>6.4</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>ALL</td>
<td>24</td>
<td>83.9</td>
<td>0.5</td>
<td>18.5</td>
</tr>
<tr>
<td>15</td>
<td>M</td>
<td>Lung</td>
<td>23</td>
<td>180.4</td>
<td>3.3</td>
<td>10.0</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>ALL</td>
<td>21</td>
<td>42.9</td>
<td>2.5</td>
<td>28.5</td>
</tr>
<tr>
<td>14</td>
<td>M</td>
<td>Lymphoma</td>
<td>24</td>
<td>58.9</td>
<td>1.8</td>
<td>4.1</td>
</tr>
<tr>
<td>14</td>
<td>F</td>
<td>Ewing sarcoma</td>
<td>25</td>
<td>21.4</td>
<td>1.8</td>
<td>42.7</td>
</tr>
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<td>13</td>
<td>F</td>
<td>Colon</td>
<td>28</td>
<td>135.7</td>
<td>-0.5</td>
<td>-2.0</td>
</tr>
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<td>missing</td>
<td>missing</td>
<td>missing</td>
</tr>
<tr>
<td>16</td>
<td>M</td>
<td>Germ cell tumor</td>
<td>missing</td>
<td>missing</td>
<td>16.6</td>
<td>1.8</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>ALL</td>
<td>26</td>
<td>60.7</td>
<td>0.5</td>
<td>-19.5</td>
</tr>
<tr>
<td>17</td>
<td>M</td>
<td>Lymphoma</td>
<td>22</td>
<td>67.9</td>
<td>3.3</td>
<td>26.4</td>
</tr>
</tbody>
</table>

<sup>a</sup> Percent of requested reports completed. Notes. AES = Acceptability E-Scale. ALL = Acute lymphoblastic leukemia. AML = Acute myeloid leukemia. BPI = Brief Pain Inventory. LCH = Langerhans cell histiocytosis. PedsQL 4.0 = Pediatric Quality of Life Inventory 4.0. PROMIS PPI-SF = Patient Reported Outcomes Measurement Information System Pediatric Pain Interference Scale Short Form.
### Table 11

**Post-study interview themes, categories, and codes**

<table>
<thead>
<tr>
<th>Theme</th>
<th>Category</th>
<th>Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceptability of the intervention</td>
<td>General impressions</td>
<td>Enjoyed use</td>
</tr>
<tr>
<td></td>
<td>Usability</td>
<td>Easy to use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Easy to understand</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Quick to complete</td>
</tr>
<tr>
<td></td>
<td>Specifically endorsed interventions elements</td>
<td>Self-care advice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Thorough assessment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Design and gamification mechanics</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Real-time any-environment reporting</td>
</tr>
<tr>
<td></td>
<td>Challenges</td>
<td>Providing specific pain ratings</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Number of assessment questions</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Notifications</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other technical problems</td>
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<tr>
<td>Potential active ingredients of the intervention</td>
<td>Self-management support</td>
<td>Engagement in self-care</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Self-monitoring of pain</td>
</tr>
<tr>
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<td></td>
<td>Patient-provider communication</td>
</tr>
<tr>
<td></td>
<td>Study nurse support</td>
<td>Value of nurse</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Timing of nurse support</td>
</tr>
<tr>
<td>Suitability of the intervention</td>
<td>Impact on daily activities</td>
<td>Perceived burden</td>
</tr>
<tr>
<td></td>
<td>Recommended usage</td>
<td>Appropriateness when ill</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Appropriateness when symptom-free</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Recommended usage</td>
</tr>
<tr>
<td>Recommendations for improvement</td>
<td>Recommended improvements</td>
<td>Additional self-care advice</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Additional gamified mechanics</td>
</tr>
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<td></td>
<td>Tutorials on use</td>
</tr>
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<td></td>
<td>Audio-visual assets</td>
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<td></td>
<td>Review data</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Self-scheduling notifications</td>
</tr>
<tr>
<td>Acceptability of the study</td>
<td>General impressions and specific likes</td>
<td>General impression</td>
</tr>
<tr>
<td></td>
<td>Motivation for participation</td>
<td>Specific likes</td>
</tr>
<tr>
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<td>Altruism</td>
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<tr>
<td></td>
<td>Challenges</td>
<td>Novel experience</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gamification</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Outcome measure assessments</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Study phone</td>
</tr>
</tbody>
</table>
**Usability.** Every adolescent endorsed the ease of use of *Pain Squad+.* Specifically, the app’s level of complexity was considered appropriate for the targeted age group: “It was really easy. It was very straightforward. It wasn’t really complicated. It was just like simplified so it was easy to use for little kids” (male, 16 years). One adolescent specifically reported that because she was familiar with smartphone-based apps, use of *Pain Squad+* was not problematic: “I’m used to that stuff so it made it easy” (female, 16 years).

The content of *Pain Squad+*, both the pain assessment questions and pain management advice, was reported as simple to comprehend. Thirteen participants in total discussed ease of understanding related to *Pain Squad+.* For instance, “It was really straightforward. I think all the questions were worded well so you could like understand what they were getting at” (female, 16 years). Two participants also endorsed the app as efficient to complete: “It was good because it was really fast and easy” (male, 14 years).

**Specifically endorsed interventions elements.** Specific elements of the *Pain Squad+* app that were cited as well-liked or helpful to adolescents were: self-care advice provided by the app in response to pain reports; the option to provide thorough pain assessment data; the app’s design and gamification mechanics (endorsed by all participants); and the ability to use the app in real-time and in any environment, especially when at home. One participant endorsed the app’s provision of self-care advice with detailed instruction:

I thought the pain help ideas were really awesome. When they suggested like different things that you could do? Those were really helpful. And they had some [pieces of pain management advice] where they would suggest like relaxation and breathing, and how do I do that. And then you click on it and there is someone talking to you, walking you through it. Like how to relax. So that’s helpful because someone can tell you to relax, but you can just be sitting there like, ‘I don’t know how’. (female, 16 years)
Referring to the ability of the app to provide pain management advice at any time and in any environment, 2 adolescents said: “I think overall it was good. Probably one of my favourite parts of it was that you could do the 8 questions in the middle [truncated ad hoc pain survey]. That helps a lot” (female, 12 years) and “There was stuff you could try at home and like do yourself. So I liked that.” (female, 15 years)

**Challenges.** Despite being generally satisfied with *Pain Squad*+, 16 adolescents cited challenges they experienced with the app. Two participants reported an issue related to rating pain specifically on the visual analog ‘slider’ scales as the app does not currently display a number corresponding to pain ratings between 0 and 10 made by an adolescent. Twelve participants stated that the scheduled long-form morning and evening pain assessments included too many questions: “It was okay and too much. Because sometimes people don’t want to like keep…um…doing the same thing over again…21 questions every time” (male, 16 years).

Nine adolescents cited challenges related to the frequency and timing of pain assessment notifications. The notification issue appeared to be related to a technical problem with the application software server where repeated notifications to complete the same pain assessment questionnaire were sent to study phones, which was “annoying” (female, 17 years) for adolescents:

Even if I did do my case [pain assessment], it would still just keep on giving notifications. And I know that after you say, ‘yes’ to the case, [the app will] follow-up [on the severity of pain 1 hour later]. But even if I would do the follow-ups, it would just keep on giving more and more [notifications]. (female, 15 years).

Technical problems experienced by adolescents were cited as a final challenge. One adolescent described an issue likely related to the app being unable to connect to the Internet:
“Sometimes it was hard for me to do it. Like 2 or 3 times I couldn’t [use the app], because like as soon as I clicked on the app the screen would just go white” (male, 14 years). Two adolescents reported an issue where scheduled reminders to complete pain assessments were not being received:

I think it was a problem with my version [of the app] but I wasn’t getting any reminders [to complete pain assessments]…So I set up just a regular alarm in the clock the phone has itself. (male, 17 years)

**Potential active ingredients of the intervention.**

**Self-management support.** The ability of *Pain Squad+* to support pain self-management was reported as being of therapeutic benefit to all participants. Aspects of the app supporting self-management included the capacity of *Pain Squad+* to support an adolescent’s ability to engage in self-care. This capacity is highlighted in the following quote:

Yeah because being like an out-patient, you’re not at the hospital all the time. And you don’t want to call the doctor every time you have something as simple as a stomachache, when you know you got tips from the app to help. (female, 14 years)

Adolescents commonly cited the capacity of the app to enable them to self-monitor pain as a valuable self-management attribute: “Yeah especially because it really helps me to track my pain and remember everything.” (male, 14 years). Improved awareness of pain was also a perceived benefit of the app: “Some of the questions were things that I didn’t really consider when I was thinking about my pain. So [*Pain Squad+] helped with [recognizing how pain] affected me and all that.” (female, 16 years). *Pain Squad+* was also cited as helping to facilitate adolescents’ communication about pain and pain control with their medical team. One adolescent highlighted this finding by saying: “I think when I had a problem at home, like
experiencing some kind of pain, after inputting it into the app and coming back to the hospital, talking to my doctor was easier.” (male, 17 years).

**Study nurse support.** Ten participants discussed interaction with the Pain Squad+ study nurse as being of potential therapeutic benefit. Both, adolescents who interacted with the study nurse and those who did not, appreciated the nurse as a feature of the app. In particular, these adolescents viewed healthcare professional involvement in Pain Squad+ as an extra layer of pain management support in the event that self-care strategies were ineffective:

I liked that when you answer questions, if you go higher [in terms of pain rating], a nurse actually calls you and like asks about your pain. It’s actually a good thing because like if you actually have pain and you don’t know what to do, she can help you. (male, 15 years)

Despite this finding, 3 adolescents reported that they did not believe nurse involvement was essential to the Pain Squad+ intervention and the recommended self-care strategies were sufficient to support pain care: “I had it pretty controlled on my own.” (female, 16 years). One adolescent commented that he experienced some difficulty in connecting with the nurse when she attempted contact him:

The part where you get the advice from the nurse was good but then sometimes I would just miss her, if I was out or my phone was on silent. So it might be better if she left you a [text] message so that you could check what she was telling you to do. (male, 14 years)

**Suitability of the intervention.**

**Impact on daily activities.** Seven participants commented that use of the app fit well with their usual daily activities. For example, 1 adolescent commented, “Oh it was good, it was good. It didn’t really take that much time and effort” (female, 17 years). Six participants
commented that the number of notifications the app sent to remind adolescents to complete pain reports was obtrusive.

**Recommended usage.** Nine participants stated that use of the app when not experiencing pain was not appropriate. Related to this notion, 1 adolescent said: “Yeah, I didn’t really have pain all of the time. So I think [the number of notifications] just wasn’t for me, but I’m sure for someone who’s going through pain it’s going to be really helpful” (male, 16 years). Another adolescent, when asked about his lack of interaction with *Pain Squad*+ said: “Like it got a little tiring sometimes. Because especially there’s days I didn’t feel any problems, like have any problems, and I felt less inclined to actually finish the surveys” (male, 17 years).

**Recommendations for improvement.**

After using the *Pain Squad*+ intervention longitudinally, participants made a number of recommendations to improve the app. Six adolescents suggested that the app include additional pieces of self-care advice that they could use (e.g., “I think if there were more ways to help you manage your pain added on, then it would be more helpful.” [male, 14 years]). When probed however, adolescents did not have any specific suggestions for additional pieces of advice that could be included. Supporting adolescent’s comments regarding the acceptability of the gamification mechanics of the app, 4 participants recommended enhancements to this aspect of the app. One adolescent stated: “Um, maybe like something a little more than just like how you ‘level up’ [by completing pain assessments and management advice]. Just…more to do with that. A little more interactive kind of thing…like even more fun.” (female, 14 years).

Three participants recommended adding tutorials to *Pain Squad*+ on how to use the pain management and gamification mechanics of the app. Another 2 adolescents recommended
converting text-based information on how to manage pain into an audio- or video-recorded format. For example:

Umm I think probably like uh a few videos from actual professionals, healthcare professionals, like doctors. Or like maybe like, err therapists, like massage therapists. If there was like maybe, for example like a massage therapist showing someone how to relieve pain in a certain area. (male, 14 years)

Finally, 1 adolescent made the recommendations to allow more flexibility in self-scheduling the timing of notifications to complete pain assessments and 3 adolescents suggested incorporating a capacity to review previously logged pain reports in order to track pain management progress.

Acceptability of the study.

General impressions and specific likes. Overall, adolescents with cancer enjoyed participating in the pilot stating that the study was “really good” (male, 15 years) and they “didn’t mind” (female, 14 years) participating. Specifically endorsed elements of the study included: the ease of participation and the ability to use the intervention for a time:

And I don’t know, I really liked…I just liked the app. I liked being able to record my pain, like without just writing it down in like a journal or something you know? I really liked how they gave me suggestions for like what I could do. I just liked it all, overall. (female, 16 years)

Two adolescents specifically cited completion of the outcome measures as a well-liked component of the study, with 1 participant stating: “I liked the questionnaires at the beginning and the end. Just to like compare sort of how you’re doing before and after.” (female, 15 years)
Motivation for participation. With respect to adolescents’ motivation for participation in the study in general, reasons included altruism, the chance to engage in a new experience, and the general gamification of the app. Two participants discussed the chance to potentially help other adolescents with cancer as their rationale for study involvement (e.g., “I just liked, you know, contributing to the development of this app. It will be a huge help to other little kids going through cancer.” [female, 16 years]). Another adolescent mentioned the novel experience of being a research participant as her motivation for participation. Last, 6 participants stated that they maintained engagement with the intervention over the course of the study because of the gamification mechanics (e.g., point and levelling system) embedded in the app. For instance: “Yeah but it was pretty cool. It made you sort of want to do it more. ‘Okay I’ve got to do this because I want to get the next level’” (female, 16 years).

Challenges. The use of the study phone loaned to participants was a challenge for 5 of the 20 adolescents who were interviewed. Having already owned a smartphone, care and use of a second phone was considered a study burden:

Half the time, I wouldn’t even hear it because it would be in a different room or something and I just totally forget about it. If [Pain Squad+] was on my actual cell phone I probably would have done it more. But it wasn’t on my actual phone that I have on me all the time. (female, 14 years)

Four participants also stated that the outcome measure questionnaires sometimes seemed repetitive or could be slightly reduced: “I think maybe reduce the questions a little bit, but not too much. But yeah they were okay.” (male, 14 years).

Secondary Outcome: Pain Squad+ Effectiveness Outcomes

The secondary research question explored the effect of the Pain Squad+ real-time pain management app on pain intensity, pain interference, health-related quality of life, and self-
efficacy after 28 days of use, compared to pre-intervention scores on each variable in adolescents with cancer. Table 12 shows the mean and SD of scores for pain intensity, pain interference, health-related quality of life, and self-efficacy at baseline and post-study, the change in scores between the 2 time points, the test statistics and \( p \)-values for exploratory inferential testing, and the Cohen’s \( d \) effect sizes across each outcome.
Table 12

Changes in adolescent health-related outcomes from baseline to post-study

| Dependent variable (possible response range) | Baseline | | | Post-study | | | | Change score | p | Cohen’s d |
| | n | M (SD) | Range | n | M (SD) | Range | M (SD) | | |
| Pain intensity (BPI; 0 – 10) | | | | | | | | | | |
| Worst pain preceding week | 33 | 7.00 (2.24) | 2 – 10 | 28 | 5.21 (3.86) | 0 – 10 | -1.79 (3.78) | 0.019 | 0.47 |
| Least pain preceding week | 33 | 1.39 (1.81) | 0 – 7 | 28 | 0.68 (1.19) | 0 – 5 | -0.71 (1.41) | 0.012 | 0.51 |
| Average pain preceding week | 33 | 3.86 (2.16) | 1 – 10 | 28 | 2.54 (2.15) | 0 – 7 | -1.32 (2.21) | 0.004 | 0.60 |
| Current pain | 33 | 2.21 (2.28) | 0 – 4 | 28 | 1.61 (2.36) | 0 – 9 | -0.61 (2.99) | 0.290 | 0.20 |
| Summary score | 33 | 3.62 (1.49) | 1 – 8 | 28 | 2.51 (1.91) | 0 – 7 | -1.11 (1.60) | 0.001 | 0.69 |
| Pain interference (PROMIS PPI-SF; 34 – 78) | | | | | | | | | | |
| Pain interference | 33 | 58.78 (9.85) | 34 – 78 | 27 | 54.41 (12.73) | 34 – 73 | -4.37 (12.58) | 0.083 | 0.35 |
Table 12 (Continued)

Changes in adolescent health-related outcomes from baseline to post-study

<table>
<thead>
<tr>
<th>Dependent variable (possible response range)</th>
<th>Baseline</th>
<th>Post-study</th>
<th>Change score</th>
<th>p</th>
<th>Cohen’s d</th>
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<td>M (SD)</td>
<td>Range</td>
<td>n</td>
<td>M (SD)</td>
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<td>10 – 100</td>
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<td>Summary score</td>
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<td>1 – 5</td>
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<td></td>
<td>(1.42)</td>
<td></td>
<td></td>
<td>(1.24)</td>
</tr>
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</table>

a researcher-developed tool.

Notes. BPI = Brief Pain Inventory. PROMIS PPI-SF = Patient Reported Outcomes Measurement Information System Pediatric Pain Interference Scale Short Form. PedsQL 4.0 = Pediatric Quality of Life Inventory 4.0. GSE-Sherer Scale = General Self-Efficacy – Sherer Scale.
**Pain intensity.** The mean change in summary score for pain intensity measured using the BPI was -1.11/10 (SD = 1.60) indicating that pain decreased over the course of *Pain Squad*+ use. Change scores for each of the scale items showed ‘worst’, ‘least’, and ‘average’ pain in the preceding week, as well as BPI-rated current pain intensity, to improve overtime. The largest and smallest mean improvement scores in pain intensity related to worst pain in the preceding week and current pain and were -1.79/10 (SD = 3.78) and -0.61/10 (SD = 2.99) respectively. With the exception of current pain ($p = 0.29$), these differences corresponded to statistically significant changes in each pain intensity item (all $p$-values $\leq 0.019$). Within-group effect sizes for each item and the summary score were small to moderate (0.20 – 0.69).

**Pain interference.** On average, participants reported less pain interference post-intervention as compared to baseline when assessed using the PROMIS PPI-SF. The mean change score across participants was from baseline to post-study approached but did not represent a significant improvement in pain interference ($p = 0.083$). The magnitude of the relationship was small with the effect size calculated as 0.35.

**Health-related quality of life.** In general, adolescent HRQL improved over the course of the study. Total scale scores on the PedsQL 4.0 improved from 53.99 (SD = 19.05) at baseline to 61.19 (SD = 17.16) at post-study, which represented a statistically significant improvement in adolescent HRQL ($p = 0.032$). Although the scale scores were indicative of impaired HRQL at baseline, at post-study, scores had improved such that adolescents could be considered no longer ‘at risk’ for HRQL impairment. The effect size for the mean difference was small (0.43). Regarding the PedsQL 4.0 subscales, significant improvements over the course of the study were observed for social functioning ($p = 0.031$) and emotional functioning ($p = 0.003$). The effect sizes for these variables were small to moderate in nature (social functioning = 0.43; emotional functioning = 0.61). The change in the physical functioning
subscale was not statistically significant ($p = 0.120$), but mean outcome scores increased from baseline to post-study ($M = 7.68; SD = 25.08$). A small effect size of 0.31 was observed for the physical functioning subscale. Conversely, scores on the school functioning subscale decreased over the time of the *Pain Squad*+ study ($M = -7.50; SD = 17.95$). The finding was not statistically significant ($p = 0.140$) and the magnitude of the effect on school functioning was small (0.42).

**Self-efficacy.** A statistically significant difference in self-efficacy measured with the GSE-Sherer Scale was not seen ($p = 0.950$) and the effect size for the mean difference was negligible (0.01). With regard to the investigator-developed self-efficacy in pain care question, the mean change score from baseline to post-study was 0.36 on a 1- to 5-point Likert scale (SD = 1.20). The difference in scores across the 2 time points was not significant ($p = 0.296$). However, the within-group baseline to post-study effect size for the self-efficacy in pain care was larger than obtained for the GSE-Sherer Scale (i.e., effect size of 0.27).
CHAPTER SIX: DISCUSSION

Study 1: Usability Testing

Discussion of Findings

This study explored the usability issues and perceptions of adolescents with cancer as they pertained to the Pain Squad+ real-time smartphone-based pain management app. Whereas many pain management apps are currently available (Lalloo et al., 2015), an app that provides adolescents with cancer with comprehensive, expert-vetted and age-appropriate pain self-management advice has not been developed to date (Jibb et al., 2014). Formal evaluation of the usability of the prototype Pain Squad+ app for adolescents with cancer allowed for identification of software malfunction, interface design flaws (i.e., responsiveness of interactive elements, burdensome number of ‘clicks’ required to navigate app), and confusing text (i.e., meaning of the concepts ‘control over pain’ and ‘pharmacological pain management’). Additionally, the refinement of the app in a user-centered manner provided evidence that Pain Squad+ is easy to use and understand, efficient, and acceptable to adolescents, including in terms of its design, content, and utility. Both positive and negative feedback from study participants regarding the design, content, organization, and utility of the app also provide insight into app function and interface principles that may be transferable to the development of other real-time self-management interventions, especially those that target the adolescent developmental stage.

Over the course of 3 usability-testing cycles, the Pain Squad+ app was refined for both ease of use and ease of understanding. All adolescent participants were either ‘comfortable’ or ‘very comfortable’ using a device and 81% owned their own smartphone. These observations are reflective of much larger national reports showing that 75% of adolescents have or have access to a smartphone (Lenhart, 2015). It might be expected then that ease of use issues,
particularly those related to using basic app functions such as clicking and swiping, would be minimal. Indeed, adolescents in this study intuitively understood how to launch and use *Pain Squad*+.

Ease of use was negatively impacted by software malfunction (i.e., app ‘crashing’) in the first cycle of testing. The malfunction prevented adolescents from adequately completing the ‘think-aloud’ usability task assigned and therefore testing was halted after 4 participants. Software malfunction is a leading reason for wasted time and user frustration with various electronic systems and results in decreased user engagement (Ceaparu, Lazar, Bessiere, Robinson, & Ben Shneiderman, 2010). Poor responsiveness of interactive app elements also inhibited ease of use and is a known factor associated with decreased mHealth user engagement and associated meaningful behaviour change (Danaher, Brendryen, Seeley, Tyler, & Woolley, 2015). Rectifying these issues refined the app such that it was considered sufficiently easy for adolescents with cancer.

Issues negatively impacting ease of understanding related to the adolescents’ inability to comprehend the text content of the app. Similar issues have been demonstrated in previous usability testing studies focused on this age group (Murphy, Sawczyn, & Quinn, 2012; Stinson et al., 2006b). In all instances of poor understandability, including those identified in this study, revising the text to be simpler succeeded in improving the readability by the intended audience. Regarding the objective evaluation of the efficiency of *Pain Squad*+, the app was quick to complete. In addition, subjective reports from adolescents regarding the time required to use the app indicated that this was considered satisfactory. This finding further supported the usability of *Pain Squad*+ as the ability for end-users to use a technology in a timely matter is considered a cornerstone of good app development (W. Brown, Yen, Rojas, & Schnall, 2013).
In general, Pain Squad+ was considered acceptable to adolescents with cancer. This favourable result agrees with other studies that evaluated the acceptability of electronic symptom assessment and management apps for adolescents with cancer. These studies have demonstrated that pediatric oncology patients aged 9 to 21 years and diagnosed with a variety of disease types found the use of such apps to be satisfactory (Baggott et al., 2012b; Macpherson et al., 2014; Rodgers, Krance, Street, & Hockenberry, 2013; Stinson, Jibb, et al., 2015a; Tomlinson et al., 2014). Together, this research suggests that mHealth applications represent a viable means to support cancer symptom assessment and management by adolescents during cancer therapy.

In particular, adolescents resoundingly endorsed the Pain Squad+ app design. Published literature has also shown adolescents to like mHealth and other Internet-based interventions that include colourful, age-appropriate graphics and videos (Schneider et al., 2015; Stinson, Gupta, et al., 2015b). It may be important to consider the use of these design elements when developing mHealth apps for this age group as these elements are expected to improve intervention engagement (Danaher et al., 2015).

The content included in the app was well endorsed by adolescents. Adolescents specifically liked having multiple options to use in describing and managing their pain, and detailed information on how to implement management interventions. Studies of adult cancer patients have likewise shown that 87% of patients surveyed desired as much information as possible about their disease and treatment (Eysenbach, 2015). Despite this desire for cancer-related information by patients, a review of electronically available cancer information showed a lack of high-quality content targeted at the adolescent reading level (Stinson et al., 2011). There is an opportunity for the development of mHealth interventions, such as Pain Squad+, to
offer reputable and effective real-time pain management advice to young cancer patients (Jibb et al., 2014).

Concerning the acceptability of navigating through the *Pain Squad*+ app, adolescents with cancer were displeased with the excessive number of steps required to complete a function. The desire to minimize complexity and maximize the convenience with which mHealth interventions can be used has been previously shown in adolescents with anaphylactic allergies (Anderson & Wallace, 2015) and asthma (Schneider et al., 2015). Further, difficult to find features of mHealth interventions have been a leading cause of user frustration and therefore may limit user interaction (Ceaparu et al., 2010). The constrained screen size of smartphones, which can diminish the capacity of a user to interact with the device, also represent a reason navigation should be streamlined (Danaher et al., 2015). In the present study, following cycle 1 of testing, the navigation path through the app was simplified successfully with no problems related to navigation noted in subsequent testing.

Adolescents’ endorsement of the utility and customizability of *Pain Squad*+ is comparable with recent studies of mHealth interventions (Anderson & Wallace, 2015; Jibb et al., 2014; Ly et al., 2015; Maguire et al., 2015; Stinson et al., 2013). These studies have shown that mHealth interventions are consistently considered useful and valuable adjuvants to routine clinical care. This study adds to this research by indicating that adolescents with cancer expect that they would use mHealth interventions such as *Pain Squad*+ over a prolonged period whenever they experience symptoms and especially in circumstances of limited access to other clinical support. This finding is particularly important in the case of adolescent cancer because recent electronic diary research has shown 95.3% of 8 – 18 year olds with cancer to experience pain at least daily, including when not in the hospital (Stinson, Jibb, et al., 2015a). Therefore
smartphone-based means to support consistent adolescent pain management in all naturalistic settings (e.g., home, school, hospital) have potential cancer care value.

The ability for adolescents to customize *Pain Squad*+ to their preferences represented the final app acceptability theme. Participants valued the capacity to personalize the pain advice that was recommended to them. A customizability capacity is in keeping with previous clinical and theoretical usability research with adolescents with health conditions (Anderson & Wallace, 2015; W. Brown et al., 2013). These studies indicate that customizability may be a valuable app usability asset because it allows users to operate a system as preferred and may therefore improve satisfaction.

**Strengths and Limitations**

The strengths of this study include the user-centered and iterative design approach to the refinement of the *Pain Squad*+ app. In addition, the credibility of the results was enhanced by triangulation of findings across data sources (i.e., observation and interviews). Several research limitations need to be highlighted. First, this study was conducted at a single tertiary pediatric center using a relatively small number of adolescents, which could represent a threat to the generalizability of the results. However, research suggests that most usability problems can be identified with testing cycles including as little as 5 participants (Kushniruk & Patel, 2004) and each cycle of testing may decrease usability related problems by 10-fold (Kushniruk, 2002). The first cycle of testing included only 4 adolescents, but the profound problems with the app (i.e., software ‘crashes’) meant that continuing with testing would have been futile.

Second, the usability of *Pain Squad*+ in adolescent environments other than the hospital (e.g., home and school) and longitudinally was not assessed. Because components of an app’s usability, such as technical difficulties and acceptability, may differ across testing
environments and with repeated testing, it is recommended to test interventions in the various environments within which it will be used (W. Brown et al., 2013; Kushniruk & Patel, 2004; McCurdie et al., 2012). This issue has been addressed in Study 2.

Third, the large majority of adolescent participants enrolled in this study were relatively newly diagnosed with cancer and were being treated on an ambulatory basis. The usability of this Pain Squad+ app by adolescents at different stages of the treatment process and by adolescents who are acutely ill or experiencing toxicities is not known. Study 2, has examined app use longitudinally in a more diverse group of adolescents with cancer.

Last, potential cognitive biases may have been introduced into the findings. For instance, experimenter bias may have been introduced as the researcher conducted the usability testing observation and interviews, as well as the analyses. However, because 2 independent observers endeavored to be present at all testing sessions and debriefed about the session afterwards and a bracketing protocol was used, this bias is expected to have been limited. Social desirability bias may also have occurred because adolescents used the app in the presence of the research team and provided feedback to the researcher. To minimize this effect, at testing onset all adolescents were encouraged to use the app naturally and provide both positive and negative feedback.

**Conclusion**

Engagement of end-users early and throughout mHealth development is highly recommended to ensure that interventions meet the explicit needs of the target group (McCurdie et al., 2012; Wootten et al., 2014). In the present study, findings from usability testing were successfully used to refine the Pain Squad+ app for ease of use, ease of understanding, efficiency, and acceptability. Pain Squad+ was subsequently piloted and will eventually be tested for its effectiveness in a RCT. If effective in improving pain outcomes for
adolescents with cancer, the *Pain Squad*+ app may represent a viable means to offer patients real-time self-management support related to a number of physical and psychosocial cancer symptoms. Finally, a usable *Pain Squad*+ app may act as a template for the remote real-time self-management of a variety of chronic and life-limiting conditions, although additional usability testing with these user groups is recommended.

**Study 2: Pilot Testing**

**Discussion of Findings**

Pain is a considerable problem for adolescents with cancer who may benefit from ‘in-the-moment’ self-management support to ameliorate the symptom. The primary aim of this study was to evaluate the ability to implement the *Pain Squad*+ real-time smartphone-based pain management app into a future RCT. The secondary aim was to obtain estimates of treatment effect on adolescent health outcomes in order to calculate an appropriate sample size for a future hypothesis-testing trial. Overall, the results suggest that it is possible to implement the *Pain Squad*+ study protocol for effectiveness testing. Adjustments to improve the fidelity of intervention delivery (i.e., sound technical functioning and prompt study nurse contact) and adolescent adherence to the intervention should be considered before a future trial. Regarding the secondary study aim, outcome scores (i.e., pain intensity, pain interference, HRQL, self-efficacy) across the 2 assessment points generally showed changes indicative of positive health outcomes. Although only exploratory in nature, analyses of baseline to post-study changes in pain intensity and HRQL in particular highlight the potential effectiveness of the *Pain Squad*+ for adolescents with cancer.

**Pain Squad**+ implementation outcomes.

**Study accrual and retention.** The demonstrated accrual and retention rates are encouraging regarding the potential to trial the *Pain Squad*+ intervention for adolescents with cancer.
cancer. Of eligible adolescents, 75% agreed to participate in the study, indicating that the study and the intervention are of interest to a majority of adolescents with cancer pain. Participant attrition from the study was 3%, suggesting that: overall, the intervention is satisfactory for this group. These accrual and retention numbers meet the a priori criteria for implementation success (i.e., accrual of >70% and attrition of <10%) and exceed those cited in other studies of symptom management- and quality of life-related interventions for adolescents with chronic or life-threatening conditions (Diorio et al., 2015; Gorman et al., 2014; Maguire et al., 2015; Weaver et al., 2015). The time to recruit the cohort of 33 participants across the 2 study sites was approximately 9 months. This suggests that a future trial will require the inclusion of additional sites to improve the recruitment rate. In addition, this accrual rate was dependent on the availability of research personnel. Therefore potentially eligible adolescents may have been missed and recruitment rates in a future trial may benefit from dedicated recruitment personnel at all study sites, as well as other types of recruitment aides (e.g., pamphlets, posters).

Reasons for participation refusal or withdrawal related to a lack of interest in the study and the belief pain would resolve without intervention. These reasons for lack of study involvement are largely in line with those previously reported (Causarano et al., 2015; Diorio et al., 2015; McGregor, Coghlan, & Dennis, 2014; V. A. Miller et al., 2013). Novel to this study is the finding that the use of the study smartphone may be a hindrance to study participation commencement and continuation. Adolescents who owned a phone at recruitment or those who feared damaging or losing the loaned phone declined to participate. As the responsibility of managing the study phone may be problematic for adolescents with cancer, installing Pain Squad+ software on to adolescents’ personal phones may further enhance recruitment and retention in a future Pain Squad+ trial.
Over the course of the study, adolescents completed 1,172 pain assessments using the *Pain Squad+* app, with 487 reports indicating the presence of pain. Adolescents used at least 1 pain management strategy in response to 138 reports of pain. Momentary pain intensity was mild when all pain reports were considered, but was on average moderate (Hirschfeld & Zernikow, 2013) when only those reports were pain was rated as > 0/10 were considered. Under these circumstances, pain unpleasantness and interference were also moderate. These findings agree with previously published electronic momentary assessment data from adolescents with cancer (Stinson, Jibb, et al., 2015a) and support the notion that pain is problematic for this group (Collins et al., 2000; Hedén et al., 2013; Hedström et al., 2003; Hockenberry & Hooke, 2007; Walker et al., 2010). Adolescents used pharmacological pain management strategies most frequently, which is reflective of previous studies into pediatric cancer pain management in home settings. (Fortier, Wahi, Bruce, Maurer, & Stevenson, 2014). In the present study, participants could also be receiving cancer therapy on an in-patient basis and pharmacological modalities to treat pain are most common in hospitals (Stevens et al., 2011). Adolescent use of pharmacological strategies may therefore be indicative of the prescribing practices of their physicians and their familiarity and comfort with the modality. Still psychological and physical pain management strategies were used in response to a large number of pain reports, suggesting that *Pain Squad+* recommendations to use these modalities are effective.

With regard to the potential impact of *Pain Squad+* on engagement in pain self-management behaviours, the average experience of control over pain in this study was 6.4/10 (SD = 2.2). This number is greater than that obtained in a previous study where pain was assessed in adolescents with cancer longitudinally, but no pain management advice was
provided (Stinson, Jibb, et al., 2015a). *Pain Squad+* may therefore be an effective tool in supporting adolescents in their capacity to self-manage cancer pain.

**Intervention fidelity.** Some issues with intervention fidelity occurred during the study, inhibiting the delivery of the core components of the *Pain Squad+* intervention as planned. Successful delivery of pain self-management support via the app is dependent on its sound technical functioning. Although the vast majority of study participants were able to complete pain assessments and receive pain self-care advice from the app (i.e., n = 27; 82%), the remainder experienced technical issues. The *a priori* implementation success criterion for technical functioning of *Pain Squad+* specified that technical difficulties would be reported by <10% of participants. This criterion was therefore not met. Technical malfunctioning of mHealth interventions is a limitation of the mode of intervention delivery and has been reported previously in other pilot studies of technology-associated health apps and web-based programs (Ameringer, Erickson, Macpherson, Stegenga, & Linder, 2015; de Wit, Dozeman, Ruwaard, Alblas, & Riper, 2015; Maguire et al., 2015). Although a relatively rare occurrence in the cited literature and present study, technical difficulties inhibit the usability of mHealth interventions like *Pain Squad+* (Makai, Melis, & Olde-Rikkert, 2014). As such, technical difficulties may limit intervention effectiveness and may also represent a safety issue for users (McCurdie et al., 2012). Indeed, in the present study, adolescents who experienced technical difficulties and participated in post-study qualitative interviews commented on these as adding unnecessary complexity and frustration to the intervention. In this study, technical issues experienced by participants were resolved quickly wherever possible. However, moving forward to a future effectiveness trial, it would be ideal if these technical issues, and in particular those related to connectivity between the hospital server and study phones, were rectified before study onset.
The second intervention fidelity issue focused on the study nurse’s capacity to efficiently contact participants following receipt of an email alert about the participant’s pain. Initially, the goal of the study was to see >80% nurse-participant contact within 12 hours of the alert being received by the nurse. This goal was not achieved with only 20% of participant contacts occurring within 12 hours of the alert. The mean time to contact was in actuality much longer at 62.5 hours. The principal reason for the length of time to contact was adolescents not answering repeated telephone calls or emails.

Previously published studies of similar real-time symptom management interventions have not reported on time to participant contact from healthcare professionals following severe symptom alerts (Cleeland, Farrar, & Hausheer, 2010; Head et al., 2011; Judson et al., 2013; Kearney et al., 2009; Kroenke et al., 2010; Maguire et al., 2015). This lack of reporting makes it difficult to place the mean time to contact observed in this study within a broader context of potential intervention fidelity. However, published studies of adults with cancer have reported on the percent of alerts issued to a healthcare professional in response to symptom reports (64%; Sundberg et al., 2015) and the percent of times the nurse was able to contact the participant issuing the report (60%; Cleeland et al., 2011). These findings are in line with those obtained presently and may represent more realistic targets for patient follow-up with remote symptom management interventions.

This study did not explore each participant’s rationale for not answering telephone calls or emails from the nurse. However, 1 adolescent reported that he did not always have his phone in close proximity and therefore missed to connect with the nurse. Other participants similarly reported issues related to use of the study phone, especially when if they owned a personal phone at study onset. These adolescents stated that they forgot to interact with Pain Squad+ because it was not accessible on their personal device. Because a delay in healthcare
professional contact could have adverse consequences for some patients (North et al., 2013),
strategies to minimize the time between nurse email receipt and adolescent contact should be
considered. To improve interaction with the study nurse, a protocol for future trial may include
the installation of the app on an adolescents’ primary phone and the nurse contacting
adolescents on this phone.

Regardless of whether or not study adolescents were contacted by the study nurse, they
generally reported valuing the nurse role in the Pain Squad+ intervention. Participants felt the
nurse was of therapeutic benefit as she provided customized and additional pain management
support to adolescents in the event that self-care strategies were ineffectual. Previous
qualitative research of adult cancer patients engaged in studies of similar real-time symptom
management interventions also showed positive feedback related to the role of a healthcare
professional in remotely monitoring symptom reports (Maguire et al., 2015; Sundberg et al.,
2015). Acceptability of the nurse suggests the role may be a valuable component of real-time
symptom management interventions for cancer patients. In the present study, only 39% of
participants actually interacted with the nurse, who represents a cost addition to the
intervention. A future Pain Squad+ trial may therefore consider using a 3-arm design (i.e.,
Pain Squad+ with nurse interaction, Pain Squad+ without nurse interaction, control) to
elucidate the therapeutic benefit of the study nurse. This design should also include a cost-
benefit analysis to elucidate the value added of including a nurse in the intervention.

**Outcome assessment piloting.** Participants completed the majority of baseline and post-
study outcome measures. The a priori criterion for implementation success was <10% of
questions being missed by participants. This criterion was met for baseline measures but was
missed for post-study measures (mean of 84.3% completed), although the small numbers of
participants in the study means data missing from only a few adolescents could dramatically
sway average completion percentages. Acute illness and treatment prevented 2 participants from completing post-study measures and 2 additional participants were lost to follow-up post-study. Because internal validity and statistical analyses depend in part on collecting maximal outcome data from participants (Fewtrell et al., 2008; Polit & Beck, 2008), strategies should be put in place to decrease loss to follow-up in a future trial. Adolescents who participated in qualitative interviews suggested that a decreased number of outcome measure questions could be more amenable. However, a meta-analysis of results from studies investigating strategies to improve follow-up in randomized trials with adults showed decreasing question number to be a relatively ineffective strategy compared to standard procedures (RR = 1.04; 95% CI = 1.00 to 1.08) (Brueton et al., 2014). The same result was found for additional reminders to complete outcome measures (RR = 1.03; 95% CI = 0.99 to 1.06). Thus, strategies to prevent loss to follow-up in a future Pain Squad+ RCT may include also sending the email alerts to the adolescents’ parent or other caregiver.

Adolescent adherence. The Pain Squad+ app represents a pragmatic study intervention in that it is flexible in terms of adolescent engagement (i.e., use of the intervention dependent on pain) and pain management strategies selection. Therefore, to set a measure of adherence that was standardized across participants, a definition based on the number of pain assessments, and not engagement with the management recommendation feature of the app, was used. The criterion for implementation success was set at completion of >80% of twice-daily pain assessments (or >80% of 56 assessments). This criterion was not achieved with adolescents completing a mean of 69.4% (SD = 40.1) of the required assessments. However, engagement with the system in general was high and a mean of 27.1 days (SD = 6.3) of interaction (at least 1 pain report completed per day) over the 28-day study. In addition, adherence in this study appeared to decrease in magnitude overtime with adherence to pain
assessment completion in week 1 being 77.2% (SD = 51.2) and adherence in week 4 being 38.5% (SD = 39.4).

Previous studies of real-time symptom assessment systems have shown variable rates of reporting adherence. For instance, a pilot study of a tele-oncology service for chemotherapy-induced nausea and vomiting support for adults with cancer showed adherence to once-daily reporting for 5 days to be 73% (Yap et al., 2013). In a separate recent prospective cohort study of adolescents with cancer self-reporting pain, mean adherence to a twice-daily reporting protocol for 14 days was 72.2% (SD = 23.1; n = 92). However, adherence decreased when adolescents were asked to complete the same protocol for 21 days in the perioperative period (M = 47.4%; SD = 25.2%; n = 14) (Stinson, Jibb, et al., 2015a). Finally, a longitudinal study of adult cancer patients electronically self-reporting a variety of cancer symptoms showed mean adherence to be 82% (SD = 25) with once-monthly reporting and only 62% (SD = 30) with once-weekly reporting (Judson et al., 2013). These authors also observed adherence to decrease over the time of study follow-up, with participants being >3-fold more likely to be compliant with self-reporting during their first 12 weeks in the study than they were after that time (OR, 3.31; p < 0.001). Together, these results suggest that adherence may be contingent on the length of symptom reporting required and potentially on symptom severity (e.g., increased pain after surgery diminishing symptom reporting frequency).

The apparent decrease in pain reporting in the present study from week 1 to week 4 with relatively little change in adherence between weeks 1, 2, and 3 may provide evidence related to the average adolescents’ preferred length of interaction with Pain Squad+ (i.e., ~3 weeks or ~21 days). However, it should be noted that several study participants did continue to interact with the app after 3 weeks, and 15 participants interacted with the app for more than the requested amount of days. This suggests that the need for adolescents with cancer to
interact with *Pain Squad+* may be highly individualized; raising the issue of the ideal number of interactions with the app adolescents should be encouraged to make. From a clinical standpoint, the optimal number of pain assessments that should be collected *per* day or the number of days over which pain should be assessed is not known (Stone & Shiffman, 2002). Research has shown that an average of 12 pain assessments completed over 4 days produces the most reliable and valid estimates of average weekly pain (Jensen & McFarland, 1993). These data were collected from adults with chronic pain and no studies to date have examined the optimal frequency of pain reporting in adolescents, including those with acute pain. Increasing the number of pain assessments *per* day and the number of days of data collection will improve the ability to detect pain when it occurs and initiate management in real-time. However, the advantage of increasing pain-reporting frequency must be weighed against the disadvantage of increased study participant burden, which may reduce adherence (Stone & Shiffman, 2002).

In the present study, adolescents with cancer provided rationale for low levels of interaction with *Pain Squad+*. Adolescents felt that interaction with the app when not in pain was not needed. Adolescents also reported that notifications to complete pain reports were burdensome. This finding is important because electronic patient-reported outcome (ePRO) assessment adherence is improved with the addition of automated reminders (Basch & Abernethy, 2011; Shields, Stone, & Shiffman, 2010). Therefore, to improve the ability to implement trialing of the *Pain Squad+* intervention, a compromise in the number of notifications promoting interaction with the app (including when adolescents are not experiencing pain) is needed. Before an effectiveness trial, additional qualitative interviews with adolescents, especially with those who participated in this longitudinal study, could determine the amount of interaction *per* day that is considered amenable. Coupled with
empirical evidence regarding the optimal notification frequency (Shields et al., 2010), these data could be used to refine Pain Squad+ such that reporting adherence is maximized and any burden associated with notifications is minimized.

**Acceptability.** Overall, adolescents were satisfied with the Pain Squad+ intervention. Quantitatively, all items on the AES received a mean score of >3/5, indicating acceptability for the item and 4 items achieved a mean score indicative of high acceptability. These findings are consistent with previous studies of real-time symptom management interventions, which have shown participants to consider the systems as easy to use, easy to understand, and quick to complete (Cleeland et al., 2011; Head et al., 2009; Sundberg et al., 2015).

Qualitative data also confirmed that adolescents with cancer considered the intervention satisfactory, despite variations in age, sex, diagnosis, level of interaction with the app, and change scores on study outcome measures. Specifically, the usability of Pain Squad+ was endorsed and use of the app was considered to fit well with adolescents’ usual daily activities. Adolescents particularly liked the capacity of the app to support self-management via the self-care advice provided (especially when at home), pain self-monitoring, and the perceived facilitation of communication with their healthcare professionals. This finding suggests that adolescents with cancer value the means by which the intervention is intended to work (i.e., by supporting the self-management of pain in real-time). Finally, as has been shown in previous studies of mHealth and other Internet-based health interventions targeted and adolescents (Stinson et al., 2013; Stinson, Gupta, et al., 2015b), all interviewed participants found the design and gamification mechanics (i.e., badges, point and leveling system) attractive and acceptable.

Some recommendations for improvement to the Pain Squad+ intervention were made and these may offer clues into how to address items on the AES that did not achieve mean
scores indicative of high acceptability. Recommendations focused on: (a) the inclusion of additional pieces self-care advice; (b) enhancements to the gamification mechanics of the app; (c) more flexibility in self-scheduling pain assessment notification timings; (d) incorporating the capacity to review previously logged pain reports in order to track pain management progress; (e) the capacity to rate pain more specifically on visual analogue scales; and (f) decreasing required interaction with the app when not experiencing pain. It is expected that addressing these issues may improve ratings of app enjoyment and helpfulness, as well as the acceptability of time to complete the app.

Regarding satisfaction with the *Pain Squad+* study protocol in general, adolescents who were interviewed reported it to be acceptable. Engagement in the study was considered easy and use of the intervention was liked. Participant reports of altruism as motivation for study participation are in line with those shown previously in studies of adolescents with cancer engaged in research (Barrera, D'Agostino, Gammon, Spencer, & Baruchel, 2005; V. A. Miller et al., 2013). Other motivations for participation included the novelty of being involved in research and the general gamification of the app. Although a relatively new adjuvant to electronic health interventions (Miller et al., 2014), gamification specifically has been shown to improve engagement with Internet- and mobile phone-based interventions (de Ridder, Kim, Jing, Khadra, & Nanan, 2016). Indeed, adolescents advocated for enhancements to the breadth of the gamification mechanics of *Pain Squad+*. Enhanced *Pain Squad+* gamification may then represent a means to further improve accrual in a future trial, as well as improve interaction with the intervention by study participants. The taxonomy of gamification mechanics described by Miller and colleagues (2014) indicates that several additional features exist, which may be added to *Pain Squad+* to bolster app use. These additional mechanics include leaderboards (leveraging potential competitiveness in users as they compete against peers), challenges and
quests, and social engagement loops (integration with existing social media platforms garnering peer support and building social capital).

**Pain Squad+ effectiveness outcomes.** Because this was a pilot study, descriptive data analysis was performed to obtain estimates of treatment effect to inform a sample size calculation for a future adequately powered RCT. Inferential testing of the data from the small sample was performed only to identify apparent trends in the health-related outcomes from baseline to post-study. Additionally, multiplicities of analyses conducted on the several health-related outcomes were conducted. Together this means that the outcome results must be interpreted cautiously. Regardless, the results are encouraging with respect to the potential health benefits of Pain Squad+ for adolescents with cancer pain.

**Pain intensity.** Ratings of ‘worst’, ‘least’, and ‘average’ pain in the preceding week, and the pain intensity summary score, all decreased significantly from baseline to post-study with calculated effect sizes being in the moderate range (0.47 – 0.69). ‘Current’ pain intensity did decrease across the 2 assessment points but the change was not significant and the effect size was small (0.20). Improvements in pain intensity related to real-time self-management support systems have been demonstrated in previous studies involving cancer patients. For instance, a RCT including 79 adults with cancer using an interactive phone system to report symptoms and receive management advice showed symptom intensity (including pain intensity) to decrease more rapidly in the intervention group than in the control group ($p = 0.003$; Cleeland et al., 2011). Another RCT of 405 adults with cancer using a similar system showed effect sizes for between-group differences in pain intensity to be 0.67 and 0.39 at 3 and 12 months respectively (Kroenke et al., 2010).

Presently, mean differences in pain intensity scores ranged from -0.61 to -1.79 on a 0- to 10-point numerical rating scale. Changes in pain intensity of these magnitudes may
represent clinically important improvements in pain for adolescents with cancer. Minimal clinically important differences (MCID) in pain intensity in adults with both acute and chronic pain due to a variety of health conditions (e.g., cancer, facial surgery, temporomandibular disorder, arthritis) have been investigated (Emshoff, Bertram, & Emshoff, 2011; Fayers et al., 2011; Salaffi, Stancati, Silvestri, Ciapetti, & Grassi, 2004; Sandhu et al., 2015). These studies have used various scales to assess pain intensity, but have shown that equivalent of decreases between 1 and 2 points on an 11-point numerical rating scale are indicative of patient-reported pain improvement. Less well-researched has been MCID cut points in pain intensity for children and adolescents (Hirschfeld, 2014), with no research on clinically important pain intensity differences in adolescents with cancer. Clinically important differences in children and adolescents with postoperative pain, however, have been determined as a 1-point difference on an 11-point numerical rating scale for pain ≤5/10 and a 2-point difference when pain was >5/10 (Voepel-Lewis, Burke, Jeffreys, Malviya, & Tait, 2011). Using these values for the present study, mean changes in ‘average’ pain in the preceding week and the BPI item summary score represent clinically meaningful improvements. The mean change in ‘worst’ pain in the preceding week also approached the cut off for clinical improvement in pain >5/10. Further, using cut points for mild, moderate, and severe pain intensity in children and adolescents with chronic pain (Hirschfeld & Zernikow, 2013) mean ‘worst’ pain from baseline to post-study moved from severe to moderate and mean ‘average’ and the item summary score both moved from moderate to mild over the course of the study. Cut points for acute cancer pain have not been established. Still, taken together, these findings suggest the possibility that, when investigated in a future trial, the Pain Squad+ intervention may improve pain intensity in adolescents in a clinically meaningful manner. Exploration of whether any intervention-
associated differences in pain intensity ratings change in magnitude and direction or are sustained over time should be outcome targets of a RCT.

**Pain interference.** Despite its importance to the assessment of the functional impact of pain on patients, pain interference is a little researched construct in the pediatric and adolescent with cancer populations (Erickson et al., 2013). This lack of research is disappointing in that functional status not only affects quality of life directly, but also indirectly through its effect on symptoms (Hsu & Tu, 2014). Furthermore, discordance between symptom severity and functional status has been demonstrated in children with cancer (Buckner et al., 2014), pointing to the importance of assessing both constructs through research and in clinical settings.

In the present study, although the change did not amount to one of statistical significance, PROMIS PPI-SF pain interference decreased from baseline (M = 58.78) to post-study (M = 54.41). The associated effect size for the change in mean scores was small (0.35). Two previous non-interventional cohort studies have administered the PROMIS-PPI to children and adolescents with cancer and reported on scale scores. First, a psychometric testing study of the PROMIS instrument with 8 to 17 year olds reported mean pain interference to be 50.2 (SD = 11.2; n = 90) for those in active treatment and 44.7 (SD = 10.2; n = 103) for survivors (Hinds et al., 2013). Second, an examination of symptom patterns and functional impairment in 8 to 17 year olds in active treatment or survivorship found mean pain interference to be 47.2 (SD = 11.3; n = 200). The mean scores obtained in this study indicate that *Pain Squad+* participants experienced more pain interference with function than previously shown. This may be reflective of the study inclusion criterion that *Pain Squad+* participants have had at least 1 episode of pain >3/10 in the previous week.

As a relatively new pediatric symptom and functional impairment measure, clinically important changes in pain interference on the PROMIS measure have not been established. The
lack of available cut points for MCID limits the clinical interpretation of the results. The finding that even in the context of a small within-group pilot study, pain interference decreases with use of the Pain Squad+ intervention is promising with respect to potential future effectiveness.

**Health-related quality of life.** Effect sizes for mean differences in adolescent HRQL from baseline to post-study were small to moderate (0.31 – 0.61). Changes that achieved statistical significance were those for the total PedsQL 4.0 HRQL score, as well as for the emotional and social subscales of the measure. Changes for the physical and school subscales were not significant and the school subscale in particular saw changes in direction indicating worse school functioning at post-study compared to baseline. Several studies in children, adolescents, and young adults with various cancer diagnoses have shown pain to be negatively correlated with HRQL (Bhat et al., 2005; Ewing, King, & Smith, 2009; Stinson, Jibb, et al., 2015a; Sung et al., 2009; Varni et al., 2004). There is reason to believe that a potential positive impact of the Pain Squad+ intervention on pain severity may mediate improvements in adolescent HRQL. This association may be the reason that preliminary evidence for positive changes in PedsQL 4.0 scores were observed in this study.

With respect to the absolute PedsQL 4.0 scores obtained, these can be directly compared to those previously published. Overall, published HRQL scores on the measure for pediatric and adolescent cancer patients have widely been shown to be less than those reported by healthy children (Ewing et al., 2009; Stinson, Jibb, et al., 2015a; Sung et al., 2009; 2011). Baseline PedsQL 4.0 scores obtained in the present study are consistent with published pediatric cancer-specific scores for the total scale score and each subscale scores. The finding that physical functioning was reported as the lowest score dimension of PedsQL 4.0 has been demonstrated previously in adolescents with cancer (Stinson, Jibb, et al., 2015a). This finding
may be related to the diagnoses (i.e., solid tumor cancers) and associated treatment modalities (i.e., radiation and surgery) that are more commonly seen the adolescent patient population (Sung et al., 2009).

The finding that real-time symptom self-management systems may improve HRQL for cancer patients is consistent with previous research. For instance, in a within-group study of 34 adults with cancer using a telehealth system that enabled the receipt of symptom self-care advice, clinically meaningful improvements in HRQL (measured with Functional Assessment of Cancer Therapy-General [FACT-G]) were observed over the study (Chumbler, Mkanta, et al., 2007b). Likewise, a pilot-RCT of 44 adults with head and neck cancers using a similar telehealth system showed system usage to be correlated with the physical well-being ($p = 0.048$) and emotional well-being ($p = 0.042$) subscales of the FACT-Head and Neck HRQL measure.

Furthermore, the mean changes observed in HRQL presently from baseline to post-study may represent clinically important differences. Varni et al. (2003) have proposed 1 SD below the mean obtained from a healthy population to represent children and adolescents ‘at-risk’ for impaired HRQL. Using 409 healthy children (5 – 18 years) Varni et al. (2002) presented self-reported PedsQL 4.0 mean ± SD scores as: total scale 83.00 ± 14.79, physical functioning 84.41 ± 17.26, emotional functioning 80.86 ± 19.64, social functioning 87.42 ± 17.18, and school functioning 78.63 ± 20.53. In this Pain Squad+ study, mean scores on the PedsQL 4.0 and all of its subscales were >1 SD below the mean at baseline. However, scores for the total scale, as well as the emotional and social subscales were within 1 SD of the mean at post-study. Movement of mean scores above the threshold for HRQL impairment suggests the intervention may serve to clinically improve dimensions HRQL in adolescents with cancer. As pain is an emotional experience, as well a sensory experience (Melzack, 2005; Melzack &
Wall, 1965), improvements in the emotional and social subscales of the PedsQL 4.0 related to improvements in pain intensity are not necessarily surprising.

The finding that school functioning decreased over the course of the study is likely related to school-related questions being inappropriate for may adolescents with cancer. Previous research into HRQL in pediatric cancer patients undergoing therapy has omitted the school subscale from analyses because these children often do not attend school (Sung et al., 2009). In the present study, the greatest amount of HRQL missing data pertained to the school functioning subscale. The resulting small sample sizes used in the analyses may have therefore independently biased the results. It is possible that the trend toward decreased school function is related to Pain Squad+ intervention, but the mechanism by which this would occur is not clear.

**Self-efficacy.** Self-efficacy did not change over the study, with the mean difference from baseline to post-study being negligible. This lack of change is not necessarily surprising. The GSE-Sherer Scale assesses the construct of self-efficacy in a general manner. Self-efficacy, however, is often considered a task-specific phenomenon such that confidence to complete a certain task does not translate into confidence to complete other tasks (Boveldt et al., 2014). As the Pain Squad+ intervention is intended to support pain-specific self-management of adolescents in real-time, the items in the GSE-Sherer Scale may have had little to no relevance to the pain-care circumstances of study participants (Bandura, 2006).

An investigator-developed pain care-specific item was added to the self-efficacy questionnaire. Concerning this item, a non-significant trend towards improvement from baseline to post-study was observed and the effect size for the mean change was small (0.27). Previous studies into interventions to improve adolescents’ task-specific self-efficacy have produced variable results. For instance, a pilot-RCT of an Internet-based self-management
program with telephone support for adolescents with arthritis showed arthritis-care self-efficacy effect sizes to range from 0.11 – 0.31 (Stinson et al., 2010). A separate pilot-RCT of a peer-support intervention for adolescents with chronic pain produced an effect size for the difference in mean chronic pain-care self-efficacy at post-study of 0.50 (Kohut et al., 2016).

Theoretical frameworks that guide symptom self-management interventions propose that improvements in symptom status are in part related to enhanced patient self-efficacy (Barlow & Ellard, 2004). Interestingly, empirical evidence from a study investigating engagement in physical activity by adolescent girls has demonstrated that, not only did self-efficacy directly impact activity; the relationship was also partially mediated by engagement in self-management strategies (Dishman et al., 2005). Therefore, if the development of self-efficacy is related to engagement in self-management skills, more self-efficacy changes related to use of the Pain Squad+ intervention might emerge after longer follow-up.

**Strengths and Limitations**

This is the first study to pilot a real-time multidimensional pain management app for adolescents with cancer. The methods employed addressed many of the limitations noted in previous research into real-time symptom management systems for patients with cancer (Aldiss et al., 2011; Chumbler, Kobb, et al., 2007a; Chumbler, Mkanta, et al., 2007b; Head et al., 2011; Kearney et al., 2009; Sundberg et al., 2015). The study was strengthened by the use of a robust collection of implementation outcomes to more holistically assess readiness for a RCT. Furthermore, the use of *a priori* implementation success criteria provided a basis for interpreting study results and determining whether to proceed to a RCT (Thabane et al., 2010).

Clear objectives and well-defined outcomes were set before the study was begun, providing a clear framework to follow (Lancaster et al., 2004). The recruitment of a heterogeneous group of adolescents with cancer across 2 study sites improved the
generalizability of findings. Valid and reliable measures to assess the secondary quantitative outcome were used. Data were entered directly into REDCap by adolescents, wherever possible, preventing any errors in data transcription. Loss to follow-up was also relatively rare. In addition, following recommendations for the conduct of pilot studies (Arain, Campbell, Cooper, & Lancaster, 2010), the analyses of data were descriptive in nature. As no formal power calculations were conducted, inferential statistical analyses were treated as preliminary and interpreted cautiously.

All interviews were conducted over the telephone, providing a degree of anonymity to participants and therefore potentially limiting reporting bias. Two individuals independently participated in data analyses and an audit trail detailing analyses decisions was kept. Additionally, a bracketing and peer debriefing procedure was used to minimize the impact of researcher subjectivity during both qualitative data collection and data analysis (Morrow, 2005)

As a whole, the study benefited from the inclusion of both quantitative and qualitative assessments of implementation success. The combination of these different data provides a more exhaustive report on the ability to implement the Pain Squad+ intervention. The conduct of a preparatory quantitative study, enhanced with direct interview-based commentary has, in advance, helped to detect key human and technical issues that pose a threat to the validity of a future RCT (Cafazzo, Seto, & Jadad, 2012b).

The study also has several limitations. First, a one-group design was used to pilot Pain Squad+. The feasibility of a randomization procedures, as well as control arm recruitment, attrition, outcome measure completion, and acceptability have not been demonstrated. A number of pilot RCTs of similar interventions with adolescents with chronic health conditions have been conducted and these have demonstrated the feasibility of these control group-
associated procedures (Kohut et al., 2016; Stinson et al., 2010). The lack of a control group also means that the preliminary effect sizes calculated for the outcome measures may be confounded in a number of ways (Kraemer et al., 2006; Leon et al., 2011). Importantly, no controls for the effects of time and attention were implemented in the design and this is reflected in the obtained effect sizes. However, regarding the effect of time in particular, the \textit{a priori} expectation that pain should necessarily decrease over a 28-day period in adolescent with cancer may not be founded. For instance, a longitudinal study of 92 adolescents at various points within the cancer treatment trajectory these adolescents to have no significant change in current pain intensity over a 2-week period (Stinson, Jibb, et al., 2015a).

Another limitation relates to the definition of adherence used in the study. To measure adherence across adolescents in a standardized way, a definition related to compliance with pain assessment reporting was used. The intervention, however, is intended to impact on adolescents’ self-management of their pain. Therefore, a means of describing adherence that is focused on engagement in self-care may have been more appropriate. For instance, based on previous research (Kroenke et al., 2010), use of self-care strategies in response to >80% of completed pain assessments positive for pain may be a useful definition.

The \textit{Pain Squad+} intervention is personalized with respect to the amount of adolescent \textit{ad hoc} pain reporting, as well as use of self-care advice and interaction with the study nurse. A highly standardized and inflexible intervention was not administered across study participants. Instead, the dose of the intervention varied between participants, which may have increased variability in study outcomes. Similarly variability may have been introduced by through the inclusion of a broad range of adolescents (e.g., differences in age, diagnosis, symptom severity at study onset). However, the use of a flexible intervention and broad inclusion criteria mean
that this study was necessarily pragmatic in nature, which benefits the study by improving the generalizability of its results.

**Conclusion**

Implementation of the *Pain Squad*+ app for future effectiveness testing in adolescents with cancer and estimates of treatment effect on adolescent health outcomes were studied. Overall, the intervention can be implemented for effectiveness testing in a future RCT, albeit with some adjustments to the study protocol. Namely, changes to improve the fidelity of the intervention and adolescent adherence to the intervention should be considered before a future trial. Intervention fidelity was impacted by technical difficulties with the app. Sound technical functioning must be established prior to a RCT to diminish the threat it poses to internal validity. The fidelity of the nurse support component of *Pain Squad*+ should also be improved if it is to be retained in the intervention. Installing the app on participants’ personal phones may improve the capacity of the nurse to more promptly interact with those adolescents who trigger an email alert and to interact with the app. Strategies to improve adherence to pain reporting by adolescents should also be considered prior to a RCT. A balance between the number of notifications needed to encourage interaction with the app and the number that is considered a nuisance by adolescents should be struck. Finally, the use of an adherence definition that considers interaction with the self-care elements of the app should be considered for a future trial. Regarding the preliminary effectiveness outcomes from the present study, the potentially positive impact of the *Pain Squad*+ intervention on pain in adolescents with cancer was demonstrated. In total, this study provides promising evidence for the success of a future *Pain Squad*+ RCT. If shown to be effective, the real-time and ecologically relevant (i.e., in everyday environments) approach employed through the *Pain Squad*+ intervention can serve to address the problem of cancer pain in adolescents.
CHAPTER SEVEN: IMPLICATIONS, KNOWLEDGE TRANSLATION, AND SIGNIFICANCE

Implications for Research

Following some modifications to the *Pain Squad*+ intervention, the primary research implication will be to inform the protocol of an adequately powered RCT. As the immediate goal of the *Pain Squad*+ intervention is to improve pain in adolescents with cancer in real-time, the primary outcome of a future trial should be pain intensity (McGrath et al., 2008). The direct and indirect effects of symptom severity on function, HRQL, and confidence to engage in self-care mean that changes in pain intensity have wide-reaching consequences (Buckner et al., 2014; Fayers et al., 2011; Sung et al., 2009). The BPI summary score item, being a composite of adolescent ratings of ‘worst’, ‘least’, and ‘average’ in the preceding week, as well as current pain, should be used to broadly assess the impact of *Pain Squad*+ on pain intensity in adolescents with cancer. In addition, in this study the decrease in the summary score for pain intensity from baseline to post-study was significant ($p < 0.001$) with a moderate effect size (0.69).

Using data obtained in this pilot study, a t-test sample size calculation has been conducted. This calculation is based on the detection of a 1.11-point difference in the BPI pain intensity summary score between the experimental and control groups, which represents a clinically important improvement in pain intensity (Voepel-Lewis et al., 2011). Assuming a mean BPI summary score of 3.62/10 in the control group, the most broad estimate of variance across the groups (post-study SD = 1.91), and a Type I error of 0.05, the number of participants needed to achieve 80% power to detect a difference of 1.11 points is 94, or 47 per group. A loss to follow-up of 15% should be assumed based on the number of outcome assessment non-
completers in the Study 2. Therefore, a future Pain Squad+ trial should aim to recruit 108 adolescents randomized to each of 2 groups (54 adolescents per group).

Recruitment of 33 participants into Study 2 required 9 months across 2 study sites. To complete accrual for a future trial involving 108 adolescents in the same amount of time, additional study sites would need to be recruited. Thus, consideration should be given to the methodology of a larger multi-site study in terms of treatment fidelity. Replication of this study as the intervention arm in such research could see server use, technical support, and study nurse support centralized at 1 lead site. This design was used in the present pilot and the centralization offered several advantages. For instance, the researcher was able to liaise with technical support personnel quickly in the event of technical difficulties. Frequent data checks were also possible because all data were stored on a single secure server. Additionally, a single study nurse was able to provide care to adolescents in a consistent manner and easily contact the adolescent’s primary care team as appropriate. If these activities were implemented on a per site basis in multi-site trial, training of technical support personnel and site nurses would need to conducted, as would intervention fidelity checks across sites.

Although pain intensity may be the primary outcome of choice in a future trial, secondary trial outcomes should also be considered. Research should focus on determining the impact of the app on patient (e.g., pain interference, HRQL, self-efficacy, self-management skills, communication with healthcare professionals, satisfaction, cost), provider (e.g., efficiency, satisfaction), and health service (e.g., healthcare utilization, cost [including of involving a nurse]) outcomes. If intervention-associated changes in pain intensity are observed in a RCT, these differences may be sustained (mediated by an enhanced capacity to engage in pain self-management) or may change in magnitude and direction overtime. Outcome assessment at longer-term follow-up should therefore be an objective of a future RCT.
The methods from the pilot may be used to inform the protocol for the intervention arm of a future RCT. However, some modifications to the Pain Squad+ intervention and study will be required. In particular, measures to enhance intervention fidelity and adolescent adherence to Pain Squad+ should be enacted. To improve the internal validity of a future trial, the technical functioning of the app should be improved. Specifically, issues with the hospital server logging participants out of the app or not sending notifications must be rectified. A RCT assessing the value added by the study nurse in terms of therapeutic benefit and cost (e.g., 3-arm trial with a Pain Squad+ app plus study nurse group, a Pain Squad+ app only group, and a control group) could be used.

Means to improve the capacity for the study nurse to reach study participants, such as installing the app on adolescents’ personal devices, should also be considered. The benefit of installing Pain Squad+ on adolescents’ devices would be the decreased burden to adolescents of having 2 phones to maintain (e.g., carry with them, charge batteries). Another benefit would be the proximity of the device to the adolescent. In this study participants reported that, if they owned a personal phone, they kept this phone on their person. This was not however true for the study phone they were loaded. The barriers to installing the Pain Squad+ app on adolescents’ personal devices include: logistics of the installation (i.e., currently would have to be installed by the hospital information technology department at the expense of time and cost) and data usage (i.e., adolescents would consume some data during the study by using Pain Squad+ and would need to be reimbursed for this cost). The first barrier could be resolved if the app were distributed via the public market (i.e., “app stores”), following thorough testing of the app across various screen sizes and device types.

Future research should focus on addressing recommendations for improvements to the Pain Squad+ intervention made by adolescents during qualitative interviewing. Specific
recommendations centered around: (a) including additional pieces of self-care advice; (b) enhancing the breadth of gamification mechanics of *Pain Squad+*; (c) increasing flexibility in scheduling pain assessment notifications; (d) incorporating a process for the review of previously logged pain reports; (e) including the ability to more clearly specify pain ratings on visual analogue scales; and (f) decreasing app interaction when an adolescent was not experiencing pain.

Addressing these recommendations has the capacity to improve *Pain Squad+* utility and therefore improve engagement with the system. Because routine, sustained AWC engagement with *Pain Squad+* is imperative to app effectiveness (McCurdie et al., 2012), it is critical that this app be modified and tested until it meets all of the expressed needs of adolescents with cancer pain. Following the implementation of adolescent recommendations, *Pain Squad+* should undergo additional iterative cycles of usability testing to ensure that, in its new format, it is still easy to use and understand, not prone to error-making, efficient, and satisfying to complete for adolescents.

Additionally, if shown to be effective in a substantive study, the smartphone pain management app could be used as a template for the monitoring and management of pain and other symptoms (e.g., nausea, fatigue) in a wide variety of chronic or life-limiting health conditions (e.g., arthritis, gastrointestinal disorders, sickle cell disease), as well as in end-of-life patients. This creates opportunities for research exploration into the remote real-time management of an array of health conditions in a wider variety of patient groups. The *Pain Squad+* app has received considerable endorsement from the adolescents with cancer sample. Adolescents with other chronic and life-limiting conditions may therefore represent a logical alternate patient population with which to begin trialing the intervention.
By virtue of the number of pain assessments completed by adolescents during this study, new knowledge related to the daily pain experience of adolescents with cancer has been generated. This dataset consists of frequent multidimensional assessments of pain that are momentary in nature, which minimizes the issue of recall bias (Stinson et al., 2014). The dataset also includes information on pain self-care strategies employed by the adolescents, as well as the frequency and content of interactions with the study nurse. These data will provide rich information on the prevalence and nature of cancer pain in adolescents, as well as on the timing and effectiveness of the self-care strategies adolescents’ use.

The impact of Pain Squad+ on health system costs should also be a target for future research. Cancer-related pain in adults represents a significant cost burden to patients, families and the healthcare system (Abernethy, Samsa, & Matchar, 2003) and is a major reason for cancer-related emergency health service use (Barbera, Taylor, & Dudgeon, 2010; Tsai, Liu, Tang, Chen, & Chen, 2009). Cost-effectiveness of the Pain Squad+ app should be determined using direct healthcare costs and family out-of-pocket costs related to pain. System costs related to app administration, database hosting, study nurse training, and study nurse time will also require assessment. Cost-utility of the Pain Squad+ intervention can further be assessed using quality-adjusted life years (QALYs) to determine cost per incremental unit of quality of life gained (Horsman, Furlong, Feeny, & Torrance, 2003; Sung & Regier, 2013).

Implications for Practice

Although the primary objectives this study were to refine Pain Squad+ for usability and examine the implementation of the app, data which have implications for pediatric oncology practice have emerged. If shown to be effective, Pain Squad+ could prove to be a useful tool for healthcare professionals, clinical educators, and managers (as well as policy advisory groups such as POGO) who are responsible for introducing clinical quality
improvement initiatives, including changing practice guidelines, policies, and procedures. The *Pain Squad*+ intervention could be used to support real-time pain assessment and management in a cancer patient population increasingly treated on an out-patient basis (Fortier et al., 2014; Hendershot et al., 2005). New or revised practice guidelines could educate healthcare professionals on how to adopt technology into practice and recommend “prescribing” the app to adolescents with cancer. In doing so, the knowledge generated by this research could be directly translated into practice.

This study also has implications for the use of innovative methods, such as remote real-time symptom assessment and management, in pediatric oncology practice. As demonstrated in this study, the use of Internet- and mobile-based technologies by adolescents is commonplace (Lenhart, 2015). Health interventions grounded in technologically based modalities therefore may represent a viable, useful, and potentially cost-effective means to improve adolescent health. This study has demonstrated that a pain self-management intervention can be delivered to adolescents with cancer using smartphones, with a high degree of acceptability. Self-management and mHealth interventions such as *Pain Squad*+ may therefore represent a novel means to improve the care delivered to children and adolescents with cancer and their use in routine practice should be considered.

The daily pain assessment and management data generated by study participants have provided information about the pain experience of adolescents with cancer and the degree of pain management they are engaging in at home. The momentary pain data collected from adolescents have shown pain to be a common occurrence (pain reported on 42% of completed pain assessments). These data have also shown that when pain is present, its intensity (4.4 ± 2.6/10) and impact on function (4.0 ± 2.3/10) are considerable. These data can be used to educate healthcare professionals about adolescents’ cancer pain. Ideally, healthcare
professionals will use this knowledge related to the problematic nature of cancer pain when planning care for adolescents undergoing treatment.

**Implications for Theory**

**Seto’s Model of Mobile Real-Time Patient Care Support**

Results from this research provide empirical support for Seto’s model (2011) of behaviour and health outcome change in response to mobile real-time patient care support (Figure 2). Seto’s model has been successfully used to provide conceptual direction to the development and effectiveness testing of the *Pain Squad*+ pain self-management intervention for adolescents with cancer. Using both the qualitative and quantitative findings from Studies 1 and 2, the value of the active ingredients in the enabling resource (i.e., *Pain Squad*+) was highlighted. The model’s interactions, which conceptualize the process of real-time support of patient behaviour and health outcome change, were examined through Study 2. Implications for the Expanded Health Belief Model and Connelly’s Model of Self-Care in Chronic Illness are not explicitly discussed because the constructs and interactions in these frameworks have been subsumed into Seto’s model.

In line with Seto’s model, the *Pain Squad*+ intervention was designed to include functionalities that would enhance adolescents’ capacities to engage in self-management behaviours. These functionalities were: (a) automated adherence alerts to self-monitor pain; (b) the provision of real-time pain self-care advice in any environment; and (c) individualized clinical support from a healthcare professional in response to sustained severe pain. Although not directly compared to a control group, engagement in self-management behaviours appears to have improved as a result of *Pain Squad*+. In addition, the ‘perceived control over pain’ scores obtained in this study were greater than those obtained in a previous study where pain was assessed in adolescents with cancer longitudinally, but no pain management advice was
provided (Stinson, Jibb, et al., 2015a). Qualitative results from both Study 1 and 2 also showed adolescents to perceive Pain Squad+ as useful adjuvant to usual pain care because of its ability to provide real-time self-management support.

Regarding the circular relationship between predisposing characteristics and self-management, Seto’s model proposes that adolescents with cancer who are motivated, feel a sense of self-efficacy related to pain management, and demonstrate awareness of their health, and in particular pain, will engage in pain self-management. The model further proposes that self-management will reciprocally improve these predisposing characteristics. Although motivation was not examined explicitly in this study, qualitative results indicated that adolescents were motivated to engage in self-management because they perceived doing so as beneficial. As suggested in the literature (Miller et al., 2014), qualitative findings showed that gamification mechanics included in the app (i.e., reward badges, point and leveling systems) were a motivating element supporting engagement in self-management behaviours. Pain severity was also a motivator for adolescents to engage with the app as many adolescents who did not experience pain, did not engage in routine pain assessments. Perceived barriers to self-management de-motivated adolescents and thereby inhibited engagement in associated behaviours. As an example, based on qualitative interviews, the hassle of carrying the study phone (in addition to an adolescent’s personal phone) was reported as diminishing interaction with Pain Squad+. Increased self-efficacy was not investigated as being predictive of engagement in self-management behaviours; however, self-efficacy did improve in a non-significant manner from baseline to post-study. Adolescents also reported feeling more confident in their ability to engage in self-management behaviours, such as communicating with their healthcare team, because of Pain Squad+. Based on post-study interviews, the ability of the intervention to promote awareness of pain also appeared to impact on self-
management. Adolescents specifically appreciated the capacity to self-monitor their pain and felt that doing so helped facilitate pain care.

Supporting Seto’s proposed positive interaction between self-management and health outcomes, the preliminary effectiveness outcomes from Study 2 showed pain intensity and HRQL to be significantly improved from baseline to post-study. These findings may indicate that engagement in pain self-management behaviours improved pain-related health outcomes. In addition, these findings agree with those of several studies showing positive physical and emotional outcomes in adolescents engaged in self-management interventions when compared to adolescents receiving medical care alone (Breakey et al., 2014; Cafazzo et al., 2012a; Rikkers-Mutsaerts et al., 2012; Ruotsalainen et al., 2015; Stinson et al., 2009; 2010).

According to Seto’s model, improvements in health outcomes will motivate adolescents with cancer by improving their perception of pain self-management strategies as beneficial. Improved health outcomes are further expected to result in enhanced feelings of self-efficacy and awareness of the effectiveness of self-care strategies on pain. This research did not directly examine whether improvements in outcomes resulted in changes in any of these predisposing characteristics for pain self-management. However, as mentioned, qualitative and preliminary quantitative data indicate that motivation, awareness, and pain care self-efficacy improved over the course of the study alongside changes in health outcomes.

Direct interactions between clinical management and predisposing characteristics as well as health outcomes are also expected according to the model. In this study, it was not possible to parse out the individual impact of clinical management via the study nurse from engagement in pain self-management. Qualitative results indicate that the study nurse is considered a valuable addition to the Pain Squad+ intervention, however Study 2 implementation outcomes show the nurse to be potentially under-utilized by adolescents with
sustained pain. Further research is needed to elucidate the value of clinical management in remote pain care from that of engagement in self-care activities.

In sum, this research has provided empirical support for the theoretical constructs and interactions proposed by Seto’s model. In particular, use of the enabling resource (i.e., Pain Squad+) appears to improve engagement in pain self-management and, in turn, health outcomes. Changes in health motivation, pain care self-efficacy, and pain awareness may also be reciprocally related to pain self-management. Further quantitative research with a larger sample size is needed to specifically examine the explanatory power of each of the model’s interactions in predicting pain self-management and health outcomes (Hoffman et al., 2009). Finally, this research expands Seto’s model by suggesting that novel methods to internally motivate patients to interact with the enabling resource, such as gamification mechanics, may serve to bolster engagement in self-care activities.

Additional Conceptual Framework Implications

Melzack’s neuromatrix theory of pain. The results of this research support the conceptualization of pain as a subjective multidimensional (sensory-discriminative, affective-motivational and cognitive-evaluative dimensions) construct as described in both the gate control and neuromatrix theories (Melzack, 1999a; 2005; Melzack & Wall, 1965). Through qualitative interviewing in both Study 1 and Study 2, adolescents with cancer were found to understand pain assessment question wording that pertained to each conceptualized dimension of pain. In addition, adolescent ratings of pain intensity, pain interference, and pain unpleasantness varied within and between participants, indicating that each construct was differentiated from the other and rated uniquely.

These findings are reflective of previous research with adolescents with cancer showing the content validity of a multidimensional pain assessment tool (Stinson et al., 2013). Because
of the known importance of all pain dimensions to pediatric cancer patients, further research is needed to understand whether younger children (e.g., 6 – 11 year olds) can also discriminate between and rate the multiple dimensions of pain. Additional studies are also required to explore the relationships between the different dimensions of pain in adolescents with cancer and how child- (e.g., sex, age), disease- (e.g., diagnosis, treatment stage), and pain management-level factors impact on each dimension.

Finally, the pain assessment data collected in this study were done so using self-report according to adolescents’ own schedules and in their natural environments. As such, rating biases introduced because of social transactions between patients and clinicians may have been avoided. Future research is needed to explore the potential value of Pain Squad+ in providing valid self-reports of pain in adolescents with cancer, as the app is capable of removing the influence of patient-clinician interaction.

**User-centered design approach.** This research provided support for the value of utilizing a user-centered approach when developing electronic self-management interventions. Incorporating users in the design of these complex systems means that the resultant products are more likely to be used as intended, which in turn impacts on intervention effectiveness (Johnson et al., 2005; Mao et al., 2005). The user-centered approach utilized presently through the preliminary research and Study 1, succeeded in creating an electronic self-management intervention that was implemented successfully in Study 2. During post-study qualitative interviews, adolescents reported understanding the purpose of Pain Squad+ and utilizing the functionalities of the intervention (e.g., pain assessments, pain self-care advice) as intended.

**Proctor’s implementation outcomes.** Last, a large body of literature exists related to the implementation of new health interventions into practice. Proctor and colleagues (2011) have specifically conceptualized a set of implementation outcomes, which are distinct from
service and clinical outcomes. The research presented presently has used a number of Proctor’s outcomes to evaluate the likelihood that the Pain Squad+ intervention and study protocol may be implemented into a large-scale RCT. Specifically, acceptability of the intervention and protocol at the individual patient level, intervention fidelity, and appropriateness (assessed in Study 1 interviews as utility) were measured. Proctor has conceptualized participant accrual and retention rates as being components of implementation feasibility. Adoption, or the uptake of the intervention, was measured as adherence to Pain Squad+ pain reporting. Additional implementation outcomes conceptualized by Proctor include cost, penetration, and sustainability. These outcomes are often assessed at the ‘late’ stage of implementation and therefore were not measured presently.

Using Study 2 data, interrelationships between the implementation outcomes proposed by Proctor were observed. Proctor has suggested that implementation outcomes are interrelated in dynamic and complex ways. This research supports that notion empirically by demonstrating that the fidelity with which Pain Squad+ could be delivered impacted on acceptability (i.e., technical limitations of the app decreased acceptability according to post-study interviews). Although more research is required, the initial observation of interrelationships between implementation outcomes suggests a theoretical model detailing how interactions can be developed.

The present study demonstrates the utility of Proctor’s implementation outcomes for novel intervention research. Proctor and colleagues (2009) have also developed a conceptual model of implementation research detailing end-points to evaluate implementation success. According to this model, the most important outcome criteria for evaluating implementation are at the patient-level (i.e., satisfaction, function, symptomology). A future RCT evaluating
the effectiveness of the *Pain Squad*+ intervention will provide clinical support for value of the implementation outcomes studied presently.

**Knowledge Translation**

**Knowledge Translation Objective and Audience**

The knowledge translation (KT) objective of this research is to generate awareness of and interest in the key findings regarding the development and preliminary evaluation of the *Pain Squad*+ app. This objective will be obtained with the use of both integrated and end-of-study KT approaches. If shown to be effective in a large-scale RCT, the KT objective should shift to imparting knowledge of the *Pain Squad*+ intervention, as well as generating behaviour and policy change (Barwick, 2013). Several audiences at whom this KT objective is targeted have been identified: (a) adolescents with cancer; (b) pediatric oncology healthcare professionals; (c) scientists; (d) local administrators; and (e) research funding agencies. These audiences have been identified as being highly relevant targets for KT of clinical research (Grimshaw, Eccles, Lavis, Hill, & Squires, 2012).

**Knowledge Translation Messages**

The KT messages for this study will center on: (a) the utility of user-centered methods to refine complex mHealth interventions; (b) specific components of the *Pain Squad*+ intervention that were endorsed by patients, as well as usability issues that have been recognized; (c) identified means to successfully implement mHealth interventions such as *Pain Squad*+ for effectiveness testing with adolescents; (d) adolescent reports of intervention and study protocol acceptability and areas for improvement; and (d) the potentially positive impact of the intervention on pain in adolescents with cancer.

The audiences for each KT message will vary. Healthcare professionals, scientists, local administrators, and research funding agencies will receive messages related to: (a) the
usability of Pain Squad+ by adolescents with cancer; (b) means to implement it for effectiveness testing; (c) adolescent-rated points of satisfaction with the intervention and study protocol; and (d) areas for intervention and protocol improvement. These audiences may use information gleaned from this research to support and develop future real-time remote self-management interventions for patients (including adolescents with cancer). The present results and discussion may be used to inform the needed requirements of these future interventions to ensure they are well used and successfully implemented into RCT testing for evaluation. The KT message related to the effectiveness of Pain Squad+ on pain in adolescents will be shared with all of the identified KT audiences in an effort to raise awareness about the potentially positive impact of the intervention.

Integrated Knowledge Translation Plan

An integrated KT approach involves active collaboration between researchers and knowledge users throughout the research process (Graham & Tetroe, 2007). Throughout this research project knowledge users, namely adolescents with cancer and their healthcare professionals, collaborated with the researcher. During the preliminary research process, pediatric pain and oncology healthcare professionals assisted in conceptualizing the Pain Squad+ intervention and its system requirements. Both adolescents with cancer and their healthcare professionals then vetted a draft set of Pain Squad+ system requirements and a pain management algorithm. During Study 1, iterative cycles of Pain Squad+ usability testing with adolescents with cancer helped to ensure ease of use, ease of understanding, acceptability, and efficiency of the app. During Study 2, adolescents participated in a longitudinal pilot study and provided qualitative feedback on their perceptions of the intervention and its study protocol in post-study interviews. Future Pain Squad+ research will see the incorporation of adolescent recommendations into both the app and protocol. The collection of evidence related to the
relative effect of KT strategies and approaches in the literature is ongoing (Grimshaw et al., 2012). However, similar to the rationale for the use of user-centered methods in intervention development (McCurdie et al., 2012), integrated KT is expected to improve the relevance of research findings to end-users and thereby enhance use (Graham & Tetroe, 2007).

**End-of-Study Knowledge Translation Plan**

End-of-study KT refers to dissemination or communication activities to a variety of different audiences following the completion of a research study (Graham & Tetroe, 2007). Adolescents with cancer and their interdisciplinary healthcare professional teams will be targeted. Scientists with interest in pediatric oncology and electronic health interventions, as well as unit and organizational leaders at both the Hospital for Sick Children and the Children’s Hospital of Eastern Ontario also represent an audience target. The final end-of-study KT audience will be the research funding agencies that have supported this research. Regarding these agencies, the Pediatric Oncology Group of Ontario (POGO) and C17: Children’s Cancer and Blood Disorders, who develop clinical guidelines and communicate with government agencies around pediatric cancer care, will be targeted.

The selection of KT strategies to be used will be dependent on the target audience as well as known strategy effectiveness (Barwick, 2013; Grol & Grimshaw, 2003). Strategies to promote KT to adolescents with cancer will include the development of a YouTube video for wide dissemination of study results and an adolescent-friendly infographic to be emailed to study participants. A 1-page plain language evidence summary of research results and a 3-page executive summary will be disseminated to healthcare professionals, unit leaders, and organizational leaders. These stakeholders are also expected to receive information through the strategies targeted at scientists described below.

KT strategies focused on scientists will include the didactic (plus question and answer
period) presentation of study findings by the researcher locally (i.e., POGO annual symposium, C17 videoconference, University Health Network Centre for Global eHealth Innovation rounds) and internationally (i.e., Annual Congress of the International Society of Paediatric Oncology). Peer-reviewed publication of the study results in open-access pediatric or oncology journals will also be used to disseminate knowledge to scientists.

Last, the research funding bodies that supported these studies will be made aware of the study results. This work has already begun. End-of-grant reports detailing study methods, results, and implications have been prepared and sent to Alex’s Lemonade Stand Foundation and the Canadian Institutes of Health Research. Oral presentations of the study results have also been made at POGO and the University of Toronto Centre for the Study of Pain.

**Required Resources and KT Impact Indicators**

The resources required to reach the KT objective include: financial, human, and information technology. Financial support for KT has been acquired from the granting agencies that have providing funding for this research. The key research personnel, including the researcher, who have been involved in this project from its inception will provide human resources. The information technology support required to produce the YouTube video and adolescent-friendly infographic will be acquired from the Hospital for Sick Children.

Indicators of KT impact will be those focused on KT reach. The aim will be to distribute 50 1-page evidence summaries to the pediatric hematology/oncology divisions at each of the study sites, 25 3-page executive summaries to each site, >30 000 YouTube video views (based on the number of YouTube views obtained by the precursor app to *Pain Squad+*), and 1 infographic email to each study participant (n = 33). Each of the 6 oral presentations described above will be made and manuscripts describing each of Study 1 and Study 2 will be drafted for publication.
Significance

Novel approaches are necessary to more effectively assess, treat, and monitor pain outcomes in adolescents with cancer in their everyday environments. A user-centered approach was used to develop and establish the testing procedures for the Pain Squad+ real-time smartphone pain app capable of providing pain management advice to adolescents with cancer. Pain Squad+ usability testing has refined the app, making it both acceptable and understandable to adolescents with cancer. Pilot testing has shown that, with modifications, the study protocol for the intervention arm of a future RTC can be implemented as intended (Pain Squad+ implementation outcomes). The pilot study has also been used to calculate the magnitude of intervention effects on pain intensity, pain interference, HRQL, and self-efficacy in order to establish a sample size for a RCT (Pain Squad+ effectiveness outcomes). Effect sizes for pain intensity items (0.20 – 0.69), pain interference (0.35), HRQL subscales (0.31 – 0.61), and pain care self-efficacy (0.27) were in the small to moderate range.

Once the identified modifications to the intervention and study protocol have been made, the immediate next step for this phased research project would be to evaluate the impact of Pain Squad+ in a multi-center RCT. If shown to be effective in terms of improved patient outcomes following a RCT, the Pain Squad+ intervention will represent a novel modality to improve pain treatment and ultimately HRQL life for adolescents with cancer. Although still requiring investigation, the app may further have the capacity to decrease healthcare system costs by supporting the management of adolescent cancer pain in real-time, thereby decreasing emergency health service use. Finally, Pain Squad+ as a care model represents an excellent opportunity to improve healthcare broadly through remotely monitoring and efficiently managing a range of physical and psychological health conditions. A paradigm shift in how care is supported for patients navigating their own health trajectories in the modern healthcare
system is required. The *Pain Squad*+ pain self-management intervention represents a unique modality that may expediently, successfully and cost-effectively provide such care to young patients with cancer.


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Appendix A: Studies Examining Effectiveness of Real-time Interventions to Remotely Manage Symptoms in Cancer Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Purpose of Study</th>
<th>Theoretical Rationale</th>
<th>Design/Participants</th>
<th>Real-time Intervention</th>
<th>Results Summary</th>
<th>Study Appraisal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldiss et al. (2011)</td>
<td>To pilot test the ASyMS-YG system in a group of adolescents with cancer.</td>
<td>Not reported.</td>
<td>Pilot randomized controlled trial of 4 adolescents (age range 13-15 years) at a single site.</td>
<td>Chemotherapy patients complete daily ASyMS-YG questionnaires on mobile device. Data are then sent in ‘real-time’ to a study server, which returns symptom management advice to the patient based on algorithms created by the research team. Severe symptoms alert a nurse via a 24-hour pager and the patient is contacted and assisted with decision-making. Daily plus ad hoc assessments completed.</td>
<td>Quantitative outcome results not analyzed. Adolescents liked the self-care advice given by the app and the communication with the care team. Also endorsed app as potentially helpful. Adolescents felt 14 days was not a long enough trial. Care providers did not experience technical issues and thought the tool would be useful as an accurate, real-time tracker of patient symptoms. Care providers felt adolescents should not be recruited at diagnosis because of the emotional burden and that ASyMS-YG should be completed for entire treatment course.</td>
<td>Conceptualization: Explanation of rationale included. Design: Appropriate to answer research questions. No attention control group. Recruitment: Recruitment rate data presented. No data regarding reasons non-participation. Methods/Results: Very small sample size. Daily and outcome symptom assessments not validated. Content and timing of nurse responses to patients not recorded. No quantitative data analysis completed because of sample size. Outcome symptom assessment measure was the same as the ASyMS-YG symptom assessment measure so was more familiar to intervention group. No a priori criteria for determining implementation success. No statistical testing conducted. Generalizability of conclusions: Limited generalizability as all recruited from a single site, and participants all male ages 13-15 years.</td>
</tr>
<tr>
<td><strong>Chumbler et al. (2007a)</strong></td>
<td>To compare the use of preventable services and cancer-related services by cancer patients using a telehealth program with those receiving standard care.</td>
<td>Not reported.</td>
<td>Matched case-control study of 125 adults (approximate mean age = 63 years) with a variety of cancers receiving chemotherapy at a single site.</td>
<td>Telehealth system enabling remote interactions between patients and care coordinators. Patients answered questions related to pain, fatigue, nausea, worry, functional limitations using a device plugged into their home telephone. The device used an evidence-based algorithm to provide self-care advice. Data were transferred to a remote care coordinator. If an agreed upon threshold for a symptom was surpassed, the coordinator contacted the patient. Coordinators used their own clinical judgment to advise patients. Assessments completed daily.</td>
<td>Telehealth patients used significantly fewer clinic visits (RR = 0.03, 95% CI = 0.00–0.24), bed days of care for all causes of hospitalization (RR = 0.50, 95% CI = 0.37–0.67), hospitalizations related to chemotherapy (RR = 0.43, 95% CI = 0.21–0.91) and bed days of care for chemotherapy hospitalizations (RR = 0.49, 95% CI = 0.34–0.71) than the control group.</td>
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<tr>
<td><strong>Conceptualization:</strong> Explanation of rationale included.</td>
<td><strong>Design:</strong> Not randomized, but some effort to control for potential confounders in analysis.</td>
<td><strong>Recruitment:</strong> No data on recruitment rates and reasons for non-participation.</td>
<td><strong>Methods/Results:</strong> Case-matching only for tumor-type and cancer stage (not age, symptoms etc.). Symptom severity not measured at baseline. No description of the symptom management advice given to participants (e.g. content, response time). Standardized definitions used to define care utilization. Adjusted RR used to determine risk for the effect of the system on utilization (adjusted for demographics but not symptom severity). Symptom severity in control group over study not known and may have influenced healthcare utilization. No report of compliance with system. Statistical analyses appropriate for to answer research question.</td>
<td><strong>Generalizability of conclusions:</strong> Limited generalizability (study included primarily male (94-95%) veterans from a single site).</td>
<td></td>
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</tr>
<tr>
<td>Chumbley et al. (2007b)</td>
<td>To examine the level of cooperation with and effectiveness (related to HRQL) of the ‘Health Buddy symptom management intervention in adult cancer patients.</td>
<td>Cancer Care Dialogues Model.</td>
<td>Post-test case series feasibility study of 34 adults (42-81 years) with a variety of cancers receiving chemotherapy from a single care centre.</td>
<td>A telehealth system enabling remote interaction between patients and care coordinators. Participants answered questions related to pain, fatigue, nausea, worry, functional limitations using the touchpad of their home telephone for 6-months. Assessments completed daily. Participants received self-care feedback specific to reported symptoms from a care coordinator. The method by which the care coordinator contacted the patient is not reported.</td>
<td>High level of engagement with the system (mean cooperation of 84%, range 4-100%) and observed clinically meaningful improvement in health-related quality of life (HRQL) over the study (greater improvement with older participants).</td>
<td>Conceptualization: Explanation of rational included. Study grounded in a theoretical rationale that is used to explain design and to interpret results. Design: No control group despite effectiveness testing. Recruitment: Recruitment rate and reasons for non-participation (too busy, moving away, treatment postponed) were reported. Methods/Results: Small sample size. No description of the symptom management advice given to participants (e.g. content, response time). Symptom assessment measure unidimensional. Statistical testing incomplete (intended to analyze the impact of engagement of HRQL, but did not present these results). Generalizability of conclusions: Limited generalizability (study included primarily white (91%) male (94%) veterans who were not living alone, recruited from a single site).</td>
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<tr>
<td>Cleeland et al. (2011)</td>
<td>To examine the effectiveness of an interactive voice</td>
<td>Not reported.</td>
<td>Randomized controlled trial of 79 adults (approximate)</td>
<td>Interactive voice response system contacted patients at home to assess pain,</td>
<td>Greater reduction in symptom threshold events in intervention group</td>
<td>Conceptualization: Explanation of rationale included.</td>
</tr>
<tr>
<td>Study</td>
<td>Objective</td>
<td>Methodology</td>
<td>Findings</td>
<td>Generalizability</td>
<td></td>
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<tr>
<td>Head et al. (2011)</td>
<td>To examine the effectiveness of a telehealth intervention on symptom distress, quality of life, self-efficacy, and care satisfaction, as well as the feasibility of use and acceptability</td>
<td>Pilot randomized controlled trial of 44 adults (mean age = 59 years) with head and neck cancers. Telehealth system enabling remote assessment and self-care management advice provision. Symptom management algorithms based on scientific evidence and interviews with patients and clinicians. Study nurse or high level of engagement with the system (mean compliance over time of 86.3%, SD of 15%). Thirty-three of 45 patients required nurse call. Unrelieved pain was the reason for 30% of nurse contacts. Overall patient satisfaction ratings with high level of satisfaction.</td>
<td>Compared to control (19% vs. 8%). More rapid decline in symptom threshold events in intervention group ($p = 0.003$). Greater average reduction in symptom interference in the intervention group (difference between groups 0.36 on a 0-10 scale, $p = 0.02$).</td>
<td>Limited generalizability as all recruited from a single site.</td>
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</tr>
</tbody>
</table>

**Comment**: The use of a telehealth system for symptom management after thoracotomy is effective in reducing symptom distress and improving quality of life, self-efficacy, and care satisfaction. The system was feasible and well-accepted by patients. The results are limited by the small sample size and single-site recruitment. Further research is needed to generalize these findings to other populations and settings.
| Kearney et al. (2009) | To determine the feasibility of and preliminarily evaluate a trial of effect the ASyMS© system on the incidence, severity and distress caused by nausea, vomiting, fatigue, mucositis, hand–foot syndrome and diarrhea related to chemotherapy. | Not reported. | Pilot randomized controlled trial of 112 adults (mean age = 56 years) with a variety of cancers receiving chemotherapy. | Chemotherapy patients complete twice-daily and ad hoc ASyMS© questionnaires on mobile device. Data are then sent in ‘real-time’ to a study server, which returns symptom management advice to the patient based on algorithms created by the research team. Severe symptoms alert a nurse via a 24-hour pager and the patient is contacted and assisted with decision-making. Twice-daily plus ad hoc assessments completed. | Moderate attrition rates (20-27%). No significant differences in attrition rates between study arms. More reports of fatigue in the control group (OR = 2.29, 95% CI = 1.04, 5.05, \( p = 0.040 \)) and less reports of hand-and-foot syndrome in the control group (OR = 0.39, 95% CI = 0.17, 0.92, \( p = 0.031 \)). Higher severity of hand-foot syndrome (OR = -0.27, 95% CI = -0.52, -0.02, \( p = 0.033 \)) and distress related to hand-foot syndrome (OR = -

Methods/Results: Quality of nurse response not documented in study. No data on the validity or dimensionality of daily symptom assessment. No data on the demographics of the control group are presented. No data regarding how nurse decisions regarding care were made or time to decision. Threshold for a nurse call is not clear. Statistical analyses appropriate to answer research question, but conducted in treatment group only.

Generalizability of conclusions: Recruited from a single site. Participants overwhelmingly male (90%).

Conceptualization: Explanation of rationale included.

Design: Appropriate to answer research questions.

Recruitment: No data on recruitment rates and reasons for non-participation.

Methods/Results: Twice-daily and outcome symptom assessments not validated. High attrition rates in both arms. Engagement on the part of patients and nurses not reported. Study was not powered to detect changes (regardless inferential
| Kroenke et al. (2010) | To examine the effectiveness of an automated telecare management pain and depression outcomes in patients with cancer. | Randomized controlled trial of 405 adults (approximate mean age = 58 years) with cancer-related pain and/or depression. | Patients used either interactive voice-recorded telephone calls or Internet surveys to report pain and/or depression. Clinical follow-up occurred in cases of inadequate symptom improvement, medication non-adherence, and suicidal ideation or on patient request. Follow-up based on standardized algorithms and discussion with primary team. Scheduled calls from a | Improved pain and depression score and number of categorical pain or depression responders in the intervention group (p < 0.001 for all). Effect sizes for between-group differences at 3 and 12 months were 0.67 (95% CI = 0.33, 1.02) and 0.39 (95% CI = 0.01, 0.77) for pain and 0.42 (95% CI = 0.16, 0.69) and 0.41 (95% CI = 0.08, 0.72) for depression. | Conceptualization: explanation of rationale included. Design: Appropriate to answer research question. Attention not controlled for in control group. Recruitment: Information on recruitment presented by reasons for non-participation not included. Methods/Results: Participants not stratified by site or intervention medium (phone or Internet). Validated and multidimensional tool used to assess symptoms. | 0.17, 95% CI = -0.33, -0.02, p = 0.028) reported by the intervention group. Statistics were calculated. Outcome symptom assessment measure was the same as the ASyMS symptom assessment measure so was more familiar to intervention group. No data regarding how nurse decisions regarding care were made or time to decision. Comparable groups with respect to demographics and disease assembled at baseline. Equivalence with respect to symptom status not known. Statistical analyses appropriate for to answer research question. Generalizability of conclusions: Patients recruited from 7 centres with diverse characteristics. |
Sundberg et al. (2015) | To pilot test an interactive smartphone-platform for which collects and manage patient reported symptoms during radiotherapy for prostate cancer. | Not reported. | One-arm pilot study of 9 adults (mean age 69 years) at 2 sites. | Radiotherapy patients complete daily symptom reports on a smartphone. Data are sent to a study server, which is monitored by a group of nurses who then contacts the patient to discuss issue for 14 days. Links to self-care advice are also provided via the phone. | Self-care advice was accessed by 85% of the patients (total of 20 viewing occasions). Qualitative interviews showed the system to be acceptable (symptom questionnaire and the self-care advice relevant; application user-friendly; nurse contact a valued asset). No technical difficulties occurred. | Comparable groups with respect to demographics, disease and symptom status assembled at baseline. Engagement on the part of patients and nurses not reported. Study was powered to detect a clinically meaningful change in pain and depression scores. Statistical analyses appropriate for to answer research question. | Generalizability of conclusions: Very specific inclusion criteria but study conducted across 16 urban and rural centres. |
| Yap et al. (2013) | To pilot a pharmacist-run tele-oncology service using text messaging to monitor nausea and vomiting in ambulatory cancer patients. | Not reported. | One-arm pilot study of 68 adults (median age 49.5 years; males and females) at a single site. | Post-chemotherapy patients complete daily text message assessments of nausea and vomiting for 5 days. Self-care advice was provided according to an algorithm and a pharmacist contacted patients in response to uncontrolled symptoms. | Study accrual rate was 37.6%. Adherence to reporting was 73.3%. Participants (90.0%) found the duration of monitoring acceptable and the self-care advice useful (61.7%). Pharmacists made 22 calls across all participants in response to uncontrolled symptoms. | Conceptualization: Explanation of rationale included. | Design: Appropriate to answer research questions. No attention control group. | Recruitment: Recruitment rate data and reasons for non-participation presented. Withdrawals and loss-to-follow-up presented. | Methods/Results: Method used to develop algorithm presented. Validated symptom assessment tools used. Several implementation outcomes assessed. No a priori criteria for determining implementation success. Rationale for and details of pharmacist contact reported. Generalizability of conclusions: Enhanced by large sample for a pilot study. Participant group heterogeneous but recruited from a single site. |

CI, confidence interval; HRQL, health-related quality of life; OR, odds ratio; RR, relative risk; SD, standard deviation.
### Appendix B: *Pain Squad*+ Pain Assessment Questions

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer type</th>
<th>Answer option(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  Did you have PAIN in the last 12 hours?</td>
<td>Discrete</td>
<td>Y or N</td>
</tr>
<tr>
<td>2  Touch the mark and move it to show how much PAIN you have right now</td>
<td>Continuous</td>
<td>Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>3  Touch the mark and move it to describe your pain when it was at its WORST in the last 12 hours</td>
<td>Continuous</td>
<td>Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>4  Touch the mark and move it to describe your pain when it was at its LEAST in the last 12 hours</td>
<td>Continuous</td>
<td>Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>5  Touch the mark and move it to describe your pain when it was at its AVERAGE in the last 12 hours</td>
<td>Continuous</td>
<td>Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>6  When you had pain the last 12 hours, how long did it USUALLY last?</td>
<td>Discrete</td>
<td>Just a few minutes, About an hour, 1 to 3 hours, 3 to 6 hours, 6 to 9 hours, 9 to 12 hours</td>
</tr>
<tr>
<td>7  Please tell us what you think your pain was DUE TO in the last 12 hours</td>
<td>Discrete</td>
<td>Your treatments (chemotherapy, radiation, medication, surgery), Your Cancer, Medical condition(s) other than your cancer (e.g. arthritis, sickle cell disease), Medical procedures (e.g. lumbar puncture, bone marrow aspirate, IV insertion, bloodwork), Everyday Pain, Other (please specify)</td>
</tr>
<tr>
<td>8  Touch the parts of the body picture to show WHERE YOU HURT in the last 12 hours</td>
<td>Continuous</td>
<td>Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>9  Touch the mark and move it to show how BOTHERSOME your pain was in the last 12 hours</td>
<td>Continuous</td>
<td>Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>10 Touch the mark and move it to show how much your pain got in the way of your SLEEP in the last 12 hours</td>
<td>Continuous</td>
<td>Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>11 Touch the mark and move it to show how much your pain got in the way of THINGS YOU DID in the last 12 hours</td>
<td>Continuous</td>
<td>Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>12 Touch the mark and move it to show how much your pain got in the way of HOW YOU FELT in the last 12 hours</td>
<td>Continuous</td>
<td>Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>13 Touch the mark and move it to show how much your pain got in the way of WALKING in the</td>
<td>Continuous</td>
<td>Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td></td>
<td>last 12 hours</td>
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<td>---</td>
<td>-------------------------------------------------------------------------------</td>
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</tr>
<tr>
<td>14</td>
<td>Touch the mark and move it to show how much your pain got in the way of RELATIONSHIPS with friends and family in the last 12 hours</td>
<td>Continuous Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>15</td>
<td>Touch the mark and move it to show how much your pain got in the way of SCHOOLWORK in the last 12 hours</td>
<td>Continuous Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>16</td>
<td>Touch the mark and move it to show how much your pain got in the way of ENJOYING LIFE in the last 12 hours</td>
<td>Continuous Visual analogue slider scale (0-100)</td>
</tr>
<tr>
<td>17</td>
<td>Touch the words that best describe how your pain felt in the last 12 hours</td>
<td>Discrete Variety of words describing pain quality</td>
</tr>
</tbody>
</table>
| 18| Please tell us what other symptoms you have experienced in the last 12 hours | Discrete | Nausea  
Feeling drowsy  
Numbness/Tingling in hands/feet  
Vomiting  
Itching  
Lack of appetite  
Difficulty swallowing  
Mouth sores  
Constipation  
Changes in skin  
Diarrhea |
| 19a| Please tell us about the medications you have taken to try to REDUCE your pain in the last 12 hours | Discrete | None  
Acetaminophen (Tylenol)  
Ibuprofen (Advil)  
Naproxen  
Codeine  
Morphine (short-acting)  
Morphine (long-acting)  
Gabapentin  
Amitriptyline  
Other (please list) |
| 19b| How helpful was using this strategy? | Discrete | Not helpful  
A little helpful  
Somewhat helpful  
Very helpful  
Don't know |
| 20a| Please tell us about other things you used to try to REDUCE your pain in the last 12 hours | Discrete | None  
Deep breathing  
Relaxation exercises  
Heat  
Cold  
Massage/rubbing  
Imagery  
Distraction (e.g. TV, books, music)  
Talking with friends/family  
Rest/sleep  
Prayer/meditation  
Other (please list) |
| 20b| How helpful was using this | Discrete | Not helpful |
| 21 | Touch the mark and move it to show how much CONTROL you felt you had over your pain in the last 12 hours | Continuous | Visual analogue slider scale (0-100) |
| 22 | Please type in anything else you want to tell us about your pain in the last 12 hours | Free-text |
## Appendix C: Studies of Pediatric Oncology Non-pharmacological Pain Management

<table>
<thead>
<tr>
<th>Therapy modality</th>
<th>Study</th>
<th>Design</th>
<th>Number of participants; Age range</th>
<th>Primary clinical condition</th>
<th>Pain source</th>
<th>Intervention group vs. comparator group</th>
<th>Pain measure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Art</td>
<td>Madden et al., 2010</td>
<td>pilot-RCT + qualitative interview</td>
<td>16; 2-13 years</td>
<td>Brain tumor, non-specified cancer diagnoses</td>
<td>Course of treatment</td>
<td>6-1 hour training sessions in dance, music and art vs. attention control</td>
<td>PedsQL Cancer Module pain subscale (parent-report)</td>
<td>Reduction in parent-reported pain ($p = 0.03$). Highlight sig results</td>
</tr>
<tr>
<td>Distraction</td>
<td>Gershon et al., 2004</td>
<td>RCT</td>
<td>59; 7-19 years</td>
<td>Leukemia, lymphoma, solid tumour</td>
<td>IVAP access</td>
<td>VR distraction + EMLA vs. non-VR distraction + EMLA vs. EMLA</td>
<td>100mm VAS (self-report, parent-report &amp; nurse-report) &amp; CHEOPS (researcher-report)</td>
<td>Nurses-reported pain to be reduced in VR distraction ($p &lt; 0.05$).</td>
</tr>
<tr>
<td></td>
<td>Hedén et al., 2009</td>
<td>RCT</td>
<td>28; 2-7 years</td>
<td>Leukemia, CNS tumor, solid tumour</td>
<td>IVAP access</td>
<td>Distraction (blowing bubbles) + EMLA vs. attention control + EMLA</td>
<td>100mm VAS (parent-report &amp; nurse-report)</td>
<td>No difference in pain.</td>
</tr>
<tr>
<td></td>
<td>Thanh Nhan et al., 2010</td>
<td>RCT</td>
<td>40; 7-12 years</td>
<td>Leukemia</td>
<td>LP</td>
<td>Self-selected music vs. attention control</td>
<td>0-10 numerical rating scale (self-report)</td>
<td>Pain reduced in the music group ($p &lt; 0.001$).</td>
</tr>
<tr>
<td></td>
<td>Windich-Biermeier et al., 2007</td>
<td>RCT</td>
<td>50; 5-18 years</td>
<td>Leukemia, lymphoma, solid tumour</td>
<td>IVAP access or venipuncture</td>
<td>Self-selected distractor + EMLA &amp; education vs. EMLA &amp; education</td>
<td>Colour analogue scale (self-report)</td>
<td>No difference in pain.</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Age Range</td>
<td>Condition</td>
<td>Intervention</td>
<td>Outcome Measure</td>
<td>Findings</td>
<td></td>
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<tr>
<td>Wint et al., 2002</td>
<td>RCT</td>
<td>30; 10-19</td>
<td>Leukemia, Lymphoma</td>
<td>LP</td>
<td>VR + midazolam, EMLA &amp; education vs. midazolam, EMLA &amp; education</td>
<td>100mm VAS</td>
<td>No difference in pain.</td>
<td></td>
</tr>
<tr>
<td>Wolitzky et al., 2005</td>
<td>RCT</td>
<td>20; 7-14</td>
<td>Non-specified cancer diagnoses</td>
<td>IVAP access</td>
<td>VR vs. non-VR distraction during procedure</td>
<td>CHEOPS (nurse-report)</td>
<td>Decrease ($p &lt; 0.05$) in nurse-rating pain in VR group.</td>
<td></td>
</tr>
<tr>
<td>Katz et al., 1987</td>
<td>RCT</td>
<td>86; 6-11</td>
<td>Leukemia</td>
<td>BMA</td>
<td>Hypnosis vs. attention control (play)</td>
<td>1-100 numerical rating scale (self-report)</td>
<td>Decreased pain ($p &lt; 0.05$) in both groups.</td>
<td></td>
</tr>
<tr>
<td>Liossi &amp; Hatira, 2003</td>
<td>RCT</td>
<td>80; 6-16</td>
<td>Leukemia, non-Hodgkin’s Lymphoma</td>
<td>LP</td>
<td>Direct hypnosis vs. indirect hypnosis vs. attention control vs. control</td>
<td>Wong-Baker Faces Scale (self-report)</td>
<td>Reduced pain in the hypnosis groups compared to control groups ($p &lt; 0.001$).</td>
<td></td>
</tr>
<tr>
<td>Liossi et al., 2006</td>
<td>RCT</td>
<td>45; 6-16</td>
<td>Leukemia, non-Hodgkin’s Lymphoma</td>
<td>LP</td>
<td>Hypnosis + EMLA vs. Attention control + EMLA vs. EMLA</td>
<td>Wong-Baker Faces Scale (self-report)</td>
<td>Reduced pain in hypnosis groups compared to control groups ($p &lt; 0.001$).</td>
<td></td>
</tr>
<tr>
<td>Liossi et al., 2009</td>
<td>RCT</td>
<td>45; 7-16</td>
<td>Non-specified cancer diagnoses</td>
<td>Venipuncture</td>
<td>Hypnosis + EMLA vs. Attention control + EMLA vs. EMLA</td>
<td>100mm VAS (self-report)</td>
<td>Reduced pain in hypnosis groups compared to control groups ($p &lt; 0.05$).</td>
<td></td>
</tr>
<tr>
<td>Zeltzer &amp; LeBaron 1982</td>
<td>pre- &amp; post-test with control</td>
<td>33; 6-17</td>
<td>Leukemia &amp; non-Hodgkin’s Lymphoma, neural tumour</td>
<td>LP or BMA</td>
<td>Hypnosis vs. distraction, deep-breathing &amp; preparation</td>
<td>1-5 numerical pain scale (self-report)</td>
<td>Hypnosis reduced BMA &amp; LP pain ($p &lt; 0.001$). CBT reduced BMA pain ($p &lt; 0.01$).</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design Type</td>
<td>Age Range</td>
<td>Disease/Procedure</td>
<td>Method of Pain Management</td>
<td>Course of Treatment</td>
<td>Pain Assessment Tools</td>
<td>Findings</td>
<td></td>
</tr>
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<td></td>
</tr>
<tr>
<td>Ackerman et al., 2012</td>
<td>Qualitative examination</td>
<td>23; 5-18 years</td>
<td>Variety of cancers &amp; bone marrow failure</td>
<td>Minimum 3-weekly massages by therapist &amp;/or parents during hospital stay</td>
<td>Open-ended interview</td>
<td>100mm VAS or Wong-Baker Faces Scale (self-report; 3-18 years) &amp; Pain Assessment Tool (parent-report; 1-2 years)</td>
<td>Parents reported that child experienced relief from pain.</td>
<td></td>
</tr>
<tr>
<td>Post-White et al., 2008</td>
<td>RCT with cross-over</td>
<td>23; 1-18 years</td>
<td>Non-specified cancer diagnoses</td>
<td>4-weekly massages vs. quiet-time control</td>
<td></td>
<td>No difference in pain.</td>
<td>Patient reported pain reported as decreased with hand-holding (especially by mother).</td>
<td></td>
</tr>
<tr>
<td>Weekes et al., 1993</td>
<td>Qualitative examination</td>
<td>20; 11-19 years</td>
<td>Leukemia, retinoblastoma</td>
<td>Holding mother or nurse’s hand</td>
<td>Semi-structured interview</td>
<td>No difference in pain.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisignano &amp; Bush 2006</td>
<td>RCT</td>
<td>30; 7-18 years</td>
<td>Variety of cancers &amp; hematological disorders</td>
<td>Venipuncture, IVAP access</td>
<td>Education, modeling, deep-breathing, distraction, imagery + EMLA vs. education, EMLA</td>
<td>0-100 numerical rating scale (self-report)</td>
<td>No difference in pain.</td>
<td></td>
</tr>
<tr>
<td>Broome et al., 1998</td>
<td>Single-group repeated measures</td>
<td>28; 4-18 years</td>
<td>Non-specified cancer diagnoses</td>
<td>LP</td>
<td>Relaxation, distraction &amp; imagery</td>
<td>Oucher scale (self-report)</td>
<td>Pain reduction ($p &lt; 0.05$).</td>
<td></td>
</tr>
<tr>
<td>Jay et al., 1987</td>
<td>Repeated measures cross-over</td>
<td>56; 3-13 years</td>
<td>Leukemia</td>
<td>BMA</td>
<td>Modeling, deep-breathing, incentive, distraction, rehearsal vs.</td>
<td>0-100 numerical rating scale (self-report)</td>
<td>Reduction in pain between CBT and control group ($p &lt; 0.01$). No</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Age Group</td>
<td>Diagnosis</td>
<td>Intervention</td>
<td>Measure of pain</td>
<td>Difference in pain</td>
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<tr>
<td>Jay et al., 1991</td>
<td>Repeated measures factorial design</td>
<td>83; 3-12 years</td>
<td>Leukemia or lymphoma</td>
<td>LP or BMA</td>
<td>Peer-modeling, cognitive restructuring, deep-breathing, distraction, incentive, rehearsal vs. same + diazepam</td>
<td>5-point faces scale (self-report)</td>
<td>Main effect of time ($p &lt; 0.01$).</td>
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<tr>
<td>Jay et al., 1995</td>
<td>Repeated measures cross-over</td>
<td>18; 3-12 years</td>
<td>Leukemia</td>
<td>BMA</td>
<td>Peer-modeling, cognitive restructuring, distraction, rehearsal vs. general anesthesia</td>
<td>5-point faces scale (self-report)</td>
<td>No difference in pain.</td>
<td></td>
</tr>
<tr>
<td>Liossi &amp; Hatira, 1999</td>
<td>RCT</td>
<td>30; 5-15 years</td>
<td>Leukemia</td>
<td>BMA</td>
<td>Direct hypnosis vs. relaxation, deep-breathing and cognitive restructuring vs. attention control</td>
<td>6-point faces scale (self-report)</td>
<td>Pain reduced over time hypnosis group and CBT group ($p &lt; 0.008$). Hypnosis and CBT more effective than control.</td>
<td></td>
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<tr>
<td>Manne et al., 1990</td>
<td>RCT</td>
<td>23; 3-9 years (mean:4.7)</td>
<td>Non-specified cancer diagnoses</td>
<td>Venipuncture</td>
<td>Parent-initiated distraction, deep-breathing &amp; positive reinforcement vs. attention control</td>
<td>FACES scale (self-report) &amp; 100mm VAS (parent-report)</td>
<td>No difference in self-reported pain. Decrease in parent-report of pain ($p &lt; 0.005$).</td>
<td></td>
</tr>
<tr>
<td>Pederson, pre- &amp; post-</td>
<td>RCT</td>
<td>8; 6-14 years</td>
<td>Leukemia</td>
<td>LP</td>
<td>Deep-breathing,</td>
<td>100mm VAS</td>
<td>No difference in</td>
<td></td>
</tr>
<tr>
<td>Year</td>
<td>Test Method</td>
<td>Control Method</td>
<td>Treatment Type</td>
<td>Outcome</td>
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<tr>
<td>1996</td>
<td>Test with control</td>
<td>Control</td>
<td>Progressive relaxation, distraction vs. control</td>
<td>Pain</td>
<td></td>
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</tr>
</tbody>
</table>

BMA, bone marrow aspirate; CBT, cognitive behavioural therapy; CNS, central nervous system; EMLA, eutectic mixture of local anesthetics; IVAP, implanted venous access port; LP, lumbar puncture; RCT, randomized controlled trial; VAS, visual analogue scale; VR, virtual reality.
Appendix D: Pain Squad+ Smartphone-Based Pain Management App Screenshots

Top row, left to right: (a) pain advice recommendation screen (advice informed by algorithm and based on adolescent pain reports; (b) sample of self-management advice; and (c) detailed view of ‘Mental Games’ self-management advice for pain. Bottom row, left to right: (d) detailed view of imbedded audio-recording of ‘Muscle Relaxation Mindfulness’ self-management advice for pain; (e) gamification mechanic (point and leveling system); and (f) game mechanic (badges)
Appendix E: Pain Management Algorithm

Legend

- no pain or pain < 30
- pain ≥ 30

Pain advice should be given as follows:

If (1) current pain, (2) pain in since last report or (3) pain getting in the way of things you did is 0 or < 30 – this would be classified as mild

If answers to any question is rated as greater than or equal to 30 it is moderate/severe

If an answer to “how much control you had since last report” is between 71 and 100 – this would be classified as mild

If a response to this question is 70 or less – this would be moderate/severe

***The most ‘severe’ response to any of these questions should drive advice – that is, (as an example) if pain now is 10, pain since last report is 20, interference is 20 and control is 40 – this would be a moderate/severe report

Email alert to healthcare provider

User receives popup alert

END
## Appendix F: *Pain Squad*+ Pain Management Advice

<table>
<thead>
<tr>
<th>Wireframe Template</th>
<th>Name of Advice</th>
<th>Duration</th>
<th>Most Effective For</th>
<th>Overview Page (eg. 9.x.1)</th>
<th>Additional Screens or Slides (eg. 9.x.1.1 and 9.x.1.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.x.4 – Scrolling Page</td>
<td>Numbing Cream</td>
<td>45 - 60 minutes</td>
<td>Before Procedures</td>
<td>Remember to apply a pain numbing cream (topical anesthetic) 45-60 minutes before the procedure if your healthcare team has said it’s okay.</td>
<td>N/A (This advice only has one screen)</td>
</tr>
<tr>
<td>9.x.4 – Scrolling Page</td>
<td>Take Your Pain Medications Regularly</td>
<td>1 minute</td>
<td>Surgery, Headaches, Abdomen Pain</td>
<td>Make sure you are sticking to the medication schedule your doctor recommends. If taking your medications is difficult, you can speak to your pharmacist about useful options such as setting reminders on a cell phone or using post-it notes. Make sure to talk to your doctor, nurse, or pharmacist if you’re having trouble taking your medications, if they are not working or if you’re having side effects from them.</td>
<td>N/A (This advice only has one screen)</td>
</tr>
<tr>
<td>9.x.4 – Scrolling Page</td>
<td>Take an “as needed” medication</td>
<td>1 minute</td>
<td>Surgery, Headaches, Abdomen Pain etc.</td>
<td>If your doctor has given you a medication for break-through pain AND it is time to take it, consider taking it now. You can talk to your</td>
<td>N/A (This advice only has one screen)</td>
</tr>
<tr>
<td>Wireframe Template</td>
<td>Name of Advice</td>
<td>Duration</td>
<td>Most Effective For</td>
<td>Overview Page (eg. 9.x.1)</td>
<td>Additional Screens or Slides (eg. 9.x.1.1 and 9.x.1.2)</td>
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<td>parents or healthcare team if you’re not sure about when and how to take these medications. Make sure to talk to your doctor, nurse, or pharmacist if you’re having trouble taking your medications, if they are not working or if you’re having side effects from them.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Step 1</td>
<td>Behaviour rehearsal helps you to prepare for an event that you think will be stressful before it even happens, like a painful procedure. What you need to do is break the situation into parts that you can imagine.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Step 2</td>
<td>Behaviour rehearsal helps you to prepare for an event that you think will be stressful before it even happens, like a painful procedure. What you need to do is break the situation into parts that you can imagine.</td>
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<tr>
<td></td>
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<td>Additional Screens or Slides (eg. 9.x.1.1 and 9.x.1.2)</td>
<td>N/A (This advice only has one screen)</td>
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<td>N/A (This advice only has one screen)</td>
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<td>N/A (This advice only has one screen)</td>
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<td>N/A (This advice only has one screen)</td>
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<td>N/A (This advice only has one screen)</td>
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</tbody>
</table>

**Behaviour Rehearsal**

- **5-10 minutes**
- **Before Procedures**

**Step 1**
Rehearse what you are going to do to relax, stay calm, and get through the procedure.

**Step 2**
Relax your muscles, breathe deeply, stay calm and use positive thoughts like “I can do this”.

**Step 3**
Imagine how you will relax during each part of the procedure.

**Step 4**
When you’ve made it through the procedure, make sure you have a plan to celebrate your success! You might not be able to cope exactly the way you wanted, but you still made it through!

**Distraction**

- **5-30 minutes**
- **During Procedures, Headaches, Abdomen Pain, Muscle Pain etc.**

By turning your attention to something else, you can block out unpleasant or stressful thoughts.

Make sure to choose pleasant things to focus your attention on.

You can do things like listen to music, play video games or concentrate on your breathing.

**Alphabet Game**

1. Think of any

**Song Lyrics**

Try to

**Count the Tiles**
<table>
<thead>
<tr>
<th>Wireframe Template</th>
<th>Name of Advice</th>
<th>Duration</th>
<th>Most Effective For</th>
<th>Overview Page (eg. 9.x.1)</th>
<th>Additional Screens or Slides (eg. 9.x.1.1 and 9.x.1.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abdomen Pain, Muscle Pain etc.</td>
<td>your mind busy with another activity. As a result, your mind isn’t available to think about pain.</td>
<td>category of interest, such as sports, cars, teams, animals, or countries.</td>
<td>remember all the words to your favourite song</td>
<td>Count the number of tiles on the floor or dots on an area of the ceiling</td>
</tr>
</tbody>
</table>

<p>| 9.x.1 – Step-by-Step Slider | Imagery | 5-30 minutes | During Procedures, Headaches, Abdomen Pain, Muscle Pain etc. | Imagery is like daydreaming except that you are doing it on purpose. Some people find it easy to use their imagination to distract themselves. Others need more practice. | <strong>Step 1</strong> Imagine being in a pleasant place, maybe on a beach or in a park with your family and friends. This is much more interesting to think about than pain! <strong>Step 2</strong> Involve as many of your 5 senses as you can. For example, if you are thinking about the beach, think about the sound of the water, all the sights on the beach, the smell of the ocean or lake, the feeling of the sand, and the taste of the water. | |
| 9.x.1 – Step-by-Step Slider | Mini-relaxation | 5 minutes | During Procedures, Headaches, Abdomen Pain, Muscle Pain etc. | Mini-relaxation is a very quick and easy way to relax when you feel stressed or are feeling pain wherever you are. | <strong>Step 1</strong> Take a deep breath in through your nose. Feel your stomach rise as you take in the deep breath. <strong>Step 2</strong> Hold your breath for a few seconds while you count to 5. <strong>Step 3</strong> Roll your shoulders in a big circle and then let them drop loose. Think “r-e-l-a-x.” <strong>Step 4</strong> Breathe out through your mouth, slow and relaxed, as if you’re softly whistling. Repeat steps and feel more relaxed each time. | |
| Physi... | Applying Cold | 15-20 minutes | Mouth Sores, Muscle Pain | Cold temperatures can help reduce pain. For instance, the cold | |</p>
<table>
<thead>
<tr>
<th>Wireframe Template</th>
<th>Name of Advice</th>
<th>Duration</th>
<th>Most Effective For</th>
<th>Overview Page (eg. 9.x.1)</th>
<th>Additional Screens or Slides (eg. 9.x.1.1 and 9.x.1.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applying Heat</td>
<td>15-20 minutes</td>
<td>Abdomen Pain, Muscle Pain etc.</td>
<td>Warm temperatures can help reduce pain.</td>
<td>For instance, the warm temperature of a hot pack can reduce muscle aches! Apply a hot pack to the area you are feeling pain. Remember not to apply heat to wounds or stitches.</td>
<td></td>
</tr>
</tbody>
</table>

| 9.x.1 – Step-by-Step Slider | 5-30 minutes | During Procedures, Headaches, Abdomen Pain, Muscle Pain etc. | Belly breathing is one of the best and easiest ways to relax. It can help you manage pain and also distract you from unpleasant situations. | Step 1  
· Lie down, knees bent, place 1 hand on your chest and 1 hand just above your belly button.  
[Step 1 animation Slide 1]  
Step 2  
· Take a deep breath in through your nose, pushing your belly out.  
· Feel your bottom hand, on your belly, move out. The top hand on your chest should stay still.  
· Notice how long your inhaled breath is by counting.  
· When your belly is all the way out,  
Step 3  
· ...now breathe out slowly, through puckered lips, to the same count you used to breathe in.  
· Let your belly come down until it is flat.  
Step 4  
· Repeat slowly a few times.  
· Notice your body beginning to feel relaxed with each breath out.  
· After you have practiced this exercise a few times, you can make the count longer to get an even deeper, more relaxing breath. |

sensation from popsicles and ice chips can be really helpful for mouth sores!  
Apply a cold pack or other cold things like ice to the area you are feeling pain.  

[Belly-breathing animation Slide 1]
<table>
<thead>
<tr>
<th>Wireframe Template</th>
<th>Name of Advice</th>
<th>Duration</th>
<th>Most Effective For</th>
<th>Overview Page (eg. 9.x.1)</th>
<th>Additional Screens or Slides (eg. 9.x.1.1 and 9.x.1.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.x.1 – Step-by-Step Slider</td>
<td>Mental Relaxation</td>
<td>10 minutes</td>
<td>Surgeries, Headaches, Abdomen Pain, Muscle Pain etc.</td>
<td>Step 1: Find a comfortable, quiet place to sit.</td>
<td>Step 2: When you hit play, an audio recording will start. The audio recording will lead you through the relaxation exercise. [Audio File Play Button]</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>pause for a moment...</td>
<td>breathing animation Slide 2</td>
</tr>
<tr>
<td>Muscle Relaxation</td>
<td></td>
<td>15 minutes</td>
<td>Headaches, Abdomen Pain, Muscle Pain etc.</td>
<td>Step 1: Find a comfortable, quiet place to sit.</td>
<td>Step 2: When you hit play, an audio recording will start. The audio recording will lead you through the relaxation exercise. [Audio File Play Button]</td>
</tr>
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</tr>
<tr>
<td>9.x.4 – Scrolling Page</td>
<td>Gentle exercise</td>
<td>10-40 minutes</td>
<td>Muscle Pain, Headache, Abdominal Pain, Surgeries</td>
<td>Try gentle exercising by going for a walk.</td>
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<tr>
<td></td>
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<td></td>
<td>Research shows that physical activity can help you manage symptoms like pain.</td>
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<td></td>
<td>It’s important to talk to your health care provider and maybe a physiotherapist before you start adding physical activity to your routine. Some types of exercise may be risky depending on the type of cancer</td>
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<td>N/A (This advice only has one screen)</td>
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<tr>
<td>Wireframe Template</td>
<td>Name of Advice</td>
<td>Duration</td>
<td>Most Effective For</td>
<td>Overview Page (eg. 9.x.1)</td>
<td>Additional Screens or Slides (eg. 9.x.1.1 and 9.x.1.2)</td>
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</tr>
<tr>
<td>9.x.3 – Drill Down Table</td>
<td>Stretching (yoga)</td>
<td>10-40 minutes</td>
<td>Muscle Pain, Headache, Abdominal Pain, Surgeries</td>
<td>Yoga aims to restore the balance between one’s body, mind, and spirit through a series of gentle exercises and breathing techniques. There are lots of poses you can do in yoga.</td>
<td>Mountain (tadasana) pose</td>
</tr>
</tbody>
</table>

Mountain (tadasana) pose

(1) Stand with feet hip-width apart and your weight evenly balanced between them.
(2) Pull up through the top of your forehead and try to make your spine feel longer.
(3) Tilt your tailbone (bottom of your spine) under so it points towards the ground, with your shoulders away from the ears.
(4) Breathe in and out smoothly.
(5) Mentally scan your body, releasing any tension. Relax your neck, face, jaw, and tongue.

Tell yourself a positive phrase like “I am strong and brave”.

[Image from TTC Website]

Archer pose

(1) While standing, step forward with your left leg so your legs are about 2.5 feet apart.
(2) Turn your right foot out at a 45-degree angle.
(3) Raise your left arm straight out in front, parallel to the ground, with your hand in a fist.
(4) Pull your right arm back as if it’s pulling back on a bowstring.
(5) Both wrists form a straight line with your shoulders. Bend your left knee and squeeze your thighs together.
(6) Look at your left fist and feel like a strong warrior.

[Image from TTC Website]

Tree pose

(1) Stand upright and shift your weight to 1 foot.
(2) When you feel stable, place your other foot either at your ankle or inner thigh. Focus on a spot in front of you to help you balance.
(3) Breathe deeply and raise your arms and put your hands together in front of your chest.

[Image from TTC Website]

Ego pose

(1) Sitting at the edge of the bed, raise your arms overhead in a V shape.
(2) Stretch your thumbs to the sky and curl your fingers onto the palms of your hand.
Breathe in and out slowly. Hold for as long as you can, up to a minute.

[Image from TTC Website]
<table>
<thead>
<tr>
<th>Wireframe Template</th>
<th>Name of Advice</th>
<th>Duration</th>
<th>Most Effective For</th>
<th>Overview Page (eg. 9.x.1)</th>
<th>Additional Screens or Slides (eg. 9.x.1.1 and 9.x.1.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ego pose</td>
<td></td>
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<td></td>
<td>then switch legs.</td>
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<td></td>
<td>[Image from TTC Website]</td>
</tr>
<tr>
<td></td>
<td>Life nerve stretch</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>[Image from TTC Website]</td>
</tr>
</tbody>
</table>

**Ego pose**

(1) Sitting at the edge of the bed, raise your arms overhead in a V shape.
(2) Stretch your thumbs to the sky and curl your fingers onto the palms of your hand.

Breathe in and out slowly. Hold for as long as you can, up to a minute.

[Image from TTC Website]

**Life nerve stretch**

(1) Sitting up, flex both feet back towards the head.
(2) Keeping a straight back, reach as far down your legs as you can – it might be your shins or your toes, or somewhere in between.

Breathe long slow breaths. Continue for 1 minute.

[Image from TTC Website]
## Appendix G: Truncated Pain Assessment Survey

<table>
<thead>
<tr>
<th>Pain survey question</th>
<th>User Entry</th>
<th>Response Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Touch the mark and move it to show how much PAIN you have right now</td>
<td>Visual analogue slider scale (0-100)</td>
<td>Drives advice given by algorithm</td>
</tr>
<tr>
<td>2 Touch the mark and move it to describe your pain when it was at its WORST since your last survey</td>
<td>Visual analogue slider scale (0-100)</td>
<td>Drives advice given by algorithm</td>
</tr>
<tr>
<td>3 Touch the mark and move it to show how much your pain got in the way of your SLEEP since your last survey</td>
<td>Visual analogue slider scale (0-100)</td>
<td>Data recorded and stored to server. May be used for review by healthcare providers at later time.</td>
</tr>
<tr>
<td>4 Touch the mark and move it to show how much your pain got in the way of THINGS YOU DID since your last survey</td>
<td>Visual analogue slider scale (0-100)</td>
<td>Drives advice given by algorithm</td>
</tr>
<tr>
<td>5 Please tell us about the medications you have taken to try to REDUCE your pain since your last survey</td>
<td>None</td>
<td>Data recorded and stored to server. May be used for review by healthcare providers at later time.</td>
</tr>
<tr>
<td></td>
<td>Acetaminophen (Tylenol)</td>
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<td></td>
<td>Ibuprofen (Advil)</td>
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<td></td>
<td>Naproxen</td>
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<td></td>
<td>Codeine</td>
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<td></td>
<td>Morphine (short-acting)</td>
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<td></td>
<td>Morphine (long-acting)</td>
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<td></td>
<td>Gabapentin</td>
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<td></td>
<td>Amitriptyline</td>
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<td></td>
<td>Other (please list)</td>
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<tr>
<td>6 Please tell us about other things you used to try to REDUCE your pain since your last survey</td>
<td>None</td>
<td>Data recorded and stored to server. May be used for review by healthcare providers at later time.</td>
</tr>
<tr>
<td></td>
<td>Deep breathing</td>
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<td></td>
<td>Relaxation exercises</td>
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<td></td>
<td>Heat</td>
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<td></td>
<td>Cold</td>
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<td></td>
<td>Massage/rubbing</td>
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<td>Imagery</td>
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<td></td>
<td>Distraction (e.g. TV, books, music)</td>
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<td></td>
<td>Talking with friends/family</td>
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<td></td>
<td>Rest/sleep</td>
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<tr>
<td></td>
<td>Prayer/meditation</td>
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<tr>
<td></td>
<td>Other (please list)</td>
<td></td>
</tr>
<tr>
<td>7 Touch the mark and move it to show how much CONTROL you felt you had over your pain since your last survey</td>
<td>Visual analogue slider scale (0-100)</td>
<td>Drives advice given by algorithm</td>
</tr>
</tbody>
</table>
Appendix H: Recruitment Email to be Sent to Healthcare Providers

Study 1 Email to Healthcare Providers

Hello,

We are conducting a study on the development and preliminary testing of a smartphone-based pain self-management app for adolescents with cancer. This project will be conducted in a phased manner. An initial phase will involve adolescents using this testing the smartphone app while at the hospital and engaging in an interview about their perceptions related to the app. This process is estimated to require ~25 minutes in total.

To participate in this phase of the study, adolescents must be between the ages of 12 and 18 years, able to speak and read English, actively undergoing cancer treatment on an in- or out-patient basis, being at least 3 months from diagnosis and having self-reported pain in the week immediately before the study.

If you are aware of any adolescents who fit these criteria and may be interested in participating, R.S.V.P to Lindsay Jibb at lindsay.jibb@sickkids.ca and we will contact you to arrange details related to meeting the adolescent.

Thank you for your time and I look forward to hearing from you.

Lindsay Jibb RN MSc
Study Investigator
PhD Student

c.c. Dr. Jennifer Stinson
Clinician Scientist
Study 2 Email to Healthcare Providers

Hello,

We are conducting a study on the development and feasibility testing of a smartphone-based pain self-management app for adolescents with cancer. This project will be conducted in a phased manner. We are now conducting the second phase of this project. Specifically, this second study will involve adolescents using the pain app during a 1-month feasibility trial with preliminary effectiveness testing (testing of app effect on health outcomes such as pain and quality of life). Adolescents will complete pain assessments on the app and receive care advice from the app or their primary care team (depending on their pain).

To participate in this phase of the study, adolescents must be between the ages of 12 and 18 years, able to speak and read English, actively undergoing cancer treatment on an in- or out-patient basis, being at least 3 months from diagnosis and having an episode of self-reported pain of at least 3/10 in the week immediately before the study.

If you are aware of any adolescents who fit these criteria and may be interested in participating, R.S.V.P to Lindsay Jibb at lindsay.jibb@sickkids.ca and we will contact you to arrange details related to meeting the adolescent. Please also contact us with any questions or comments related to this study.

Thank you for your time and I look forward to hearing from you.

Lindsay Jibb RN MSc
Study Investigator
PhD Student

c.c. Dr. Jennifer Stinson
Clinician Scientist
Appendix I: Study Participation and Audio-Recording Consent Forms

Study 1 Consent Form for Youth

Title of Research Project:
Usability Testing as Part of the User-Centered Design of a Smartphone App to Support Real-time Pain Management for Adolescents with Cancer

Investigator(s):
- Dr. Jennifer Stinson RN PhD, SickKids
- Lindsay Jibb RN MSc, SickKids
- Dr. Bonnie Stevens RN PhD, SickKids
- Dr. Paul Nathan MD MSc FRCPC, SickKids
- Dr. Joseph Cafazzo PhD PEng, University Health Network
- Dr. Emily Seto PhD PEng, University Health Network
- Dr. Donna Johnston MD FRCPC, Children’s Hospital of Eastern Ontario

Purpose of the Research:
We want to improve the way this smartphone app works for adolescents with cancer by getting adolescents to try it out and then share their opinions about it with us.

Description of the Research:
To find out how easy the smartphone app is to use, you will be a part of a ~25 minute testing process and interview with two researchers. We will give you a story about an adolescent with cancer who is experiencing pain and ask you to use this app, pretending to be that adolescent. You will record pain using that app and the app will give you an example of a pain solution you could use. While you use the app, we will ask you to think out loud about any problems you are having with the diary. We will watch the process and take notes. We will also audiorecord the process. After you have used the app, we will ask you questions about your experience. The whole process will be used to help us learn about how we can improve the app. The recordings will be kept safe and only the people on the research team will be able to listen to them. If there are any questions you do not want to answer you do not have to answer them and you can stop the interview at any time. We will also ask you some questions about yourself and how you feel about using smartphones (like iPhones). We will also gather some information about your cancer from your medical record.

Potential Harms:
We do not think there are any bad things that could happen because of the study.

Potential Discomforts or Inconvenience:
You may experience emotional upset talking about cancer and pain. If you do have problems or become upset at any time during the course of the interview, you can stop the interview. A member of your health care team (like a doctor, nurse or social worker) will be available if you need them. Participation in this study may also cause you some inconvenience because of the time involved in using the app and participating in the interview.

**Potential Benefits:**

**To individual subjects:**
We do not think there are any especially good things that could happen to you because of the study.

**To society:**
The good thing about this study is that you will help us to improve the pain app, making it more useful for other adolescents with cancer.

**Confidentiality:**
Only you and the research team will know about what you did in the study. If we feel your health may be in danger, we may have to report your results to your doctor.

**Reimbursement:**
You will be given a small gift as a token of our appreciation.

**Participation:**
It is your choice to take part in this study. You can stop at any time. The care you get at Sick Kids will not be affected in any way by whether or not you take part in this study. Your participation may contribute to the creation of an app that may be worth some money. Although we may make money from these findings, we cannot give you any of this money now or in the future because you took part in this study. You will be given a copy of this consent form for your records.

**Sponsorship:**

**Conflict of Interest:**
I, and the other research team members have no conflict of interest to declare.

**Consent:**
By signing this form, I agree that:

1) You have explained this study to me. You have answered all my questions.

2) You have explained the possible harms and benefits (if any) of this study.

3) I know what I could do instead of taking part in this study. I understand that I have the right not to take part in the study and the right to stop at any time. My decision about taking part in the study will not affect my health care at Sick Kids.

4) I am free now, and in the future, to ask questions about the study.

5) I have been told that my medical records will be kept private except as described to me.

6) I understand that no information about who I am will be given to anyone or be published without first asking my permission.

7) I agree, or consent, to take part in this study.
Printed Name of Subject & Age__________________________

Subject’s signature & date

Printed Name of person who explained consent__________________________

Signature of Person who explained consent & date

Printed Witness’ name (if the subject/legal guardian does not read English)__________________________

Witness’ signature & date

If you have any questions about this study, please call Lindsay Jibb at

If you have questions about your rights as a subject in a study or injuries during a study, please call the Research Ethics Manager at
Title of Research Project:
Usability Testing as Part of the User-Centered Design of a Smartphone App to Support Real-time Pain Management for Adolescents with Cancer

Investigator(s):
Dr. Jennifer Stinson RN PhD, SickKids
Lindsay Jibb RN MSc, SickKids
Dr. Bonnie Stevens RN PhD, SickKids
Dr. Paul Nathan MD MSc FRCP, SickKids
Dr. Joseph Cafazzo PhD PEng, University Health Network
Dr. Emily Seto PhD PEng, University Health Network
Dr. Donna Johnston MD FRCP, Children’s HOpsital of Eastern Ontario

Confidentiality:
The recordings produced from this study will be stored in a secure, locked location. Only members of the research team will have access to them. Following completion of the study the recordings will be kept for 7 years following the last publication from this study. They will then be destroyed.

Consent:

By signing this form,

1) I agree to be audio taped during this study. These audio recordings will be used to determine how easy it is for youth with cancer to use the electronic pain diary.

2) I understand that I have the right to refuse to take part in this study. I also have the right to withdraw from this part of the study at any time. (e.g., before or even after the recordings are made). My decision will not affect my health care at SickKids.

3) I am free now, and in the future, to ask questions about the recordings.

4) I have been told that my medical records will be kept private. You will not give anybody information about me, unless the law requires you to.

5) I understand that no information about me (including these recordings) will be given to anyone or be published without first asking my permission.

6) I have read and understood pages 1 to 2 of this consent form. I agree, or consent, to having being recorded as part of the study.
In addition, I agree or consent for this recording to be used for:

1. Other studies on the same topic □
2. Teaching and demonstration at SickKids □
3. Teaching and demonstration at meetings outside SickKids □
4. Not to be used for anything else □

In agreeing to the use of the recording(s) for other purposes, I have been offered a chance to hear the recording(s). I also have the right to withdraw my permission for other uses of the recording(s) at any time.
Study 2 Consent Form for Youth

Title of Research Project:
Feasibility Testing of a Smartphone App to Support Real-time Pain Management for Adolescents with Cancer

Investigator(s):
Dr. Jennifer Stinson RN PhD, SickKids
Lindsay Jibb RN MSc, SickKids
Dr. Bonnie Stevens RN PhD, SickKids
Dr. Paul Nathan MD MSc FRCPC, SickKids
Dr. Joseph Cafazzo PhD PEng, University Health Network
Dr. Emily Seto PhD PEng, University Health Network
Dr. Donna Johnston MD FRCPC, Children’s Hospital of Eastern Ontario

Purpose of the Research:
We want to see if the study we have designed to test this smartphone app that helps adolescents with cancer to manage pain works. We also want to see if this app is effective in helping adolescents with pain.

Description of the Research:
The study lasts for 4 weeks. There is one visit during your regular check up at the hospital and one telephone call.

First visit (today)
At your first visit, you will meet a researcher. You will answer questions about yourself and your pain. You will enter your answers to these questions on a computer. The research will also look at your medical chart and collect information about your cancer. You will then be shown how to use the smartphone app. You will be asked to take home an iPhone that has the app on it and use it every day for 4 weeks.

Filling out the diary
The iPhone will tell you when it is time to enter information about your pain because it will make a beeping noise. The diary will beep two times a day: when you wake up and just before bed. Each time you fill out the diary, you will be asked to rate how much pain you have, show where you hurt on a body diagram, choose words that describe your pain, and rate how the pain affects the things you do. You will also be asked to record pain medicines that you use and any other things you do to reduce your pain. If you tell the app you have pain, the app will give you some strategies to use to help decrease that pain. It will then check-up on you 1 hour later to see if you are doing better. If your pain is bad and the strategies the app is giving you are not
helping, the app will tell someone from your healthcare team and they will call you to check-up on you. If you are in pain in-between the times the app will usually beep, you can use the app to get the same pain help. You do not have to wait for the next beep. The app will take you about 10 minutes each day to do. You will also be able to call the researcher telephone help-line if you have questions about the app.

After the study
When you finish the study, the app will beep and ask you to log onto a website to complete some questionnaires. We will also call you to remind you to complete these questionnaires and ask you to send the smartphone back to us. We might also ask you at this time to participate in a telephone interview with us. During this interview we will ask you about what you thought about the study and using the app. We will use the information you give us to improve the study and the app.

Potential Harms:
We do not think there are any bad things that could happen because of the study.

Potential Discomforts or Inconvenience:
You may experience emotional upset talking about or thinking about your cancer or pain. If you do have problems or become upset at any time during this study, you can stop participating. A member of your health care team (doctor, nurse) will be available if you need them.

Participation in this study may also cause you some inconvenience because of the time using the app, filling out the questionnaires and participating in the interview.

Potential Benefits:

To individual subjects:
We do not think there are any especially good things that could happen to you because of the study.

To society:
The good thing about this study is that you will help us to improve the app and the way we study it, making it more useful for other adolescents with cancer.

Confidentiality:
Only you and the research team will know about what you did in the study. If we feel your health may be in danger, we may have to report your results to your doctor.

Reimbursement:
You will be given a small gift as a token of our appreciation.

Participation:
It is your choice to take part in this study. You can stop at any time. The care you get at Sick Kids will not be affected in any way by whether or not you take part in this study. Your participation may contribute to the creation of a new app that may be worth some money. Although we may make money from these findings, we cannot give you any of this money now
or in the future because you took part in this study. You will be given a copy of this consent form for your records.

**Sponsorship:**

**Conflict of Interest:**
I, and the other research team members have no conflict of interest to declare.

**Consent:**
By signing this form, I agree that:

1) You have explained this study to me. You have answered all my questions.
2) You have explained the possible harms and benefits (if any) of this study.
3) I know what I could do instead of taking part in this study. I understand that I have the right not to take part in the study and the right to stop at any time. My decision about taking part in the study will not affect my health care at Sick Kids.
4) I am free now, and in the future, to ask questions about the study.
5) I have been told that my medical records will be kept private except as described to me.
6) I understand that no information about who I am will be given to anyone or be published without first asking my permission.
7) I agree, or consent, to take part in this study.

______________________________  ________________
Printed Name of Subject & Age  Subject’s signature & date

__________________________  ______________________
Printed Name of person who explained consent  Signature of Person who explained consent & date

__________________________
Printed Witness’ name (if the subject/legal guardian does not read English)  Witness’ signature & date

If you have any questions about this study, please call Lindsay Jibb at

If you have questions about your rights as a subject in a study or injuries during a study, please call the Research Ethics Manager at
Study 2 Audio Recording Consent Form

Title of Research Project:
Feasibility Testing of a Smartphone App to Support Real-time Pain Management for Adolescents with Cancer

Investigator(s):
- Dr. Jennifer Stinson RN PhD, SickKids
- Lindsay Jibb RN MSc, SickKids
- Dr. Bonnie Stevens RN PhD, SickKids
- Dr. Paul Nathan MD MSc FRCPC, SickKids
- Dr. Joseph Cafazzo PhD PEng, University Health Network
- Dr. Emily Seto PhD PEng, University Health Network
- Dr. Donna Johnston MD FRCPC, Children’s Hospital of Eastern Ontario

Confidentiality:
The recordings produced from this study will be stored in a secure, locked location. Only members of the research team will have access to them. Following completion of the study the recordings will be kept for 7 years following the last publication from this study. They will then be destroyed.

Consent:

By signing this form,

1) I agree to be audio taped during this study. These audio recordings will be used to determine how easy it is for youth with cancer to use the electronic pain diary.

2) I understand that I have the right to refuse to take part in this study. I also have the right to withdraw from this part of the study at any time. (e.g., before or even after the recordings are made). My decision will not affect my health care at SickKids.

3) I am free now, and in the future, to ask questions about the recordings.

4) I have been told that my medical records will be kept private. You will not give anybody information about me, unless the law requires you to.

5) I understand that no information about me (including these recordings) will be given to anyone or be published without first asking my permission.

6) I have read and understood pages 1 to 2 of this consent form. I agree, or consent, to having being recorded as part of the study.
In addition, I agree or consent for this recording to be used for:

1. Other studies on the same topic □

2. Teaching and demonstration at SickKids □

3. Teaching and demonstration at meetings outside SickKids □

4. Not to be used for anything else □

In agreeing to the use of the recording(s) for other purposes, I have been offered a chance to hear the recording(s). I also have the right to withdraw my permission for other uses of the recording(s) at any time.
Thank you for participating in this study!

If you would like to receive a newsletter with a summary of the study results, please let us know by providing your email address or mailing address below.

Sincerely,

Lindsay Jibb RN MSc
Study Researcher

Participant Name: _______________________________

☐ NO thank you. I would not like to be sent a newsletter telling me about the study results.
☐ YES, please send me a newsletter telling me about the study results. (Fill in information below)

<table>
<thead>
<tr>
<th>Name:</th>
<th>Email address:</th>
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<tbody>
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</table>

Alternate Contact information:
Appendix J: Adolescent Demographics and Disease Questionnaire

**Date:** YEAR ___ ___ MONTH ___  ___  DAY ___ ___

**Directions:** Please complete the following items.

1. **Gender:**
   - [ ] 1 Female
   - [ ] 2 Male

2. **Date of birth:** YEAR _____ MONTH ____  ____  DAY ____  __

3. **Ethnicity:**
   - [ ] 1 Aboriginal (Inuit, Metis, North American Indian)
   - [ ] 2 Arab/West Asian (e.g., Armenian, Egyptian, Iranian, Lebanese, Moroccan)
   - [ ] 3 Black (e.g., African, Haitian, Jamaican, Somali)
   - [ ] 4 Chinese
   - [ ] 5 Filipino
   - [ ] 6 Japanese
   - [ ] 7 Korean
   - [ ] 8 Latin American
   - [ ] 9 South Asian
   - [ ] 10 South East Asian
   - [ ] 11 White (Caucasian)
   - [ ] 12 Other (please specify): _______________

4. **Primary cancer diagnosis:**
   - [ ] 1 ALL
   - [ ] 2 AML
   - [ ] 3 lymphoma
   - [ ] 4 osteosarcoma
   - [ ] 5 brain tumor
   - [ ] 6 neuroblastoma
   - [ ] 7 Ewing’s sarcoma
   - [ ] 8 Other (please specify): _______________

5. **Cancer stage/risk:** _______________

6. **Relapse?:**
   - [ ] 1 yes
   - [ ] 2 no

7. **Type of cancer treatment:**
   - [ ] 1 chemotherapy
   - [ ] 2 radiation
   - [ ] 3 surgery
   - [ ] 4 bone marrow/stem cell transplant
☐ 5 other (please specify): _______________

8. Date of diagnosis: YEAR ___ ___ MONTH ___ ___ DAY ___ ___
Appendix K: Smartphone Comfort Questionnaire

Date: Year ___ ___ Month ___ ___ Day___ ___

Identification number

Directions:

Please answer the following questions. Ask the research assistant for help if you need it.

1. Do you have a smartphone?
   - [ ] Yes
   - [ ] No

2. How often do you use your smartphone everyday? (fill in ONE only)
   - [ ] never
   - [ ] 1-3 times a day
   - [ ] 4-6 times a day
   - [ ] 7-10 times a day
   - [ ] over 10 times a day
   - [ ] I don’t have a smartphone

5. What do you use your Smartphone to do? (check as many as you would like)
   - [ ] calling people
   - [ ] texting people
   - [ ] listening to music
   - [ ] using apps
   - [ ] playing games
   - [ ] emailing people
   - [ ] I don’t have a smartphone

5. Please circle the number that goes with how comfortable you feel using a smartphone?

   1  2  3  4
   not at all comfortable  a little comfortable  comfortable  very comfortable

   [ ]
Appendix L: Standardized Pain Vignettes for *Pain Squad*

**Pain Vignettes for Girls Testing Pain Squad**

“The following example is about a girl with cancer like you. The example I will talk about will tell you about how much pain she has (it could be a little, quite a bit, or a lot of pain), whether she is or is not upset about the pain, and whether the pain is or is not affecting different parts of her life. You will use the smartphone app to rate how much you think the pain hurts, how upsetting the pain is, and how much the pain is affecting her.

The app will then give some ideas about what she could do to help with the pain. You will have to pick one of these ideas for this girl. The app is then going to ask if she used the idea to help with her pain and if she liked the idea. You will have to imagine you are her and choose.”

Okay, go ahead and try.”

When she woke up, Jane had a medium amount of sharp pain in the upper left side of her chest around her port-a-cath that was inserted 2 days ago. Jane is pretty upset about this horrible pain. Because of her pain, Jane had a really hard time sleeping, woke up in a pretty bad mood, felt very tired and didn’t feel like eating.

**Pain Vignettes for Boys Testing Pain Squad**

“The following example is about a boy with cancer like you. The example I will talk about will tell you about how much pain he has (it could be a little, quite a bit, or a lot of pain), whether he is or is not upset about the pain, and whether the pain is or is not affecting different parts of his life. You will use the smartphone app to rate how much you think the pain hurts, how upsetting the pain is, and how much the pain is affecting him.

The app will then give some ideas about what he could do to help with the pain. You will have to pick one of these ideas for this boy. The app is then going to ask if he used the idea to help with his pain and if he liked the idea. You will have to imagine you are him and choose.”

Okay, go ahead and try.”

When he woke up, John had a medium amount of sharp pain in the upper left side of his chest around his port-a-cath that was inserted 2 days ago. John is pretty upset about this horrible pain. Because of his pain, John had a really hard time sleeping, woke up in a pretty bad mood, felt very tired and didn’t feel like eating.
Appendix M: Study 1 Semi-Structured Interview Guide

1) How easy was it to use this smartphone app to rate cancer pain and get pain help ideas?

   Probes: What did you find easy to understand about this app? Can you tell me more about that?

2) What did you like best about this smartphone app?

   Probes: Rating pain? Getting ideas about help with pain? Rating how much you liked the pain help ideas the app gave? Design of app?
   Detective theme? Time to complete app? Can you tell me more about that?

3) What did you like least about this smartphone app?

   Probes: Rating pain? Getting ideas about help with pain? Rating how much you liked the pain help ideas the app gave? Design of app?
   Detective theme? Time to complete app? Can you tell me more about that?

4) What did you find hard to use about this smartphone app?

   Probes: Rating pain? Getting ideas about help with pain? Rating how much you liked the pain help ideas the app gave? Can you tell me more about that?

5) What did you find easy to use about this smartphone app?

   Probes: Rating pain? Getting ideas about help with pain? Rating how much you liked the pain help ideas the app gave? Can you tell me more about that?

6) What did you find hard to understand about this smartphone app?

   Probes: Wording of questions? Wording of pain help ideas? How to use the app to get pain help when needed? How you could do the things the app recommended? Can you tell me more about that?

7) What did you find easy to understand about this smartphone app?

8) What would you like to change about this smartphone app?

   Probes: Number of pain assessments? Length of pain assessments?
   Wording of pain assessment questions and pain help ideas? Type of pain help ideas? Can you tell me more about that?

9) What would you like to add to this smartphone app that would help you to better manage your cancer pain?

   Probes: Can you tell me more about that? Can you give me an example?

10) Would you be willing to try this smartphone app out for four weeks?

    Probes: If not, how long would you be willing to use it for?

11) What about this smartphone app would make you want to use (or to not use it)?

    Probes: Can you tell me more about that? Can you give me an example?

12) Is there anything else you would like to tell us about this smartphone app?

    Probes: Can you tell me more about that?
Appendix N: Cancer Pain Management Recruitment Log

<table>
<thead>
<tr>
<th>Date</th>
<th>Number of eligible patients as assessed by healthcare team</th>
<th>Number of team-assessed patients with self-reported pain in previous week</th>
<th>Number recruited</th>
<th>Reason for nonparticipation</th>
<th>Notes</th>
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### Appendix O: Cancer Pain Management Activity Log

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>Details of adverse event/safety issue identified (date, time, event, action taken)</th>
<th>Notes</th>
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<tbody>
<tr>
<td></td>
<td>Reason for attrition</td>
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<tr>
<td></td>
<td>Completed study? (Y/N)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Date technical problem resolved</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nature of technical problem</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Date technical problem experienced</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Technical problem experienced? (Y/N)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Compliance rate</td>
<td></td>
</tr>
</tbody>
</table>

- Details of adverse event/safety issue identified: Provide specific details about adverse events or safety issues encountered during the study, including the date, time, nature of the event, and any actions taken to address it.
- Notes: Provide any additional notes or comments relevant to the identified adverse event or safety issue.
- Reason for attrition: Specify the reason for attrition and any relevant details.
- Completed study: Indicate whether the study was completed (Y) or not (N).
- Date technical problem resolved: Record the date when the technical problem was resolved.
- Nature of technical problem: Describe the nature of the technical problem encountered during the study.
- Date technical problem experienced: Record the date when the technical problem was experienced.
- Technical problem experienced: Indicate whether a technical problem occurred (Y) or not (N).
- Compliance rate: Calculate and report the compliance rate of the study participants.
Appendix P: Study 2 Semi-Structured Interview Guide

1) How easy was it to use this smartphone app to rate cancer pain and get pain help ideas?
   Probes: What did you find easy to understand about this app? Can you tell me more about that?

2) What did you like best about this smartphone app?
   Probes: Rating pain? Getting ideas about help with pain? Rating how much you liked the pain help ideas the app gave? Design of app? Detective theme? Time to complete app? Can you tell me more about that?

3) What did you like least about this smartphone app?
   Probes: Rating pain? Getting ideas about help with pain? Rating how much you liked the pain help ideas the app gave? Design of app? Detective theme? Time to complete app? Can you tell me more about that?

4) What did you find hard to use about this smartphone app?
   Probes: Rating pain? Getting help with pain? Rating how much you liked the pain help ideas? Can you tell me more about that?

5) What did you find easy to use about this smartphone app?
   Probes: Rating pain? Getting ideas about help with pain? Rating how much you liked the pain help ideas the app gave? Can you tell me more about that?

6) What did you find hard to understand about this smartphone app?
   Probes: Wording of questions? Wording of pain help ideas? How to use the app to get pain help when needed? How you could do the things the app recommended? Can you tell me more about that?

7) What did you find easy to understand about this smartphone app?
   Probes: Wording of questions? Wording of pain help ideas? How to use the app to get pain help when needed? How you could do the things the app recommended? Can you tell me more about that?

8) What would you like to change about this smartphone app?
   Probes: Number of pain assessments? Length of pain assessments? Wording of pain assessment questions and pain help ideas? Type of pain help ideas? Can you tell me more about that?

9) What would you like to add to this smartphone app that would help you to better manage your cancer pain?
   Probes: Can you tell me more about that? Can you give me an example?

10) What about this smartphone app would make you want to use (or to not use it)?
   Probes: Can you tell me more about that? Can you give me an example?
11) Is there anything else you would like to tell us about this smartphone app?
   \textit{Probes: Can you tell me more about that?}

12) What did you like best about participating in this study?
   \textit{Probes: Can you tell me more about that?}

13) What did you like least about participating in this study?
   \textit{Probes: Can you tell me more about that?}

14) Would you be willing to use this smartphone app for longer than 4 weeks?
   \textit{Probes: How long would you be willing to use it for? Why?}
Appendix Q: Healthcare Provider Cancer Pain Intervention Log

<table>
<thead>
<tr>
<th>Participant ID</th>
<th>Time of incoming pain alert</th>
<th>RN description of incoming pain alert</th>
<th>Time of patient contact</th>
<th>RN description of pain advice given</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix R: Criteria for Rating the Research Base Providing Evidence for a Psychometric Measure

<table>
<thead>
<tr>
<th>Category</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Well-established</td>
<td>The measure must have been presented in at least two peer-reviewed articles by different investigators or investigatory team.</td>
</tr>
<tr>
<td></td>
<td>Sufficient detail about the measure to allow critical evaluation and replication (e.g., measure and manual provided or available upon request).</td>
</tr>
<tr>
<td></td>
<td>Detailed (e.g., statistics presented) information indicating good validity and reliability in at least one peer-reviewed article.</td>
</tr>
<tr>
<td>Approaching well-established</td>
<td>The measure must have been presented in at least two peer-reviewed articles, which might be by the same investigators or investigatory team.</td>
</tr>
<tr>
<td></td>
<td>Sufficient detail about the measure to allow critical evaluation and replication (e.g., measure and manual provided or available upon request).</td>
</tr>
<tr>
<td></td>
<td>Validity and reliability information presented in either vague terms (e.g., no statistics presented) or moderate values.</td>
</tr>
<tr>
<td>Promising</td>
<td>The measure must have been presented in at least one peer-reviewed article.</td>
</tr>
<tr>
<td></td>
<td>Sufficient detail about the measure to allow critical evaluation and replication (e.g., measure and manual provided or available upon request).</td>
</tr>
<tr>
<td></td>
<td>Validity and reliability information presented in either vague terms (e.g., no statistics presented) or moderate values.</td>
</tr>
</tbody>
</table>

Reproduced from Cohen et al. (2008).
Appendix S: Acceptability E-Scale (modified)

We would like to ask you about your thoughts on using *Pain Squad*+.

<table>
<thead>
<tr>
<th>1. How easy was <em>Pain Squad</em>+ for you to use?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>very difficult</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. How understandable were the questions?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>difficult to understand</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>3. How much did you enjoy using <em>Pain Squad</em>+?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>not at all</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4. How helpful was <em>Pain Squad</em>+ in describing your pain?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>very unhelpful</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. How helpful was <em>Pain Squad</em>+ in treating your pain?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>very unhelpful</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. Was the amount of time it took to complete <em>Pain Squad</em>+ acceptable?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>very unacceptable</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. How would you rate your overall satisfaction with <em>Pain Squad</em>+?</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
</tr>
<tr>
<td>Very dissatisfied</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>8. How long would you be willing to use <em>Pain Squad</em>+?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Same amount of time</td>
</tr>
</tbody>
</table>
Appendix T: Pain Intensity Subscale of Brief Pain Inventory

12) Please rate your pain by circling the one number that best describes your pain at its **worst** in the last week.

0  1  2  3  4  5  6  7  8  9  10
No Pain  Pain as bad as you can imagine

13) Please rate your pain by circling the one number that best describes your pain at its **least** in the last week.

0  1  2  3  4  5  6  7  8  9  10
No Pain  Pain as bad as you can imagine

14) Please rate your pain by circling the one number that best describes your pain on the **average**.

0  1  2  3  4  5  6  7  8  9  10
No Pain  Pain as bad as you can imagine

15) Please rate your pain by circling the one number that tells how much pain you have at **now**.

0  1  2  3  4  5  6  9  10
No Pain  Pain as bad as you can imagine
Appendix U: PROMIS Pain Interference – Short Form Questionnaire

**Pediatric Pain Interference - Short Form**

Please respond to each item by marking one box per row.

<table>
<thead>
<tr>
<th>In the past 7 days.....</th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>I had trouble sleeping when I had pain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I felt angry when I had pain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>I had trouble doing schoolwork when I had pain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>It was hard for me to pay attention when I had pain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>It was hard for me to run when I had pain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>It was hard for me to walk one block when I had pain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>It was hard to have fun when I had pain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>It was hard to stay standing when I had pain.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
Appendix V: PedsQL 4.0 Health-Related Quality of Life Questionnaire

Note: The instructions for the below forms read “in the past ONE month”. This study will use the acute version, which reads “in the past 7 days”
In the past **ONE month**, how much of a **problem** has this been for you ...

### ABOUT MY HEALTH AND ACTIVITIES (problems with...)

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Almost</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. It is hard for me to walk more than one block</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. It is hard for me to run</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. It is hard for me to do sports activity or exercise</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. It is hard for me to lift something heavy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. It is hard for me to take a bath or shower by myself</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. It is hard for me to do chores around the house</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. I hurt or ache</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. I have low energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

### ABOUT MY FEELINGS (problems with...)

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Almost</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I feel afraid or scared</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. I feel sad or blue</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. I feel angry</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. I have trouble sleeping</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. I worry about what will happen to me</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

### HOW I GET ALONG WITH OTHERS (problems with...)

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Almost</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I have trouble getting along with other kids</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Other kids do not want to be my friend</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. Other kids tease me</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. I cannot do things that other kids my age can do</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. It is hard to keep up when I play with other kids</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

### ABOUT SCHOOL (problems with...)

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Almost</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. It is hard to pay attention in class</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. I forget things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. I have trouble keeping up with my schoolwork</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. I miss school because of not feeling well</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. I miss school to go to the doctor or hospital</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
**PedSQL™**
**Pediatric Quality of Life Inventory**

Version 4.0

**TEEN REPORT (ages 13-18)**

**DIRECTIONS**

On the following page is a list of things that might be a problem for you. Please tell us how much each one has been a problem for you during the past ONE month by circling:

- 0 if it is never a problem
- 1 if it is almost never a problem
- 2 if it is sometimes a problem
- 3 if it is often a problem
- 4 if it is almost always a problem

There are no right or wrong answers. If you do not understand a question, please ask for help.
**PedsQL 2**

*In the past ONE month, how much of a problem has this been for you...*  

<table>
<thead>
<tr>
<th>ABOUT MY HEALTH AND ACTIVITIES (problems with...)</th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. It is hard for me to walk more than one block</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. It is hard for me to run</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. It is hard for me to do sports activity or exercise</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. It is hard for me to lift something heavy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. It is hard for me to take a bath or shower by myself</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. It is hard for me to do chores around the house</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. I hurt or ache</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. I have low energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ABOUT MY FEELINGS (problems with...)</th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I feel afraid or scared</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. I feel sad or blue</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. I feel angry</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. I have trouble sleeping</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. I worry about what will happen to me</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HOW I GET ALONG WITH OTHERS (problems with...)</th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I have trouble getting along with other teams</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Other teens do not want to be my friend</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. Other teens tease me</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. I cannot do things that other teens my age can do</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. It is hard to keep up with my peers</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ABOUT SCHOOL (problems with...)</th>
<th>Never</th>
<th>Almost Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Almost Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. It is hard to pay attention in class</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. I forget things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. I have trouble keeping up with my schoolwork</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4. I miss school because of not feeling well</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. I miss school to go to the doctor or hospital</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>
Appendix W: Modified General Self-Efficacy – Sherer Scale

For each of the following statements, indicate your agreement on a scale of 1 to 5:

1 = strongly disagree
2 = disagree
3 = neutral
4 = agree
5 = strongly agree

1. If something looks too complicated, I will not even bother to try it.
2. I avoid trying to learn new things when they look difficult.
3. When trying something new, I soon give up if I am not initially successful.
4. When I make plans, I am certain I can make them work.
5. If I can’t do a job the first time, I keep trying until I can.
6. When I have something unpleasant to do, I stick to it until I finish it.
7. When I decide to do something, I go right to work on it.
8. Failure just makes me try harder.
9. When I set important goals for myself, I rarely achieve them.
10. I do not seem to be capable of dealing with the most important problems that come up in my life.
11. When unexpected problems occur, I don’t handle them very well.
12. I feel insecure about my ability to do things.

Self-efficacy in pain-care question

13. I am certain that I have the ability to manage pain I experience.