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Pain Squad+ smartphone app to support real-time pain treatment for adolescents with cancer: protocol for a randomised controlled trial

Lindsay Jibb ,[1,2] Paul C Nathan,[1,3,4,5,6] Vicky Breakey,[7,8] Conrad Fernandez,[9,10] Donna Johnston,[11,12] Victor Lewis,[13,14] Sarah McKillop,[15,16] Serina Patel,[17,18] Christine Sabapathy,[19,20] Caron Strahlendorf,[21,22] J. Charles Victor,[3,6] Myla E Moretti,[1] Cynthia Nguyen,[1] Amos Hundert,[1] Celia Cassiani,[1] Graziella El-Khechen Richandi,[1] Hayley Insull,[20] Rachel Hamilton,[1] Geoffrey Fang,[5] Susan Kuczynski,[23] Jennifer Stinson[1,2,3]

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For numbered affiliations see end of article.

Correspondence to
Dr Lindsay Jibb;
lindsay.jibb@sickkids.ca

ABSTRACT

Introduction Pain negatively affects the health-related quality of life (HRQL) of adolescents with cancer. The Pain Squad+ smartphone-based application (app), has been developed to provide adolescents with real-time pain self-management support. The app uses a validated pain assessment and personalised pain treatment advice with centralised decision support via a registered nurse to enable real-time pain treatment in all settings. The algorithm informing pain treatment advice is evidence-based and expert-vetted. This trial will longitudinally evaluate the impact of Pain Squad+, with or without the addition of nurse support, on adolescent health and cost outcomes.

Methods and analysis This will be a pragmatic, multicentre, waitlist controlled, 3-arm parallel-group superiority randomised trial with 1:1:1 allocation enrolling 74 adolescents with cancer per arm from nine cancer centres. Participants will be 12 to 18 years, English-speaking and with ≥3/10 pain. Exclusion criteria are significant comorbidities, end-of-life status or enrolment in a concurrent pain study. The primary aim is to determine the effect of Pain Squad+, with and without nurse support, on pain intensity in adolescents with cancer, when compared with a waitlist control group. The secondary aims are to determine the immediate and sustained effect over time of using Pain Squad+, with and without nurse support, as per prospective outcome measurements of pain interference, HRQL, pain self-efficacy and cost. Linear mixed models with baseline scores as a covariate will be used. Qualitative interviews with adolescents from all trial arms will be conducted and analysed.

Ethics and dissemination This trial is approved by the Hospital for Sick Children Research Ethics Board. Results will provide data to guide adolescents with cancer and healthcare teams in treating pain. Dissemination will occur through partnerships with stakeholder groups, scientific meetings, publications, mass media releases and consumer detailing.

Trial registration number NCT03632343 (*ClinicalTrials.gov*).

Strengths and limitations of this study

- This study is a large trial evaluating an innovative method to address pain in adolescents with cancer, the most common and distressing symptom experienced by this group.
- This pragmatic design of the trial means that our approach to study eligibility criteria, intervention intensity and participant adherence will determine intervention effect under real-world conditions.
- Former adolescent cancer patients are core members of this study team and have, and will continue to, guide and support study design, study conduct and results dissemination.
- Adolescents with cancer, their caregivers and the study nurse will not be blinded to participant group as this is prohibited by the nature of the intervention.

INTRODUCTION

Adolescents with cancer report pain as the most commonly occurring and distressing cancer-related symptom experienced.[1–3] Pain negatively impacts health-related quality of life (HRQL),[4–6] represents a significant cost burden to patients, families and the health system[7] and is a major reason for cancer-related emergency health service use in adult patients.[8–11] However, the successful identification of pain, including in and outside of the hospital setting, does not equate to its adequate treatment and pain is often undertreated in adolescents.[12–15]

Due to improvements in therapeutic regimes, supportive care and changes in the health system, adolescents with cancer now spend less time in hospital and more time at home.[16–18] Thus, adolescents and their families are increasingly responsible for managing

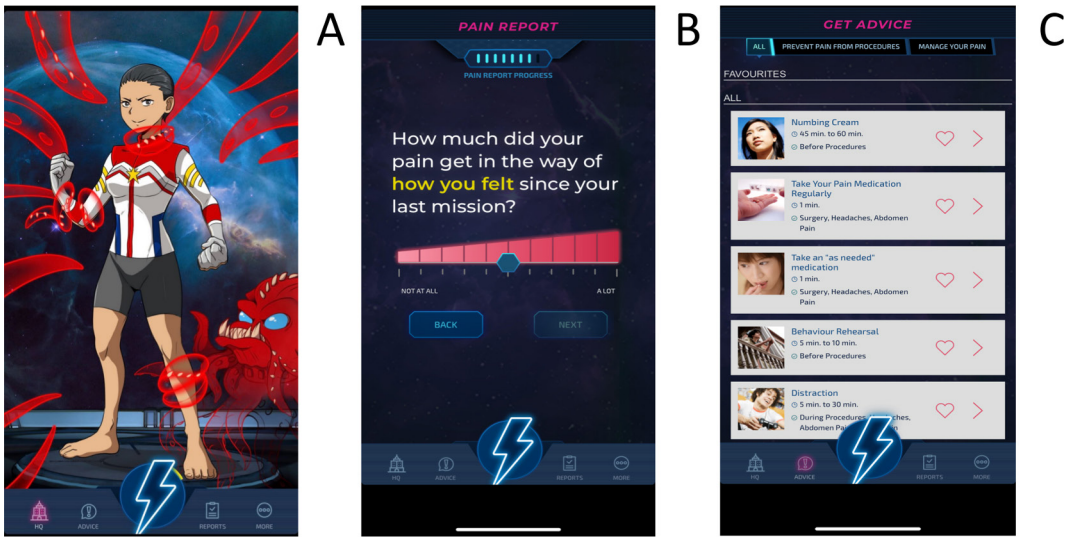

Figure 1 Pain Squad+ smartphone application screenshots of the application landing screen (A), a visual analogue slider scale for pain assessment (B) and a portion of the library of pain self-management advice. Photos used in this figure are stock photos and are under license from the copyright owners.

cancer-associated pain in environments with less supervision from healthcare professionals.[13 19] Adolescents are more vulnerable in these environments as they often lack the knowledge, skills and self-efficacy needed to adequately react to symptoms and may ignore or inappropriately accept changes in pain.[13 16 20 21] Digital health technologies are widely used by adolescents[22] and can empower adolescents with cancer to engage in remote and real-time pain treatment in all of their natural environments (eg, hospital, home, school). Studies have indicated that digital real-time symptom monitoring and treatment improves HRQL and decreases emergency service use and hospitalisation rates in adults with cancer,[23 24] but no such research has been conducted with adolescents.

The Pain Squad+ smartphone-based real-time pain treatment application

Using a phased-centred and user-centred approach, our team has developed a smartphone application (app), called Pain Squad+, capable of providing adolescents with real-time pain treatment support (figure 1).[25–31] Pain Squad+ uses a truncated 8-item version of a valid and reliable automated questionnaire to assess adolescent pain (severity, interference, location and capacity to self-manage pain).[12] When pain is reported using Pain Squad+, self-management advice is presented to users in real-time according to a vetted and standardised clinical care algorithm.[25 28] Advice is based on a library of pharmacological (eg, medication adherence reminders), psychological (eg, distraction techniques) and physical (eg, yoga instruction) advice that aligns with typical recommendations provided to adolescents by their healthcare teams.[32] Three consecutive moderate-to-severe reports of pain intensity (ie, ≥3/10)[33] trigger an email to be sent to a paediatric oncology-trained registered nurse. The nurse then contacts the adolescent and/or their healthcare team to discuss the case and initiate healthcare professional-driven intervention, which may be outside of the scope of the self-management algorithm (eg, adjusting a prescribed medication regime). To encourage engagement with Pain Squad+, the app is 'gamified' with users playing the role of superheroes who receive rewards for adherence to pain assessment and treatment recommendation completion.[19]

The most recently completed phase of Pain Squad+ testing was a 1-group, baseline-poststudy pilot that demonstrated the feasibility (ie, intervention fidelity, outcome measure completion, adherence, acceptability) of evaluating the app in a randomised controlled trial (RCT), as well as small-to-moderate effect sizes (Cohen's d: 0.23 to 0.67).[30] This protocol details the methods to be used in the next phase of Pain Squad+ testing: a RCT aimed at longitudinally evaluating the impact of Pain Squad+, with or without the addition of nurse support, on adolescent health and cost outcomes.

Specific objectives

Primary objective and hypothesis

To examine the effect of 4 weeks of Pain Squad+ app use, with and without nurse support, on pain intensity in adolescents with cancer, when compared with a waitlist control group. We hypothesise that 4 weeks of Pain Squad+ use, with or without nurse support, will result in improved pain intensity scores, compared with a waitlist control group.

Secondary objectives and hypotheses as appropriate

Objective related to the effect of Pain Squad+ on health outcomes overtime.

To examine the effect of each of 2, 4 and 8 weeks of Pain Squad+ app use, with and without nurse support, on each of pain intensity, pain interference, HRQL and pain management self-efficacy in adolescents with cancer, when compared with a waitlist control group. We

hypothesise that Pain Squad+ use, with or without nurse support, for 2, 4 and 8 weeks will result in improved pain intensity, pain interference, HRQL and self-efficacy scores, compared with a waitlist control group.

Objective related to maintenance of potential therapeutic gains from Pain Squad+ use

To examine the effect of the Pain Squad+ app, with and without nurse support, on each of pain intensity, pain interference, HRQL and pain management self-efficacy in adolescents with cancer compared with a waitlist control group, when assessed after intervention use has ceased (ie, 8 weeks post-use of the intervention). We hypothesise that improvements in pain intensity, pain interference, HRQL and self-efficacy scores related Pain Squad+ use, with or without nurse support, will be sustained when assessed after intervention use has ceased.

Objective related to the effect of Pain Squad+ on health system and societal costs.

To examine the cost-effectiveness and cost utility of the Pain Squad+ app, with and without nurse support as compared with standard care from both a health system and societal perspective.

Objective related to treatment arm satisfaction.

To explore adolescent with cancer-rated acceptability (including engagement with pain treatment strategies) of the Pain Squad+ app and the study following participation.

METHODS

Trial design

This will be a pragmatic, multicentre, waitlist group-controlled, investigator and analyst-blinded, 3-arm parallel-group superiority RCT with 1:1:1 allocation (figure 2). Randomisation will be stratified by recruitment site to account for differences in care across centres[34] with block sizes of 6 and 9 within each stratum. Reporting of this protocol is in accordance with the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) guidelines[35] (see online supplementary additional file for SPIRIT checklist).

Study setting

Adolescent and caregiver recruitment will occur across nine Canadian paediatric oncology programmes that treat a diversity of paediatric cancers (often based on the same standardised protocols). All of these programmes are located in tertiary care centres that serve paediatric

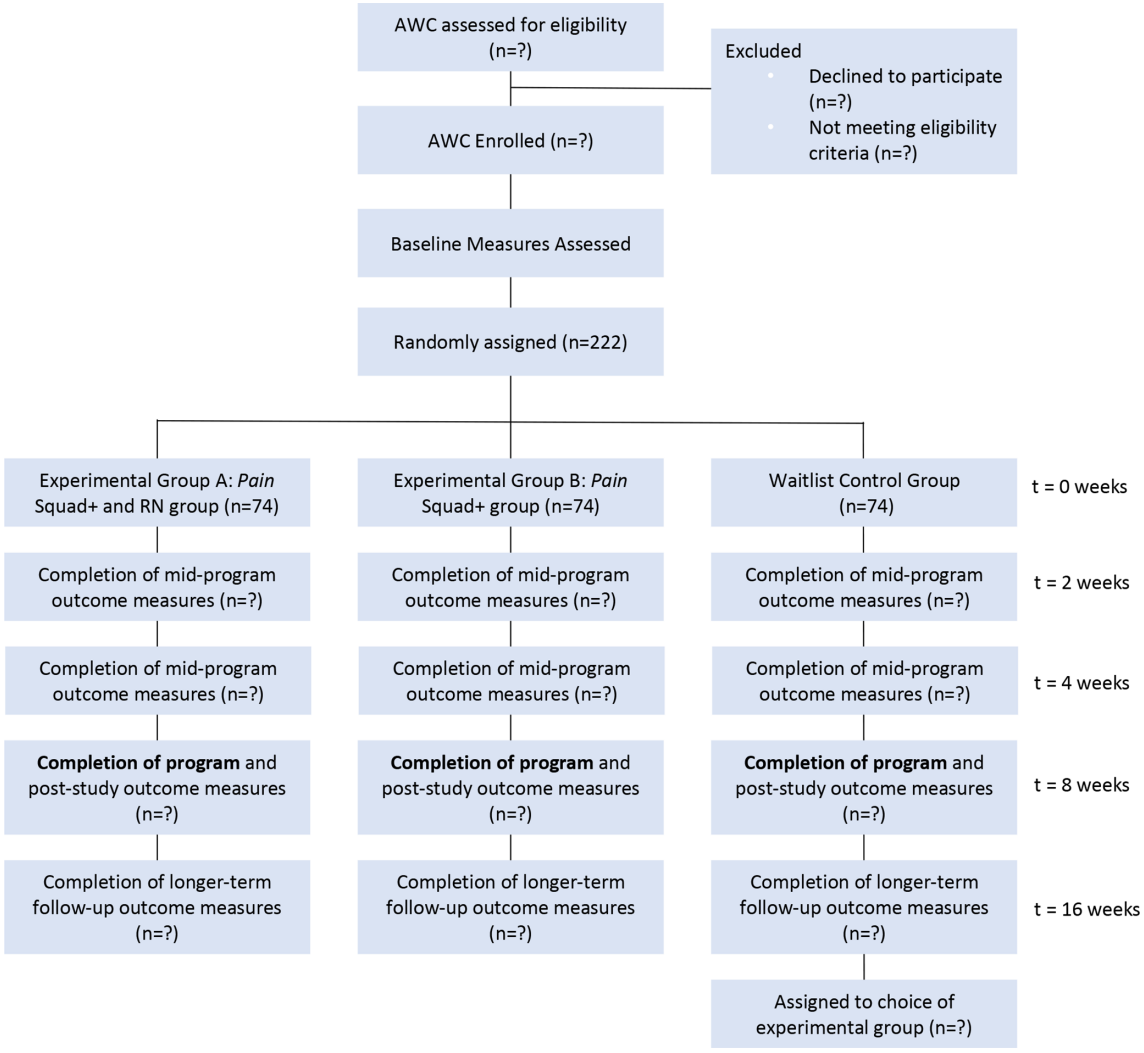

Figure 2 Flowchart of Pain Squad+ trial protocol. AWC,adolescents with cancer.

Table 1 Pain Squad+ RCT participation eligibility criteria

Criterion	Rationale	Source
Inclusion criteria		
12 to 18 years of age	Study restricted to AWC	Medical chart
Diagnosed with cancer (all disease types) and receiving cancer-directed therapy	Study restricted to AWC	Medical chart
English-speaking and reading	Pain Squad+ app currently available in English only	AWC self-report
Average pain score of ≥3/10 over the preceding week	Value describes moderate-severe pain in adolescents[33] and RCTs of similar interventions in adults with cancer pain.[36 37] In our pilot, 75% of AWC reported average pain of ≥3/10 in the week prior to enrolment.	AWC self-report measured using an 11-point numerical rating scale
English-speaking and reading caregiver who is willing and able to complete outcome measures related to healthcare encounters	English-speaking caregivers required to complete outcome measure related healthcare utilisation and associated costs.	AWC or caregiver self-report
Exclusion criteria		
Significant cognitive impairments or comorbid illnesses	Would limit interaction with Pain Squad+ or outcome measure assessment	Healthcare team report
Currently participating in other pain treatment studies	Concomitant intervention represents a threat to internal validity	AWC or caregiver self-report
Not expected to survive past 16 weeks	Terminal data collection point is at 16 weeks post-randomisation	Healthcare team report

app, application; AWC, adolescents with cancer; RCT, randomised controlled trial.

populations with considerable racial, ethnic and socioeconomic diversity. The lead study site is the Hospital for Sick Children (SickKids).

Eligibility criteria

The eligibility criteria for this study, with the rationale for each criterion and the sources of associated data collection, are shown in table 1. No restrictions will be placed on analgesia use or hospitalisations, however data related to medication and other pain treatment strategy use, as well as inpatient stays (ie, reason, duration, pain-related treatment received), will be collected during the study.

Interventions

Experimental group A

The deployment of the Pain Squad+ app to adolescent's personal phones will be done through the Apple App Store and Google Play Store. The research team will loan an iPhone or Android phone to those without a smartphone. All adolescents will be trained to use Pain Squad+ using a standardised procedure. Three repeated audible smartphone alerts over a 30 min window will signal each adolescent to complete the 8-item pain assessment using Pain Squad+ every morning and evening for 8 weeks. The timing of morning and evening pain assessments will be individualised according to participant's daily and weekly schedules. An automated 30 min window within which each assessment must be completed will be set, or the assessment will be registered as 'missed'. Adolescents will also have the option of completing ad hoc pain assessments anytime between the automated alert times. Algorithm-driven pain self-management advice will be issued in response to pain, providing real-time decision support (see online supplementary appendix A). One hour after a recommendation is made, the app will alert adolescents to complete a pain reassessment and additional advice will be offered as appropriate. All pain assessment and treatment advice data logged will be encrypted and wirelessly transferred to a secure server at SickKids for storage. Email alerts related to three consecutive reports of pain >3/10 will be sent to the study nurse who will log into the Analytics Platform to Evaluate Effective Engagement (APEEE) platform[36] to review the adolescent's pain report history. The nurse may liaise with the adolescent's healthcare team regarding the case and will contact the adolescent within 12 hours of receiving the alert, including on weekends. The time of nurse contact and the details of the pain treatment conversation will be recorded. A research coordinator will provide telephone-based technical assistance (weekdays 09:00 to 17:00 EST) to participants if required.

Experimental group B

Adolescents randomised to this group will complete pain assessments and receive the same smartphone-based algorithm-driven pain treatment advice as in Experimental Group A but will not receive nurse-initiated pain support.

Waitlist control group

Adolescents randomised to this group will be waitlisted to receive the Experimental Group B condition within 1 month of completing all post-study outcome measures.

All study groups

Regardless of study group, adolescents will continue to receive standard medical care from their treating healthcare teams. All groups will be reminded to pursue help using the usual channels (calling oncology clinic, 'on-call' team or 911) should any medical emergencies arise during the study.

Outcomes

All outcome measures have demonstrated validity and reliability in 12 to 18 year olds with cancer and will be assessed according to the schedule shown in figure 3. A 1 week recall period will be used for all health-related outcomes.

Primary outcome

The primary outcome is average pain intensity, measured using Brief Pain Inventory (BPI). The BPI assesses current pain and 'worst', 'least' and 'average' pain in the preceding week using an 11-point numerical rating scale

	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			Close-out
TIMEPOINT**	$-t_1$	0	t_1 (2 weeks)	t_2 (4 weeks)	t_3 (8 weeks)	t_4 (16 weeks)
ENROLMENT:						
Eligibility screen	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
Experimental Group A Standard care + *Pain Squad*+ smartphone app + RN support						
Experimental Group B Standard care + *Pain Squad*+ smartphone app						
Waitlist Control Group Standard care						
ASSESSMENTS:						
Baseline Variables • Adolescent with cancer socio-economic, demographic, pain, and cancer-related characteristics • Adolescent ownership and use of smartphones • Adolescent expectation about treatment effectiveness • Caregiver demographics	X	X				
Health Quality Variables • Pain intensity [BPI] • Pain interference [PROMIS] • Quality of life [PedsQL 4.0] • Pain self-efficacy [Porter's scale])		X	X	X	X	X
Cost Variables • Cost effectiveness and utility [HUI2/3])		X			X	X

Figure 3 Pain Squad+ schedule of enrolment, interventions and assessments. app,application; RN, registered nurse.

(NRS) with verbal anchors 'no pain' at 0 and 'pain as bad as you can imagine' at 10.[37 38] Item scores may also be averaged to give a Pain Intensity Summary Score.[39]

Secondary outcomes

a. ***Pain interference*** will be assessed using the Patient Reported Outcomes Measurement Information System (PROMIS) Pediatric Pain Interference Short-form Scale. The PROMIS instrument is a valid 8-item scale assessing the impact of pain on function.[40 41] Higher scores represent greater interference with function.
b. ***HRQL*** will be assessed using the Pediatric Quality of Life Inventory (PedsQL) 4.0. The PedsQL 4.0 is a valid and reliable 23-item instrument not specific to pain.[2 42] It is comprised of 4 subscales (physical functioning, emotional functioning, social functioning and school functioning), which are summed to provide a total score. Higher scores represent better quality of life.
c. ***Pain management self-efficacy*** will be assessed with Porter's scale which assesses self-efficacy for managing pain, symptoms and function in cancer patients.[43 44] This 16-item scale includes a valid and reliable 5-item subscale assessing cancer pain management self-efficacy with higher scores indicating more certainty and is adapted from a scale that has been successfully administered to adolescents.[21 45]
d. ***Cost effectiveness and cost utility*** analyses will determine the incremental costs (or savings) of the Pain Squad+ app, with and without nurse support, when compared with a waitlist control group in reducing pain over the study. Quality-adjusted life years will be calculated using data from the valid and reliable Health Utility Index Mark 2/3 (HUI2/3)[46] completed by adolescents. Direct healthcare costs will include the intervention costs as well as costs for health service utilisation during the trial. Family out-of-pocket expenses, indirect costs due to lost productivity and health service use will be ascertained using standardised customised data collection forms completed by caregiver report.
e. ***Satisfaction with treatment*** will be assessed using qualitative interviews with a subset of participating adolescents. These interviews will specifically be used to explore the perceptions of adolescents with cancer as they relate to the acceptability (including engagement with pain treatment strategies) of Pain Squad+, with and without nurse support or the waitlist control condition.

Sociodemographic-related and disease-related data baseline

Adolescent age, sex, ethnicity, school grade, diagnosis, stage/risk, relapse-status, treatment-type, date of diagnosis, comorbid conditions and medications, pain history; as well as caregiver age, sex, ethnicity, educational attainment and financial characteristics; adolescent ownership and use of smartphones and adolescent expectation about treatment effectiveness (assessed using a valid NRS scale with verbal anchors 'don't think it will help at all' at 0 and 'think it will help a lot' at 10).

Participant timeline

An 8-week treatment period will be used (figure 3). The primary outcome, and health-related secondary outcomes will be assessed at baseline and 2, 4, 8 and 16 weeks post-randomisation. Cost-related outcomes will be assessed at baseline, 8 and 16 weeks post-randomisation. The primary endpoint will be at 4 weeks post-randomisation selected as our primary endpoint because, based on our pilot, it is feasible to administer the intervention for this period and significant pain improvements are observed at 4 weeks.[30] To examine whether duration of Pain Squad+ use changes the magnitude or direction of outcome changes, adolescents in the experimental groups will continue to use the app until 8 weeks post-randomisation and outcomes will be assessed at 2 and 8 weeks (specifically examining the effect of shortening or extending intervention use on health quality). A longer-term follow-up (16 weeks) will be used to examine the maintenance of any Pain Squad+ therapeutic gains after discontinuation of the intervention. Qualitative interviews will be conducted at study completion or withdrawal.

Sample size

The sample size is calculated based on detecting a difference of 1.1 points between any two treatment groups in the primary outcome, average pain intensity reported on the BPI, at 4 weeks post-randomisation. This difference in pain intensity represents one of minimal clinical significance (the smallest difference that patients perceive as beneficial) for pain intensity improvement on a 0 to 10 scale in adolescents.[47] Our pilot study showed that the effect size for a 1.1-point change in pain intensity in adolescents following Pain Squad+ was 0.52.[30] We have used a conservative approach which accounts for the 1-group design of our pilot and have powered this RCT to detect a primary outcome effect size of 0.5. Using a sample size calculation for analysis of covariance models and controlling for baseline pain intensity,[48] sample sizes of 63 per group, or 189 in total, will be required to achieve 80% power to detect an effect size of 0.5 between any two treatment groups. This calculation assumes an overall Type I error set at 0.05 allowing for Bonferroni-corrected pairwise comparisons of treatment arms, and a conservative correlation between baseline and follow-up measurements of 0.5. To account for the 5% drop out and 10% loss to follow-up rates observed in the pilot study,[30] we will recruit 222 (ie, 189/0.85) adolescents into the study, or 74 per group.

Recruitment

Each site research assistant (RA) will coordinate with the clinic healthcare team to determine eligibility. Identified eligible potential participants will be recruited via telephone call (following a mailed or emailed study information letter) or in-person at the hospital. Recruitment will begin in November 2019 and is projected to end in April 2022.

Allocation and blinding

A centrally controlled, online randomisation service will be used to assign adolescent to each study group using a 1:1:1 allocation model. When an adolescent is ready to be randomised, the lead site RA will enter a unique identification number and information about the stratification variable (recruitment site) into the online programme. Group allocation will be assigned with block sizes of 6 and 9 within each stratum. The RA, who has no role in allocation sequence generation, will then inform the adolescent of their group assignment and instruct them on the procedures to be followed. The investigators, including data analysts, will be blind to group allocation. Treatment allocation may be unblinded only by the principal investigators when knowledge of the actual treatment is essential for further treatment of the patient,[49] as determined by the adolescent's treating oncologist.

Data collection methods

Pre-randomisation procedures

Eligible adolescents who are hospital inpatients or have a scheduled clinical appointment during the recruitment period will be invited to participate. Site RAs will obtain informed consent from adolescents and one of their primary caregivers. The research coordinator will track the number of eligible adolescents approached and reasons for refusal on an investigator-developed form. The lead site RA will obtain baseline data on adolescents (sociodemographic-related and disease-related characteristics) from their medical records and administer online pre-intervention measures on the secure password-protected Research Electronic Data Capture (REDCap) site.

Post-randomisation procedures

At 2, 4, 8 and 16 weeks post-randomisation, the lead site RA will contact adolescents and caregivers up to three times by text message, email and/or telephone and ask them to complete all outcome measures. To do so, participants will log into REDCap using an Internet-enabled device and their unique identifier. Outcome measure data will be time-stamped by REDCap when entered and participants will be encouraged to complete measures immediately after contact with the RA. The RA will provide telephone troubleshooting in the case of REDCap or questionnaire problems. Adolescents will receive a gift certificate for each outcome assessment completed in recognition of their time and effort. Loaned phones will be returned. All data will be exported from REDCap to SAS statistics[50] on the secure server at SickKids for analysis. Qualitative interviews will be conducted with a subset of adolescents from each trial arm. Adolescents who vary across age, sex, diagnosis and study engagement will be recruited. Interviews will be conducted until data saturation (ie, no new data generated in an interview). We anticipate conducting a total of 45 interviews. A semi-structured interview guide that is based on the guide used in our pilot[25–31] and has been refined by former adolescent cancer patients will be used. Interviews will be audio-recorded and may be conducted in-person or over the telephone. Field notes will be taken by the interviewer.

Data management and confidentiality

All outcome data will be collected online using REDCap and the associated database will be regularly backed up by SickKids. All data files (including backups) will be kept in a secured environment in Canada and are available for recovery. The secure digital platform APEEE will be used to collect adolescent-entered pain assessment and treatment data, as well as data related to app engagement, for each of the intervention groups. Data will be accessible only by the study team and staff. Any hardcopy documentation (eg, consent forms) will be stored in locked cabinets in locked offices at study sites, separate from the stored data. All staff will be provided with training on the use of REDCap and APEEE and maintaining participant confidentiality.

Data analyses methods

Health outcome analyses

Pain intensity, pain interference, HRQL and self-efficacy data will be analysed using an intent-to-treat approach.[51] Background variable data collected at baseline will be described using measures of central tendency and variance. If outcome data meet the requirements for parametric statistics (eg, approximate normality, linear distribution), linear mixed models will be used to assess the effects of the intervention on primary and secondary outcomes with baseline scores used as covariates. Regarding our HRQL outcome, as with our pilot, we will separately analyse the physical, emotional, social and school subscales of the PedsQL, as well as the total scale score. To explore the effects of demographic, disease-related variables and pain treatment strategies used on outcomes, separate linear mixed models with these variables as covariates will be used. A significance level of 0.05 will be used for all outcomes (with adjustment made for serial analyses).

Economic analyses

Cost effectiveness and cost utility analyses will be conducted using both a health system and societal perspective. Cost effectiveness and cost utility will be expressed as incremental cost effectiveness ratios (ICERs), calculated by dividing the incremental costs between treatment arms by the incremental difference in average pain intensity or the incremental change in utility scores, measured by the HUI2/3. Multiple ICERs will be calculated comparing each of the three study groups in a pairwise fashion for both the cost effectiveness and cost utility analyses. Deterministic and probabilistic sensitivity analysis will be performed to evaluate the robustness of the results. A 95% CI for incremental costs, incremental effects and the ICER will be calculated from study data.

Qualitative interview analyses

Audio-recorded interviews will be transcribed verbatim. Transcribed data will be managed using NVivo 12.0 software (QRS International). Data analysis will occur shortly after each interview is conducted so that identified issues can be used to inform subsequent interview content. Data will be read several times by the study team for overall understanding and to identify data codes. Data will then be coded using a line-by-line approach according to study objective. Codes will be grouped into categories based on between-code relationships. Category development will occur until all data can be classified under the existing categories. Categories will then be grouped into themes. Field notes and relevant sociodemographic and disease characteristics will be integrated into the analysis process to illustrate or clarify emerging categories and themes.

Patient and public involvement statement

Adolescents with cancer have been directly and actively involved in all stages of the development and evaluation of the Pain Squad+ app, including determining the feasibility of this study, evaluating any potential burden on adolescent participants and in the development of this research protocol. An adolescent with cancer advisory committee has been established to guide trial conduct and results interpretation and dissemination from a patient perspective and will report to the principal investigators. This advisory committee will meet regularly with the lead investigators to ensure the trial is guided by the priorities and experiences of adolescents with cancer.

ETHICS AND DISSEMINATION

Trial steering and data safety and monitoring committees

The trial steering committee consists of the lead study team. Virtual progress meetings with all steering committee members will be routinely collected to ensure the smooth running of the study. A datasafety and monitoring committee (DSMC) guided by a prepared charter of roles and responsibilities (available from corresponding author) and consisting of a statistical expert, a paediatric oncology nurse scientist and a paediatric anaesthesiologist who are independent of the research team has been established. The DSMC will meet biannually to review recruitment, accumulating study data and adverse events and will provide guidance to the study team regarding any needed action.

Safety appraisal and protocol amendment reporting

Based on our pilot and similar studies conducted by our group,[12] there are no known risks to adolescents enrolled in the experimental or control groups. Any adverse events reported by adolescents, their healthcare teams or the study nurse will be tracked on a critical incident form and reported to treating oncologists as soon as possible. Site ethics boards and the DSMC will also be contacted as soon as possible after the occurrence of any adverse event. Any major amendments to the protocol that may impact the conduct of the study or participant benefits or harms will be agreed on by the trial steering committee, as well as the adolescent with cancer advisory committee and approved by all site ethics boards before they are instituted. These amendments will also be communicated with study participants as soon as possible by site RAs.

Dissemination and knowledge translation plan

We have and will continue to involve patient, healthcare professional, policymaking and research stakeholders in all stages of the research process. We will present research findings at international oncology and paediatric conferences and publish in leading journals. Our knowledge translation strategy will also include: a one-page brochure for distribution to oncology healthcare professionals, a~3 min video for adolescents with cancer, which will be posted on websites such as YouTube, media releases (ie, for newspaper, magazines), posting on partner organisation, hospital and university websites and supporting adolescents and caregivers in translating results into fact sheets to support these key stakeholders in educating their healthcare professionals about results (ie, consumer detailing).

Author affiliations
[1]Child Health Evaluative Sciences, Hospital for Sick Children, Toronto, Ontario, Canada
[2]Lawrence S. Bloomberg Faculty of Nursing, University of Toronto, Toronto, Ontario, Canada
[3]Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada
[4]Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada
[5]Division of Hematology/Oncology, Hospital for Sick Children, Toronto, Ontario, Canada
[6]Institute for Clinical Evaluative Sciences, Toronto, Ontario, Canada
[7]Division of Hematology/Oncology, McMaster Children's Hospital, Hamilton, Ontario, Canada
[8]Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada
[9]Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada
[10]Division of Hematology/Oncology, IWK Health Centre, Halifax, Nova Scotia, Canada
[11]Division of Hematology/Oncology, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada
[12]Faculty of Medicine, University of Ottawa, Ottawa, Ontario, Canada
[13]Division of Hematology/Oncology, Alberta Children's Hospital, Calgary, Alberta, Canada
[14]Cumming School of Medicine, University of Calgary, Calgary, Alberta, Canada
[15]Division of Hematology/Oncology, Stollery Children's Hospital, Edmonton, Alberta, Canada
[16]Faculty of Medicine and Dentistry, University of Alberta, Edmonton, Alberta, Canada
[17]Division of Hematology/Oncology, London Health Sciences Centre Children's Hospital, London, Ontario, Canada
[18]Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada
[19]Division of Hematology/Oncology, Montreal Children's Hospital, Montreal, Quebec, Canada
[20]Faculty of Medicine, McGill University, Montreal, Quebec, Canada
[21]Division of Hematology/Oncology, BC Children's Hospital, Vancouver, BC, Canada
[22]Faculty of Medicine, The University of British Columbia, Vancouver, BC, Canada
[23]Ontario Parents Advocating for Children with Cancer, Toronto, Ontario, Canada

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Contributors LJ and JS conceived of this trial and designed and developed the Pain Squad+ intervention. LJ, PCN, VB, DJ, VL, SM, SP, CSa, CSt, JCV, MEM, CN, AH, CS, GE-KR, HI, RH, GF, SK and JN contributed to the design of the trial from a methodological standpoint, including design of the data analyses plans (JCV and MEM). LJ drafted the manuscript and PCN, VB, DJ, VL, SM, SP, CSa, CSt, JCV, MEM, CN, AH, CS, GE-KR, HI, RH, GF, SK and JN read or revised and approved the final version.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not required.

Ethics approval Ethics approval for this study has been obtained from the Hospital for Sick Children Research Ethics Board.

Provenance and peer review Not commissioned; peer reviewed for ethical and funding approval prior to submission.

ORCID iD

Lindsay Jibb http://orcid.org/0000-0001-6995-2825

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