REFINEMENT AND EARLY EVALUATION OF SPARK, AN APPROACH TO ENABLE SYMPTOM SCREENING AND MONITORING BY CHILDREN RECEIVING CANCER TREATMENTS

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Summary

Questions: Children with cancer and hematopoietic stem cell transplant (HSCT) recipients frequently experience severe and bothersome symptoms because treatments are intensive. Symptoms may remain unaddressed even during healthcare encounters because children do not complain or ask for help, and clinicians do not appreciate symptoms because they fail to ask about them.

In order to address these gaps, we developed SPARK (Supportive care Prioritization, Assessment and Recommendations for Kids), a website devoted to facilitating symptom screening by children receiving cancer treatment and dissemination of supportive care guidelines. This proposal is focused on symptom screening.

Aims are: (1) To refine the SPARK platform to promote self-report symptom screening; (2) To determine the proportion of children who complete symptom screening on at least 60% of inpatient days and to determine the most effective ways to communicate symptom screening results to children; and (3) To determine the feasibility of a randomized controlled trial (RCT) of symptom feedback to healthcare providers.

Core Expertise: Dr. Sung is a Pediatric Oncologist and Clinician Scientist. She chairs Cancer Control and Supportive Care in the Children's Oncology Group. Dr. Dupuis is a Pediatric Oncology Pharmacist and a Clinician Scientist. She has a research program focused on chemotherapy-induced nausea and vomiting prevention. Dr. Gladstone has expertise in qualitative methods and patient engagement. Dr. Soman is a leading scholar in the area of behavioral insights and choice architecture. The site collaborators have an excellent track record for patient accrual and high data quality.

Methods: For aim 1, participants will be children with cancer or HSCT recipients who are 8-18 years of age and who can understand English. Aim 1 is cross-sectional; we will perform individual interviews to evaluate and refine the symptom screening component of SPARK. The think aloud (TAL) technique will be used to evaluate understandability and usability among 40-80 participants.

Participants eligible for aims 2 and 3 will be children who meet eligibility for aim 1 and who are expected to be in hospital or in clinic daily for 5 days. For aim 2, we will ask 30 participants to complete symptom screening daily for 5 days. We will determine the proportion of children who complete at least 60% of evaluations. We will also evaluate preferences for, and understanding of symptom reports. Interviews will be conducted on day 5.

Aim 3 will be a pilot multi-center RCT in which we will randomize children to either undergo daily symptom screening for 5 days with symptom reports provided to the healthcare team or standard of care. Feasibility will be met if at least 30 participants are enrolled within one year and at least 75% complete at least 60% of evaluations.

Expected Results: In our future vision, symptom control will become a metric by which to judge the quality of healthcare. In order to realize this vision, we need a feasible mechanism by which children with cancer and HSCT recipients can be enabled to report and track symptoms and for this information to be readily available to clinicians. The expected result is a transformation from our current non-systematic healthcare provider-centered approach to symptom management to a systematic child-centered

approach. The ultimate result will be improved symptom control and better quality of life (QoL) for children receiving cancer treatment.

Concept

Quality of the Idea

Children receiving cancer treatment have excellent survival outcomes, in part, related to the provision of intensive therapies. Unfortunately, most children suffer and experience severe and bothersome treatment-related symptoms.[1] Symptoms not only impact on QoL and morbidity but, in addition, may negatively influence future psychosocial functioning.[2]

Symptoms remain unaddressed even during healthcare encounters because children do not complain and clinicians fail to ask about them. We recently developed SSPedi, a pediatric-specific symptom screening tool on an iPad. SSPedi, however, consists only of the questions which ask about symptoms. SPARK is the web-based application which will facilitate access to SSPedi, encourage symptom screening, generate reports and allow children to track their symptoms. Careful thought to design is required to ensure SPARK optimizes future use and has clinical utility. The proposed project output is a product that facilitates longitudinal symptom screening and provides the groundwork for a future RCT of symptom feedback.

SPECIFIC OBJECTIVES

Among children with cancer and HSCT recipients:

1. To refine the SPARK platform to promote self-report symptom screening. Evaluation will focus on understandability and usability.

2. To determine the proportion of children who complete symptom screening on at least 60% of on-study days during a 5 day longitudinal study and to determine the most effective ways to communicate symptom screening results to children.

3. To determine the feasibility of an RCT of symptom feedback to healthcare providers compared with standard of care. Feasibility will be evaluated by the number of children enrolled during a one year period and compliance with symptom screening.

Importance of the Idea

Children with cancer and HSCT recipients frequently experience severe and bothersome symptoms because treatments are intensive. Common symptoms include pain, mouth sores, nausea, fatigue, sadness and worry. Symptoms remain unaddressed even during healthcare encounters because children do not complain, clinicians do not appreciate symptoms because they fail to ask about them, clinical practice guidelines (CPGs) addressing most symptoms do not exist and a mechanism to facilitate access to CPGs is not available. This application focuses on improving symptom screening and communication.

In adult oncology patients, routine patient-reported outcome (PRO) measurement and provision of PRO reports to healthcare providers improves patient QoL.[3-5] In Ontario, improved health outcomes were observed following wide implementation of routine symptom screening of a validated instrument.[6] Implementation led to decreased emergency room visits and higher symptom scores triggered clinical actions.[7, 8]

In contrast to these efforts, data in children are limited.[9] We recently developed SSPedi (Symptom Screening in Pediatrics Tool),[10] the only comparable pediatric symptom screening tool[11, 12] and just developed SPARK. SPARK is a web application which consists of two components: (1) symptom screening component centered on web-based SSPedi; and (2) supportive care CPG component. SSPedi is a 15 item symptom screening tool for children receiving cancer treatment. We confirmed understandability and content validity of the paper version of SSPedi.[11] Subsequently, we finalized an electronic iPad version of SSPedi that is easy to use and understand with features specifically designed to facilitate child self-report (Figure 1).[12]

Based upon the initial favorable psychometric properties of SSPedi, we are continuing the development of a web-based application of SSPedi integrated within SPARK. Products to be evaluated in this proposal are external to SSPedi questions and include design to encourage children to complete SSPedi, to facilitate longitudinal completion, to view reports and to track symptoms. Future work beyond this proposal will promote healthcare provider access to CPG specific recommendations based upon symptoms reported by children within SPARK.

SPARK has been developed and preliminarily evaluated with research staff (Figure 2). However, SPARK has not yet been evaluated by users. This proposal will refine the symptom tracking and communication modules of SPARK to optimize understandability and usability. We define usability as ease of use and design to maximum likelihood and volume of use. We will also evaluate daily SSPedi completion rates and refine symptoms reports such that they are understood by children. We will also conduct a pilot RCT of symptom feedback to healthcare providers via SPARK which will lay the foundations for a future definitive trial.

In our future vision, symptom control will become a metric by which to judge the quality of healthcare. In order to realize this vision, we need a feasible mechanism by which

children with cancer and HSCT recipients can be enabled to report and track symptoms and for this information to be readily available to clinicians. The expected result is a transformation from our current non-systematic healthcare provider-centered approach to symptom management to a systematic child-centered approach. The ultimate result will be improved symptom control and better QoL for children receiving cancer treatment.

METHODOLOGY

Overall Eligibility: We will include children with cancer and HSCT recipients who are 8-18 years of age at enrollment and who can understand English. Participants may be inpatients or outpatients, and may be actively receiving cancer treatment or may have completed treatment. Exclusion criteria will be illness severity, cognitive disability, or visual impairment that precludes utilization of SPARK according to the healthcare team. Additional criteria apply to aims 2 and 3.

Sites: Aims 1 and 2 will occur at a single site, The Hospital for Sick Children (SickKids) in Toronto. Aim 3 will occur at 5 sites: SickKids and the children's hospitals in Vancouver, London, Hamilton and Ottawa.

Ethics: Research Ethics Board (REB) approval will be obtained at all sites. Informed consent and assent (if applicable) will be obtained from all participants.

SPARK Development: With support from an Infrastructure Grant from the Garron Cancer Centre, we worked with a website developer (Translucent Computing) and a choice architecture expert (Soman) to create a draft version of SPARK (Figure 2).

SPARK development has incorporated several design features. First, efforts have focused on maximizing the use of icons and images rather than text based upon choice architecture expert input. Second, usability has been emphasized. In order to account for the wide age and developmental ability range, we have integrated audio assistance and synonym lists for younger children. Third, SPARK is accessible on multiple platforms such as a personal computer, tablet or smartphone. Fourth, we have developed an on-line, secure database located at SickKids. Data transmission occurs via wireless network systems and all processes are HIPPA/PHIPPA compliant. Fifth, SSPedi reports allow each child to track his/her symptoms over time and will permit healthcare providers to view their patients' SSPedi results. Currently, SPARK has only been evaluated by research team members. The following describes the specific methodology for each aim.

Objective 1: To refine the SPARK platform to promote self-report symptom screening.

Specific Eligibility: All participants meeting overall eligibility criteria.

Procedure: After collection of demographic data, we will ask children to evaluate SPARK. In-person, individual interviews will be conducted with a semi-structured format using the TAL technique of cognitive interviewing. Participants will be purposively sampled in groups of five to maximize variation by age, diagnosis, inpatient status and treatment status active/completed. This aim will occur on a laptop.

We will ask the participant to explore the SPARK landing page (Figure 2) which contains 3 icons representing children receiving cancer treatment, family members and

healthcare providers. Next, we will ask the participant to click the child icon which will take him/her to the patient main page (Figure 2). The patient main page includes 3 icons which direct the user to: (1) Do SSPedi now; (2) See reports; and (3) View description of the benefits of using SSPedi. Finally, from “See reports”, the participant will be asked to view and describe four hypothetical SSPedi reports. Two reports will illustrate single SSPedi administrations: one represents highly bothersome symptoms and one represents symptoms that are not bothersome. Two reports will illustrate trends over time: one showing improving and one showing worsening of symptoms.

To evaluate understandability, with each page, the participant will be asked what each icon or element means and will be encouraged to click on icons to progress through SPARK. Participants will be asked to verbalize their thought process as they navigate through SPARK and will be continuously prompted to TAL. The interviewer will be a trained clinical research associate or research nurse with expertise in qualitative approaches and cognitive interviewing. We have previous experience both with the TAL approach and with iterative instrument development in this patient population.[13, 11] A second research associate will observe the interview and rate understandability of each SPARK element and the symptom reports on a 4-point Likert scale ranging from 1=“completely incorrect” to 4=“completely correct”.

To evaluate usability, at the end of the interview, we will ask participants what they like and don’t like about SPARK and solicit suggestions for modifications. We will ask participants to rate ease of use on a 5-point Likert scale ranging from 1=“very hard” to 5=“very easy”. He/she will also rate usefulness for children receiving cancer treatment on 5-point Likert scale ranging from 1=”not useful at all” to 5=”extremely useful”.

Evaluation will occur in 2 phases, namely low and high-fidelity testing. Low-fidelity testing focuses on understandability; SPARK will not have color, design elements will be drafts and SSPedi will not be functional. High-fidelity testing will incorporate graphic and visual communication design expertise via Catalyst Inc. This version of SPARK will be fully functional and will allow SSPedi data entry and real-time report generation. High-fidelity evaluation will be similar to low-fidelity evaluation except that participants will complete SSPedi and the actual SSPedi report will be shown in addition to the 4 hypothetical reports. Questions about color and design will also be added. This 2-phased approach is more cost efficient than initial development at high-fidelity.

At both low and high-fidelity testing, interview results will be summarized and reviewed after every 5 interviews by research team members to determine whether our approach or the script requires modification. Minor edits to SPARK may also be made. After every 10-20 participants (2-4 iterations) and with the proposed final version, a larger Review Panel will be convened to evaluate responses and deliberate whether SPARK requires modification. The Review Panel will be composed of the investigators, the Design Team (Translucent and Catalyst), the choice architecture expert (Soman), the qualitative expert (Gladstone), 2 pediatric cancer survivors and a parent advocate.

Analysis and Sample Size: Low-fidelity iterations will continue until saturation is reached

and no further edits to promote understandability are required. Saturation will be defined as the absence of substantive new comments identified during a round of five interviews. Next, high-fidelity iterations will focus on both understandability and usability and will continue until: (1) saturation is reached; (2) at least 9 of the last 10 participants state that SPARK is easy or very easy to use; and (3) qualitative comments suggest that no further modifications are required.

We will describe the proportion of participants who state that SPARK is easy or very easy to use, who rate usefulness as 4 or 5 (5=”extremely useful”) and who correctly interpret each SPARK element. Analysis of qualitative comments will be descriptive. Based upon our previous experience with this technique, we anticipate the conduct of between 8-16 iterations with 5 participants per iteration for a total of 40-80 participants.

Objective 2: To determine the proportion of children who complete symptom screening on at least 60% of on-study days and to determine the most effective ways to communicate symptom screening results during a longitudinal study.

Specific Eligibility: Participants meeting overall eligibility criteria and who are expected to be in hospital or in clinic daily for at least 5 days.

Procedure: Participants will complete symptom screening using refined SPARK from aim 1, once daily on a study-supplied iPad, for 5 days. Five days was chosen to allow longitudinal daily evaluation but preserve feasibility as few children are admitted or seen daily for longer than 5 days. For inpatients, daily reminders to complete SSPedi will appear on the iPad, by text or by email depending on preferences and availability. Reports will be available to the child at any time. For outpatients, research associates will provide the iPad in person daily and reports may be viewed at those encounters.

Individual interviews will be conducted on day 5±1 using a semi-structured format similar to that used in aim 1. The interviewer will ask if the participant viewed any of the reports and what was done with the information, including whether the information was shared with healthcare providers. Next, the interviewer will generate that child’s last SSPedi report and all reports since study entry. If the child did not complete any SSPedi evaluations, then hypothetical reports will be shown. The participant will be asked to interpret the reports in a similar fashion as aim 1 using TAL. Suggestions for modifications to improve clarity and meaning will be solicited, particularly if the child is incorrect in report interpretation.

Next, we will ask about the participant’s experience with daily SSPedi completion. We will ask about potential facilitators and barriers to daily reporting. At the end of the interview, questions regarding general impressions and ratings of ease of use and usefulness will be the same as in aim 1.

Interview results will be summarized and reviewed after every 5 interviews by research

team members to determine whether our approach or the script requires modification. Minor edits to SPARK may be made. After 15 and 30 participants have been enrolled, the same Review Panel from aim 1 will meet to evaluate the comments and decide whether to modify SPARK. If compliance is low after 15 participants, we may provide the iPad in person daily for inpatients (similar to outpatients) for the next 15 participants.

Analysis and Sample Size: We will describe the proportion of children who complete screening on at least 60% of on-study days, or 3 of 5 days. Based upon our experience with SSPedi, we anticipate that at least 75% of participants should be able to achieve this level of compliance.

We will describe the proportion of participants who state that SPARK is easy or very easy to use, who rate usefulness as 4 or 5 (5=”extremely useful”) and who correctly interpret SSPedi reports. Analysis of qualitative comments will be descriptive.

We will include 30 participants. Assuming that 75% of participants achieve SSPedi completion on at least 60% of days, this sample size provides a two-sided 95% confidence interval with limits of 56-89%; this precision will be adequate for our purposes.

Objective 3: To determine the feasibility of an RCT of symptom feedback to healthcare providers versus standard of care.

Specific Eligibility: Same as aim 2.

Procedures: In this pilot multi-center RCT, we will randomize children to either undergo daily symptom screening for 5 days with symptom reports provided to the healthcare team or standard of care. The primary endpoint, feasibility, will be met if at least 30 participants are enrolled within one year and if at least 75% complete symptom screening on at least 60% of on-study days. Participants will be randomly allocated 1:1 to the intervention group or to the control group. The randomization sequence will be computer generated and stratified by HSCT versus non-HSCT and institution. Block sizes will not be disclosed and the allocation sequence will be concealed.

For those randomized to the intervention arm, symptom screening using SPARK will be completed once daily for 5 days on an iPad using the approach refined in aim 2. Daily SSPedi reports will be printed and provided in the patient chart. On days 1 and 3±1, a report describing symptoms that are “a lot” or “extremely” bothersome will be emailed to the physician providing direct medical care..

For those randomized to the control arm, a clinical research associate will visit the participant on days 1 and 5±1 and will obtain SSPedi scores on an iPad. Reports will not be printed or emailed to the physician.

For both arms, participants will be interviewed on day 5±1 using a semi-structured

format. We will identify aspects of the study which they liked and which they didn't like and potential barriers and facilitators to participation in a future RCT. Secondary endpoints will also be collected. For the intervention arm, questions regarding general impressions and ratings of ease of use and usefulness will be the same as in aim 1.

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The primary outcome feasibility will be met if at least 30 participants are enrolled within one year and at least 75% complete at least 60% of evaluations.

Secondary endpoints include potential efficacy outcomes for the definitive RCT; they will be obtained on day 5±1. We will include SSPedi total scores and individual symptom scores. We will also include a pain scale (Faces Pain Scale Revised) and the PedsQL 3.0 Acute Cancer Module. This measure is a multidimensional instrument that is reliable and valid in children with cancer.[13-17] It assesses pain and hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, perceived physical appearance and communication. The self-report 7 day recall version will be used. We will also measure documentation of symptoms and intervention provision for symptom control as abstracted from the health record.

Analysis and Sample Size: Feasibility will be defined as ability to enroll 30 participants within one year and compliance with SSPedi evaluations as defined above. For the SSPedi, pain and QoL scores, we will calculate variance to facilitate sample size calculations for the future definitive trial. Description of symptoms and intervention provision will be descriptive. In the event of missing data, multiple imputation approaches will be used.

JUSTIFICATION FOR METHODOLOGICAL CHOICES

Cohort: A lower age limit of 8 years was chosen as this is the youngest age for which SSPedi has been evaluated. We plan to conduct this study among English-speaking children because SSPedi is currently only available in English. Translation to other languages will be an important future initiative.

Timing: Early psychometric testing of SSPedi has been promising. Even though psychometric evaluation of SSPedi is in progress, it is appropriate to begin evaluation of SPARK. In the unlikely scenario that SSPedi total score is not reliable or valid, individual SSPedi items can still be incorporated into SPARK and only the overall SSPedi scores would be deleted.

Focus on inpatients and clinic patients: There are many contexts in which SPARK may be helpful including inpatient, clinic, home and following completion of therapy. We have chosen to begin this research program with those seen for 5 consecutive days but appreciate that expanding to other contexts is a priority.

FEASIBILITY, TIMELINE AND FUTURE WORK

At SickKids, there are 350 new cancer diagnoses and 100 HSCT procedures performed annually. Thus, we anticipate 150 eligible patients for aim 1 and 50 eligible patients for aims 2 and 3 annually. Assuming 40-60% acceptance rate, each aim will require 1 year for enrollment (aim 3 occurs at 5 sites).

Aims 1 and 2 will require 2.5 years which incorporates time for Review Panel meetings and software development and modifications. Aim 3 will require 1.5 years to allow time for study start-up at the 4 non-SickKids sites. One final year will be required for analysis and manuscript preparation, resulting in a total timeline of 5 years.

In the future, we plan to link the data from the longitudinal studies of SSPedi and SPARK to data in the Cancer in Young People – Canada (CYP-C) program. CYP-C is a national pediatric cancer database which includes all children 0 to < 15 years of age with cancer since 2001. Linking these data sets will allow us to develop predictive models of symptom burden using patient and institutional characteristics and to describe survival outcomes associated with uncontrolled symptoms. Therefore we plan to ask participants in this randomized trial for permission to link trial data with the data in CYP-C.

Expertise, Experience and Resources

Expertise and Experience: This group of investigators is inter-professional and brings together expertise in pediatric oncology, pharmacy, qualitative and quantitative methodology, choice architecture, and patient engagement.

Dr. Sung (6 hrs/wk) is a Pediatric Oncologist with a PhD in Clinical Epidemiology. She is the Chair of Cancer Control and Supportive Care in the Children's Oncology Group (COG), the world's largest pediatric cancer clinical trial consortium. Dr. Sung has an independent research program focused on the measurement and treatment of symptoms. She is the co-Principal Investigator of the CCSRI Impact Grant which supported the development of SSPedi (the symptom screening tool). She has an excellent track record of successfully leading multi-center supportive care trials.

Dr. Dupuis (4 hrs/wk) is a Pediatric Oncology Pharmacist and a Clinician Scientist. She is the Chair of the COG Antiemetic Sub-Committee and Co-Chair of the Pediatric Oncology Group of Ontario Supportive Care Committee. She has a research program focused on chemotherapy-induced nausea and vomiting prevention. She also chairs the International Pediatric Oncology Guidelines in Supportive Care (iPOG) Network (http://www.sickkids.ca/research/ipog/), which brings pediatric cancer supportive care CPG developers together worldwide.

Dr. Gladstone (2 hrs/wk) has expertise in qualitative methods and patient engagement in research. She is the Associate Director of the Center for Critical Qualitative Research at the University of Toronto and a CIHR New Investigator. Dr. Gladstone is recognized internationally for her innovative research with young people. She uses participatory research methods to bring young people's voices into debates about their health and social care needs by engaging families, clinicians, educators and other decision makers in an integrated knowledge creation and translation process.

Dr. Soman (2 hrs/wk) is a Professor at the Rotman school of Management and a leading scholar in the area of behavioral insights and choice architecture. His research (summarized in his book *The Last Mile*[18]) studies the manner in which people make choices, and identifies ways in which choice environments can be structured to help them make better choices.

Site Collaborators (2 hrs/wk) are all supportive care champions in their institutions. We have had extensive collaborations with all sites and they all have an excellent track record for patient accrual and high quality of data.

Preliminary Data: We previously identified the need for a new symptom screening tool for children with cancer and HSCT recipients.[19, 20] We were awarded a CCSRI Impact Grant (Jan 2014) to develop and validate a new tool named SSPedi. Based upon input from children receiving cancer treatments and their parents, we developed and refined the paper[11, 10, 21] and electronic versions of SSPedi and confirmed content validity, understandability and ease of use. SPARK builds upon SSPedi and is important as it

promotes access, encourages and facilitates use, allows children to view reports and enables symptom tracking.

Resources: Drs. Sung and Dupuis are Scientists in Child Health Evaluation Sciences, Research Institute, SickKids. SickKids is the largest pediatric institution in Canada and is one of the largest pediatric cancer centers in North America. We have sufficient space and infrastructure to support our research group and to conduct the described research.

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