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Development and Testing of a Videogame Intervention for Symptom Management among Children with Cancer: A Study Protocol

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TITLE

Development and Testing of a Videogame Intervention for Symptom Management among Children with Cancer: A Study Protocol

ABSTRACT

Introduction

Evidence shows that cancer treatment-related symptoms could be managed effectively in 8–18-year-old children through Digital Health Interventions (DHIs), consequently improving their Health-related Quality of Life (HRQOL). However, limited research is available about digitally mediated educative health interventions for children with cancer from Low and Middle-Income Countries like Pakistan. This study aims to develop a videogame intervention for children with cancer and test the clinical efficacy of the videogame concerning HRQOL and cancer treatment-related symptoms. Moreover, the following feasibility outcomes will be recorded: acceptability, appropriateness, cost, feasibility, and intervention fidelity.

Methods and analysis

An exploratory sequential mixed methods design is used in this study. In the first phase of the study, we interviewed 28 participants (14 child-parent dyads) and assessed their symptom experiences affecting children's HRQOL. Moreover, their preferences for the development of the videogame were also elicited. Based on the findings from relevant literature and the interviews, we developed the videogame in collaboration with clinical and digital experts in the study's second phase. In the third phase of the study, a Pilot Randomized Controlled Trial (Pilot-RCT) will be conducted at a Tertiary Care Hospital in Karachi, Pakistan. There will be two groups: the intervention group and the control group. The intervention group children will receive the videogame application for eight weeks, during which symptom management strategies will be taught to them. Children in the attention control group will receive weekly WhatsApp messages on healthy behaviours.

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The primary outcome will be the HRQOL of children, and the secondary outcome will be cancer symptoms frequency and distress. These outcomes will be assessed pre- and eight weeks post-intervention. The feasibility outcomes will be assessed quantitatively and quantitatively through a questionnaire, videogame dashboard, interviews with a subset of intervention group child-parent dyads, and a focus group discussion with nurses and doctors, post-intervention respectively.

Ethics and dissemination

The study has been approved by the Ethics Review Committee of the Aga Khan University (2022-6833-21251). Data is accessible only to the research team in a secure form. The findings will be disseminated through publications.

Trial registration

ClinicalTrials.gov Identifier NCT05796895, registered in April 2023.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

- Evidence from High-Income Countries (HICs) shows that optimum symptom management in children with cancer through Digital Interventions significantly improves their HRQOL.
- Among several interventions, videogame-based interventions have demonstrated efficacy in the HICs.

WHAT THIS STUDY HOPES TO ADD?

- The study will add to the scientific knowledge on the clinical efficacy and feasibility of the videogame intervention on children with cancer from an LMIC Pakistan.
- A mixed methods approach will help understand the research problem and the best possible practical solutions.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY?

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- If the intervention efficacy is established, it will improve the healthcare practice through a digitally mediated intervention.
- It will enhance nurses' role in educating and promoting innovative strategies for symptom management among children with cancer.

Introduction

Approximately 400,000 children aged up to 19 years are estimated to be diagnosed with cancer annually worldwide [1]. With the global rise in the incidence of childhood cancer worldwide, Low and Middle-Income Countries (LMICs), including Pakistan, suffer a disproportionate burden [2,3]. The National Cancer Registry reveals that approximately 17,457 children are diagnosed with cancer in Pakistan yearly [4]. Global evidence suggests that 8 out of 10 children may get completely cured of childhood cancer upon receiving evidence-based, accessible treatment and support services [5]. Although cancer treatment is complex and lengthy, children respond better to treatment than adults and reach survivorship [5]. Early identification and treatment of childhood cancer through multimodality therapies is critical for better survival. Chemotherapy and radiation are the most common treatment modalities for childhood cancers [5]. However, these therapies result in severe cancer treatment-related symptoms, compromising children's daily functioning and HRQOL [6-7]. Several studies suggest that children with cancer below 18 years of age report similar treatment-related symptoms affecting physiological and psychosocial domains of their HRQOL [8-9]. Common physiological problems include pain, fatigue, GI-related symptoms, hair loss, and infection [9-11]. Commonly reported psychosocial symptoms include anxiety, depression, and isolation from friends [9-11]. Children's school attendance and academic progress are also affected during their treatment, which has future implications for them [12]. Suboptimal symptom management negatively affects children's physiological and psychological health, cognitive functions, academic performance, social relationships, and

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overall HRQOL and well-being [12-13]. Additionally, poor symptom management can have implications for delayed or abandoned treatment, poor treatment tolerance, unnecessary frequent emergency visits, and poor psychological outcomes [13-15]. Therefore, education and support about symptom management are critical to optimizing children's HRQOL and preventing symptom worsening [7,16].

During the prolonged trajectory of childhood cancer, the responsibility of treatment-related symptom management keeps switching from healthcare providers in the hospital to the children and their parents at home. Effective symptom management at home leads to better symptom outcomes, treatment adherence, less morbidity, fewer rehospitalizations, and improved HRQOL among children [17-18]. Studies have shown that children who actively participate in learning about self-management of their symptoms understand their disease well, have better preparedness to manage their symptoms, and contribute to more informed health decisions [19-20]. Developmental psychology theories highlight that children learn best when engaged in activity and play [21-23]. Digital technologies such as interactive mobile apps, virtual reality (VR), and videogames allow children to engage in their learning. For these reasons, healthcare providers have started using digital devices in children with asthma, diabetes, cancer and other chronic health conditions to educate them about symptom monitoring and management [17,24].

Studies from High-Income Countries have shown that implementing Digital Health Interventions (DHIs) has significantly improved the HRQOL [18,25,26], knowledge [20], self-efficacy [20] and has decreased pain and fatigue [18], anxiety, and depression [27] in children with cancer. Among various DHIs, videogames have emerged as one of the promising modes of education to help children learn symptom management. The evidence regarding the efficacy of DHIs, especially from LMICs, is still limited, and more studies are recommended to determine the efficacy of these interventions on the health outcomes of

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children with cancer. To our knowledge, no similar study has been conducted in Pakistan. The aim of this study, therefore, is to develop a videogame intervention for children (age 8-18 years) with cancer and test its clinical efficacy concerning HRQOL and cancer treatment-related symptoms in children, and also to observe the feasibility of the intervention in terms of acceptability, appropriateness, cost, and intervention fidelity.

Symptom management theory (SMT)

As shown in Figure 1, the Symptom Management Theory (SMT) comprises three interrelated concepts: (a) symptom experience, (b) symptom management strategies, and (c) symptom status outcomes. Symptom experience explains the perception of change in a patient's usual health status. Symptom management strategies are approaches used to prevent, delay, or lessen the symptom experience. Symptom outcomes are measurable outcomes, such as improvement in the HRQOL or recovery from illness, assessed pre-and post-implementation of a symptom strategy [28].

In accordance with the SMT, in the first phase of the study, we identified the experience of symptoms from child-parent dyads and symptom management strategies from them and the relevant literature. The findings informed the development of the videogame in the second phase of the study. In the third phase of the study, we plan to teach symptom management to children through a videogame intervention and assess their HRQOL and symptom frequency and distress.

Methods and analysis

Design

As shown in Figure 2 [29], this study employs a mixed methods design (qual → QUAN) having three phases:

1. Phase I – Need Assessment.
2. Phase II – Videogame Intervention Development.

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3. Phase III – Videogame Intervention Testing.

Study phase I – need assessment

In Phase I of the study, a qualitative descriptive exploratory design was used to understand the experiences and perceptions of children with cancer and their parents regarding children's HRQOL, treatment-related symptoms, management strategies, and preferences informing the development of the videogame. In-depth interviews were conducted with 28 participants (14 child-parent dyads). Participants elicited strategies for the management of the following symptoms and healthy behaviours to be translated into the videogame: pain, fever, mucositis, nausea, vomiting, hair loss, missing school, throat irritation, constipation, staying physically active, balancing balance between rest and activity, knowing alarming signs, preventing infection, eating healthy, fighting sickness, and maintaining psychological and spiritual health.

Study phase II – videogame intervention development

During Phase II of the study, a multi-disciplinary team comprised of children with cancer, parents, clinical experts (oncology nurses and physicians), and digital design specialists (videogame developers and information technologists) collaborated in an iterative design process for the videogame. A series of brainstorming sessions employed an iterative methodology to refine the game's content, visual design, and narrative flow (storyboard). Upon development completion, user acceptance testing (UAT) was conducted with the child participants, parents, and research team members. This UAT phase served to identify and rectify any software bugs or usability issues within the videogame.

Features of the videogame

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As shown in Figure 3, in the game, a player (study participant) enters the game and selects language (English or Urdu), gender (boy or girl), and environment (city or town). After selecting the avatar, the game interface opens, and a Mascot (a gender-neutral cartoon character - bunny) welcomes the child. The Mascot provides the player with necessary instructions about the gameplay.

There are fourteen levels in the videogame. The child plays each level, which targets one symptom for which the child is taught symptom management or health behaviour. Moreover, feedback messages also pop up on the videogame screen to highlight the significance of the action performed. With that, the player progresses to the next level. Each day, the player can unlock two to three game levels. The game content is the same for all children; however, few variations are kept for younger (8-12 years old) and older children (13-18 years old). For example, some game levels provide more lifelines and hints to younger children. The videogame is auto-locked at 30 minutes for younger children to avoid exceeding the screen time limit. Younger children can play two game levels daily, whereas older children can play three. While older children can navigate the game icons, a tutorial about the gameplay is provided to younger children. Table 1 presents the game levels, symptoms and concerns, and details about game levels.

Table 1

The Videogame Levels, Symptoms and Concerns, and Details about the Game

Levels	Symptom or Health Concern	Symptom Management Strategies/ Behaviours (Game Activity)	Game Mechanism	Feedback/ Important Message for Children
Level one	Mucositis	Perform oral care by toothbrushing and protect oral cavity.	The player clicks on all the steps of toothbrushing and tongue cleaning on the game avatar to score coins.	1. Brush your teeth with a soft brush twice a day. 2. Avoid brushing teeth when platelet counts are low.

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Level two	Risk for Infection	Identify alarming signs of worsening symptoms and inform the doctor or nurse.	The player bursts all the balloons one by one. On popping each balloon, a text message shows one alarming sign of infection.	Know these alarming signs. If you have them, tell your doctor and nurse immediately and visit the hospital.
Level three	Risk for Infection And Constipation	Perform hygiene care regularly.	The player clicks on several steps of maintaining good hygiene (bathing, brushing teeth, shampooing, hand washing, passing stool daily, cutting nails, using sunscreen, and wearing a scarf or hat).	1. Keep yourself clean to maintain a healthy body. 2. If you are constipated, talk to your doctor and nurse.
Level four	Pain	To relieve pain, take analgesics on time and perform deep breathing exercises at least 3-4 times a day.	The player takes the prescribed analgesics and performs deep breathing exercises.	Take the medicine as prescribed by your doctor and do deep breathing exercises.
Level five	Fever	Take antipyretics as prescribed by the doctor to get relief from fever.	The player clicks on the steps of taking temperature, identifying fever, taking medicine as prescribed, rechecking temperature after an hour, informing the doctor if fever persists, and going to the hospital if needed.	Talk to your doctor if your fever persists and go to the hospital.
Level six	GI-related symptoms	Differentiate between healthy and unhealthy food options which are appropriate during sickness to stay healthy.	The player identifies healthy food options and collect them in a basket to score points.	Eat healthy food and avoid unhealthy food.
Level seven	Hair Loss	Accept that hair fall will occur and protect the scalp by covering it.	The player wears different head gears (hats, scarves, hair extensions). The player learns about hair fall and return of hair after completion of treatment.	1. Protect your scalp. 2. Hairfall is temporary, and hair will return after treatment is completed.

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Level eight	Fighting sickness	Identify measures that can be taken when feel sick and practice them.	The player bursts all the balloons one by one. On popping each balloon, a text message shows one measure to take when the child falls sick. The player must read and learn the measures.	Practice the measures taught to you when you feel sick.
Level nine	Mucositis	Gargles should be performed as prescribed by the doctor to prevent oral mucositis.	The player clicks on all the steps to gargle with the prescribed mouthwash. The player must read the message about adhering to this behaviour in a timely manner to prevent oral mucositis.	Gargle with the prescribed solution as advised by your doctor to prevent mucositis.
Level ten	Missing School	Perform a visual puzzle activity to find differences between two images. Keep your mind engaged, learn observation, attention to detail, and critical thinking skills, and do not miss school. Also, paint a few images for fun.	The Mascot advises the player to do activities at his school and some puzzles to remember fun at school. The player finds differences between the two images and paints several pictures.	When you miss your school and school activities, do some learning and fun activities at home.
Level eleven	Nausea, vomiting, and anorexia	Take antiemetics as prescribed and take small frequent meals to deal with nausea, vomiting, and anorexia.	The mascot advises the player to take antiemetics as prescribed and eat small, frequent meals. Several healthy eating options appear on the table one by one. The player chooses between them through a 'yes' or 'no'.	Take the medicine as prescribed and eat a small, frequent meal every 2-4 hours in a day, choosing healthy food options.
Level twelve	Throat Irritation	Identify and eat soothing food items to decrease oral ulcers and throat irritation.	The avatar has oral ulcers and an irritating throat. Several soothing and soft food options appear before the player. S/he can choose from them and eat to soothe their mouth. The player selects a 'yes' for the food option s/he likes.	You have several soothing and soft food options to soothe your irritating throat. Select whichever food item you like and eat it.

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Level thirteen	Psychological symptoms	Try various activities such as yoga, spending time in the garden, engaging in activities you enjoy, communicating with your friends, and practicing meditation and prayer to gain inner strength.	The mascot asks the player to do some yoga exercises, observe things around, talk to friends, and meditate and pray. The player performs these steps one by one and scores coins.	Do yoga and deep breathing to keep your mind relaxed. If you miss friends, call them. Meditate and pray.
Level fourteen	Fatigue	Maintain a balance between exercise/play and rest not to get fatigued.	The player clicks on several icons to help the avatar do exercises like walking, running, jumping, and hopping to score points. The avatar returns home and sleeps when tired.	Maintain a balance between exercise/play and rest not to get fatigued.

*The scoring and reward mechanism comprises coins, claps, celebration animation, and messages of applaud upon activity completion.

Study phase III – intervention testing (Pilot-RCT)

There are two objectives of this phase.

1. To determine the efficacy of the videogame intervention on the HRQOL and cancer symptoms frequency and distress of children with cancer in the intervention group as compared to the children in the attention control group at pre and eight weeks post-intervention.
2. To determine the intervention feasibility outcomes: acceptability, appropriateness, cost, feasibility, and fidelity.

Design

A Pilot Randomized Controlled Trial (Pilot-RCT) with an attention control will be used to attain the set objectives.

Study setting

The study is conducted at the Aga Khan University Hospital's (AKUH) in- and outpatient chemotherapy and radiation therapy units. The AKUH is a not-for-profit, resource-intensive,

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tertiary care, and Joint Commission International (JCI) accredited university hospital recognized for providing high-quality, compassionate care for several speciality services. The oncology department offers specialized cancer services [30]. There is one inpatient clinical area for chemotherapy and two outpatient areas for radiation and chemotherapy for children. In the inpatient area, there are separate beds assigned for children for chemotherapy [30].

Study population

Children having cancer and receiving chemotherapy or radiation are the study population.

Inclusion criteria

- Children aged 8-18 years.
- Diagnosed with any type and stage of cancer within six months.
- Can comprehend Urdu or English language.
- Have access to an Android smartphone/tablet for at least 30 minutes/day.

Exclusion criteria

- Critically ill children.
- Receiving palliative treatment.
- Have any diagnosed sight, hearing, cognitive impairment, or upper limb deformity.
- If already playing any videogame with similar content.

Sample size and sampling technique

The sample size was calculated for the primary outcome of HRQOL. Keeping the study power at 80%, significance level at 5%, maximum standard deviation of 18.6 [18], and true difference value of 13.5 points [17], a sample of 31 patients per group is desired for this study. Adjusting for 10% attrition, the final sample size is 35 patients per study group. For a pilot trial, a sample size of 35 participants per study group is considered adequate [31]. Children will be selected using a non-probability purposive sampling technique.

Participant recruitment

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A Research Associate (RA) will screen potential study participants using the patients' list available at the inpatient and outpatient oncology units and through communication with the staff nurses. The RA will assess the child for eligibility and explain the study to them and will approach the child in the presence of the parent. The RA will explain the study and random allocation to any study group. The child's written assent and parent's consent will be obtained if they agree to participate.

Randomization, blinding, and allocation concealment

Children will be randomized in a 1:1 ratio to the intervention or attention control group. Using a computer-generated randomization scheme, a random block of 4 and 6 will be used. A person, not a research team member, will generate the randomization list and prepare sealed and opaque envelopes, ensuring allocation concealment. The RA will open the envelope in front of the child/parent. Further steps would follow according to the child's assignment. The study will be non-blinded as group assignments cannot be hidden from the participants and research team members in a behavioural intervention [32].

Intervention group

Children in the intervention group will receive the videogame for eight weeks. The RA will provide instructions about the videogame. S/he will call the child and parent every week to ensure participant adherence in the study and to inquire if they have any questions related to the videogame content or worsening of symptoms and will answer in consultation with the clinical expert (oncologist in the research team). A call log of the conversation will be maintained.

Attention control group

The attention control group will be selected to ensure that the study outcomes are not attributable to the unequal attention given to the intervention group [33]. Children will receive weekly WhatsApp messages on healthy behaviours based on the National Cancer

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Institute's guidelines for childhood cancer. The RA will call the child and parent weekly to inquire about the child's health, and a call log of the conversation will be maintained.

Figure 4 presents the CONSORT flow diagram.

Study outcomes

Primary outcome – HRQOL

The HRQOL of children with cancer will be assessed using the Pediatric Quality of Life Inventory Generic Core Scale (PedsQL 4.0) and Cancer Module (PedsQL 3.0).

Secondary outcome - Cancer symptoms frequency and distress

The cancer symptoms frequency and distress will be assessed using the Memorial Symptom Assessment Scale Short Form (MSAS-SF).

Permission was obtained from the tool distributors for all the tools and to translate PedsQL 3.0 into Urdu. The tools were pre-tested on 10% of the sample (n=7 children). Their data will be excluded from the analysis. The Content Validity Index and post-hoc reliability measures of the tools in our sample will be reported.

Feasibility outcomes

The following feasibility outcomes will be assessed: intervention acceptability, appropriateness, cost, feasibility, and fidelity.

Data collection

The primary and secondary outcomes will be assessed at pre-intervention (Baseline) and eight weeks post-intervention (Endline) using quantitative tools. The feasibility outcomes will be assessed eight weeks post-intervention using quantitative and qualitative measures. Moreover, participants' sociodemographic information will be obtained via a checklist.

Table 2 presents the study outcomes, data collection tools, and data ascertainment time points.

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Table 2

Study Outcomes, Tools, and Data Ascertainment Time Points

Outcome	Instrument | Description	Data Collection Time-Point
Clinical Efficacy Outcomes		
Primary Outcome - HRQOL	**Pediatric Quality of Life Inventory Generic Core Scale (PedsQL 4.0)** [34]. • It comprises 23 items and has four dimensions (physical, emotional, social, and school functioning) • Have a 5-point Likert response scale (0 = never to 4 = almost always a problem). • A higher score = better HRQOL. • Adequate construct and predictive validity and reliability values of >0.8 have been reported in multiple studies. • The scales specific for 8-12- and 13-18-year-old children will be used in this study.	Pre-intervention, And Eight weeks post-intervention
	Pediatric Quality of Life Inventory Cancer Module (PedsQL 3.0). [34] • It comprises 27 items and has eight domains about cancer symptoms. • Have a 5-point Likert scale (0 = never to 4 = almost always a problem). • A higher score = better HRQOL. • Sufficient construct validity and reliability values of >0.8 in all domains have been reported in multiple studies. • The scales specific for 8-12- and 13-18-year-old children will be used in this study.	Pre-intervention, and Eight weeks post-intervention
Secondary Outcome - Cancer Symptoms Frequency and Distress	**Memorial Symptom Assessment Scale Short Form (MSAS-SF).** [35]. • It comprises 30 items and has a 5-point Likert Scale (0 = not at all to 4 = very much). • A higher score = more distress and higher frequency. • Sufficient convergent and criterion validity measures and internal consistency reliability values ranging from 0.76 to 0.87 have been reported in earlier studies.	Pre-intervention, and Eight weeks post-intervention
Feasibility Outcomes		
Acceptability and Appropriateness	Acceptability E-scale [36] will be used to determine the acceptability and appropriateness of the intervention in the study population.	Eight weeks post-intervention

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	In-depth interviews will be conducted with 7-8 child-parent dyads of the intervention group to obtain insights into their experiences regarding the intervention (appropriateness, satisfaction, learning, challenges, and recommendations).	
	One focus group discussion (FGD) will be conducted with 5-6 oncologists and nurses to identify the challenges in implementing the intervention in the clinical setting.	
Cost	The cost of the intervention development will be reported in Pakistani rupees.	
Feasibility	The number and proportions will be reported for: • Participant recruitment. • Participant refusals. • Lost to follow-up participants, with reasons.	
Fidelity	Data on children's progress in the videogame will be retrieved from the dashboard. The following data will be reported: • Total game score • Number and reason for contacting the RA by children in both groups	

Data management

The data will be entered in the Statistical Package for Social Sciences (SPSS), double-entered, secured, and managed by the research team.

Data analysis plan

The intention to treat (ITT) principle of analysis will be used. Depending on the data distribution, continuous variables will be reported as means and standard deviations or medians and interquartile ranges as appropriate. The categorical variables will be reported as frequencies and proportions. The intervention efficacy will be reported using Cohen's d. The associations between independent and dependent variables will be conducted through regression analysis. The group differences will be calculated through independent samples t-

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test/Mann-Whitney U test as appropriate. No interim analysis is planned. The details are summarised in Table 3.

Table 3

Plan of Data Analysis

The Intention to treat (ITT) principle of analysis will be used in this study.	
Clinical Efficacy Outcomes	
Types of Analysis	**TESTS**
Descriptive Analysis	
Continuous variables (example: age, time since diagnosis)	Means with standard deviations (SD) [symmetrical distribution] or median with interquartile ranges (IQR) [asymmetrical distribution] as appropriate
Categorical data (example: gender, type of cancer, education status)	Frequencies with proportions
Associations	
Associations between independent variables and the dependent variable of HRQOL	Regression analysis based on data distribution. We will retain variables in the final model based on statistical and clinical significance.
Group Differences	
Between-group differences for HRQOL and cancer symptoms frequency and distress	Independent Samples t-test/Mann Whitney U test as appropriate
Within-group differences	Paired t-test/Wilcoxon signed-rank test as appropriate
Estimate of intervention efficacy	Intervention Effect Size using Cohen's d
Feasibility Outcomes	
Acceptability and Appropriateness	• Mean (SD) or median (IQR) of quantitative variables. • Thematic analysis of qualitative findings.
Cost	Cost of the videogame development
Feasibility and Fidelity	• Frequencies with proportions for categorical variables. • Thematic analysis of qualitative findings.

Study rigor

The CONSORT extension guidelines [37] will be used to report the process and findings of the study.

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Patient and public involvement

The parents, children with cancer, doctors, and nurses were involved in developing the interview guide for the study Phase I. The PedsQL 3.0 was translated into Urdu, and parents and children were involved in assessing the items' readability and comprehension. The videogame was developed with input from parents, children, doctors, nurses, and digital health experts.

Ethics and dissemination

The study has received ethical approval from the Ethics Review Committee of the study setting (2022-6833-21251). The study PI (first author) will train the research staff on the study and ethics. Written informed assent and parental consent are being obtained from children and their parents for participation in the interviews, UAT, pilot-RCT, and post-intervention interviews. Written informed consent will also be obtained from the healthcare providers before the FGD. Participants are being explained about their withdrawal from the study without any ramifications. Principles of confidentiality, privacy, and anonymity will be maintained by providing unique identification numbers and pseudonyms to the participants for the questionnaires, FGDs, and interviews, respectively. Any adverse events or changes to the protocol will be communicated to the ERC. The study data will be encrypted and remain in the custody of the research team members only. Moreover, only aggregated study findings will be disseminated through publications.

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Authors' Contributions: SeS (first author) was responsible for the conception and design of the study. She led the finalization of the study protocol, ensuring its methodological rigour and alignment with research objectives. SeS also obtained approvals from ERC, clinicaltrials.gov, and the study setting, and wrote the manuscript. RB and RG supervised and mentored SeS throughout the study, refining the study protocol and providing critical input on the manuscript. SS mentored SeS, providing oversight for the development and deployment of the videogame. ZF and ANA contributed to finalizing the study protocol and content of the videogame, and they will direct the operational implementation of the intervention in the clinical setting. All authors have reviewed the manuscript.

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Competing Interests Statement:

The authors declare that they have no competing interests.

Data availability statement

This is the study protocol and there is no data available yet for the Pilot-RCT.

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Study Figures

Figure 1

Symptom Management Theory [28]

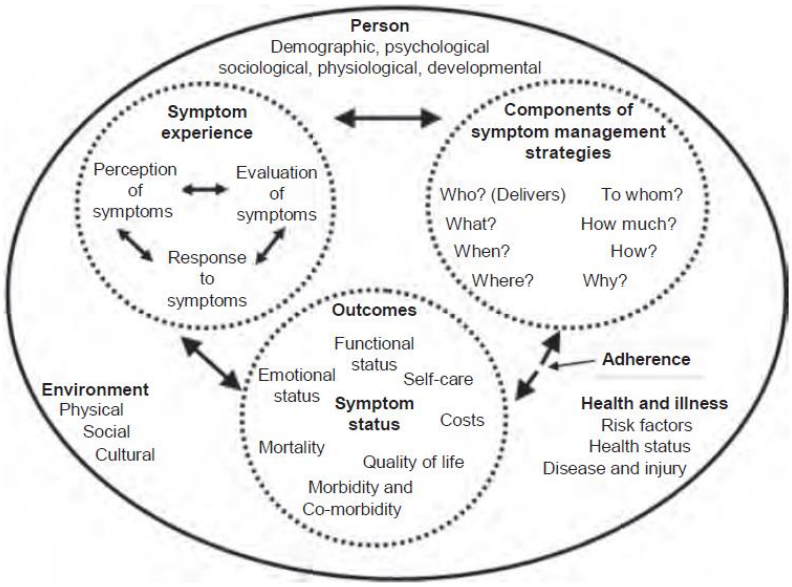

FIGURE 8.1 Symptom Management Theory.

Source: Adapted from Dodd, M., Janson, S., Facione, N., Faucett, J., Froelicher, E. S., Humphreys, J., . . . Taylor, D. (2001). Advancing the science of symptom management. *Journal of Advanced Nursing*, *33*, 668–676.

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Figure 2

Study Design [29]

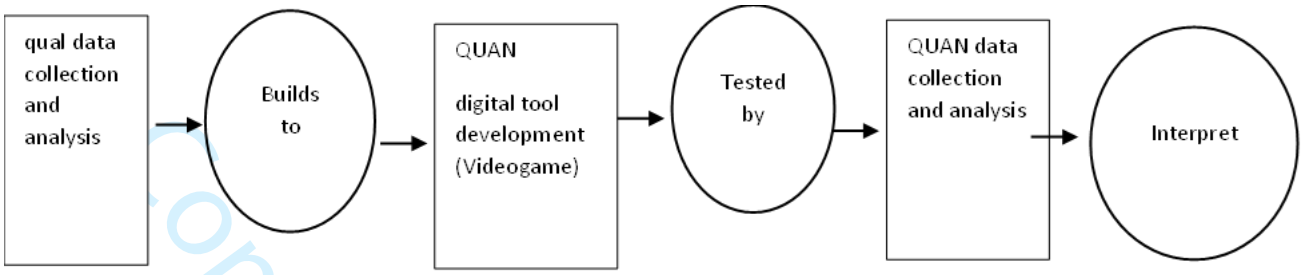

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Figure 3

The Videogame Interface

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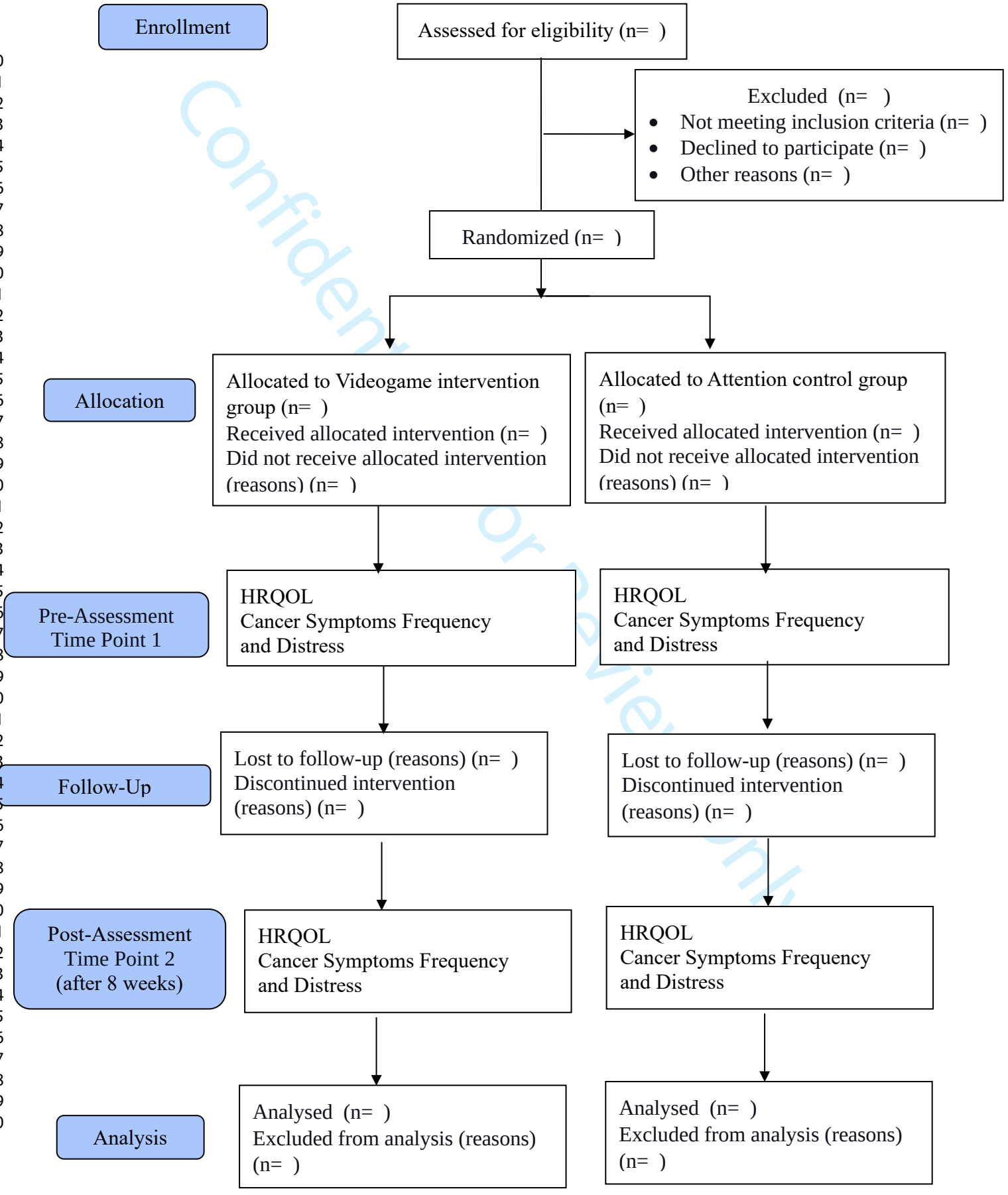
Figure 4

CONSORT Flow Diagram



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TITLE

Development and Testing of a Videogame Intervention for Symptom Management among 8-18-Year- Old Children with Cancer: A Study Protocol

ABSTRACT

Introduction

Evidence shows that cancer treatment-related symptoms could be managed effectively in 8–18-year-old children through Digital Health Interventions (DHIs), consequently improving their Health-related Quality of Life (HRQOL). However, limited research is available about digitally mediated educative health interventions for children with cancer from Low and Middle-Income Countries like Pakistan. This study aims to develop a videogame intervention for children with cancer and test the clinical efficacy of the videogame concerning HRQOL and cancer treatment-related symptoms. Moreover, the following feasibility outcomes will be recorded: acceptability, appropriateness, cost, feasibility, and intervention fidelity.

Methods and analysis

An exploratory sequential mixed methods design is used in this study. In the first phase of the study, we interviewed 28 participants (14 child-parent dyads) and assessed their symptom experiences affecting children's HRQOL. Moreover, their preferences for the development of the videogame were also elicited. Based on the findings from relevant literature and the interviews, we developed the videogame in collaboration with clinical and digital experts in the study's second phase. In the third phase of the study, a Pilot Randomized Controlled Trial (Pilot-RCT) will be conducted at a Tertiary Care Hospital in Karachi, Pakistan. There will be two groups: the intervention group and the control group. The intervention group children will receive the videogame application for eight weeks, during which symptom management strategies will be taught to them. Children in the attention control group will receive weekly WhatsApp messages on healthy behaviours.

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The primary outcome will be the HRQOL of children, and the secondary outcome will be cancer symptoms frequency and distress. These outcomes will be assessed pre- and eight weeks post-intervention. The feasibility outcomes will be assessed quantitatively and qualitatively through a questionnaire, videogame dashboard, interviews with a subset of intervention group child-parent dyads, and a focus group discussion with nurses and doctors, post-intervention respectively.

Ethics and dissemination

The study has been approved by the Ethics Review Committee of the Aga Khan University (2022-6833-21251). Data is accessible only to the research team in a secure form. The findings will be disseminated through publications.

Trial registration

ClinicalTrials.gov Identifier NCT05796895, registered in April 2023.

WHAT IS ALREADY KNOWN ON THIS TOPIC?

- Evidence from High-Income Countries (HICs) shows that optimum symptom management in children with cancer through Digital Interventions significantly improves their HRQOL.
- Among several interventions, videogame-based interventions have demonstrated efficacy in the HICs.

WHAT THIS STUDY HOPES TO ADD?

- The study will add to the scientific knowledge on the clinical efficacy and feasibility of the videogame intervention on children with cancer from an LMIC Pakistan.
- A mixed methods approach will help understand the research problem and the best possible practical solutions.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY?

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- If the intervention efficacy is established, it will improve the healthcare practice through a digitally mediated intervention.
- It will enhance nurses' role in educating and promoting innovative strategies for symptom management among children with cancer.

Introduction

Approximately 400,000 children aged up to 19 years are estimated to be diagnosed with cancer annually worldwide [1]. With the global rise in the incidence of childhood cancer worldwide, Low and Middle-Income Countries (LMICs), including Pakistan, suffer a disproportionate burden [2,3]. The National Cancer Registry reveals that approximately 17,457 children are diagnosed with cancer in Pakistan yearly [4]. Global evidence suggests that 8 out of 10 children may get completely cured of childhood cancer upon receiving evidence-based, accessible treatment and support services [5]. Although cancer treatment is complex and lengthy, children respond better to treatment than adults and reach survivorship [5]. Early identification and treatment of childhood cancer through multimodality therapies is critical for better survival. Chemotherapy and radiation are the most common treatment modalities for childhood cancers [5]. However, these therapies result in severe cancer treatment-related symptoms, compromising children's daily functioning and HRQOL [6-7]. Several studies suggest that children with cancer below 18 years of age report similar treatment-related symptoms affecting physiological and psychosocial domains of their HRQOL [8-9]. Common physiological problems include pain, fatigue, GI-related symptoms, hair loss, and infection [9-11]. Commonly reported psychosocial symptoms include anxiety, depression, and isolation from friends [9-11]. Children's school attendance and academic progress are also affected during their treatment, which has future implications for them [12]. Suboptimal symptom management negatively affects children's physiological and psychological health, cognitive functions, academic performance, social relationships, and

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overall HRQOL and well-being [12-13]. Additionally, poor symptom management can have implications for delayed or abandoned treatment, poor treatment tolerance, unnecessary frequent emergency visits, and poor psychological outcomes [13-15]. Therefore, education and support about symptom management are critical to optimizing children's HRQOL and preventing symptom worsening [7,16].

During the prolonged trajectory of childhood cancer, the responsibility of treatment-related symptom management keeps switching from healthcare providers in the hospital to the children and their parents at home. Effective symptom management at home leads to better symptom outcomes, treatment adherence, less morbidity, fewer rehospitalizations, and improved HRQOL among children [17-18]. Studies have shown that children who actively participate in learning about self-management of their symptoms understand their disease well, have better preparedness to manage their symptoms, and contribute to more informed health decisions [19-20]. Developmental psychology theories highlight that children learn best when engaged in activity and play [21-23]. Digital technologies such as interactive mobile apps, virtual reality (VR), and videogames allow children to engage in their learning. For these reasons, healthcare providers have started using digital devices in children with asthma, diabetes, cancer and other chronic health conditions to educate them about symptom monitoring and management [17,24].

Studies from High-Income Countries have shown that implementing Digital Health Interventions (DHIs) has significantly improved the HRQOL [18,25,26], knowledge [20], self-efficacy [20] and has decreased pain and fatigue [18], anxiety, and depression [27] in children with cancer. Among various DHIs, videogames have emerged as one of the promising modes of education to help children learn symptom management. The evidence regarding the efficacy of DHIs, especially from LMICs, is still limited, and more studies are recommended to determine the efficacy of these interventions on the health outcomes of

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children with cancer. To our knowledge, no similar study has been conducted in Pakistan. The aim of this study, therefore, is to develop a videogame intervention for children (age 8-18 years) with cancer and test its clinical efficacy concerning HRQOL and cancer treatment-related symptoms in children, and also to observe the feasibility of the intervention in terms of acceptability, appropriateness, cost, and intervention fidelity.

Symptom management theory (SMT)

As shown in Figure 1, the Symptom Management Theory (SMT) comprises three interrelated concepts: (a) symptom experience, (b) symptom management strategies, and (c) symptom status outcomes. Symptom experience explains the perception of change in a patient's usual health status. Symptom management strategies are approaches used to prevent, delay, or lessen the symptom experience. Symptom outcomes are measurable outcomes, such as improvement in the HRQOL or recovery from illness, assessed pre-and post-implementation of a symptom strategy [28].

In accordance with the SMT, in the first phase of the study, we identified the experience of symptoms from child-parent dyads and symptom management strategies from them and the relevant literature. The findings informed the development of the videogame in the second phase of the study. In the third phase of the study, we plan to teach symptom management to children through a videogame intervention and assess their HRQOL and symptom frequency and distress.

Methods and analysis

Design

As shown in Figure 2 [29], this study employs a mixed methods design (qual → QUAN) having three phases:

1. Phase I – Need Assessment.
2. Phase II – Videogame Intervention Development.

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3. Phase III – Videogame Intervention Testing.

Study phase I – need assessment

In Phase I of the study, a qualitative descriptive exploratory design was used to understand the experiences and perceptions of children with cancer and their parents regarding children's HRQOL, treatment-related symptoms, management strategies, and preferences informing the development of the videogame. In-depth interviews were conducted with 28 participants (14 child-parent dyads). Participants elicited strategies for the management of the following symptoms and healthy behaviours to be translated into the videogame: pain, fever, mucositis, nausea, vomiting, hair loss, missing school, throat irritation, constipation, staying physically active, balancing balance between rest and activity, knowing alarming signs, preventing infection, eating healthy, fighting sickness, and maintaining psychological and spiritual health.

Study phase II – videogame intervention development

During Phase II of the study, a multi-disciplinary team comprised of children with cancer, parents, clinical experts (oncology nurses and physicians), and digital design specialists (videogame developers and information technologists) collaborated in an iterative design process for the videogame. A series of brainstorming sessions employed an iterative methodology to refine the game's content, visual design, and narrative flow (storyboard). Upon development completion, user acceptance testing (UAT) was conducted with the child participants, parents, and research team members. This UAT phase served to identify and rectify any software bugs or usability issues within the videogame.

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Features of the videogame

As shown in Figure 3, in the game, a player (study participant) enters the game and selects language (English or Urdu), gender (boy or girl), and environment (city or town). After selecting the avatar, the game interface opens, and a Mascot (a gender-neutral cartoon character - bunny) welcomes the child. The Mascot provides the player with necessary instructions about the gameplay.

There are fourteen levels in the videogame. The child plays each level, which targets one symptom for which the child is taught symptom management or health behaviour. Moreover, feedback messages also pop up on the videogame screen to highlight the significance of the action performed. With that, the player progresses to the next level. Each day, the player can unlock two to three game levels. The game content is the same for all children; however, few variations are kept for younger (8-12 years old) and older children (13-18 years old). For example, some game levels provide more lifelines and hints to younger children. The videogame is auto-locked at 30 minutes for younger children to avoid exceeding the screen time limit. Younger children can play two game levels daily, whereas older children can play three. While older children can navigate the game icons, a tutorial about the gameplay is provided to younger children. Table 1 presents the game levels, symptoms and concerns, and details about game levels.

Table 1

The Videogame Levels, Symptoms and Concerns, and Details about the Game

Levels	Symptom or Health Concern	Symptom Management Strategies/ Behaviours (Game Activity)	Game Mechanism	Feedback/ Important Message for Children
Level one	Mucositis	Perform oral care by toothbrushing and protect oral cavity.	The player clicks on all the steps of toothbrushing and tongue cleaning on the game avatar to score coins.	1. Brush your teeth with a soft brush twice a day. 2. Avoid brushing teeth when platelet counts are low.

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Level two	Risk for Infection	Identify alarming signs of worsening symptoms and inform the doctor or nurse.	The player bursts all the balloons one by one. On popping each balloon, a text message shows one alarming sign of infection.	Know these alarming signs. If you have them, tell your doctor and nurse immediately and visit the hospital.
Level three	Risk for Infection And Constipation	Perform hygiene care regularly.	The player clicks on several steps of maintaining good hygiene (bathing, brushing teeth, shampooing, hand washing, passing stool daily, cutting nails, using sunscreen, and wearing a scarf or hat).	1. Keep yourself clean to maintain a healthy body. 2. If you are constipated, talk to your doctor and nurse.
Level four	Pain	To relieve pain, take analgesics on time and perform deep breathing exercises at least 3-4 times a day.	The player takes the prescribed analgesics and performs deep breathing exercises.	Take the medicine as prescribed by your doctor and do deep breathing exercises.
Level five	Fever	Take antipyretics as prescribed by the doctor to get relief from fever.	The player clicks on the steps of taking temperature, identifying fever, taking medicine as prescribed, rechecking temperature after an hour, informing the doctor if fever persists, and going to the hospital if needed.	Talk to your doctor if your fever persists and go to the hospital.
Level six	GI-related symptoms	Differentiate between healthy and unhealthy food options which are appropriate during sickness to stay healthy.	The player identifies healthy food options and collect them in a basket to score points.	Eat healthy food and avoid unhealthy food.
Level seven	Hair Loss	Accept that hair fall will occur and protect the scalp by covering it.	The player wears different head gears (hats, scarves, hair extensions). The player learns about hair fall and return of hair after completion of treatment.	1. Protect your scalp. 2. Hairfall is temporary, and hair will return after treatment is completed.

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Level eight	Fighting sickness	Identify measures that can be taken when feel sick and practice them.	The player bursts all the balloons one by one. On popping each balloon, a text message shows one measure to take when the child falls sick. The player must read and learn the measures.	Practice the measures taught to you when you feel sick.
Level nine	Mucositis	Gargles should be performed as prescribed by the doctor to prevent oral mucositis.	The player clicks on all the steps to gargle with the prescribed mouthwash. The player must read the message about adhering to this behaviour in a timely manner to prevent oral mucositis.	Gargle with the prescribed solution as advised by your doctor to prevent mucositis.
Level ten	Missing School	Perform a visual puzzle activity to find differences between two images. Keep your mind engaged, learn observation, attention to detail, and critical thinking skills, and do not miss school. Also, paint a few images for fun.	The Mascot advises the player to do activities at his school and some puzzles to remember fun at school. The player finds differences between the two images and paints several pictures.	When you miss your school and school activities, do some learning and fun activities at home.
Level eleven	Nausea, vomiting, and anorexia	Take antiemetics as prescribed and take small frequent meals to deal with nausea, vomiting, and anorexia.	The mascot advises the player to take antiemetics as prescribed and eat small, frequent meals. Several healthy eating options appear on the table one by one. The player chooses between them through a 'yes' or 'no'.	Take the medicine as prescribed and eat a small, frequent meal every 2-4 hours in a day, choosing healthy food options.
Level twelve	Throat Irritation	Identify and eat soothing food items to decrease oral ulcers and throat irritation.	The avatar has oral ulcers and an irritating throat. Several soothing and soft food options appear before the player. S/he can choose from them and eat to soothe their mouth. The player selects a 'yes' for the food option s/he likes.	You have several soothing and soft food options to soothe your irritating throat. Select whichever food item you like and eat it.

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Level thirteen	Psychological symptoms	Try various activities such as yoga, spending time in the garden, engaging in activities you enjoy, communicating with your friends, and practicing meditation and prayer to gain inner strength.	The mascot asks the player to do some yoga exercises, observe things around, talk to friends, and meditate and pray. The player performs these steps one by one and scores coins.	Do yoga and deep breathing to keep your mind relaxed. If you miss friends, call them. Meditate and pray.
Level fourteen	Fatigue	Maintain a balance between exercise/play and rest not to get fatigued.	The player clicks on several icons to help the avatar do exercises like walking, running, jumping, and hopping to score points. The avatar returns home and sleeps when tired.	Maintain a balance between exercise/play and rest not to get fatigued.

*The scoring and reward mechanism comprises coins, claps, celebration animation, and messages of applaud upon activity completion.

Study phase III – intervention testing (Pilot-RCT)

There are two objectives of this phase.

1. To determine the efficacy of the videogame intervention on the HRQOL and cancer symptoms frequency and distress of children with cancer in the intervention group as compared to the children in the attention control group at pre and eight weeks post-intervention.
2. To determine the intervention feasibility outcomes: acceptability, appropriateness, cost, feasibility, and fidelity.

Design

A Pilot Randomized Controlled Trial (Pilot-RCT) with an attention control will be used to attain the set objectives.

Study setting

The study is conducted at the Aga Khan University Hospital's (AKUH) in- and outpatient chemotherapy and radiation therapy units. The AKUH is a not-for-profit, resource-intensive,

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tertiary care, and Joint Commission International (JCI) accredited university hospital recognized for providing high-quality, compassionate care for several speciality services. The oncology department offers specialized cancer services [30]. There is one inpatient clinical area for chemotherapy and two outpatient areas for radiation and chemotherapy for children. In the inpatient area, there are separate beds assigned for children for chemotherapy [30].

Study population

Children having cancer and receiving chemotherapy or radiation are the study population.

Inclusion criteria

- Children aged 8-18 years.
- Diagnosed with any type and stage of cancer within six months.
- Can comprehend Urdu or English language.
- Have access to an Android smartphone/tablet for at least 30 minutes/day.

Exclusion criteria

- Critically ill children.
- Receiving palliative treatment.
- Have any diagnosed sight, hearing, cognitive impairment, or upper limb deformity.
- If already playing any videogame with similar content.

The eligibility criterion was selected based on existing literature indicating poor health-related quality of life (HRQOL) in children across all age groups and cancer types and stages (9, 31-32). Additionally, as this is an educational video game, it will be provided to all children over 8 years old experiencing cancer symptoms to educate them about symptom management. Narrowing the inclusion criteria could limit the generalizability of the study's findings. Randomization will address the distribution of demographic and clinical variables in both groups.

Sample size and sampling technique

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The sample size was calculated for the primary outcome of HRQOL. Keeping the study power at 80%, significance level at 5%, maximum standard deviation of 18.6 [18], and true difference value of 13.5 points [17], a sample of 31 patients per group is desired for this study. Adjusting for 10% attrition, the final sample size is 35 patients per study group. For a pilot trial, a sample size of 35 participants per study group is considered adequate [33]. Children will be selected using a non-probability purposive sampling technique.

Participant recruitment

A Research Associate (RA) will screen potential study participants using the patients' list available at the inpatient and outpatient oncology units and through communication with the staff nurses. The RA will assess the child for eligibility and explain the study to them and will approach the child in the presence of the parent. The RA will explain the study and random allocation to any study group. The child's written assent and parent's consent will be obtained if they agree to participate.

Randomization, blinding, and allocation concealment

Children will be randomized in a 1:1 ratio to the intervention or attention control group. Using a computer-generated randomization scheme, a random block of 4 and 6 will be used. A person, not a research team member, will generate the randomization list and prepare sealed and opaque envelopes, ensuring allocation concealment. The RA will open the envelope in front of the child/parent. Further steps would follow according to the child's assignment. The study will be non-blinded as group assignments cannot be hidden from the participants and research team members in a behavioural intervention [34].

Intervention group

Children in the intervention group will receive the videogame for eight weeks. The RA will provide instructions about the videogame. S/he will call the child and parent every week to ensure participant adherence in the study and to inquire if they have any questions related to

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the videogame content or worsening of symptoms and will answer in consultation with the clinical expert (oncologist in the research team). A call log of the conversation will be maintained.

Attention control group

The attention control group will be selected to ensure that the study outcomes are not attributable to the unequal attention given to the intervention group [35]. Children will receive weekly WhatsApp messages on healthy behaviours based on the National Cancer Institute's guidelines for childhood cancer. The RA will call the child and parent weekly to inquire about the child's health, and a call log of the conversation will be maintained.

Figure 4 presents the CONSORT flow diagram.

Study outcomes

Primary outcome – HRQOL

The HRQOL of children with cancer will be assessed using the Pediatric Quality of Life Inventory Generic Core Scale (PedsQL 4.0) and Cancer Module (PedsQL 3.0).

The PedsQL 4.0, already available in Urdu, is provided by the MAPI Research Trust. We conducted the Urdu translation of PedsQL 3.0 following MAPI Research Trust guidelines, and it has been approved for use in this study. The Content Validity Index (CVI) for PedsQL 3.0 is 0.70 for reliability and 0.74 for clarity. The approved Urdu versions of both tools will be used in the study. The tools will be pre-tested on 10% of the sample (n=7 children). Their data will be excluded from the analysis. The post-hoc reliability measures of the tools in our sample will be reported.

Secondary outcome - Cancer symptoms frequency and distress

The cancer symptoms frequency and distress will be assessed using the Memorial Symptom Assessment Scale Short Form (MSAS-SF).

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Feasibility outcomes

The following feasibility outcomes will be assessed: intervention acceptability, appropriateness, cost, feasibility, and fidelity.

Data collection

The primary and secondary outcomes will be assessed at pre-intervention (Baseline) and eight weeks post-intervention (Endline) using quantitative tools. The feasibility outcomes will be assessed eight weeks post-intervention using quantitative and qualitative measures. Moreover, participants' sociodemographic information will be obtained via a checklist. Table 2 presents the study outcomes, data collection tools, and data ascertainment time points.

Table 2

Study Outcomes, Tools, and Data Ascertainment Time Points

Outcome	Instrument | Description	Data Collection Time-Point
Clinical Efficacy Outcomes		
Primary Outcome - HRQOL	**Pediatric Quality of Life Inventory Generic Core Scale (PedsQL 4.0)** [36]. • It comprises 23 items and has four dimensions (physical, emotional, social, and school functioning) • Have a 5-point Likert response scale (0 = never to 4 = almost always a problem). • A higher score = better HRQOL. • Adequate construct and predictive validity and reliability values of >0.8 have been reported in multiple studies. • The scales specific for 8-12- and 13-18-year-old children will be used in this study.	Pre-intervention, And Eight weeks post-intervention
	Pediatric Quality of Life Inventory Cancer Module (PedsQL 3.0). [36] • It comprises 27 items and has eight domains about cancer symptoms. • Have a 5-point Likert scale (0 = never to 4 = almost always a problem).	Pre-intervention, and Eight weeks post-intervention

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	• A higher score = better HRQOL. • Sufficient construct validity and reliability values of >0.8 in all domains have been reported in multiple studies. • The scales specific for 8-12- and 13-18-year-old children will be used in this study.	
Secondary Outcome - Cancer Symptoms Frequency and Distress	**Memorial Symptom Assessment Scale Short Form (MSAS-SF).** [37]. • It comprises 30 items and has a 5-point Likert Scale (0 = not at all to 4 = very much). • A higher score = more distress and higher frequency. • Sufficient convergent and criterion validity measures and internal consistency reliability values ranging from 0.76 to 0.87 have been reported in earlier studies.	Pre-intervention, and Eight weeks post-intervention
Feasibility Outcomes		
Acceptability and Appropriateness	Acceptability E-scale [38] will be used to determine the acceptability and appropriateness of the intervention in the study population.	Eight weeks post-intervention
	In-depth interviews will be conducted with 7-8 child-parent dyads of the intervention group to obtain insights into their experiences regarding the intervention (appropriateness, satisfaction, learning, challenges, and recommendations).	
	One focus group discussion (FGD) will be conducted with 5-6 oncologists and nurses to identify the challenges in implementing the intervention in the clinical setting.	
Cost	The cost of the intervention development will be reported in Pakistani rupees.	
Feasibility	The number and proportions will be reported for: • Participant recruitment. • Participant refusals. • Lost to follow-up participants, with reasons.	
Fidelity	Data on children's progress in the videogame will be retrieved from the dashboard. The following data will be reported: • Total game score • Number and reason for contacting the RA by children in both groups	

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Data management

The data will be entered in the Statistical Package for Social Sciences (SPSS), double-entered, secured, and managed by the research team.

Data analysis plan

The intention to treat (ITT) principle of analysis will be used to preserve the benefits of randomization. Analysis conducted through ITT will also reflect effectiveness of the intervention in praxis. Depending on the data distribution, continuous variables will be reported as means and standard deviations or medians and interquartile ranges as appropriate. The categorical variables will be reported as frequencies and proportions. The intervention efficacy will be reported using Cohen's d. The associations between independent and dependent variables will be conducted through regression analysis. The group differences will be calculated through independent samples t-test/Mann-Whitney U test as appropriate. A subgroup analysis will be performed to compare sociodemographic and clinical variables and their impact on children's HRQOL. No interim analysis is planned. The details are summarised in Table 3.

Table 3

Plan of Data Analysis

The Intention to treat (ITT) principle of analysis will be used in this study.	
Clinical Efficacy Outcomes	
Types of Analysis	**TESTS**
Descriptive Analysis	
Continuous variables (example: age, time since diagnosis)	Means with standard deviations (SD) [symmetrical distribution] or median with interquartile ranges (IQR) [asymmetrical distribution] as appropriate
Categorical data (example: gender, type of cancer, education status)	Frequencies with proportions
Associations	

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Associations between independent variables and the dependent variable of HRQOL	Regression analysis based on data distribution. We will retain variables in the final model based on statistical and clinical significance.
Group Differences	
Between-group differences for HRQOL and cancer symptoms frequency and distress	Independent Samples t-test/Mann Whitney U test as appropriate
Within-group differences	Paired t-test/Wilcoxon signed-rank test as appropriate
Estimate of intervention efficacy	Intervention Effect Size using Cohen's d
Feasibility Outcomes	
Acceptability and Appropriateness	• Mean (SD) or median (IQR) of quantitative variables. • Thematic analysis of qualitative findings.
Cost	Cost of the videogame development
Feasibility and Fidelity	• Frequencies with proportions for categorical variables. • Thematic analysis of qualitative findings.

Study rigor

The CONSORT extension guidelines [39] will be used to report the process and findings of the study.

Patient and public involvement

The parents, children with cancer, doctors, and nurses were involved in developing the interview guide for the study Phase I. The PedsQL 3.0 was translated into Urdu, and parents and children were involved in assessing the items' readability and comprehension. The videogame was developed with input from parents, children, doctors, nurses, and digital health experts.

Ethics and dissemination

The study has received ethical approval from the Ethics Review Committee of the study setting (2022-6833-21251). The study PI (first author) will train the research staff on the study and ethics. Our research team has two pediatric clinical oncologists who will help

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identify children at risk in critical stages and manage them as necessary. Written informed assent and parental consent are being obtained from children and their parents for participation in the interviews, UAT, pilot-RCT, and post-intervention interviews. Written informed consent will also be obtained from the healthcare providers before the FGD. Participants are being explained about their withdrawal from the study without any ramifications. Principles of confidentiality, privacy, and anonymity will be maintained by providing unique identification numbers and pseudonyms to the participants for the questionnaires, FGDs, and interviews, respectively. Any adverse events or changes to the protocol will be communicated to the ERC. The study data will be encrypted and remain in the custody of the research team members only. Moreover, only aggregated study findings will be disseminated through publications.

Figure 1: (Symptom Management Theory [28])

Figure 2: (Study Design [29])

Figure 3: (The Videogame Interface)

Figure 4: (CONSORT Flow Diagram)

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Authors' Contributions: SeS (first author) was responsible for the conception and design of the study. She led the finalization of the study protocol, ensuring its methodological rigour and alignment with research objectives. SeS also obtained approvals from ERC, clinicaltrials.gov, and the study setting, and wrote the manuscript. RB and RG supervised and mentored SeS throughout the study, refining the study protocol and providing critical input on the manuscript. SS mentored SeS, providing oversight for the development and deployment of the videogame. ZF and ANA contributed to finalizing the study protocol and content of the videogame, and they will direct the operational implementation of the intervention in the clinical setting. All authors have reviewed the manuscript. SeS is responsible for the overall content [as guarantor].

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5. Extramural support (NA).

Competing Interests Statement:

The authors declare that they have no competing interests.

Data availability statement

This is the study protocol and there is no data available yet for the Pilot-RCT.

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Figure 1

Symptom Management Theory [28]

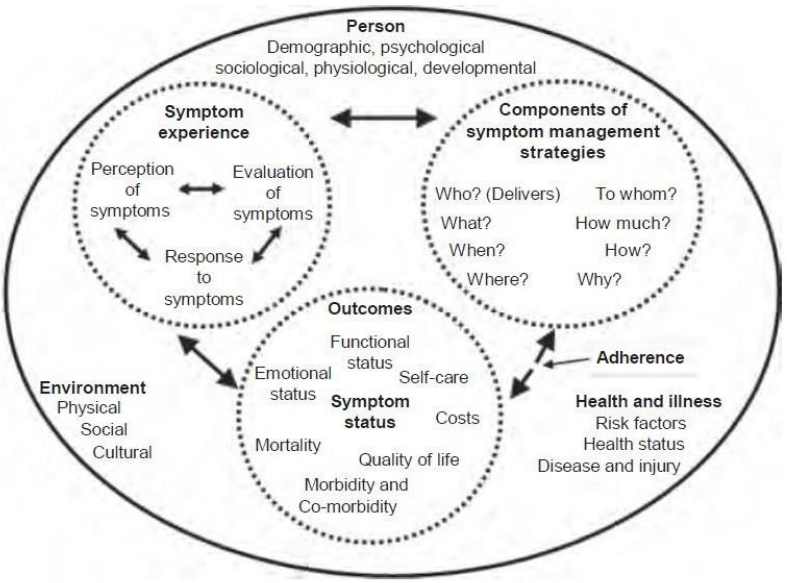

FIGURE 8.1 Symptom Management Theory.

Source: Adapted from Dodd, M., Janson, S., Facione, N., Faucett, J., Froelicher, E. S., Humphreys, J., . . . Taylor, D. (2001). Advancing the science of symptom management. *Journal of Advanced Nursing*, *33*, 668–676.

Symptom Management Theory [28]

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Figure 2

Study Design [29]

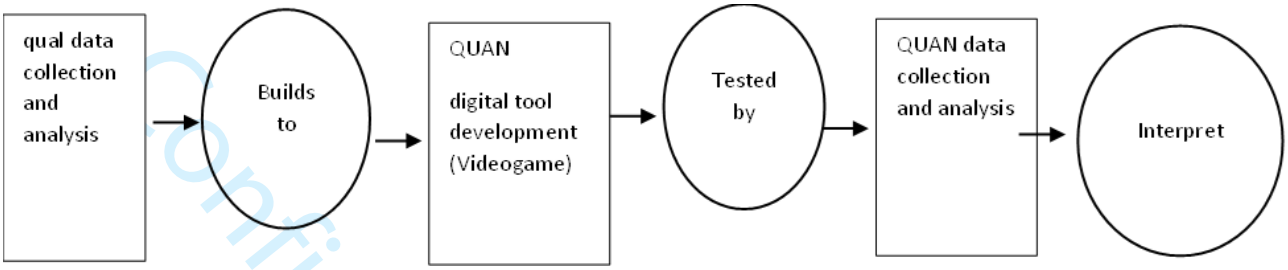

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Figure 3

The Videogame Interface

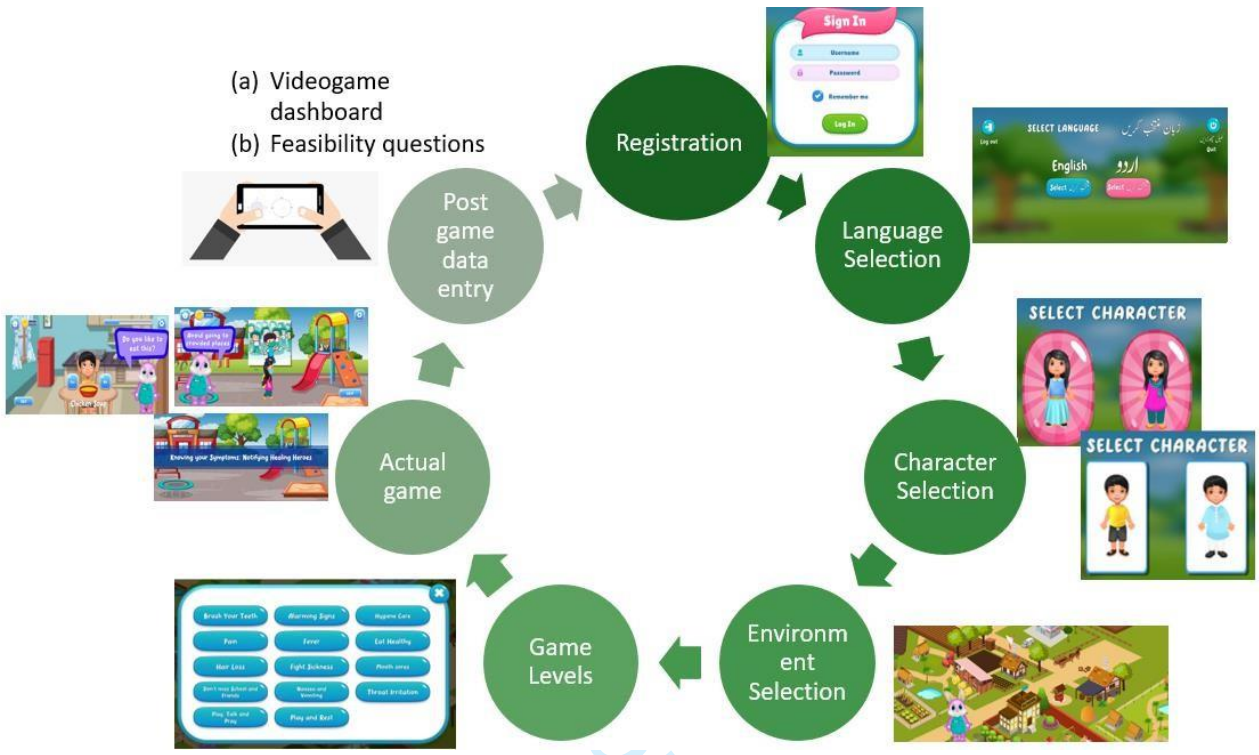

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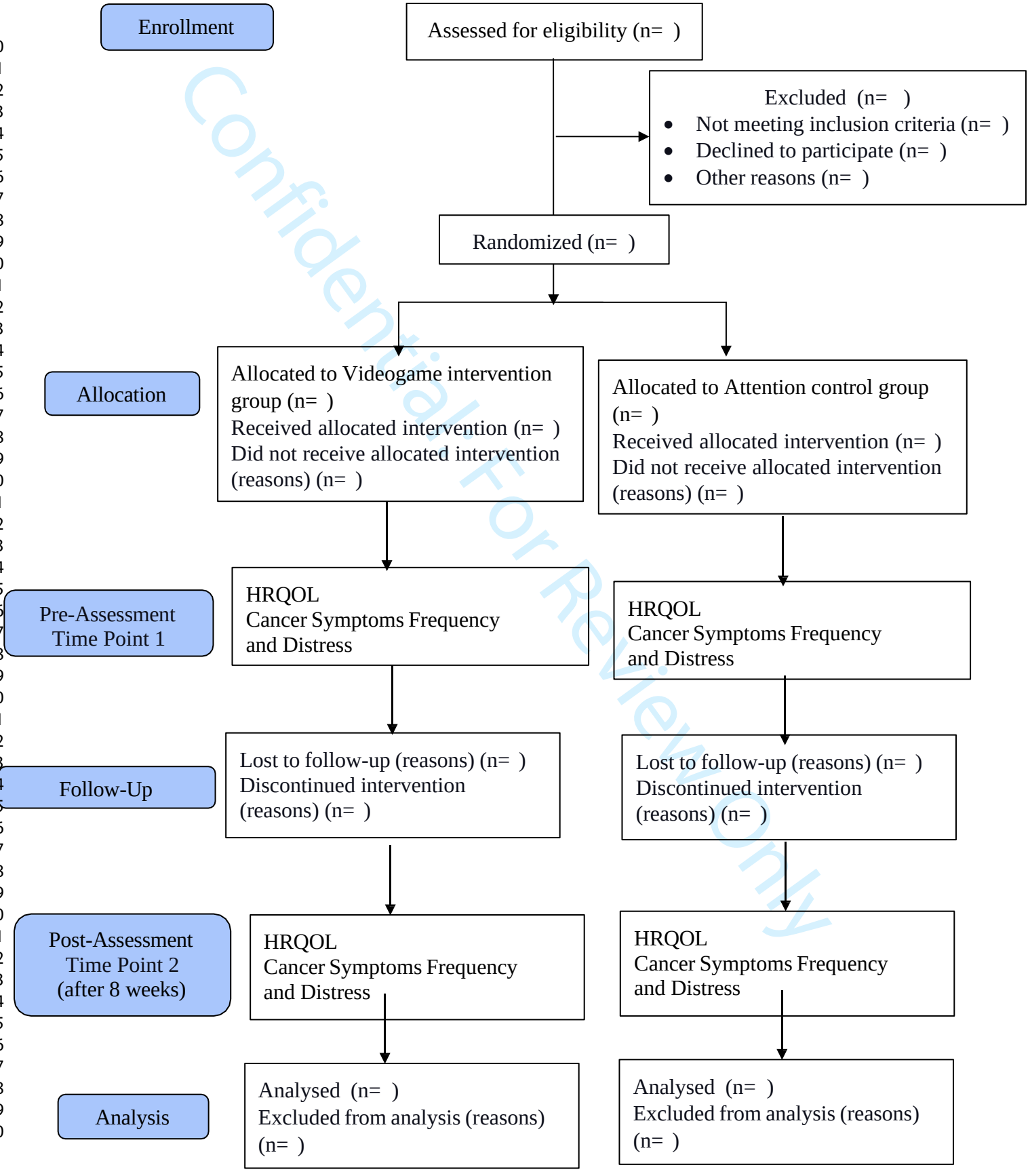
Figure 4



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