

**Developing a Stepped-Care Intervention for Emotional and Behavioral Health  
in Children with Leukemia: A Study Protocol**

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ClinicalTrials.gov.)

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June 2025

**Completion Date:**

December, 2026

## **Developing a Stepped-Care Intervention for Emotional and Behavioral Health in Children with Leukemia: A Study Protocol**

### **ABSTRACT**

**Aim:** To develop and culturally adapt a stepped-care intervention for emotional and behavioral health in children with leukemia in a low-income country.

**Design:** This study follows a multi-stage process guided by the Intervention Mapping framework and the Medical Research Council (MRC) guidelines for complex interventions. The study design comprises four interrelated stages: 1. Systematic review and expert consultation, 2. Mixed methods needs assessment with 30 children and 10 caregivers/professionals, 3. Intervention refinement through focus groups and e-Delphi, 4. Ongoing 12-week pilot RCT evaluating feasibility, acceptability, and preliminary outcomes using the RE-AIM framework.

**Methods:** Following ethical approval, the study progresses through the outlined stages, gathering qualitative and quantitative data to inform the development of a culturally sensitive, theory-driven stepped-care intervention. The pilot trial will focus on feasibility and preliminary effectiveness.

**Results:** The outcomes will inform the design of a future fully powered randomized controlled trial (RCT). Initial findings are expected to demonstrate the feasibility of a culturally adapted psychosocial intervention that addresses emotional and behavioral health in children with leukemia in resource-constrained settings.

**Conclusion:** This research integrates both qualitative and quantitative data to create an evidence-based stepped-care model. The model aims to address the current absence of psychosocial support for children with leukemia in low-resource settings.

**Implications for the Profession and Patient Care:** This study protocol will provide nurses and allied health professionals with an evidence-based, culturally adapted framework to address emotional and behavioral challenges among children with leukemia. The intervention may support integration of psychosocial care into pediatric oncology services, improve treatment adherence and well-being, and reduce psychosocial morbidity in resource-limited settings.

**Reporting Method:** This study adheres to the GUIDED guideline for reporting intervention development studies.

**Patient or Public Contribution:** Children with leukemia, caregivers, and healthcare professionals contributed to the needs assessment and intervention refinement phases, informing the cultural adaptation and structure of the stepped-care intervention.

## **Summary**

### **Contribution to the wider global clinical community**

- Provides a novel, culturally adapted stepped-care protocol to address emotional and behavioral health in children with leukemia in low-income countries (e.g., Pakistan).
- Combines scalable, family-involved strategies with non-specialist delivery (trained mental health nurses) to enhance accessibility of pediatric psychosocial care in resource-limited settings.

### **What is already known?**

- Children with leukemia experience anxiety, depression, and treatment non-adherence, yet psychosocial support is absent in most low- and middle-income countries.
- Existing evidence-based interventions (CBT, family counselling) are not culturally adapted or scalable for resource-constrained environments.

### **What this paper adds**

- A structured, multi-stage protocol (literature review, mixed-methods needs assessment, e-Delphi refinement, pilot RCT) for developing a stepped-care intervention.
- Integration of cognitive behavioral, family systems, resilience, and self-regulation frameworks within a seven-step model (universal education to specialized therapy).

### **Implications for practice and policy**

- Offers nurses and allied health professionals an evidence-based framework to improve treatment adherence and well-being in pediatric leukemia.
- Advocates for policy integration of stepped-care psychosocial support into pediatric oncology standards in low-income countries.

## **1 Introduction**

Childhood leukaemia, particularly acute lymphoblastic leukaemia (ALL), is the most common pediatric malignancy worldwide, accounting for approximately 30% of childhood cancer diagnoses (Ward et al., 2019). While advances in chemotherapy and supportive care have significantly improved survival rates, the psychological burden of the disease remains substantial (Pui & Evans, 2013). Children with leukaemia experience pervasive emotional and behavioural

disturbances across the treatment course, including anxiety, depression, trauma symptoms, irritability, social withdrawal, and treatment non-adherence, that disrupt normative development and compromise treatment efficacy (Borrescio-Higa & Valdés, 2022) (Compas et al., 2012; Krull et al., 2013). These challenges are further compounded by family factors, as parental distress and limited coping capacity are consistently linked to poorer child outcomes, underscoring the need for systemic interventions that address both the child and their caregiving environment (Alderfer & Kazak, 2006; Ferraz et al., 2024; Mavrides & Pao, 2014).

In low- and middle-income countries (LMICs) such as Pakistan, these psychosocial needs remain almost entirely unmet. Paediatric oncology services are concentrated in a few urban tertiary centres, leaving vast geographical areas underserved. Families face prohibitive travel costs, lost wages, treatment delays, and high rates of treatment abandonment stressors that compound the inherent difficulties of cancer care (Al-Sudairy et al., 2014; Mostert et al., 2008). These socioeconomic adversities intersect with a severely under-resourced mental health infrastructure and pervasive cultural stigma surrounding psychological problems, creating formidable barriers to help-seeking (Hodgkinson et al., 2017; Kovach et al., 2023). Consequently, the emotional and behavioural needs of children with leukaemia in Pakistan remain entirely unaddressed within routine oncology care.

International consensus guidelines mandate routine psychosocial risk screening and the provision of structured, evidence-based support as essential standards in pediatric oncology (Kazak et al., 2024; Kolb & Meshinchi, 2015; Wiener et al., 2015). Interventions such as cognitive-behavioural therapy, psychoeducation, and family-centred counselling have demonstrated efficacy in reducing distress among children with cancer (Kendall et al., 2011; Orgel et al., 2016). However, implementation of these programmes remains highly inconsistent

globally and is almost entirely absent in LMICs, where the majority of children with cancer reside (Lam et al., 2019; Sandra et al., 2025). This gap reflects not merely a resource limitation but a failure of service design: resource-constrained health systems require models of care that are effective, scalable, sustainable, and capable of matching intervention intensity to clinical need.

The stepped-care model offers a promising framework for addressing this challenge. Originally developed in general mental health contexts, stepped-care allocates interventions according to patient need, delivering low-intensity, low-cost support as a first step and stepping up to more intensive, specialist care only for those who do not respond (Bower & Gilbody, 2005). This tiered approach optimizes resource allocation, prevents patients from falling through gaps in care, and is particularly well-suited to resource-constrained settings (Patel et al., 2018). Despite its proven utility, the application of stepped-care within pediatric leukemia remains critically underexplored. To date, no study has systematically adapted or tested a stepped-care framework to address the bidirectional psychological distress affecting children with leukemia and their caregivers in LMICs.

This paper presents a protocol for the systematic development and cultural adaptation of a stepped-care intervention programme designed to support the emotional and behavioural health of children with leukaemia in low-income countries such as Pakistan. Guided by the Intervention Mapping framework and the Medical Research Council guidance on complex interventions, this research seeks to co-design a contextually feasible, scalable model in partnership with families, healthcare providers, and other stakeholders. The resulting programme will provide a pragmatic, resource-sensitive pathway to translate international standards of psychosocial care into

sustainable practice in one of the world's most challenging healthcare environments, with the ultimate goal of informing a future randomised controlled trial.

## **2 Protocol**

### **2.1 General goal of the study**

To understand the emotional and behavioral challenges experienced by children with leukemia in Pakistan and to comprehend the contextual, familial, and healthcare factors influencing their psychological well-being.

To develop and pilot test a culturally adapted, theory-driven Step Care intervention program aimed at enhancing emotional and behavioral well-being in children with leukemia, with the intention of informing a future large-scale randomized controlled trial (RCT) if feasibility and preliminary outcomes are favorable.

### **2.2 Specific Objectives**

#### *Stage 1: Gap Definition.*

To explore existing psychosocial care practices and identify gaps in emotional and behavioral support for children with leukemia through a comprehensive literature review and expert consultation.

#### *Stage 2: Design a Model Intervention.*

To investigate the emotional and behavioral needs of children with leukemia and their families using a mixed-methods study, and to construct a culturally adapted, theory-informed Stepped Care intervention model by integrating findings from the literature review, expert input, and mixed-methods investigations.

#### *Stage 3: Refine the Model Intervention.*

To revise and finalize the Stepped Care model into a structured draft intervention protocol suitable for pilot testing.

#### *Stage 4: Pilot RCT*

To evaluate the feasibility and acceptability of the Stepped Care intervention among children with leukemia and their caregivers, and to determine the most appropriate outcome measures for a full-scale trial.

## **2.3 Method**

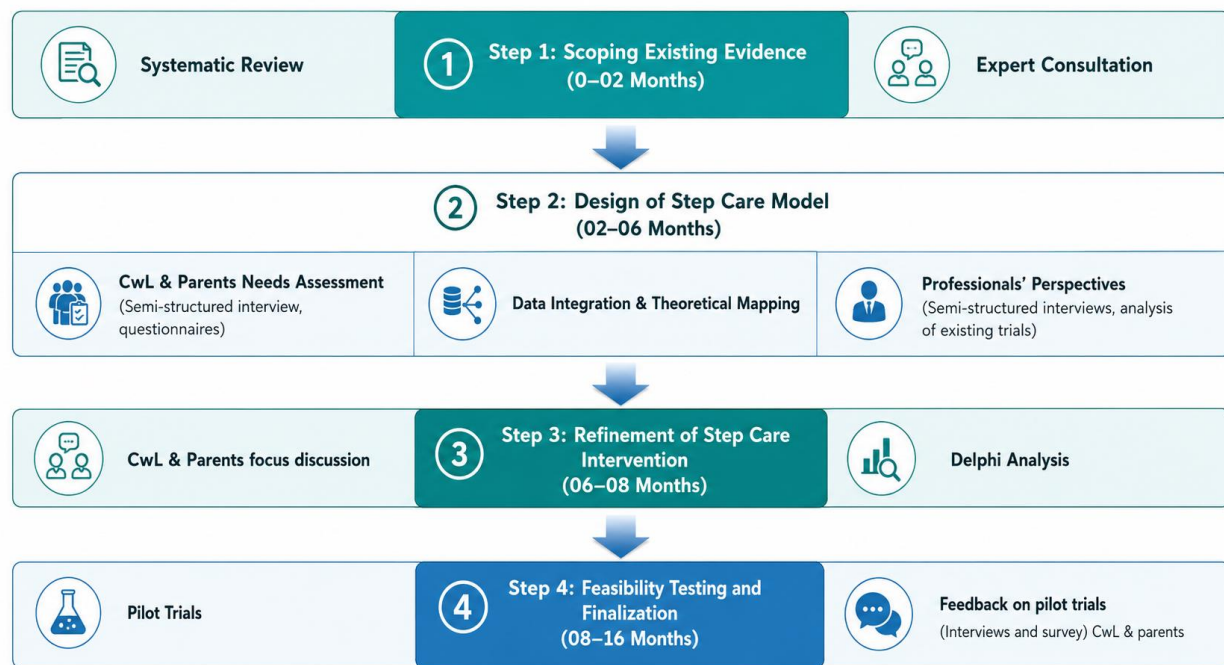
### **2.3.1 Study Design**

This study employs a **mixed-methods sequential design** guided by the Intervention Mapping framework (Fernandez et al., 2019) and the Medical Research Council framework for complex interventions (Skivington et al., 2021). The research follows a logically structured progression across four stages, integrating qualitative and quantitative approaches. Given the limited availability of structured psychosocial interventions for children with leukemia in Pakistan, greater emphasis is initially placed on exploratory qualitative methods. Quantitative components subsequently inform screening thresholds, feasibility indicators, and pilot evaluation parameters. The study proceeded through four sequential stages consistent with the Intervention Mapping and MRC frameworks:

- Stage 1 (Gap Definition): This stage involved a systematic literature review and expert consultation.
- Stage 2 (Model Development): The mixed-methods needs assessment, including qualitative data collection from 30 children and 10 caregivers/professionals.
- Stage 3 (Intervention Refinement): Focus groups and a two-round e-Delphi process for intervention refinement.
- Stage 4 (Pilot RCT and Finalization): This stage will focus on feasibility, acceptability, and preliminary outcome data being actively collected.

The study will officially complete in December 2026, after 16 months from the study start date in June 2025. This sequential, stage-gated design ensured that each phase informed the next,

aligning with best practices for developing complex interventions in resource-constrained settings.



**FIGURE 1:** Flow chart of the chronological and synchronized stages in the intervention development for Children with leukemia (CwL)

### 2.3.2 Sampling and Recruitment

Participants across all stages include: (1) children with leukemia, (2) caregivers, and (3) multidisciplinary experts. Sampling strategies are summarized below:

*Stage 1-Expert Consultation:* Purposive sampling will be used to recruit 15–20 multidisciplinary experts (pediatric oncologists, oncology nurses, clinical psychologists, child psychiatrists, and medical social workers) from tertiary care hospitals across Pakistan. Sample size is determined by the need for diverse disciplinary perspectives to comprehensively map care gaps.

*Stage 2 -Mixed-Methods Study:* For the quantitative component, 30 children with leukemia will be recruited. This sample size is sufficient for descriptive statistics and exploratory analysis in the context of a developmental study. For the qualitative component, 10 parent caregivers will be



recruited. This sample is justified by information saturation principles, as qualitative studies in similar populations have demonstrated that thematic saturation is typically achieved within 8–12 interviews. Participants will be purposively sampled to ensure representation across child age groups (7–14 years), gender, and disease phases (remission and maintenance). For professional interviews, 8–12 professionals will be recruited to achieve diversity in clinical roles and institutional settings.

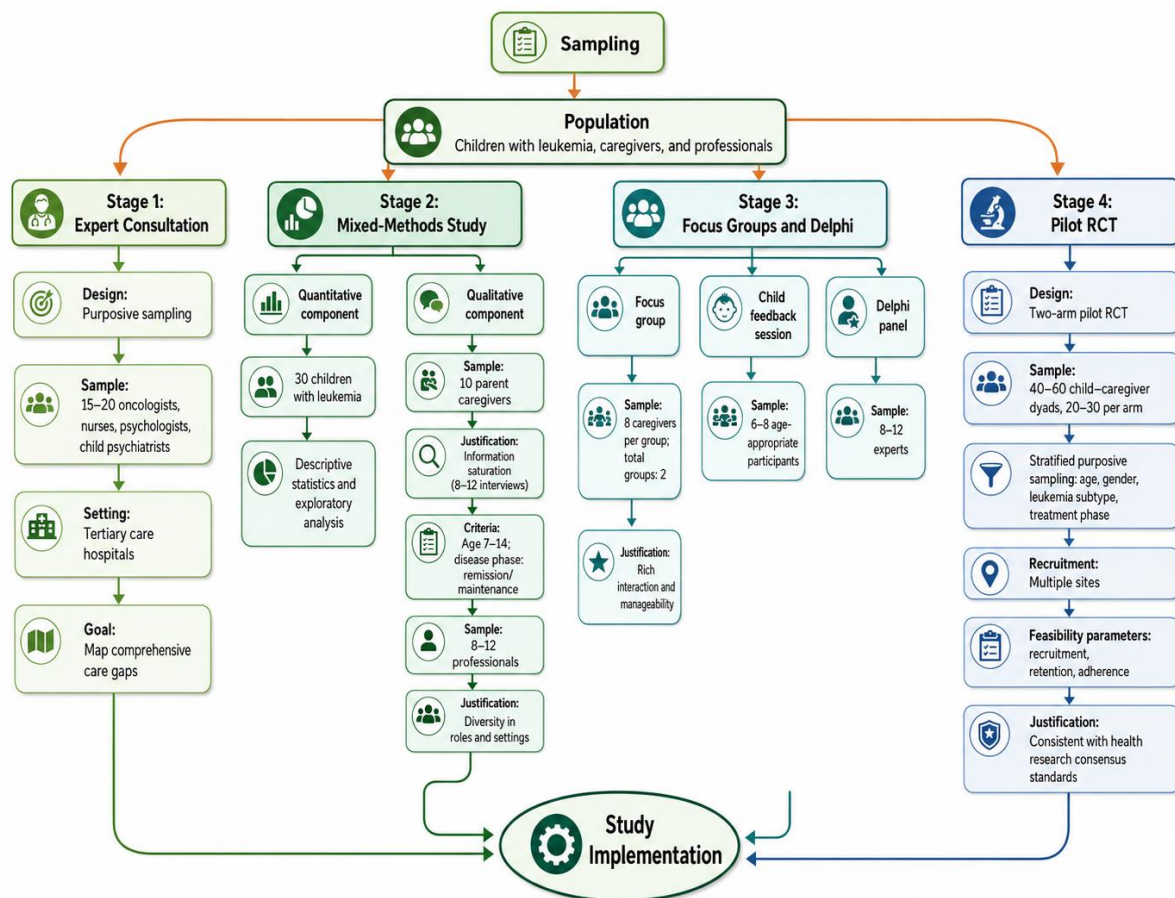
*Stage 3-Focus Groups and Delphi:* Focus groups will include approximately 8 parent caregivers per group, with two groups conducted to capture varied experiences. Sample size is justified by the goal of generating rich group interaction while maintaining manageability for in-depth discussion. Age-appropriate feedback sessions will include 6–8 children. The Delphi panel will comprise 8–12 experts, a size consistent with recommendations for achieving stable consensus in health research.

*Stage 4 -Pilot RCT:* A total of 40–60 child-caregiver dyads will be recruited (20–30 per arm). This sample size is consistent with pilot trial recommendations to estimate feasibility parameters recruitment rate, retention, and adherence without the need for formal power calculations. Sampling will ensure representativeness across child age, gender, leukemia subtype, and treatment phase. Representativeness will be ensured through stratified purposive sampling based on age, gender, and disease phase, with recruitment from multiple clinical sites where feasible.

*Eligibility Criteria:*

**Children:** Aged 7–14 years with leukemia, in stable health during remission or maintenance phases. Those in acute treatment phases are excluded to ensure meaningful engagement.

**Caregivers:** Primary caregivers directly involved in daily care and emotional support.



**Figure 2:** Flow Chart of the Protocol for Sampling and Recruitment

Experts: Healthcare professionals from oncology, pediatrics, nursing, psychology, and mental health disciplines.

Representativeness: Stratified purposive sampling based on child age (7–14 years), gender, leukemia subtype, and disease phase (remission/maintenance) will be applied, with recruitment from multiple clinical sites where feasible. Figure 2 presents a flowchart of the sampling and recruitment protocol.

### 2.3.3 Settings

Online: Expert consultations and Delphi rounds to facilitate wide geographical participation.

In-person: Interviews, focus groups, and the pilot RCT will be conducted at tertiary care hospitals and oncology centers in Pakistan, with locations agreed with participants.

#### **2.3.4 Data analysis**

**Quantitative Data Analysis:** Descriptive statistics (means, standard deviations, frequencies, percentages) will be used to summarize demographic characteristics, clinical variables, and feasibility indicators (recruitment rate, retention rate, session attendance, fidelity scores). For the pilot RCT, preliminary effect sizes will be calculated using appropriate parametric or non-parametric tests based on data distribution.

**Qualitative Data Analysis:** Qualitative data will be analyzed using the approach described by Mayring (Mayring, 2000). This method involves systematic, rule-guided coding of textual data into categories derived both deductively (from theoretical frameworks) and inductively (from emerging themes). Analysis will proceed through: (1) unitization of text into meaning units; (2) development of a coding framework; (3) iterative coding and refinement; and (4) abstraction into higher-order themes. Rigors will be measures through double coding of  $\geq 20\%$  of transcripts, with intercoder agreement calculation, expert review of coding frameworks and thematic interpretations, member checking with a subset of participants, maintenance of an audit trail documenting analytical decisions and reflexivity through researcher journals.

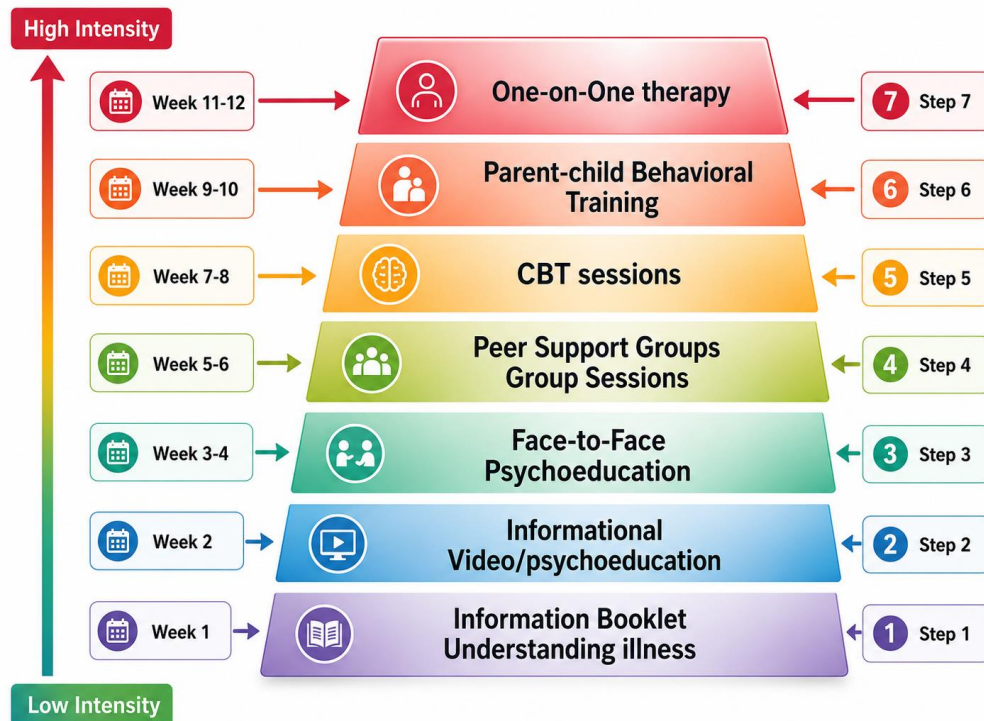
#### **2.4 Stepped Care Intervention Contents**

The clinical pathway begins at the universal level with step 1 (week 1), during which all children and caregivers receive a comprehensive information booklet to foster illness understanding and normalize emotional responses. Step 2 (week 2) utilizes an informational video to reinforce psychoeducational content through an accessible visual format. Step 3 (weeks 3–4) introduces

targeted, face-to-face psychoeducation sessions, establishing a foundational platform for direct emotional support and coping skill development.

For children exhibiting emerging emotional or behavioral difficulties, the model advances to step 4 (weeks 5–6), facilitating peer support groups to cultivate social connection and collective resilience. Step 5 (weeks 7–8) delivers structured cognitive behavioral therapy (CBT) sessions, incorporating cognitive restructuring and problem-solving skills for those requiring moderate-intensity intervention. Step 6 (weeks 9–10) implements parent-child behavioral training, equipping caregivers with essential strategies to support their child's emotional regulation at home.

At the apex of the clinical pathway, Step 7 (weeks 11–12) provides one-on-one therapy for children with severe or persistent psychological distress. This highest level of care delivers individualized therapeutic intervention and, when clinically indicated, facilitates seamless referral to specialized psychological or psychiatric services. Figure 3 illustrates the sequential steps of intervention delivery.



**FIGURE 3** Step Care Intervention Delivery Steps

## 2.5 Theoretical Framework

The development of the stepped-care program adheres to a modified form of the Intervention Mapping framework, while the MRC framework for complex interventions guides assessment of intervention complexity across multiple domains, including intervention components, contextual influences, and implementation processes.

The program is grounded in an integrated theoretical framework combining Cognitive Behavioral Theory, Stress and Coping Theory, Resilience Theory, Family Systems Theory, the Social Ecological Model, Self-Regulation Theory, and the Stepped Care Model. Collectively, this framework supports the development of a culturally sensitive, developmentally appropriate, and contextually adaptable intervention aimed at improving emotional regulation, adaptive coping, behavioral adjustment, and family support. Table 1 maps each theoretical framework to its corresponding intervention step and specific application.

**TABLE 1** Theoretical Foundation for Step Care Intervention

Theoretical Framework	Step-Care Step	Specific application in Intervention design
Cognitive Behavioral Theory (CBT)	Step 5: Specialized Psychological Intervention	Cognitive restructuring to modify maladaptive illness-related beliefs (e.g., helplessness, self-blame). Behavioral activation to reduce avoidance and increase engagement in developmentally appropriate activities (Chand et al., 2025).
Stress and Coping Theory	Step 2: Family Education & Coping Skills Workshop	Primary appraisal of leukemia-related stressors. Coping skills training (problem-solving, emotional regulation, and seeking social support) for both the child and primary caregivers (Biggs et al., 2017).
Resilience Theory	Step 3: Group-Based Resilience Building	Strengthening protective factors (optimism, self-efficacy, social connectedness) through structured peer-group activities to facilitate positive adaptation despite illness-related adversity (Southwick et al., 2014).
Family Systems Theory	Step 6: Family Therapy Sessions	Addressing relational dynamics and communication patterns. Parent-child training to reduce conflict, improves cohesion, and align family functioning with the child's psychological needs (Johnson & Ray, 2016).
Social Ecological Model	Step 1: Universal Screening & Referral Mapping	Multilevel assessment of individual, family, community, and healthcare system factors. Culturally responsive navigation to address barriers specific to Pakistani healthcare settings (Lopez et al., 2021).
Self-Regulation Theory	Step 4: Psychoeducation & Symptom Monitoring	Aligning illness perceptions with emotional responses. Teaching self-monitoring techniques to help children and families anticipate and manage treatment-related distress proactively (Cameron & Leventhal, 2012).
Stepped Care Model	Steps 1-7 (Structural Framework)	Operationalizing the stepped-care structure: Matching intervention intensity (from universal education to specialized therapy) to symptom severity and treatment response to ensure efficient resource allocation (Bower & Gilbody, 2005).

## 2.6 Intervention Complexity Features

In preliminary expert consultation and literature scoping, several layers of complexity were identified. Table 2 outlines these complexity dimensions guided by the MRC framework, including the nature of associations between intervention components, actions required by professionals and participants, outcome measures, personalization mechanisms, and theoretical understanding of change.

**TABLE 2** Intervention Study Complexity Dimensions Guided by Medical Research Council Guidelines (Skivington et al., 2021b)

Dimension	Reason for Complexity
Nature of associations between the intervention components	To reduce the risk of bias, research assistants blinded to the groups within the intervention will conduct assessments from baseline to the end of the intervention. Mental health nurses will administer the intervention supervised by a psychologist
Complexity of actions needed by professionals conducting the intervention	The principal researcher will train mental health nurses to administer the step care intervention. A supervising psychologist will manage any adverse reaction during the intervention and respond to participant concerns.
Complexity of actions needed by child participants and their caregivers	Understand and speak about problem and complete assignments required at each intervention stage.
Quantity and range of outcome measures	To make the home environment conducive to adolescent recovery, we will measure outcomes such as improved emotions and behavior, reduced stress, family environment, and coping.
Degree of personalization and influence on progress and evaluation	Since every child is different and has unique emotional patterns, the intervention will have to be personalized and individualized.

Notwithstanding this, the structure of the intervention will be a manualized, replicable, and module-oriented approach for each child and caregiver to meet their needs. It will be culturally adapted so that participants can identify with the program.

Theoretical understanding of how the intervention leads to change

Previous research and clinical insights indicate that each intervention part can be associated with specific transitional effects and ultimate outcomes.

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## **2.7 Stage 1: Gap Definition and Evidence Scoping of Psychosocial Interventions in Pediatric Leukemia**

### **2.7.1 Systematic Review of Literature**

*Objective:* To evaluate the effectiveness of psychosocial and stepped-care interventions in improving emotional and behavioral health in children with leukemia and psychological adaptation among parent caregivers.

*Method:* A systematic electronic database search will follow PRISMA guidelines. Search terms will include combinations of: child OR pediatric AND leukemia OR childhood cancer AND emotional OR behavioral OR psychological adaptation AND caregiver OR parent AND psychosocial intervention OR stepped care OR coping OR outcome. Databases will include MEDLINE, CINAHL, EMBASE, Web of Science, PsycINFO, Scopus, and will be register with ClinicalTrials.gov PRS

Studies will be included if: (1) they are randomized controlled trials; (2) participants are children aged 7–14 years diagnosed with leukemia; (3) the intervention includes a parent or caregiver component; (4) a control or comparison group is present; and (5) emotional, behavioral, or psychosocial adaptation outcomes are reported.



*Analysis:* Two independent reviewers will screen titles and abstracts. Risk of bias will be assessed using the Cochrane Risk of Bias 2 tool. Evidence certainty will be evaluated using GRADE. Intervention reporting completeness will be assessed using the TIDieR checklist.

### **2.7.2 Gap Identification from Expert Professionals**

*Objective:* To identify unmet psychosocial care needs in pediatric leukemia management in tertiary care hospitals in Pakistan.

*Method:* Two structured expert consultation meetings will be conducted with pediatric oncologists, oncology nurses, clinical psychologists, child psychiatrists, and medical social workers. Participants will respond to questions regarding psychosocial gaps, emotional and behavioral challenges, barriers to intervention delivery, and culturally feasible stepped-care strategies.

*Analysis:* Expert responses will undergo thematic analysis to identify priority gaps, service constraints, and system-level barriers.

## **2.8 Stage 2: Model Intervention Development**

The primary objective of Stage 2 is to systematically gather modules that will form the basis of a culturally adapted, stepped-care psychosocial intervention. A series of integrated research activities will be conducted to identify context-specific emotional needs, behavioral manifestations of distress, and optimal implementation strategies.

### **2.8.1 Identifying Modules from Children and Parent Caregivers**

*Objective:* To identify emotional and behavioral challenges of children with leukemia and adaptation difficulties among their caregivers.

*Design:* Mixed-methods study conducted in a tertiary care hospital in Pakistan.

*Participants:* Thirty children diagnosed with leukemia and 10 parent caregivers.

*Quantitative Component:* Researcher-administered questionnaires will assess emotional symptoms, behavioral difficulties, treatment-related stress, and coping strategies.

*Qualitative Component:* Semi-structured interviews will explore emotional distress, adjustment challenges, coping patterns, and support expectations.

*Analysis:* Descriptive statistics will summarize quantitative findings. Qualitative data will undergo content analysis following Mayring's approach.

### **2.8.2 Identifying Modules from Professionals**

*Objective:* To determine the most appropriate intervention content and delivery mode from the professional perspective.

*Method:* Semi-structured interviews will be conducted with pediatric oncologists, Oncology nurses, Clinical psychologists and Hospital administrators. A TOWS matrix will be applied to compare, internal strengths & weaknesses, and external opportunities & system constraints (Chopra et al., 2025). This structured appraisal will determine the feasible delivery frequency, Personnel training needs and Integration within routine hospital workflow. Interview transcripts will be analyzed using content analysis supported by qualitative software. See Table 3

**TABLE 3** Studies in the intervention development process.

Study	Purpose	Design& Participants	Setting	Data Analysis
Expert Consultation (Gap Identification)	To identify unmet psychosocial care needs in pediatric leukemia management.	Structured expert consultation meetings with Pediatric oncologists, nurses, clinical psychologists, child psychiatrists, and medical social workers.	Tertiary care hospitals in Pakistan.	Thematic analysis of expert responses to identify priority gaps, service constraints, and system-level barriers.
Mixed-Methods Study (Module Identification)	To identify emotional and behavioral challenges of children with leukemia and adaptation difficulties among their caregivers.	Quantitative: Researcher-administered questionnaires with 30 children. Qualitative: Semi-structured interviews with 10 parent caregivers.	A single tertiary care hospital in Pakistan.	Quantitative: Descriptive statistics. Qualitative: Content analysis following Mayring's approach.
Semi-structured Interviews (Module Identification)	To determine the most appropriate intervention content and delivery mode from the professional perspective.	Semi-structured interviews with pediatric oncologists, oncology nurses, clinical psychologists, and hospital administrators, analyzed using a TOWS matrix.	Tertiary care hospitals in Pakistan.	Content analysis of interview transcripts using qualitative software.
Focus Group & Delphi (Model Refinement)	To evaluate the feasibility, cultural appropriateness, and acceptability of the draft intervention.	Focus groups with approximately 8 parent caregivers per group, and age-appropriate sessions with children. A two-round e-Delphi process with 8–12 multidisciplinary experts.	Focus groups at participating tertiary care facilities. Delphi process conducted online.	Focus Groups: Qualitative content analysis of transcribed discussions. Delphi: Analysis of agreement indices for concentration, coordination, and stability of expert opinions
Pilot Trial (Pilot Testing)	To evaluate the feasibility, acceptability, and preliminary effectiveness of the Step Care Program.	Two-arm pilot randomized controlled trial (intervention vs. routine care) with children aged 5–18 with leukemia and their primary caregivers.	A single tertiary care hospital in Pakistan.	Feasibility: Descriptive statistics on recruitment, retention, and fidelity. Acceptability: Thematic analysis of feedback interviews. Preliminary Outcomes: Analysis of changes in emotional and behavioral functioning.

## **2.9 Stage 3: Model Refinement into Draft Intervention**

The preliminary model constructed from stage 1 and 2 will undergo iterative refinement through focus groups with children and parent dyads and a Delphi process with experts.

### **2.9.1 Focus Group and Delphi Process**

*Objective:* To evaluate the feasibility, cultural appropriateness, and acceptability of the draft intervention.

*Method:* Focus groups lasting 1–2 hours will be conducted with parent caregivers (approximately 8 per group, two groups). Age-appropriate feedback sessions will be organized with children (6–8 participants). Discussions will explore clarity of materials, cultural relevance, practical burden, and acceptability of session length and format.

A two-round e-Delphi process will be conducted with 8–12 multidisciplinary experts representing pediatric oncology, clinical psychology, psychiatry, nursing, behavioral sciences, and public health.

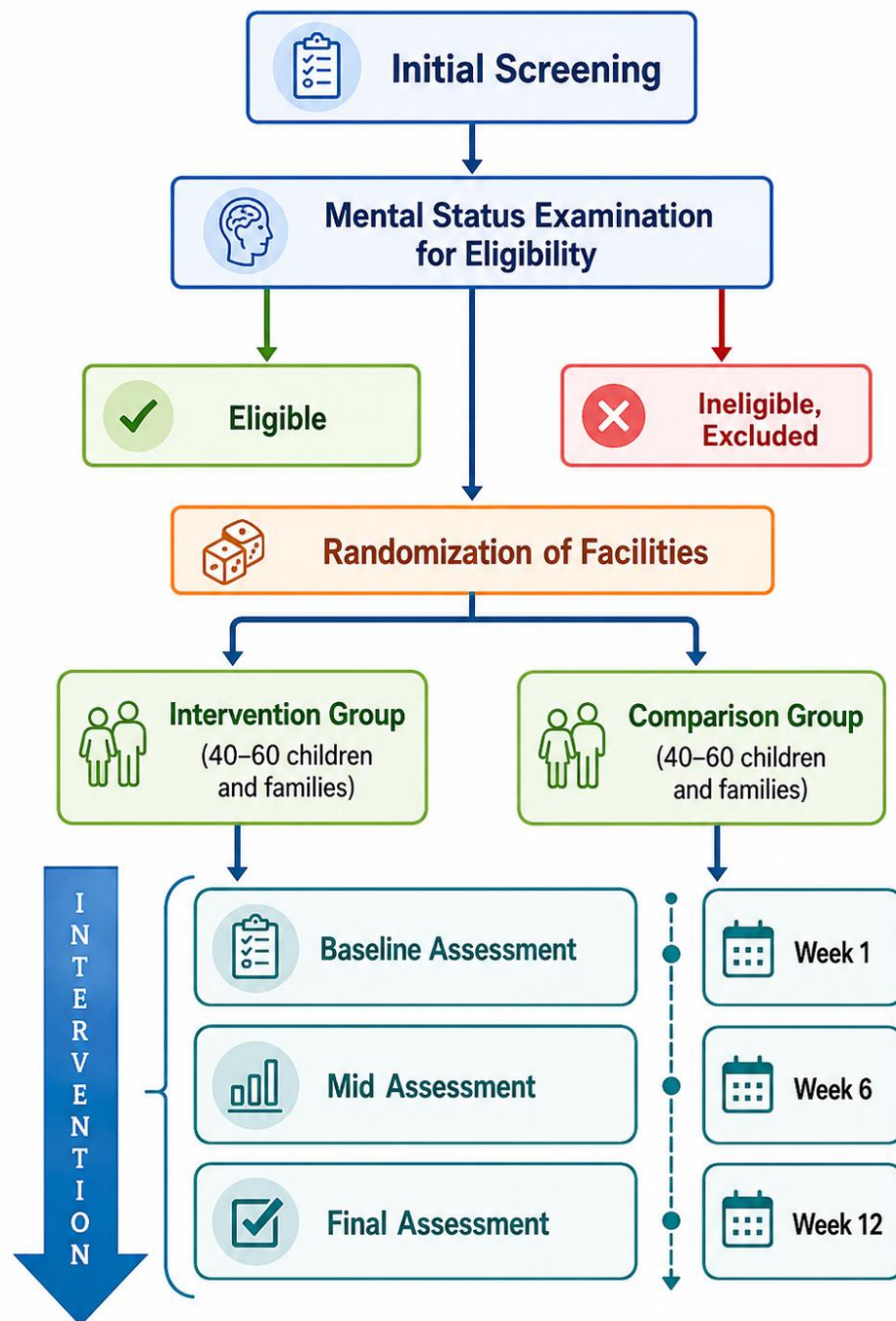
*Analysis:* Focus group data will be analyzed using qualitative content analysis. Delphi results will be analyzed using agreement indices to assess concentration, coordination, and stability of expert opinions.

## **2.10 Stage 4: Pilot Trial of the Draft Intervention**

### **2.10.1 Study Design**

This stage employs a two-arm pilot randomized controlled trial and will be conducted in tertiary care hospitals. Participants will be individually randomized to either the intervention group (stepped-care program plus routine care) or control group (routine care only). Consistent with pilot trial recommendations, the primary purpose is to assess feasibility, acceptability, and

implementation processes rather than to test definitive hypotheses(Eldridge et al., 2016). Figure 4 presents a flow chart of the pilot RCT design.



**FIGURE 4** Flowchart of pilot RCT of step care intervention draft

## 2.10.2 Participants and Procedures

### Inclusion Criteria:

- Children diagnosed with leukaemia (confirmed by medical records).
- Aged between 7–14 years at the time of diagnosis.
- Primary carers (parents, guardians, or immediate family members) who are directly involved in the child's care and treatment.
- Ability to comprehend and communicate in the local language (e.g., Urdu, Pashto).
- Child in the stable remission or maintenance phase of leukaemia treatment.
- Willingness to participate in the study and provide informed consent (child assent and parental consent).

### Exclusion Criteria:

- Acute medical instability requiring intensive care.
- Cognitive impairment preventing meaningful participation.
- Severe mental health conditions (e.g., active psychosis, extreme depression) in the child.
- Non-primary carers without direct responsibility for the child's care.
- Active substance abuse or impairing conditions in the primary carer.
- Non-English/non-Urdu/Pashto-speaking participants.

*Study Procedures:* The pilot RCT spans 12 weeks. After obtaining informed consent and baseline assessments, participants will be randomized. Outcome assessments will occur at baseline, mid-intervention (week 6), and post-intervention (week 12). Intervention fidelity will be monitored through structured checklists, session logs, and supervision meetings. Feasibility indicators will include recruitment rates, retention, adherence, and completeness of outcome measures. Acceptability will be assessed through satisfaction questionnaires and post-intervention feedback interviews.

### **2.10.1 Outcome and Process Evaluation**

Since this study is currently in progress, the results section will reflect preliminary findings and expected outcomes based on the design and methods outlined. Upon completion, actual data will be included.

#### ***Preliminary Results (Expected)***

##### **Feasibility Indicators:**

- **Recruitment Rate:** Expected target of 70–80% of eligible participants.
- **Retention Rate:** Preliminary data suggests a retention rate of approximately 75% after the first 6 weeks.
- **Session Attendance:** The intervention aims for 85% attendance rate across all sessions, with deviations primarily due to logistical barriers.

##### **Acceptability:**

- **Participant Satisfaction:** Early feedback from focus groups and pilot testing indicates a high level of acceptability, with preliminary satisfaction scores averaging 4.5 out of 5.
- **Cultural Appropriateness:** Preliminary focus group results suggest that the intervention's cultural adaptation is well-received by caregivers and children, with minor recommendations for improvement in materials.

#### ***Preliminary Effectiveness (Secondary Outcomes):***

##### **Emotional and Behavioral Health:**

- **Pediatric Quality of Life Inventory (PedsQL):** Expected improvement in quality of life scores from an average baseline score of 55 to 75 post-intervention.
- **Strength and Difficulties Questionnaire (SDQ):** Anticipated reduction in behavioral difficulties, with SDQ scores decreasing from an average of 25 to 18.
- **Patient Health Questionnaire (PHQ-9):** Initial results suggest a decrease in depressive symptoms, with average scores reducing from 14 (moderate depression) to 9 (mild depression).

##### **Psychosocial Well-Being:**

- **Pediatric/Procedural Anxiety Distress Thermometer:** Expected decrease in anxiety scores, with an average reduction from 8 (high anxiety) to 4 (moderate anxiety).

- Sleep Disturbance Scale for Children (SDSC): Early indications suggest that children in the intervention group report a significant improvement in sleep quality, with SDSC scores decreasing from 7 (severe disturbance) to 4 (mild disturbance).

#### **Treatment Adherence:**

- Adherence Rates: Preliminary results show an increase in adherence rates to treatment protocols, with average adherence rising from 75% to 90% after 12 weeks of intervention.
- Family Environment (Family Functioning Scale): Expected improvements in family dynamics, with scores increasing from a baseline of 50 (moderate dysfunction) to 80 (strong family functioning).

**TABLE 4** Measuring tool for emotions and behaviors for Leukemia Children.

Questionnaires
Socio-demographic information
Patient Health Questionnaire-PHQ 9 (Kroenke et al., 2001)
The strength and difficulties Questionnaire -SDQ (Goodman, 1997)
Pediatric Quality of Life Inventory PedsQL (Varni et al., 2002)
Sleep Disturbance Scale for Children (SDSC) (Bruni et al., 1996)
Distress Thermometer (Pediatric/Procedural Anxiety) (Cuffe et al., 2022)

*Implementation Evaluation:* The RE-AIM framework (Reach, Effectiveness, Adoption, Implementation, and Maintenance) will guide systematic assessment of public health impact and implementation feasibility (Holtrop et al., 2021).

### **2.11 Data Integration**

The findings generated from the quantitative and qualitative components across all stages of the study will be integrated using triangulation principles, following methodological guidance on mixed-methods integration (Brannen, 2005). This process will involve systematically



bringing together results from needs assessment, model development, refinement, and pilot testing phases.

Integration will include cross-referencing quantitative outcomes (e.g., changes in emotional and behavioral measures, feasibility indicators) with qualitative findings (e.g., participant feedback, expert consensus, acceptability interviews) to confirm, complement, or explain results. Converging evidence will strengthen interpretation, while discrepancies between data sources will be examined to generate deeper insights and guide further refinement of the intervention.

The weighting of evidence will consider methodological rigor, sample characteristics, and contextual applicability within the Pakistani pediatric oncology setting. Greater weight will be assigned to findings derived from robust data collection procedures and those demonstrating consistency across multiple sources. Final interpretations will be determined collaboratively by the research team, ensuring that conclusions reflect both empirical strength and contextual relevance for implementation.

## **2.12 Sharing and Management of data**

The principal investigator will oversee the collection, storage, and management of data across all stages of the program. All research data will be stored in password-protected digital files and used solely for research purposes. Identifiable participant information will be stored separately from research datasets to ensure confidentiality. Each participant will be assigned a unique de-identified code to maintain anonymity in all study documents, databases, and electronic records. Both quantitative and qualitative data will be entered and stored using these coded identifiers.

Access to study data will be restricted to authorized investigators and, where required, regulatory authorities. Audio recordings from interviews and focus groups will be securely stored and deleted after transcription has been verified for accuracy. All research data will be retained securely for a period of 10 years following study completion, after which records will be permanently destroyed in accordance with institutional data protection policies.

### **2.13 Dissemination**

Dissemination will occur at two levels. Internally, iterative reports will guide real-time refinement of the intervention. Externally, findings will be disseminated through peer-reviewed publications, conference presentations, and tailored outputs:

<b>Audience</b>	<b>Output</b>
Academic and research community	Systematic review, care gap analysis, intervention protocol, pilot RCT results, intervention manual
Healthcare institutions and clinicians	Training manuals, facilitator guides, fidelity checklists
Policymakers and health planners	Policy briefs (Urdu and English)
Families and patient advocacy groups	Lay summaries, infographics

These outputs will translate findings into practice by equipping clinicians with standardized training tools, informing policy decisions, and empowering families through accessible resources.

### **2.14 Timeline**

The overall timeline of the study will span 16 months. Stage 1 will be conducted within the first 2 months of the project. Stage 2 will take place from month 2 to month 6. Stage 3 will be

implemented between month 6 and month 8. Finally, stage 4 will be carried out from month 8 to month 16 of the study period.

### **2.15 Ethics**

Ethical and institutional approval was granted as follows:

- Ethical approval was granted by the university, approval # ZZUIRB-2025-03.
- Ethical Permission was also secured from the tertiary care hospital, approval No. 2370, prior to the commencement of data collection and pilot study.

The study is expected to be completed in December 2026, started from June 2025.

## **3 DISCUSSION**

This protocol details the systematic development of a stepped-care intervention to enhance emotional and behavioral health in children with leukemia, guided by Intervention Mapping and MRC frameworks for complex interventions. The integration of qualitative and quantitative methods across four sequential stages ensures the final intervention is both culturally adaptable and methodologically rigorous.

This research directly addresses critical deficiencies in pediatric psycho-oncology within resource-constrained settings, where specialized psychosocial support remains scarce despite the well-documented prevalence of childhood leukemia. Emotional and behavioral disturbances during diagnosis and treatment are extensively evidenced, with untreated distress associated with poorer quality of life, compromised treatment adherence, and adverse developmental outcomes. Our stepped-care intervention aligns with global health priorities to integrate mental health services into existing systems.

Several implementation challenges must be addressed. Stigma surrounding mental health may discourage engagement; our design mitigates this through culturally sensitive recruitment, developmentally appropriate materials, and integration of locally relevant coping concepts. Participant retention may be influenced by socioeconomic factors; we address these barriers

through flexible scheduling, coordination with routine appointments, and travel reimbursement. Intervention fidelity is maintained through standardized protocols, structured training, regular clinical supervision, and session checklists.

The primary objective is sustainable integration within pediatric oncology services. Employing the MRC's translational framework, we delineate a phased scale-up approach: (1) pilot testing to establish feasibility, (2) refinement based on stakeholder feedback, (3) expansion across diverse contexts, and (4) policy advocacy for integration into standards of care. The stepped-care model's inherent efficiency delivering intensity proportionate to psychological risk which makes it particularly suitable for resource-constrained environments.

### **Limitations**

This pilot will be conducted within a single tertiary hospital, potentially limiting applicability to urban, well-resourced settings. Future research should encompass multiple centers, including rural and underserved populations. The focus on feasibility precludes definitive efficacy conclusions; a fully powered trial will be required following successful pilot outcomes. Reliance on self-reported and parent-reported measures may introduce social desirability bias; future studies should integrate clinician-rated or observational measures. The 12-week follow-up limits understanding of longer-term effects; extended assessments are needed. Finally, while designed for cultural adaptability, further contextual adaptation may be necessary for specific subpopulations, a consideration for future implementation research.

### **Declaration of Interests**

We declare no competing interests.

### **Data Sharing**

The identified participant data collected for this study, including data dictionaries, will be made available upon reasonable request to the corresponding author, subject to institutional ethics approval.

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