Study Title:

Development of a stage matched psychosocial intervention to enhance psychological adaptation among parent caregivers of children with leukemia in Pakistan: a study protocol

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Abstract

Purpose: To develop a structured, systematic and cultural adapted stage-matched psychosocial intervention to improve psychological adaptation in parent caregivers of children with leukemia in Pakistan.

Methods: This protocol study adopts a multi-stage approach guided by the Intervention Mapping framework and MRCguidance for complex interventions, this four stage protocol includes: (1) Identifying psychological adaptation gaps through literature review and expert consultation; (2) a mixed-methods needs assessment; (3) intervention refinement via focus groups and e-Delphi; and (4) a pilot cluster-randomized controlled trial (N=88) in a tertiary care Pakistani pediatric oncology unit.

Results: The protocol will produce a manualized, stage matched intervention modified to the local cultural and healthcare context. Feasibility, acceptability, and preliminary efficacy will be evaluated.

Conclusion: This protocol addresses a critical gap in supportive care for caregivers in low resource settings. If successful, the intervention will provide an evidence-based, scalable tool for integration into routine oncology care in Pakistan.

Key words: Parent caregivers, psychological adaptation, childhood leukemia, Stage matched intervention, intervention development, Pakistan

Introduction

There is a growing global recognition that childhood cancer represents a significant public health challenge and is one of the leading cause of global burden of childhood diseases(Metrics, 2019). The World Health Organization estimates that over 400,000 children and adolescents are diagnosed with cancer annually(WHO, 2021), with leukemia accounting for approximately for one-third of cases,(Ferlay et al., 2018). Childhood leukemia is the most common pediatric malignancy in Pakistan, with an estimated 8,000–12,000 new pediatric cancer cases diagnosed annually, the majority being leukemia(Graetz et al., 2023).Although improvements in treatment protocols, survival rate in Pakistan still remains below 50%, significantly lower than those reported in high-income countries(Graetz et al., 2025) . This survival gap is attributable to multiple factors, including delayed diagnosis, treatment abandonment, financial constrains, significant psychosocial barriers and limited availability of comprehensive psychosocial support services with in pediatric oncology healthcare system(Maryam et al., 2022), Furthermore, pervasive stigma surrounding mental health issues in Pakistani society prevent parent caregivers from seeking or accepting psychological support even when services are available(Rafiq et al., 2025). This insight highlights the urgent need for contextually relevant psychosocial interventions to support parent caregivers navigating childhood leukemia.

The diagnosis of leukemia in a child constitutes a profound psychological crisis for parents, who typically assume the primary caregiving role(Huang et al., 2023). The treatment process, often extending over 2–3 years, involves intensive chemotherapy, repeated hospitalizations, and management of distressing side effects(Liu et al., 2021). Children frequently experience physical discomfort and psychological difficulties, including fear, irritability, anxiety, and social withdrawal, which increase their dependence on caregivers(Tang et al., 2022). Consequently, parent caregivers face sustained emotional, physical, and financial demands that significantly elevate their psychological burden(Saeed et al., 2024), and potentially threatening the child's survival and quality of life(Wechsler et al., 2024).

Empirical evidence consistently demonstrates that caregivers of children with cancer experience significantly higher levels of psychological distress compared to the general population. Elevated rates of anxiety, depression, and post-traumatic stress symptoms have been widely reported(Bashir et al., 2024). In similar contexts, up to 87.8% of caregivers exhibit symptoms of anxiety, while 45.9% experience depression(Wang et al., 2025). In Pakistan, recent findings indicate that approximately 52.94% of caregivers of pediatric cancer patients report high levels of post-traumatic stress symptoms, with female caregivers and those with lower educational attainment being particularly vulnerable(Bashir et al., 2025). These psychological challenges can undermine caregivers' coping capacity, reduce their ability to effectively support treatment adherence, and ultimately impact the child's health outcomes and quality of life(Kumari et al., 2018). Moreover, evidence suggests a reciprocal relationship between caregiver and child adjustment, highlighting the importance of addressing caregiver well-being as part of comprehensive pediatric oncology care.

Caregiver adaptation to a child's illness is not a static outcome but a dynamic process that evolves across different phases of the disease over time(Ververidou et al., 2023). The initial diagnosis phase is often characterized by shock, disbelief, and acute emotional distress(Mess et al., 2022). During the intensive treatment phase, caregivers must continuously adjust to demanding treatment regimens, frequent hospital visits, and uncertainty regarding outcomes(Rachmad, 2022),that enable individuals to function effectively and to ease distress.(Avsec et al., 2022). The maintenance or survivorship phase introduces additional challenges, including fear of relapse, management of long-term treatment effects, and reintegration into daily life(Perkins, 2022). Each phase imposes unique adaptive requirements, necessitating different coping strategies and supportive interventions.

In Pakistan, the process of caregiver adaptation is further complicated by structural and sociocultural factors. Pediatric oncology services are limited and primarily concentrated in urban centers, creating barriers to access for many families(Faran and Ahmed, 2018). Financial hardship associated with treatment costs, travel, and loss of income places additional strain on caregivers(Bekui et al., 2023). Cultural norms, including strong family interdependence and gender role expectations, influence caregiving responsibilities and coping behaviors(Javed and Nazir, 2025). At the same time, stigma surrounding psychological distress also prevents caregivers from expressing their needs or seeking help(Salyani et al., 2025). Despite these challenges, there remains a notable absence of structured, evidence-based psychosocial interventions specifically designed for parent caregivers within Pakistani pediatric oncologycare settings.

Interventions that are responsive to the evolving needs of caregivers across the illness journey are increasingly recognized as essential. Stage-matched interventions, which adopt support according to the individual's phase of adaptation, offer a promising approach to addressing this need. Such interventions align the content, timing, and intensity of support with caregivers' changing emotional and behavioral requirements, thereby enhancing their relevance and effectiveness(Norcross et al., 2011). Evidence from diverse populations suggests that stage-matched approaches yield better outcomes compared to non-tailored interventions, particularly in improving coping skills and reducing psychological distress(Romain et al., 2018). However, most existing interventions have been developed and tested in high-income countries, limiting their applicability to low- and middle-income contexts such as Pakistan, where healthcare systems, cultural norms, and resource availability differ substantially(Tran et al., 2025). Additionally, there is limited research focusing specifically on caregiver supportive care needs within the Pakistani context(Raza et al., 2021). Therefore it is crucial to enhance psychological adjustment of parent caregivers through relavent modified intervention program.

In response to these gaps, the present study protocol aims to develop, implement, and evaluate a longitudinal stage-matched psychosocial intervention designed to enhance the psychological adaptation of parent caregivers of children with leukemia in Pakistan. The intervention will be developed using the Intervention Mapping framework to ensure systematic, theory-informed design and contextual relevance(Eldridge et al., 2016). Furthermore, the Medical Research Council framework for complex interventions will guide the development and evaluation process, ensuring methodological rigor and feasibility within real-world healthcare settings(Skivington et al., 2021a).. By addressing the evolving psychosocial needs of caregivers within a culturally sensitive framework, this study seeks to contribute to improving caregiver well-being and, ultimately, pediatric cancer outcomes in Pakistan.

2 Protocol

2.1 General goal of the study program

To understand and improve the psychological adaptation challenges and adaptive coping of parent caregivers of children diagnosed with leukemia in Pakistan.

To develop and pilot test a culturally adapted, theoretically informed stage-matched intervention aimed at enhancing the psychological adaptation of parent caregivers of children with leukemia that can be rolled out in a large- scale randomized controlled trial (RCT) if the results of this development program seem favorable.

2.2 Specific objectives

Stage 1: Gap Definition**.**

To explore the psychological adaptation pattern and gaps among parent caregivers through systematic literature search and expert review.

Stage 2: Design a Model Intervention.

To investigate the psychological adaptation needs and care giving challenges of parent caregivers of children with leukemia using a mixed-methods study.

To develop a culturally sensitive, theory-driven stage-matched intervention model by integrating findings from the literature search, expert review, and mixed-methods investigations.

Stage 3: Refine the Model Intervention.

To revise and finalize the model intervention into a draft intervention for pilot testing

Stage 4: Pilot Randomized Controlled Trial of Draft Intervention.

To evaluate the feasibility, acceptability, and preliminary efficacy of the stage-matched intervention by parent caregivers of children with leukemia. To determine the most appropriate outcome measures for a fully complete trial, including the impact on psychological adaptation of parent caregivers and outcomes of their well-being and caring capacity.

2.3 Method/ Design

The development approach of our stage-matched intervention Program will follow a multi-stage, mixed-methods design and will adhere to a modified form of the Intervention Mapping (IM) framework as described by(Eldridge et al., 2016), and the updated Medical Research Council (MRC) framework for developing and evaluating complex intervention (Skivington et al., 2021b)**.** The IM framework offers a structured, theory-informed, and evidence-based step-by-step approach for designing health promotion interventions. Specifically, it includes: (1) Needs Assessment (Logic Model of the Problem), (2) Matrices of Change Objectives (Program Outcomes and Objectives), (3) Theory-Based Methods and Practical Strategies, (4) Program Production (Design and Materials), (5) Implementation Plan, and (6) Evaluation Plan.

The present protocol study, comprises four logical and sequential stages representing the modified form of IM steps.Stages 1 and 2 of the current study presents a modified form of IM steps 1 to 4, while Stages 3 and 4 represent IM Steps 5 and 6.

The Medical Research Council (MRC) guidance framework for complex interventions (Skivington et al., 2021b) which provides a structured approach to assessing complexity by examining multiple interacting dimensions. These include the distinguishing features of the intervention elements e.g.(number of stages in the model, flexibility and interactions), contextual influences e.g.(healthcare infrastructure, sociocultural beliefs regarding childhood cancer, family roles and stigma), and the dynamic process involved in implementation (e.g., adaptation, stakeholder involment, unintended consequences). In assessing each relevant aspect of complexity outlined as shown in Table 1.

TABLE 1 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.	The intervention includes family needs assessment, stage-matched psychoeducation (based on the family's adaptation phase), dyadic communication support, problem-solving skills training, and linkage to social and spiritual resources. These components are delivered in a sequence that follows the family's evolving adaptation process rather than a rigid protocol. To minimize bias, assessments at baseline, post-intervention, and follow-up will be conducted by research assistants blinded to group allocation. Trained mental health nurses will deliver the intervention under the supervision of a clinical psychologist to ensure fidelity to the Transactional Family Adaptation Model.
Complexity of actions needed by professionals conducting the intervention.	The intervention requires mental health nurses to assess the family's current adaptation status, including demands (e.g., illness severity, financial strain), capabilities (e.g., coping resources, family cohesion), and appraisal processes (e.g., meaning-making, sense of coherence). Based on this assessment, nurses must select and apply appropriate modules to strengthen family adjustment. The principal researcher will provide rigorous training on the Transactional Family Adaptation Model, cultural nuances of family dynamics in Pakistan. A supervising psychologist will oversee sessions, address any adverse psychological reactions, and ensure that religious and cultural sensitivities are respectfully integrated into the intervention.

The complexity of actions needed by parent caregivers.	Parent caregivers must engage in structured sessions that involve reflecting on family strengths, identifying sources of stress, participating in joint problem-solving with their spouse or extended family, and practicing communication skills to coordinate caregiving roles. The intervention accommodates varying literacy levels by using verbal delivery and pictorial aids in Urdu, and sessions are scheduled flexibly around treatment cycles to reduce attrition, recognizing that multiple family members may need to participate.
The quantity and range of outcome measures.	To capture the multidimensional impact of the intervention, outcomes will include caregiver's adaptation, burden, perceived social support and psychological distress such as depression, anxiety and Stress. Exploratory outcomes will assess caregiver problem-solving capacity and child treatment adherence, where feasible. Unintended outcomes will be qualitatively explored through process evaluation..
The degree to which the intervention permits personalization and how this influences progress and evaluation.	The intervention is inherently personalized, as it responds to each caregiver's unique constellation of demands (e.g., illness phase, socioeconomic status, family structure), capabilities (e.g., social support, financial resources, religious coping), and appraisal processes (e.g., how the family makes meaning of the illness). However, to maintain replicability, the intervention is manualized with structured, module-based content that addresses common adaptation challenges. Cultural adaptation is embedded across all modules, incorporating religious coping strategies , collectivist family dynamics, and the hierarchical decision-making structures typical in Pakistani families. This balance between standardization (to ensure fidelity) and flexibility (to meet individual caregiver needs) allows for meaningful evaluation.

Theoretically, it is necessary to comprehend how the intervention leads to change, pinpointing and enhancing any vulnerable links in the cause-and-effect sequence.	Previous research and clinical insights suggest that each component of the intervention is linked to specific transitional effects, ultimately influencing the desired outcomes and ultimately reducing caregiver distress and improving the child's care environment.

The timing for each stage of the intervention program is derived from prospective longitudinal research. Stage 1 (Acute) will target caregivers within the first to three month following their child's diagnosis. Stage 2 (Early Treatment) will occur at approximately three to six months post-diagnosis. Stage 3 (Ongoing Treatment) will be delivered at approximately nine months post-diagnosis. Stage 4 (Transition) will be implemented for families who have completed active treatment, and Stage 5 (Bereavement) will be offered to families a minimum of three months following the death of their child, following established ethical guideline

Further, We will apply a modified version of the MRC guidance framework to assess the complexity within the context of pediatric oncology in Pakistan. To ensure a thorough and contextually relevant development process, we will use a mixed-methods sequential design, combining qualitative and quantitative methods across different stages. Given the limited published data for quantitative methods, our approach will focus on exploratory and qualitative techniques to deeply understand caregivers' experiences, adaptation, and needs. This will involve in-depth interviews with parents and healthcare professionals to explore cultural perceptions of psychological adaptation, coping strategies, family dynamics, and service gaps. Following this, quantitative methods will help determine screening thresholds, feasibility metrics, and pilot evaluation criteria. The stages of the research program are outlined in Figure 1.

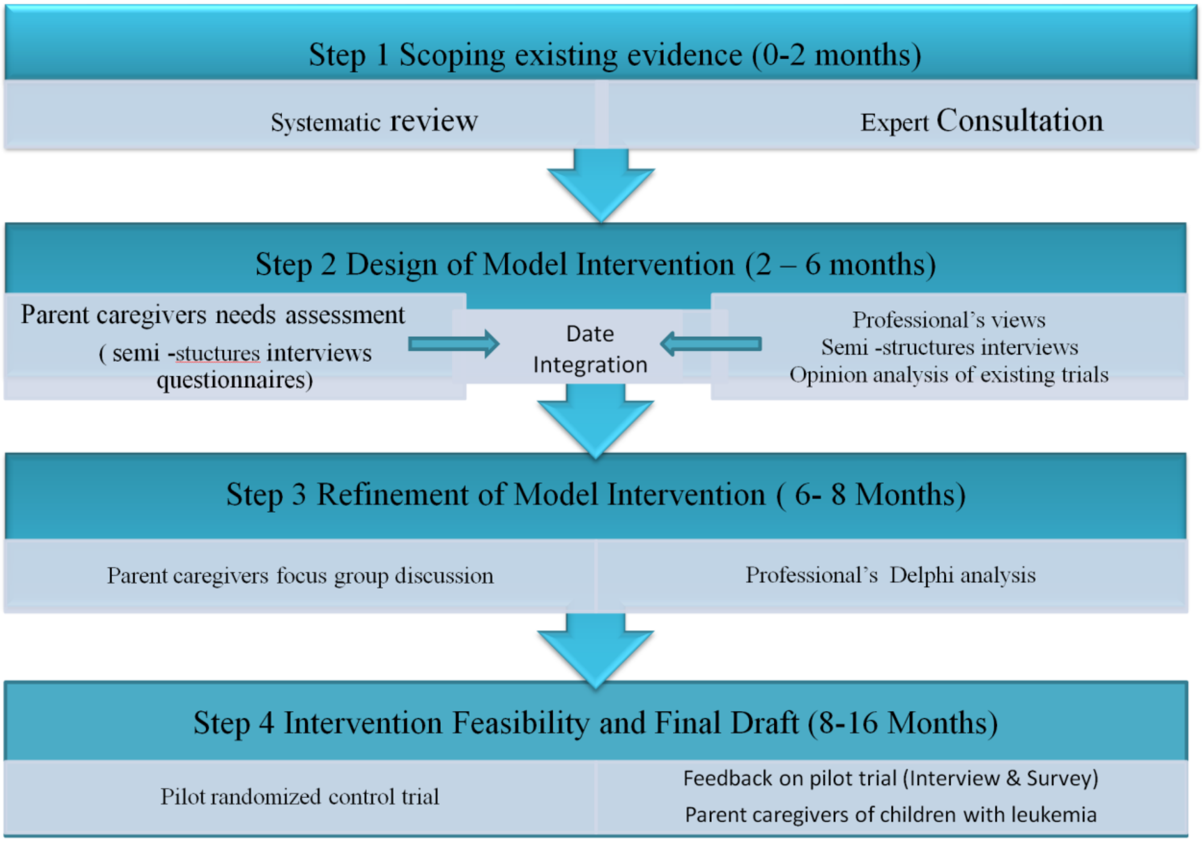

Figure 1 Flowchart of the chronological and synchronized stages in the intervention development.

Prior to intervention development establishing a strong theoretical foundation is essential. The components of the Stage-Matched Intervention Program designed to enhance the psychological adaptation of caregivers of children with leukemia in Pakistan is based on an integrated framework combining the transactional theory of stress and coping, proposed by

Folkman and Lazarus in 1984(Lazarus, 1984). This theory views stress as a complex process that arises when an individual's demands exceed their capacity to manage them. It emphasizes that stress is a dynamic transaction between the person and their environment. This framework has been foundational in stress and coping research across various fields(Biggs et al., 2017). Additionally, the Double ABC-X Model of family stress and adaptation, developed as an extension of the ABC-X Model by Reuben Hill (1949)(Lavee et al., 1985), serves as a guiding framework. The Double ABC-X Model explains how families (or caregivers) respond to stress, accumulate resources, and adapt over time. It highlights the cumulative effects of stressors and emphasizes that family adaptation is an ongoing process, not a one-time event(Lavee et al., 2003). This model helps to understand why some families adapt well to chronic stress while others experience maladaptation. It is widely used in studies of family dynamics under stress, such as caregiving situations. Together, these frameworks provide a culturally sensitive, developmentally appropriate, and contextually adaptable basis for the intervention.

This study protocol aims to improve the psychological adaptation of caregivers of children with leukemia through modified interventions that align with their stage of caregiving and readiness to adapt. The caregivers experience significantly viewed through the lens of family stress and adaptation, making the Double ABC-X Model an ideal fit to explore the relationship between stressors (child’s leukemia illness), resources (support systems), perceptions (caregiver’s cognitive appraisal), and outcomes (adaptation or maladaptation).From the above perspectives, the potential factors affecting the psychological adaptation of caregivers in pakistan are explored to provide a reference for promoting their Psychological adaptation.

Drawing upon the stage matched and the Double ABC-X Model, the intervention is expected to adopt a structured format encompassing several vital elements. These include (1) the identification of psychologically maladaption patterns, (2) the provision of resources to support the learning and practical application of newly acquired skills, and (3) the enhancement and promotion of sincere and empathetic level of adaptation through consistent monitoring and evaluation. The objective of this stage match intervention is to ensure that it is both suitable and convenient for the parent caregivers, with their active involvement. This intervention intends to establish a nurturing and peaceful environment that enhance cargivers adaptation, their wellbeing and care giving capacity as outlined in figure 2.

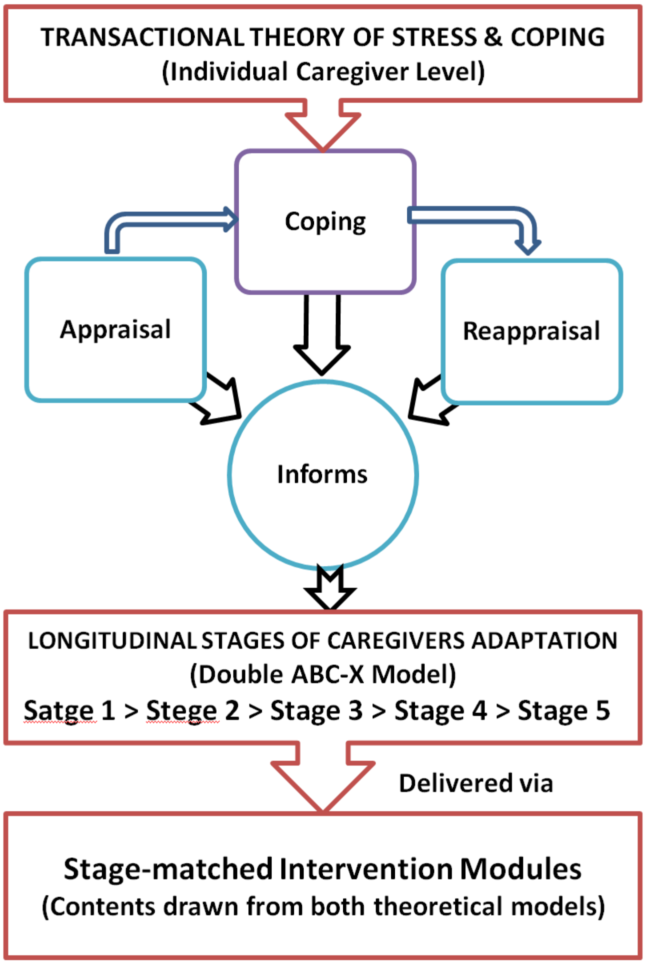

Figure 2 Conceptual Framework of the transactional family adaptation model

Further explanation of the transactional family adaptation model describes that how this integration works and significant use of stage matched intervention content as shown in Table 2.

Table 2: Integration of transactional family adaptation model

Longitudinal Stage	Double ABC-X Focus	Transactional Theory Focus	Stage Matched Intervention Content
Stage 1 **Diagnosis**	Stabilizing the A + X crisis	Addressing primary appraisal (threat, loss)	Psychoeducation, emotional validation, spiritual support, connecting with initial resources
Stage 2 **Early Treatment**	Mobilizing B resources; managing Aa pile-up	Strengthening secondary appraisal; introducing problem focused coping	Resource mapping, family communication skills, introduction to support groups

Stage 3 **Ongoing Treatment**	Addressing resource depletion; supporting Cc meaning making	Evaluating coping effectiveness; refining emotion focused coping	Caregiver burnout prevention, couples communication, meaning making interventions (e.g., narrative therapy, spiritual reframing)
Stage 4 **Transition**	Managing reduced Aa; consolidating Xx adaptation	Reappraising the situation as "new normal"	Transition planning, fear of relapse management, family reintegration, celebration of resilience
Stage 5 **Survivorship/Bereavement**	Long-term Xx outcomes	Sustaining adaptive coping; addressing grief	Maintenance planning, peer mentorship, grief support, referral pathways

The timing for each stage of Intervention Program is derived from prospective longitudinal research. Stage 1 (Acute) will target caregivers within the first to three month following their child's diagnosis. Stage 2 (Early Treatment) will occur at approximately three to six months post-diagnosis(Sulkers et al., 2015). Stage 3 (Ongoing Treatment) will be delivered at approximately six to twelve months post-diagnosis(Sharp et al., 2022). Stage 4 (Transition) will be implemented for caregiver, his/her child has completed active treatment , 0-24 months post treatment(Bradford et al., 2025)(Lemmen et al., 2025), and Stage 5 (Bereavement) will be offered to families a minimum of three months following the death of their child, following established ethical guidelines(Helton et al., 2022).

The Stage Matched Intervention Program is operationalized through a structured framework designed to deliver proportionate, evidence-based psychosocial support to parent caregivers of children with leukemia. This model progresses linear and systematically from stage to stage, universal interventions, specialized care, ensuring that the level of support is precisely calibrated to the caregivers evolving psychological needs and adaptation over the twelve-weeks intervention period. The clinical pathway commences at the universal level with stage 1 where the caregivers are in the phase of Acute Crisis, Stage 2 in optimistic phase, stage 3 in instability phase, stage4 in cohesion and stage 5 is in the phase of adjustment. Figure 3 outlines the stages comprising the entire intervention strategies focusing key contents in the relevant weekly session.

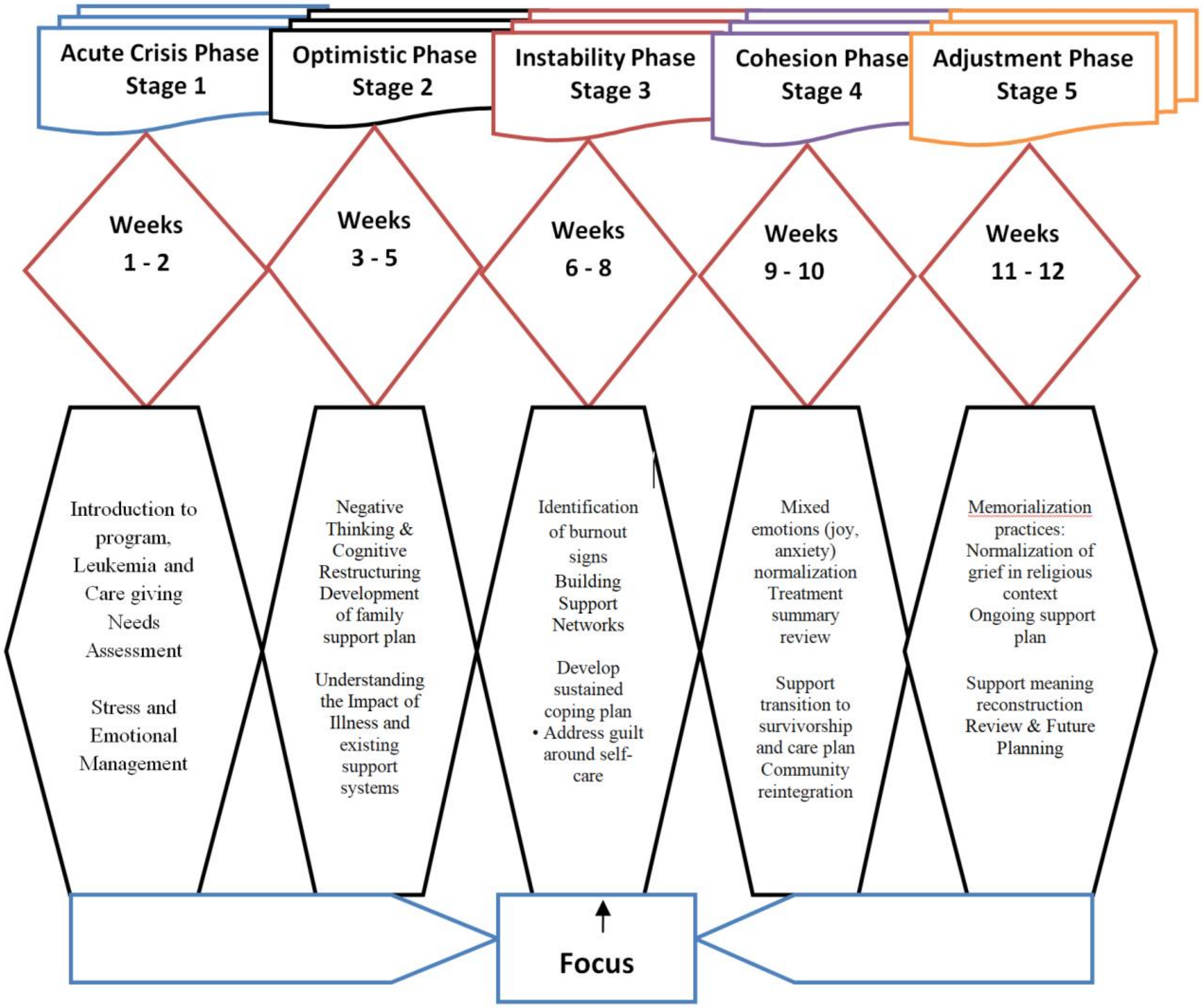

Figure 3: Stage Matched intervention delivery stages and time period

Through this graded and responsive structure, the Stage-Matched Intervention Program employs a structured, responsive approach to ensure caregivers receive the appropriate intervention at the optimal time from the most suitable provider, thereby enhancing clinical outcomes and the efficient use of healthcare resources. The stage-matched intervention is modified to be practical within Pakistani tertiary oncology care settings, culturally appropriate, mindful of resource limitations, and adaptable to local constraints. Additionally, the program's carefully designed yet flexible development process guarantees that the intervention is grounded in theory, contextually relevant, and methodologically sound.

2.4 Intervention Complexity Features and strategies for Stage Matched Intervention Program design

During our initial expert consultations and literature review to identify existing gaps, we identified several layers of complexity. These factors must be carefully considered in the development of the intervention. Table 3 outlines the sub- studies.

By the conclusion of this stage of the study, we will have established:

- The assessment method for (a) the psychological adaptation patterns of parent caregivers of children with leukemia and (b) the key challenges these caregivers face in managing their emotional and behavioral health, to modify the intervention to individual needs.
- What the contents of the intervention will be.
- How the intervention will be implemented, including the duration, frequency, venue, and mode of delivery.

Table 3 : Studies in the intervention development process.

Study	Purpose	Design and participants	Setting	Data analysis
Expert Consultation	To seek opinions of experts on the gaps in understanding the psychological adaptation challenges and possible stage-matched solutions for parent caregivers in Pakistan.	Expert professionals (clinical psychologists, pediatric oncologists, oncology nurses, psychiatric social workers) will: 1. Discuss the assessment and support of parent caregivers. 2. Analyse existing psychosocial interventions implementation.	Online/ face to face meetings	Transcription and content analysis of deliberations.
Needs analysis survey	To investigate the psychological adaptation needs and stage-specific challenges of parent caregivers of children with leukemia.	Parent caregivers will respond to a series of questionnaires to investigate their psychological distress, coping strategies, and stage of adaptation.	Participants will be recruited from the two pediatric oncology facilities included in the study.	Variable relationships will be explored using regression analyses.
Interviews with parent caregivers and healthcare professionals	Exploration of the psychological adaptation difficulties and stage-matched needs of parent caregivers of children with leukemia.	Semi-structured interviews will be conducted with parent caregivers and healthcare professionals (oncologists, nurses), Questions will focus on the adaptation challenges and support needs across different treatment stages.	At tertiary care hospital in Pakistan.	Nvivo software/ thematic analysis will be used to analyse transcribed content.
Focus group and Delphi	To elicit comments on the model stage-matched intervention.	Parent caregivers will be engaged in focus groups to give their opinions on the model intervention developed from integrated information from earlier stages. Professionals	Delphi will be e-Delphi, and focus groups will be at participating tertiary care facilities.	As with the first interview, transcription and content analysis of discussions will be done. Expert opinion will be analysed using two indicators: the degree of concentration and coordination

		(psychologists, oncologists, nurses) will give feedback through the Delphi process.		of experts' opinions.
Pilot RCT of Draft Intervention	To test the stage-matched psychological adaptation intervention for parent caregivers of children with leukemia in Pakistan.	A stage-matched intervention lasting 12 weeks with assessments conducted at baseline, mid-intervention, and end of intervention. 34 parent caregivers from each of the two study facilities (total N = 68).	A tertiary care hospital in Pakistan	Qualitative data will be transcribed and analysed. Two-tailed t-tests will be run for parametric quantitative data using 95% confidence intervals. Hedges' g formula, will be used to calculate effect sizes. Feasibility and acceptance will be measured by participants' ratings of the intervention's overall helpfulness. Baseline, midway, and post-intervention psychological adaptation and distress outcomes assessments will inform the program's initial efficacy.

2.5 Participants

During the program, we will interact with following sets of participants: (1) parent caregivers of children with leukemia from the two study facilities, (2) experts (working group) from across Pakistan. The detailed criteria for including or excluding members from each set will be specified further in the description of each phase. All participants must be able to provide consent to participate. These include:

i. Parent caregivers (biological parents or step-parents) primarily responsible for the daily care of a child diagnosed with leukemia, regardless of the child's treatment stage (diagnosis, active treatment, maintenance, or post-treatment).

ii. Professionals from disciplines related to the program's goals (pediatric oncology, clinical psychology, psychiatric social work, pediatric nursing, and community health).

2.5.1 Settings

The expert consultations and Delphi will take place online. The sub-studies (interviews, focus groups, and pilot intervention) will be conducted at hospitals, oncology centers, and convenient sites convenient sites agreed upon with parent caregivers.

2.5.2 Recruitment

The literature and professional contacts will inform the recruitment of expert participants. We will recruit parent caregivers of children with leukemia from pediatric oncology facilities in Pakistan (e.g., one in a major urban center like Peshawar and in a secondary city to capture diverse socioeconomic and cultural contexts).

2.6 Step-by-Step Design, Methods and Analyses

We have segmented the development program into four stages to accomplish our goals: (1) Identify the care gap and examine the current evidence on the influence of stage-matched interventions on psychological adaptation of parent caregivers of children with leukemia, (2) construct a model stage-matched intervention, (3) refine the model and draft an intervention, and (4) pilot the draft intervention.

2.7 Stage 1: Gap Definition and Evidence Scoping of the Impact of Stage-Matched Interventions on Psychological Adaptation of Parent Caregivers

2.7.1 Systematic Review of Literature

Objective: To evaluate the impact of stage-matched and psychosocial interventions on psychological adaptation, coping, and distress reduction in parent caregivers of children with leukemia.

Method: A systematic electronic database search will follow the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. The following key terms and their synonyms will be used: parent caregiver OR mother OR father OR family AND childhood leukemia OR pediatric cancer OR hematologic malignancy AND psychological adaptation OR coping OR distress OR quality of life OR mental health AND stage-matched intervention OR psychosocial support OR psychoeducation OR family intervention. Databases will include MEDLINE, Google Scholar, Cochrane Central Register of Controlled Trials, CINAHL, EMBASE, Web of Science, PsychINFO, Scopus, ClinicalTrials.gov, and the WHO international clinical trials registry. Bibliographies of relevant papers will also be searched to supplement data. Studies that report only child outcomes without parent outcomes will be excluded.

Studies will be included if:

1. They are randomised controlled trials, quasi-experimental studies.
2. Participants are parent caregivers (biological or non-biological) of children (aged 0–18 years) diagnosed with leukemia.
3. Interventions are psychosocial, psychological, or stage-matched targeting parent adaptation.
4. Outcomes include psychological adaptation, coping, distress, anxiety, depression, or quality of life.
5. Studies are published in English.

Analysis: Two independent researchers will screen titles and abstracts. If necessary, the supervisor will settle any disagreements through discussion. The following information will be extracted from the selected studies:

- Study characteristics: number of participants, parent age and gender, child age and leukemia subtype.
- Intervention design features: content and type of intervention, stage-matched components, duration and number of sessions, delivery mode, and follow-up period.

- Comparator: control group intervention (e.g., treatment as usual, waitlist, or alternative support).
- Outcome: data collection points, psychological adaptation measures, coping strategies, distress levels, and method of measurement.

The Cochrane Risk of Bias 2 tool(Cumpston et al., 2019) will be used to assess bias, and the analysed data will be documented in a narrative review. The GRADE(Guyatt et al., 2008) methodology will be employed to evaluate the certainty of evidence, and implementation will be checked against the TIDieR checklist.

The interventions in the included studies will be evaluated based on their impact on parent psychological adaptation, coping, distress, and quality of life, as well as the use of validated outcome measures and their theoretical basis. Studies that report effect sizes will be compared for intervention efficacy. These findings will inform the content and delivery strategies of the stage-matched intervention to be developed.

2.7.2 Gap Identification from Expert Professional's Experience

Objective: To gain insight from experts in the fields of pediatric oncology, clinical psychology, psychiatric social work, and pediatric nursing about the psychological adaptation challenges faced by parent caregivers of children with leukemia and potential stage-matched solutions to address these challenges.

Method: Two structured discussion meetings will be held. Each participant will share their responses to these questions: Could you outline the main areas of knowledge that are lacking in your professional opinion regarding parent caregivers of children with leukemia? What difficulties could arise if parent caregivers experience poor psychological adaptation? What potential stage-matched solutions would you propose for addressing these challenges across different phases of the child's treatment (diagnosis, active treatment, maintenance, relapse, or post-treatment)? The experts will be advised to focus on their direct research and clinical experience.

Participants: Expert professionals selected through a quick review of literature and recommendations from practitioners in the field will be invited for an expert consultation. These experts will cover various disciplines and will come from across Pakistan, including both urban and rural healthcare settings.

Analysis: Thematically we will analyse the experts' responses to identify priority gaps.

2.8 Stage 2: Model Stage-Matched Intervention Development

At this stage, our important goal is to compile a set of modules to promote psychological adaptation in parent caregivers of children with leukemia and provide examples of the implementation of psychosocial interventions in pediatric oncology settings. These will be used to create a model stage-matched intervention. We will conduct various research activities aimed at identifying the key challenges to psychological adaptation and determining the most effective methods for implementing intervention, incorporating insight from experts, parent caregivers, and where appropriate, children with leukemia.

To ensure the stage-matched intervention is rigorous and relevant contextually, the systematic review and expert interview findings will be integrated into each phase of the intervention design. The systematic review will synthesise existing evidence regarding psychosocial support strategies and their effects on parent caregiver adaptation, highlighting key themes such as effective coping techniques, stage-specific needs, and identifying gaps in current approaches. The findings will inform the theoretical foundation of the intervention, specifically the integration of stage-matched models (e.g., transactional family adaptation model) and psychological adaptation frameworks.

Additionally, insights from expert interviews with pediatric oncologists, psychologists, nurses, and parent caregivers will offer practical perspectives on implementation challenges and cultural nuances in Pakistan. Interviews may identify specific barriers, such as stigma, financial stress, family dynamics, and gender roles, which can be addressed through tailored psychoeducational components. Thematic analysis of interview data will enhance intervention delivery methods and ensure content accessibility across diverse literacy levels and linguistic backgrounds.The research team will utilise the Intervention Mapping framework to synthesize these inputs, converting evidence into actionable behavioural objectives, such as enhancing problem-focused coping, seeking social support, and employing emotion regulation techniques, and employing theory-based change methods, including role-playing exercises, guided imagery, and peer support. Discrepancies between the literature and stakeholder feedback will be addressed through consensus in the e-Delphi process, ensuring that the final intervention integrates evidence-based rigour with practical feasibility. This iterative approach guarantees that the final intervention maintains a balance between evidence-based rigour and real-world feasibility, rendering it both theoretically strong and practically suitable for the needs of parent caregivers of children with leukemia in Pakistan.

2.8.1 Identifying the Modules and Intervention Implementation from the Viewpoints of Parent Caregivers

Objective: To establish the psychological adaptation challenges of parent caregivers of children with leukemia from the perspectives of the caregivers themselves and, where appropriate, their children.

Method: This will be a mixed-methods research at the two study sites. The quantitative part will be a researcher-administered survey of parent caregivers of children with leukemia. The questionnaires will include: (1) sociodemographic information, (2) Psychological Adaptation Scale (PAS), (3) Caregiver burden scale, (4) Depression Anxiety and Stress Scale (DASS-21), (5) Perceived Social Support Questionnaire).

The qualitative study will consist of semi-structured interviews with parent caregivers of children with leukemia. This will attempt to identify the psychological adaptation challenges, coping mechanisms, and support needs across different treatment stages (diagnosis, active treatment, maintenance, relapse, bereavement, or survivorship).

Sample size: We will recruit 20 parent caregivers from each study facility (n = 40).

Participants: Parent caregivers (biological parents or guardians) of children diagnosed with leukemia, regardless of the child's treatment stage.

Analysis: Descriptive and quantitative methodologies will be used to analyse questionnaire data to determine the psychological adaptation challenges and their correlates. Transcribed audio recordings will undergo thematic analysis(Braun and Clarke, 2006). Drawing upon existing literature and theoretical basis, a research inquiry will be formulated to establish a framework for identifying pertinent data. The subsequent phase of data coding will entail category extraction from the data determined to be relevant to the research inquiry. Significant parent caregiver areas of need will be identified through an analysis that examines the main categories and discussion topics.

2.8.2 Identifying the Modules and Intervention Implementation from the Viewpoints of Professionals

We will use semi-structured interviews to elicit experts' viewpoints on the most appropriate intervention content and mode of implementation for stage-matched psychological adaptation support.

2.8.2.1 Expert Consultation

Objective: To elicit experts' opinions on assessing and managing psychological adaptation challenges of parent caregivers of children with leukemia.

Method: Expert consultation will analyse the implementation methods of existing psychosocial management trials for parent caregivers in pediatric oncology settings.

Analysis: We will utilise an expert forum to gather insights on the application of selected published protocols for psychosocial interventions in parent caregivers of children with cancer. The study team will select trials based on rigorous methodology, such as randomised, fully powered, rater-blinded, and placebo-controlled efficacy trials focusing on parent caregiver adaptation and adherence to MRC Guidance on complex interventions in hospital or home-based settings.

Further, the experts will be requested to evaluate the available possibilities and choose the most appropriate approach for implementing our stage-matched communication and adaptation intervention. The options appraisal will employ the TOWS approach(Chopra et al., 2025). This tool functions as a decision-support framework, using a matrix to systematically compare and evaluate external threats ("T") and opportunities ("O") against the internal strengths ("S") and weaknesses ("W") of the study team's capabilities. The matrix will draw upon the various methodologies utilized throughout the trials. The results generated by this decision-making tool will guide the selection of the implementation model for the upcoming stage-specific support trial.

2.8.2.2 Professionals' Semi-Structured Interviews

Objective: To determine the psychological adaptation needs of parent caregivers of children with leukemia from the professionals' perspective.

Method: A variety of pertinent specialists, both clinical and academic, will participate in semi-structured interviews to explore the psychological adaptation difficulties that parent caregivers of children with leukemia encounter. The structure of the interviews will be similar to parent caregiver interviews.

Participants: Pediatric oncologists, clinical psychologists, psychiatric social workers, pediatric oncology nurses, and community health workers will be interviewed.

Analysis: Transcribed interviews from all participants will be analysed with Nvivo(Dhakal, n.d.) and be subjected to thematic analysis(Braun and Clarke, 2006).

2.9 Stage 3: Model Stage-Matched Intervention Refinement in to a Draft

The components of the intervention model, developed based on insights collected in Stages 1 and 2, will be further refined for clarity and effectiveness. The model will be sent to expert professionals for their recommendations and. corrections This will include semi-directed focus groups with parent caregivers and a Delphi with relevant professionals. During each study activity, we will present the details of the model intervention and ask in-depth questions to gather perspectives and feedback on the practicality, acceptability, and how tolerable each aspect of the model intervention is.

2.9.1 Focus Group and Delphi process

Objective: To identify means of intervention application and the contents of the model from the perspectives of parent caregivers of children with leukemia, and experts.

Method: We will organize focus groups, each lasting 1 to 2 hours, with parents caring for children with leukemia. During these sessions, the intervention model developed from available resources and insights gathered in earlier stages, will be reviewed. The focus groups will evaluate the materials in terms of their effectiveness, usability, and capacity to support the psychological adaptation of parent caregivers. In parallel, experts will provide ratings and feedback on the model through an e-Delphi process.

Participants: Focus groups will consist of eight participants per group (parent caregivers of children with leukemia) per facility. Delphi will consist of multidisciplinary experts (approximately 8–10 members) across the various disciplines.

Analysis: Transcription and thematic analysis will be applied to the conversations.the degree of concentration and coordination of experts' opinions will be analysed through Delphi process.

2.10 Stage 4: Pilot Trial of the Stage-Matched Intervention Draft

The last stage of the program involves testing the stage-matched psychological adaptation intervention with a population representing the participants expected to participate in a large-scale randomised controlled trial if the pilot trial produces positive productive result results. This stage is only described briefly; although the detailed procedure will be described in a protocol for the pilot trial.

Objective: The pilot trial aims to:

1. Evaluate the feasibility of the stage-matched psychological adaptation intervention among parent caregivers of children with leukemia and the acceptability of the intervention by participants.
2. Preliminarily investigate the efficacy of the intervention in improving psychological adaptation, coping, and reducing distress in parent caregivers.
3. Examine the acceptability of the stage-matched psychological adaptation intervention among parent caregivers of children with leukemia.

Method: This study will use a two-arm pilot randomized controlled trial design involving parent caregivers of children with leukemia in two facilities of a tertiary care hospital in Pakistan. To simplify implementation and minimize contamination, each facility will be randomly assigned to either the intervention or control group.

The intervention group will receive stage-matched psychological adaptation program alongside routine medical care, while the control group will continue with standard routine medical care. Cluster randomization at the facility level is employed to prevent potential spillover effects that could occur with individual randomization within the same setting. This approach reflects real-world practice, where interventions are typically implemented at the organizational level across entire facilities rather than targeting individual participants. Using cluster randomization also enhances intervention fidelity by allowing consistent delivery and standardized staff training within each facility. Moreover, it aligns the study design with practical implementation conditions by accounting for variations in resources, workflows, and procedures across different facilities.

Participants: Parent caregivers (biological parents or step-parents of children diagnosed with leukemia. Participants who plan to relocate outside the study area during the study period will be excluded. The sample size estimation was initially derived using individual-level power calculations.

Sample size: The sample size was selected to (1) provide precise estimates of key feasibility parameters (e.g., recruitment rate, retention, adherence), (2) align with published pilot trial recommendations (Ying et al., 2025),and (3) reflect sample sizes used in comparable psychosocial intervention pilots in pediatric oncology settings(Koyu and Kilicarslan, 2024). We aim to recruit N = 70 parent caregivers (35 per arm). This sample size allows estimation of a 75% retention rate with a 95% confidence interval width of ±13%. Accounting for an anticipated 25% attrition rate common in LMIC psychosocial trials, we will recruit up to 88 participants. This sample is sufficient to assess feasibility, acceptability, and preliminary effects, while informing sample size calculations for a future definitive RCT.

Setting: The study will be conducted in a tertiary care hospital in Pakistan providing pediatric oncology services.

Study procedures: The study will be conducted over 12 weeks, with interventions delivered by trained mental health professionals and outcome assessments carried out by research assistants. After recruitment, participants will provide informed consent and be screened for eligibility. Caregivers in the intervention group will receive a stage-matched psychological adaptation program based on the transactional family adaptation model and culturally adapted coping strategies. The final intervention protocol will be developed after the initial three stages.

Outcome evaluations will be conducted at baseline, mid-intervention, and post-intervention to assess feasibility, acceptability, adherence, and effectiveness, using methods such as diaries, observations, and satisfaction measures. At the end of the study, caregivers will participate in semi-structured interviews and complete questionnaires to evaluate outcomes. Additionally, professionals delivering the intervention will be interviewed to identify strengths of the trial and assessment methods. Key outcomes include improved psychological adaptation, reduced distress, enhanced coping skills, and better quality of life among caregivers. Figure 4 summarizes the whole procedure for the pilot RCT.

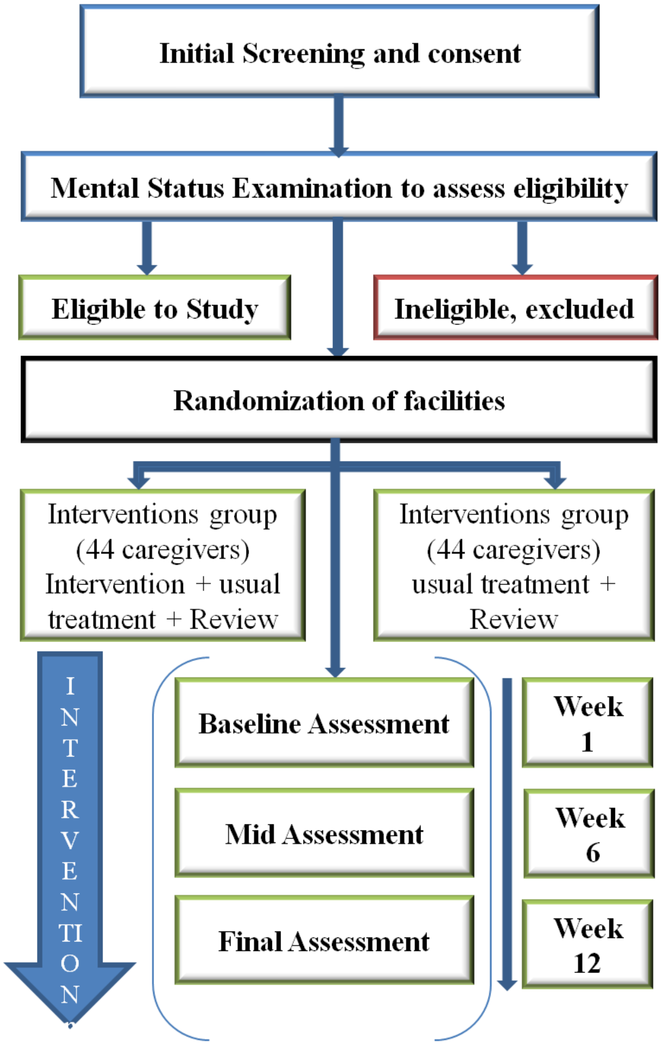

Figure 3 Flowchart of pilot RCT of stage matched intervention draft

2.10.1 Method of Outcome and Process Evaluation

Preliminary psychosocial outcomes (psychological adaptation, distress, coping, and quality of life) will be assessed using validated tools such as the (1) sociodemographic information, (2) Psychological Adaptation Scale (PAS)(Biesecker et al., 2013), (3) Depression Anxiety and Stress Scale (DASS-21) (Lovibond&Lovibond, 1995), (4) Caregiver burden scale(Zarit et al., 1980)., (5) Perceived Social Support Questionnaire) l(Zimet et al., 1988).The Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM)(Glasgow et al., 1999) framework will be utilized for implementation outcomes.Process evaluation will examine feasibility outcomes (fidelity, acceptability, participant compliance, attendance, and assignment completion records, journal entries, qualitative interviews on perceived changes, and recruitment rate). The Client Satisfaction Questionnaire (CSQ-8) will be used for acceptability, with measures such as audio recordings, direct observation, and supervision logs as fidelity monitoring procedures.

Analyses: Detailed demographic and baseline characteristics will be provided, and all findings will be systematically analysed and documented. Quantitative analysis will cover recruitment and retention rates, participants' responses to the intervention, and session frequency and duration, as measured by the Client Satisfaction Questionnaire (CSQ). Qualitative interview data will be analysed using the same approach applied in the earlier stages of the program. The preliminary findings from the pilot RCT will decide whether we will advance to a comprehensive efficacy trial. This decision will be based on a comprehensive process evaluation of the intervention components, implementation, and trial procedures. Key considerations will include participant feedback on the acceptability, feasibility, and tolerability of the intervention, as well as the relevance and practicality of the outcome measures. These criteria and decision-making processes will be clearly specified in the pilot RCT protocol.

2.11 Integrating Data From the Outputs of Various Stages

The results from each stage of the program will be integrated using triangulation principles, following the guidance provided byBrannen(Brannen, 2005). This process will involve carefully integrating all collected data, taking into account the relative weight of each piece of evidence. Methods will include cross-referencing multiple sources to validate findings, adding contextual details to enrich results, and using conflicting data to generate new research questions. The study team will determine the weight assigned to each evidence source, guided by existing literature and the rigor of the data collection methods.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 researcher will oversee the collection and management of data at each stage of the program. All data will be securely stored in password-protected files and used exclusively for research purposes. Identifiable participant information will be kept separately to maintain confidentiality. Access to the data will be limited to authorized investigators and regulatory bodies. Each participant will be assigned a unique code to ensure anonymity in all documents and electronic records. Quantitative and qualitative data will be entered using pseudonyms, and audio recordings will be deleted once notes are reviewed. All study records will be permanently destroyed 10 years after the completion of the research.

2.13 Distribution

The distribution strategy for this program has two main objectives. First, it will generate internal reports that summarize the outcomes of each program activity, helping the research team make informed decisions for future phases. Second, it will produce manuscripts and reports for external dissemination, including lay-language materials about the intervention and scholarly articles for peer-reviewed journals. Scientific contributions will include systematic literature reviews, analyses of psychological adaptation challenges from the perspectives of caregivers and healthcare professionals, a detailed account of the pilot-tested stage-matched intervention, a process evaluation of the pilot RCT, preliminary effectiveness reports, and documentation of the program development protocol.

2.14 Timeline

The overall timeline will take approximately 16 months to complete. Stage 1 of the study will be within the first 2 months, Stage 2 from the 2nd to 6th month, Stage 3 from the 6th to 8th month, and Stage 4 from the 8th to the 16th month of the study period..

2.15 Ethics

Ethical approval was obtained from the Ethics Review Board of Zhengzhou University in China (ZZUIRB2025-02) Administrative approval(2773-2025) was also obtained from the respective tertiary care hospital administrations in Pakistan prior to the commencement of data collection. Further Informed consent was be obtained from all parent caregivers,

3 Discussion

This protocol outlines the systematic development of a stage-matched intervention designed to enhance the psychological adaptation of parent caregivers of children with leukemia in Pakistan, following the Intervention Mapping**(Eldridge et al., 2016)** framework and MRC**(Skivington et al., 2021b)** guidance for complex interventions . The combination of qualitative and quantitative approaches ensures a culturally appropriate intervention while maintaining methodological integrity. This study is grounded in an integrated framework combining the transactional theory of stress and coping and the double ABC-X model of family stress and adaptation. Moreover this protocol establishes a robust foundation for addressing the multifaceted psychological needs of this vulnerable population. This discussion addresses the critical need for such an intervention, the challenges specific to the Pakistani context, the evidence base for stage-matched approaches, and the implementation considerations for low- and middle-income countries (LMICs). Specifically it addresses significant deficiencies in Pakistan's mental health support system for families affected by childhood cancer. Pakistan has a childhood cancer incidence of approximately 8,000–12,000 new cases annually(Sohail AfzaL, 2020),**(Graetz et al., 2023)**, yet psychosocial support services remain severely limited into routine cancer care, with few dedicated pediatric psycho-oncology programs available. Furthermore, studies from Pakistan have demonstrated that parent caregivers experience high levels of anxiety, depression, and caregiver burden**(Sajjad et al., 2025)(Salyani et al., 2025)**, with treatment access hindered by stigma, financial constraints, and geographic disparities. Our supportive care, stage-matched intervention is consistent with national objectives to decentralize mental health care beyond hospital based approaches. By adapting evidence-based models to local cultural frameworks, this protocol presents a scalable solution to diminish psychological distress and ehnace adaptation in parent caregivers of children with leukemia while utilizing existing hospital infrastructure and personnel.

Several challenges and considerations must be addressed to enhance the intervention's applicability and scalability. Stigma represents a considerable obstacle in mental health interventions for parent caregivers of children with cancer, potentially discouraging family involvement and help-seeking behaviour**(Kaushal et al., 2022)**. Our design will incorporate sensitization programs and anonymous feedback mechanisms to promote engagement through culturally sensitive recruitment, developmentally appropriate materials, and integration of locally relevant coping concepts.. Retention of the participants also significantly influenced by socioeconomic factors, including transportation expenses, lost wages from time off work, and conflicting caregiving obligations **(Marusak et al., 2018)**. We address this obstacle by providing flexible scheduling, for those living far from the facilities and their coordination with the healthcare facilities.

Ensuring intervention fidelity can be difficult, particularly when delivery relies on non-specialists in low-resource settings. To address this, standardized manuals for both facilitators and participants will be used, along with regular supervision by clinical psychologists and session audio recordings for quality monitoring. These strategies align with the RE-AIM framework’s implementation domain**(Glasgow et al., 1999)**, emphasizing adherence to protocols while allowing for necessary contextual adjustments. The complexity of the intervention requires strong monitoring systems to ensure consistent delivery across participants, settings, and over time.

The primary objective of this intervention is to achieve integration within Pakistan's pediatric oncology and mental health services. Using the MRC translational framework to guide the process(Skivington et al., 2021a), we delineate a phased scale-up pathway: (1) pilot testing to establish feasibility,(2) Refined based on stakeholder feedback, and (3) policy advocacy for integration into standards of care services Pakistan. This method reflects the effective scale-up of analogous interventions (LSMIP) in low- and middle-income countries where both health care infrastructures and professionals are limited.

Sustainability depends on the development of capacity. Hospital staff will be trained to deliver the intervention, a strategy shown to maintain fidelity even after the trial ends. Additionally, feasibility and acceptability data from the pilot will directly inform implementation planning for policymakers and administrators, focusing on the adoption and maintenance dimensions of RE-AIM.

Limititions

This pilot will be conducted within a single tertiary hospital, potentially limiting applicability to urban, well-resourced settings. Future research should involve multiple centers, including rural and underserved areas, where childhood cancer cases are diagnosed later and mental health resources are scarce. The study's reliance on self-reported measures may introduce social desirability bias, so integrating clinician-rated or observational assessments is recommended. The 12-week follow-up is insufficient for assessing long-term effects, so extended evaluations are needed. While culturally adaptable, further contextual adjustments may be required for specific subpopulations. Additionally, the pilot's small sample size limits statistical power; thus, a larger, multi-site trial is necessary to confirm efficacy. Lastly, excluding parents of children in the acute illness phase means findings may not reflect the highest-stress periods of the cancer journey. Additionally, the pilot RCT design with only two clusters (one intervention, one control facility) limits the statistical power for definitive hypothesis testing; therefore, the primary goal of this pilot study is to assess feasibility, acceptability, and preliminary efficacy, following CONSORT guidelines for pilot and feasibility trials(Eldridge et al., 2016). A fully powered multi-site randomized controlled trial would be required to establish definitive efficacy.

References

Avsec, A., Eisenbeck, N., Carreno, D.F., Kocjan, G.Z., Kavčič, T., 2022. Coping styles mediate the association between psychological inflexibility and psychological functioning during the COVID-19 pandemic: A crucial role of meaning-centered coping. J. Context. Behav. Sci. 26, 201–209.

Bashir, N., Ain, Q. ul, Karim, N.-E.-, Niazi, H., Khan, M.I., Asghar, A.K., 2024. Assessment of Post-Traumatic Stress Disorder and Role of Spirituality Amongst Caregivers of Pediatric Cancer Patients in Pakistan. Life Sci. 5, 08–08. https://doi.org/10.37185/LnS.1.1.440

Bashir, N., Khan, M.A., Ikram, S., Hassan, M.S. ul, Siddiqui, R., Rafaqat, N., 2025. Assessing Post Traumatic Stress Disorder (PTSD) and Evaluating Gratitude-Based Coping Strategies for Caregivers of Pediatric Cancer Patients. J. Postgrad. Med. Inst. 39. https://doi.org/10.54079/jpmi.39.3.3522

Bekui, B.A., Ohene, L.A., Badzi, C., Ampomah, M.O., Aziato, L., 2023. Physical and socioeconomic burden of caregiving on family caregivers of children with cancer at a tertiary Hospital in Ghana. Nurs. Open 10, 915–925.

Biesecker, B.B., Erby, L.H., Woolford, S., Adcock, J.Y., Cohen, J.S., Lamb, A., Lewis, K.V., Truitt, M., Turriff, A., Reeve, B.B., 2013. Development and validation of the Psychological Adaptation Scale (PAS): Use in six studies of adaptation to a health condition or risk. Patient Educ. Couns. 93, 10.1016/j.pec.2013.05.006. https://doi.org/10.1016/j.pec.2013.05.006

Biggs, A., Brough, P., Drummond, S., 2017. Lazarus and Folkman’s psychological stress and coping theory. Handb. Stress Health Guide Res. Pract. 349–364.

Bradford, N., Cashion, C., Sharwood, E., Rumble, S., Condon, P., Cossio, D., Stratton, H., Ekberg, S., Semerci, R., Bowers, A., 2025. Co-Design and Evaluation Protocol for the RECOVER Model of Care After Childhood Cancer Treatment, in: Healthcare. MDPI, p. 454.

Brannen, J., 2005. Mixing Methods: The Entry of Qualitative and Quantitative Approaches into the Research Process. Int. J. Soc. Res. Methodol. 8, 173–184. https://doi.org/10.1080/13645570500154642

Braun, V., Clarke, V., 2006. Using thematic analysis in psychology. Qual. Res. Psychol. 3, 77–101.

Chopra, A., Shastry, S., Mohan, G., Chenna, D., Rajendran, V., 2025. A Comprehensive SWOT and TOWS analysis of transfusion medicine: Indian Perspective. Transfus. Apher. Sci. 64, 104061. https://doi.org/10.1016/j.transci.2024.104061

Cumpston, M., Li, T., Page, M.J., Chandler, J., Welch, V.A., Higgins, J.P., Thomas, J., 2019. Updated guidance for trusted systematic reviews: a new edition of the Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Database Syst. Rev. 10, ED000142. https://doi.org/10.1002/14651858.ED000142

Dhakal, K., n.d. NVivo. J. Med. Libr. Assoc. JMLA 110, 270–272. https://doi.org/10.5195/jmla.2022.1271

Eldridge, S.M., Chan, C.L., Campbell, M.J., Bond, C.M., Hopewell, S., Thabane, L., Lancaster, G.A., 2016. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. bmj 355.

Faran, K., Ahmed, A., 2018. Challenges faced by Pakistani healthcare system: clinician’s perspective.

Ferlay, J., Colombet, M., Soerjomataram, I., Dyba, T., Randi, G., Bettio, M., Gavin, A., Visser, O., Bray, F., 2018. Cancer incidence and mortality patterns in Europe: Estimates for 40 countries and 25 major cancers in 2018. Eur. J. Cancer 103, 356–387. https://doi.org/10.1016/j.ejca.2018.07.005

Glasgow, R.E., Vogt, T.M., Boles, S.M., 1999. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. Am. J. Public Health 89, 1322–1327. https://doi.org/10.2105/AJPH.89.9.1322

Graetz, D., Ahmad, A., Raza, M.R., Hameed, A., Naheed, A., Najmi, A., Tul Quanita, A., Munir, S., Ferrara, G., Staples, C., Rodriguez Galindo, C., Hamid, S.A., Jeha, S., Mack, J.W., 2023. Barriers and

Facilitators of Quality Family-Centered Communication in Pakistan. JCO Glob. Oncol. e2300178. https://doi.org/10.1200/GO.23.00178

Graetz, D.E., Wardell, J., Hameed, A., Najmi, A., Ahmad, S., Shafiq, M., Naheed, A., Munir, S., Ferrara, G., Staples, C., 2025. Communication practices and information exchange for caregivers of children with cancer in Pakistan. Front. Oncol. 15, 1616467.

Guyatt, G.H., Oxman, A.D., Vist, G.E., Kunz, R., Falck-Ytter, Y., Alonso-Coello, P., Schünemann, H.J., GRADE Working Group, 2008. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 336, 924–926. https://doi.org/10.1136/bmj.39489.470347.AD

Helton, G., Beight, L., Morris, S.E., Wolfe, J., Snaman, J.M., 2022. One Size Doesn't Fit All in Early Pediatric Oncology Bereavement Support. J. Pain Symptom Manage. 63, 366–373. https://doi.org/10.1016/j.jpainsymman.2021.10.016

Huang, Y., Chen, M., Zhang, Y., Chen, X., Zhang, L., Dong, C., 2023. Finding family resilience in adversity: A grounded theory of families with children diagnosed with leukaemia. J. Clin. Nurs. 32, 5160–5172.

Javed, S., Nazir, A., 2025. Cultural Narratives, Social Norms, and Mental Health Stigma in Peshawar, Pakistan: Implications for Help-Seeking Behavior. J. Int. Relat. Soc. Dyn. 4, 85–96.

Kaushal, T., Satapathy, S., Bakhshi, S., Sagar, R., Chadda, R.K., 2022. A parent–child conjoint psychological intervention for children in maintenance phase of acute lymphoblastic leukemia: Feasibility and preliminary outcomes from a randomized control pilot trial. Arch. Pédiatrie 29, 145–152. https://doi.org/10.1016/j.arcped.2021.11.004

Koyu, H.O., Kilicarslan, E., 2024. Efficiency of the Technology-Based "HomeCARE-Family EmPow" for Children with Cancer and Their Parents: A Study Protocol for a Randomized Controlled Trial. Semin. Oncol. Nurs. 40, undefined-undefined. https://doi.org/10.1016/j.soncn.2024.151616

Kumari, R., Kohli, A., Malhotra, P., Grover, S., Khadwal, A., 2018. Burden of caregiving and its impact in the patients of acute lymphoblastic leukemia. Ind. Psychiatry J. 27, 249. https://doi.org/10.4103/ipj.ipj_75_18

LAVEE, Y., MCCUBBIN, H.I., PATTERSON, J.M., 2003. THE DOUBLE ABCX MODEL OF. Fam. Stress Class. Contemp. Read. 123.

Lavee, Y., McCubbin, H.I., Patterson, J.M., 1985. The double ABCX model of family stress and adaptation: An empirical test by analysis of structural equations with latent variables. J. Marriage Fam. 811–825.

Lazarus, R.S., 1984. Stress, appraisal, and coping. Springer.

Lemmen, J., Mageto, S., Vik, T., Olbara, G., Kaspers, G., Njuguna, F., 2025. Non-randomised prospective clinical trial to improve follow-up adherence, survivorship knowledge and late effects documentation at a childhood cancer clinic in Western Kenya: a study protocol. BMJ Open 15, e096741.

Liu, Q., Petrini, M.A., Luo, D., Yang, B.X., Yang, J., Haase, J.E., 2021. Parents' Experiences of Having a Young Child With Acute Lymphoblastic Leukemia in China. J. Pediatr. Oncol. Nurs. 38, 94–104. https://doi.org/10.1177/1043454220975463

Lovibond, P.F., Lovibond, S.H., 1995. The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories. Behav. Res. Ther. 33, 335–343.

Marusak, H.A., Iadipaolo, A.S., Harper, F.W., Elrahal, F., Taub, J.W., Goldberg, E., Rabinak, C.A., 2018. Neurodevelopmental consequences of pediatric cancer and its treatment: applying an early adversity framework to understanding cognitive, behavioral, and emotional outcomes. Neuropsychol. Rev. 28, 123–175. https://doi.org/10.1007/s11065-017-9365-1

Maryam, B., Saeed, T., Altaf, S., Ali, B., 2022. Comparing the needs of supportive care for families and patients with pediatric cancer: A perspective of patients, caregivers and oncology health professionals. Pak. J. Rehabil. 11, 115–125.

Mess, E., Misiąg, W., Klaszczyk, T., Kryś, K., 2022. Depressive and Anxiety Disorders of Parents of Children with Cancer. J. Clin. Med. 11, 5670. https://doi.org/10.3390/jcm11195670

Metrics, I., 2019. Evaluation, Global Burden of Disease Collaborative Network. Global Burden of Disease Study 2016 (GBD 2016) Results. 2017. Inst. Health Metr. Eval. Seattle.

Norcross, J.C., Krebs, P.M., Prochaska, J.O., 2011. Stages of change. J. Clin. Psychol. 67, 143–154. https://doi.org/10.1002/jclp.20758

Organization, W.H., 2021. Summary report on the regional consultation meeting on the Global Initiative for Childhood Cancer, virtual meeting, 25-26 January 2021. World Health Organization. Regional Office for the Eastern Mediterranean.

Perkins, A., 2022. Trauma and growth in parents of children with chronic illness and brain injury (PhD Thesis). University of East Anglia.

Rachmad, Y.E., 2022. Psychological Adaptation Theory.

Rafiq, K., Batool, S.Y., Fatima, K., Mushtaq, M., Sultana, N., Saify, Z.S., 2025. Barriers and Attitudes toward Psychotherapy in Pakistan: A Cross-Sectional Study. Yemeni J. Med. Sci. 19.

Romain, A.J., Bortolon, C., Gourlan, M., Carayol, M., Decker, E., Lareyre, O., Ninot, G., Boiché, J., Bernard, P., 2018. Matched or nonmatched interventions based on the transtheoretical model to promote physical activity. A meta-analysis of randomized controlled trials. J. Sport Health Sci. 7, 50–57. https://doi.org/10.1016/j.jshs.2016.10.007

Saeed, S., Malik, M.G.R., Khan, M.H., Malik, S.A.R., Aziz, B., 2024. Care for the caregiver: an exploration of caregiver burden of children with chronic medical conditions at a tertiary care hospital in Karachi, Pakistan–a mixed-methods study. BMJ Open 14, e083088.

Sajjad, S., Barolia, R., Gul, R.B., 2025. Living With Cancer: Child–Parent Dyads' Perspectives and Experiences From a Private Tertiary Care Hospital in Pakistan. Qual. Health Res. 35, 174–189. https://doi.org/10.1177/10497323241255636

Salyani, A.N.A., Rattani, S., Khowaja, A., Altaf, S., Resham, S., Badruddin, P., Aslam, Z., 2025. Parents' perspective of caring for their children identified with oncological disorders: a qualitative study. Int. J. Palliat. Nurs. 31, 562–570. https://doi.org/10.12968/ijpn.2025.0002

Sharp, K., Tillery, R., Long, A., Wang, F., Pan, H., Phipps, S., 2022. Trajectories of resilience and posttraumatic stress in childhood cancer: Consistency of child and parent outcomes. Health Psychol. 41, 256.

Skivington, K., Matthews, L., Simpson, S.A., Craig, P., Baird, J., Blazeby, J.M., Boyd, K.A., Craig, N., French, D.P., McIntosh, E., 2021a. Framework for the development and evaluation of complex interventions: gap analysis, workshop and consultation-informed update. Health Technol. Assess. Winch. Engl. 25, 1.

Skivington, K., Matthews, L., Simpson, S.A., Craig, P., Baird, J., Blazeby, J.M., Boyd, K.A., Craig, N., French, D.P., McIntosh, E., Petticrew, M., Rycroft-Malone, J., White, M., Moore, L., 2021b. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. https://doi.org/10.1136/bmj.n2061

SOHAIL AFZAL, M., 2020. Childhood Cancer in Pakistan. Iran. J. Public Health 49, 1579. https://doi.org/10.18502/ijph.v49i8.3908

Sulkers, E., Tissing, W.J.E., Brinksma, A., Roodbol, P.F., Kamps, W.A., Stewart, R.E., Sanderman, R., Fleer, J., 2015. Providing care to a child with cancer: a longitudinal study on the course, predictors, and impact of caregiving stress during the first year after diagnosis. Psychooncology. 24, 318–324. https://doi.org/10.1002/pon.3652

Tang, X., Mo, L., Liu, Q., Liu, Yixuan, Yu, L., Liu, Yang, Gao, C., 2022. Adverse experiences of social adaptation in children with leukaemia: a qualitative study from China. BMJ Open 12, e051953. https://doi.org/10.1136/bmjopen-2021-051953

Tran, S.T., Bieniak, K., Bedree, H., Adler, M., Ogunmona, S., Kovar-Gough, I., Ma, W., Thabrew, H., Cunningham, N.R., 2025. Systematic review and meta-analysis of the effect of psychological interventions on anxiety in children and youth with chronic medical conditions. J. Pediatr. Psychol. 50, 658–675.

Ververidou, M., Petarouda, N., Vaina, A., Perdikaris, P., 2023. The psychological aspects of parents who take care of children with chronic illnesses: A Review of the literature. World J. Adv. Res. Rev. 19, 1136–1176. https://doi.org/10.30574/wjarr.2023.19.2.1612

Wang, M.-J., Chang, M.-Y., Gu, C.-F., Zhang, R.-X., 2025. Psychological adaptation profiles are associated with coping style, social support, and family intimacy in caregivers of children with hematologic malignancies: a cross-sectional study. BMC Nurs. 24, 221. https://doi.org/10.1186/s12912-025-02873-9

Wechsler, A.M., Bragado-Álvarez, C., Hernández-Lloreda, M.J., Lopes, L.F., Perina, E.M., 2024. Parental perspective on the psychological adjustment of children in cancer relapse or remission. Estud. Psicol. Camp. 41, e210164. https://doi.org/10.1590/1982-0275202441e210164

Ying, X., Freedland, K.E., Powell, L.H., Stuart, E.A., Ehrhardt, S., Mayo-Wilson, E., 2025. Determining sample size for pilot trials: a tutorial. BMJ 390, e083405. https://doi.org/10.1136/bmj-2024-083405

Zarit, S.H., Reever, K.E., Bach-Peterson, J., 1980. Relatives of the impaired elderly: correlates of feelings of burden. The gerontologist 20, 649–655.

Zimet, G.D., Dahlem, N.W., Zimet, S.G., Farley, G.K., 1988. The multidimensional scale of perceived social support. J. Pers. Assess. 52, 30–41.