Efficacy of a culturally tailored cognitive-behavioural intervention for Ethiopian children with haematological malignancies: study protocol for randomised controlled trial

Tenaw Gualu Melesse1,2*, Janita Pak Chun Chau1 and William Ho Cheung Li1

Abstract

Background: Paediatric cancer patients often experience anxiety and depression. Evidence suggests that cognitive-behavioural interventions may help reduce anxiety and depression in children undergoing cancer treatment. However, only a few studies evaluated its impact on the psychological well-being and quality of life of paediatric cancer patients globally. In Ethiopia, there has been no published study to date. Thus, this trial aims to evaluate the efficacy of a culturally tailored cognitive-behavioural intervention for Ethiopian children with haematological malignancies receiving chemotherapy.

Methods: A single-blinded, parallel-group, two-arm, repeated measure randomised controlled trial will be conducted. Eighty children aged 8 – 18 years with haematological malignancy receiving chemotherapy will be recruited and randomly assigned to experimental or control groups. The experimental group will receive five sessions of introducing cognitive-behavioural intervention, identifying and modifying maladaptive thoughts and behaviour, behavioural activation, practising deep breathing exercises, reassessing goals or treatment plans, and encouraging participants to maintain changes. Each session will be conducted face-to-face for 30–35 min a week. The control group will receive usual care. The outcomes will be measured at baseline, post-intervention, and one month after the intervention using the Revised Child Anxiety and Depression Scale and Paediatric Quality of Life Inventory Generic Core Score 4.0.

Discussion: The findings of this study will provide evidence to support the integration of culturally effective cognitive-behavioural intervention strategies into paediatric oncology practice and thus, add new knowledge to the literature and help improve the care of children with haematological malignancies receiving chemotherapy. If the cognitive-behavioural intervention is shown to be effective and culturally acceptable, it will provide evidence to include the intervention as a standard of care in paediatric haematology/oncology.

Trial registration: ClinicalTrials.gov NCT05270655. Registered on March 8, 2022.

Keywords: Cognitive-behavioural intervention, Children, Haematological malignancy

Background

Haematological malignancies include malignancies of the blood, bone marrow, and lymph nodes. Leukaemia, lymphoma, and myeloma are the most common types of paediatric cancer all over the world [1–3]. In Ethiopia,
evidence shows that more than 50% of childhood cancers are haematological malignancies [4, 5]. The course of childhood cancer causes various stressful symptoms among children [6]. The diagnosis, course of treatment such as painful medical procedures and chemotherapy side effects, and challenges in social life such as missing the opportunity to play with friends, separation from family members, and school absence are major stressors among children [7, 8]. Although most paediatric cancer patients experience various psychological problems, anxiety and depression are among the most frequently reported problems [9, 10]. Childhood cancer also significantly impedes their quality of life (QOL) [11–16].

Poorly managed anxiety and depression significantly impact QOL and survival status [17, 18]. Unmanaged anxiety predicts fatigue [7], anticipatory pain, nausea and vomiting during the subsequent medical procedures [19] and increases off-therapy anxiety [20]. Poorly treated depression impairs relationships and psychological functioning [21], increases the burden of symptoms and mortality [9], and affects motivation to change behaviour and evidence suggests these patients are less likely to adhere to treatment [22]. Non-adherence to treatment including chemotherapy decreases prognosis increases relapse [23, 24], morbidity and hospital readmissions [17] and treatment costs, and has a negative impact on QOL [25]. Likewise, poor QOL is associated with emotional, behavioural, and social problems such as difficulty establishing or maintaining friendships and poor school performance [26].

Psychosocial problems, such as anxiety and depression in children with cancer are given little attention and are poorly managed [27] as more emphasis is given to the physical aspect of the illness. Thus, a tailored psychosocial intervention that has been found to be effective should be incorporated into the current medical treatment [9]. Psychosocial interventions including music-based interventions [28–30], art therapies [31–34], play-based interventions [35–37] and cognitive-behavioural interventions (CBI) [38–40] show promising effects in improving the health outcomes of children with cancer. Among psychosocial interventions, CBI is most frequently recommended to manage anxiety and depression in paediatric cancer patients due to its effectiveness and feasibility [38–41].

Evidence suggests that CBI helps improve psychosocial and health-related outcomes in children with cancer [42–46]. However, as most previous studies were conducted in developed countries, adopting and applying CBI approaches and strategies in other countries might be ineffective. In addition, in most studies, the theory guiding CBI development was not identified. Thus, developing and evaluating a theory-guided CBI in a different country such as Ethiopia is essential.

CBI is a structured and tailored psychotherapeutic intervention based on cognitive and behavioural approaches [47, 48], and helps to modify distorted thinking and beliefs, reduce maladaptive behaviour, and increase coping skills [49]. CBI enables patients to manage their problems independently and to maintain behavioural changes [47, 50].

In this study, we developed a CBI for children with haematological malignancies guided by Beck’s cognitive model [50]. The model describes the associations among cognition, emotion, and behaviour [47]. Distorted thoughts and unhelpful coping strategies often cause emotional problems such as anxiety and depression [51–53]. For instance, in Ethiopia, most patients experience extreme stress as they believe that there is no hope of childhood cancer being cured with modern medicine. They abandon treatment because they believe religious and spiritual therapies, or alternative forms of treatment such as visiting traditional healers and using holy water, are more effective [54, 55]. Thus, CBI strategies help identify and modify distorted thoughts and unhelpful behaviour [48] and promote the development of positive coping strategies, and cognitive and behavioural adaptation [47, 56]. Positive changes in the cognitive process and development of positive coping behaviour help reduce stressful feelings such as anxiety and depression and, in turn, could improve psychosocial functioning and QOL [57].

Methods
Objectives
The objectives of this study are to evaluate whether a theory-based CBI achieves (1) reduced anxiety and depression and (2) improved quality of life post-intervention in the experimental group compared to the control group receiving usual care.

Study design
This trial is designed as a multi-centre, assessor-blinded, two-arm parallel-group, repeated measure randomised controlled trial (RCT). The protocol for this trial was registered at ClinicalTrials.gov (NCT05270655). A multi-centre trial helps recruit adequate and representative participants and thus, improves the generalisability of the study findings [58].

The schedule of enrolment, interventions and assessments of the study protocol follows the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Figure (Fig. 1) and SPIRIT Checklist (Additional File 1) [59].
Study setting
Participants will be recruited from the paediatric haematology-oncology wards in two university-affiliated specialised hospitals. These hospitals are among the largest specialised hospitals providing medical services to many children with cancer in Ethiopia.

Participants
Participants (1) aged 8 to 18 years old, (2) diagnosed with haematological malignancy, (3) undergoing chemotherapy, (4) able to communicate in Amharic, and (5) with written parental consent and oral child assent will be recruited. Participants (1) with evidence of developmental, psychological and/or psychiatric illness or problems, (2) unable to collaborate in the study due to acute illness, and/or (3) having hearing or speech problems that could affect the study process will be excluded.

Sample size
The sample size was estimated using the G*Power (version 3.1.9.7) sample size calculator based on the effect size of CBI on anxiety, the primary outcome of this study. Evidence shows that the effect size of CBI ranges from 0.7 to 3.9 [43, 45, 46, 60]. Using the smallest effect size of 0.7, 80% power, 5% significance level and a potential 15% attrition rate, 80 participants (40 per group) will be recruited.
**Participant recruitment**
A research assistant (RA) in each hospital with the help of nurses in the paediatric oncology ward will approach children and their parents to identify their eligibility, explain the study procedures, and provide a detailed information sheet. For participants who agree to join the study, the RA will obtain written parent consent and oral child assent, collect baseline clinical and demographic data, and provide the participants with an appointment card.

**Randomisation**
Participants will be stratified based on their age groups, i.e. ≤ 12 years and ≥ 13 years in each hospital [61]. Evidence shows that age influences the level of anxiety, depression, and QOL [11, 62, 63]. Stratified randomisation balances comparability between the groups and increases the power of the study [64]. The principal investigator will generate a computerised random sequence with a 1:1 allocation using a block size of 4 and 6 for each stratum of each hospital.

**Allocation concealment**
Participants, research assistants (RAS) and intervention providers would not know to which group the participants will be assigned. The allocation sequence will be concealed in a sequentially numbered, sealed, and opaque envelope until treatment assignment.

**Blinding**
The outcome evaluators are paediatric nurses who are not working in the study hospitals and will be blinded to the study groups. To ensure blinding, participants will be advised not to disclose their group assignment to outcome evaluators. However, due to the nature of the intervention, it is not possible to blind participants and intervention providers. This is an open-label trial with only patient-outcome assessors being blinded so emergency unblinding will not occur.

**Intervention procedures**
Guided by Beck's cognitive model [50], the content and dose of CBI are determined by reviewing international guidelines on CBI [48, 50, 65], and the findings of the systematic review and meta-analysis [66]. Beck's model describes how thought, feeling, and behaviour interact. Hence, CBI helps identify and modify maladaptive thoughts and behaviour and develops coping skills. Intervention content and strategies for the experimental group will be tailored to the child's age and health conditions and include psychoeducation, guided discovery or Socratic questioning, discussion, drawing/painting or writing, and play supplemented with home-based practices.

**Experimental group**
The experimental group will receive five weekly face-to-face sessions (30–35 min each). The intervention will be delivered by two psychologists with master's degree who have clinical and research experience in CBI. The contents include (1) an introduction to CBI, (2) identifying, evaluating, and challenging maladaptive thoughts, beliefs and behaviour, (3) behavioural activation, (4) practising deep breathing exercises, and (5) reassessing goals or treatment plans, and encouraging participants to maintain changes.

The intervention will be delivered in the hospital before the children undergo chemotherapy to avoid excessive fatigue and increase their engagement with the interventions. Additionally, to establish a strong family support system and enhance intervention delivery, parents or primary caregivers of the child will be invited to attend the introduction of the first session, the summary of each session, and whenever else necessary. However, the role of the parents/caregivers is only to facilitate the intervention delivery, such as providing information when needed.

To enhance the retention rate, interventions will be delivered during participants’ medical appointments at the hospitals. In addition, each participant will be provided with an appointment card containing the date and time of the next CBI appointment, and the RA will remind them with a phone call 2 days before the next appointment. The participants will continue receiving the usual psychosocial care provided by the nurses in the paediatric oncology ward.

**Control group**
The control group will receive the usual psychosocial care such as information and health education about the course of the illness and treatments provided by the nurses in the paediatric oncology ward. Additionally, the RA will offer them attention every week for 30 min about treatment adherence and other concerns. Parents will be invited to attend if they wish to do so.

**Outcomes and measurements**

**Primary outcome**
Anxiety will be assessed using the anxiety subscale of the self-report 25-items Revised Child Anxiety and Depression Scale (RCADS) (α=0.91 for anxiety scale) in the original study [67], before the intervention (T0, baseline),
immediately after the intervention (T1, at 6 weeks) and one month after completion of the intervention (T2, at 10 weeks). In this study, the Amharic version of the RCADS will be used. The Amharic version of the scale exhibited satisfactory validity and reliability in our other study (α = 0.95 and α = 0.96 for the anxiety sub-scale and total scale respectively) [unpublished data]. Each item will be rated on a four-point Likert scale (0–3), and the total raw anxiety score ranges from 0 to 45 [68]. To calculate the total anxiety score, the raw scores will be converted into $T$-scores, with $T$-scores of ≥ 65 to 70 and ≥ 70 being borderline and above the clinical threshold, respectively [69]. A higher anxiety score corresponds to higher levels of anxiety.

**Secondary outcomes**

For the secondary outcomes, depression and QOL will be assessed at T0, T1, and T2. The level of depression will be assessed using the depression subscale of the RCADS (α = 0.80 for the depression scale in the original study) [67], and α = 0.94 for the Amharic version in our study [unpublished data]. A higher score reflects higher depression.

QOL will be measured using a child-report PedsQL™ 4.0 GCS for ages (8 – 12 and 13 – 18 years) [70]. The Amharic version of the scale demonstrated good reliability and validity in our other study (α = 0.96) [unpublished data]. To calculate the total score, each item will be scored on a five-point Likert scale (0–4), and the 0 – 4 scale items will be reversely scored and linearly transformed to 0–100 [71]. A higher score indicates high QOL.

**Other measures**

Participants’ demographic and clinical characteristics will be recorded at baseline using a demographic and clinical datasheet. The overall study process is summarised in Fig. 2.

**Data analysis**

The analysis will be conducted using Statistical Package for the Social Sciences (IBM SPSS statistics 26). To check discrepancies in data entry, the principal investigator and a RA will independently enter the coded data twice into SPSS. While categorical data will be summarised using frequencies and percentages, continuous data will be summarised using means, standard deviations, median and interquartile ranges depending on normality distribution. Depending on the types of data and normality distribution, the characteristics of the groups will be compared using independent t-tests, Mann–Whitney U tests, Chi-square tests, and Fisher’s exact tests. Outcome analysis will be conducted as an intention-to-treat analysis. Missing value analyses will be conducted to determine the need for multiple imputations. A generalised estimation equation (GEE) model will be applied to determine the intervention effect between the groups in terms of a group, time, and group*time interaction. Variability in effect will be assessed by performing a sub-group analysis. Given that this trial is studying a low-risk or no-risk intervention, there are no stopping rules or plans for interim analyses. The significance level will be determined at 5% (two-sided) for all statistical tests.

**Oversight and monitoring**

The coordinating centres are composed of the principal investigator and the research team (clinical psychologists and research assistants) and are responsible for the day-to-day organisational support for the trial. The PI will meet them every 2 weeks to discuss the trial progress and any issues that arise during the trial. The steering committee includes the PI, site supervisors (pediatric haematologists-oncologists), and a psychiatrist who will meet every 2 months. However, as the intervention of this trial is a low or no-risk intervention, there is no data monitoring committee. To review the trial conduct, the study team will meet every 2 weeks led by the PI throughout the study. The steering committee will also meet every 2 months. Finally, a progress report will be submitted to the Ethics committees at the end of the trial.

**Discussion**

Most previous trials that evaluated CBI in paediatric oncology focused on parent or caregiver outcomes. Other studies that evaluated child outcomes were conducted in developed countries. However, CBI strategies in these countries might not be acceptable for patients with diverse backgrounds and the effects of the interventions may differ when adopted and applied in different cultural contexts such as Ethiopia. In addition, most of these trials had methodological limitations and the authors recommended conducting further rigorous trials [66].

This RCT can be considered the first to evaluate CBI for children with cancer in Ethiopia. It aims to evaluate the effects of a theory-based and age-appropriate cognitive behavioural intervention to improve anxiety, depressive symptoms, and QOL of children with haematological malignancies. Thus, if the intervention is found to be effective and acceptable, it will pave the way for
the integration and implementation of CBI into paediatric haematology-oncology to improve the psychological symptoms and QOL of paediatric cancer patients.

**Trial status**
Protocol version 2, September 2022.
Participant recruitment commenced in May 2022 and the study will be completed in November 2022.

**Abbreviations**
CBI: Cognitive-behavioural intervention; CUHK-NTEC CREC: Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee; QOL: Quality of life; RCADS: Revised Child Anxiety and Depression Scale; SPIRIT: Standard Protocol Items: Recommendations for Interventional Trials; SPSS: Statistical Package for the Social Sciences.

**Supplementary Information**
The online version contains supplementary material available at https://doi.org/10.1186/s13063-022-06768-x.

**Dissemination**
The findings of this study will be disseminated via publication in a peer-reviewed scientific journal.

**Authors' contributions**
TGM initiated and designed the study and wrote the manuscript. JPCC and WHCL provided feedback on the design of the study and manuscript and edited the manuscript. All named authors adhere to the authorship guidelines of Trials and have agreed to publication. No professional writers have been involved. The author(s) read and approved the final manuscript.
Available as there are no personal identifiers of participants presented in this protocol. However, a model consent form can be obtained from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

We obtained ethical approval from the Joint Chinese University of Hong Kong (CUHK)- New Territories East Cluster Clinical Research Ethics Committee (NTEC CREC) (CREC Ref. No. 2021.729-T), Institutional Ethical Review Board of the University of Gondar (Ref VP/RTT/05/815/2022) and Ethics and Research Committee of Department of Paediatrics and Child Health, School of Medicine, College of Health Sciences, Addis Ababa University (Ref. No Ped/ Mf/343/14). We will also obtain written parent or legal guardian consent and oral child assent to participate in the study. Participants will be informed that they have the full right not to participate in the study or withdraw from the study anytime if they feel uncomfortable and/or have any concerns. Participants will be asked if they agree to their data being used should they choose to withdraw from the trial. They will also be asked for permission for the research team to share relevant data with people from the Universities taking part in the research or from regulatory authorities, where relevant. This trial does not involve collecting biological specimens for storage. All the collected data from the participants will be kept confidential using codes instead of personal identifiers and will be meant only for this study. Any significant changes to the protocol will require approval from and Research and Ethics committees and this will be communicated to the responsible parties. Regarding provisions for post-trial care, there is no anticipated harm and compensation for trial participation.

Consent for publication

Not applicable as there are no personal identifiers of participants presented in this protocol. However, a model consent form can be obtained from the corresponding author upon request.

Competing interests

The authors declare that they have no competing interests.

Author details

1Nethersole School of Nursing, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong, Hong Kong; 2Department of Paediatrics and Child Health Nursing, College of Health Sciences, Debre Markos University, Debre Markos, Ethiopia.

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References

1. Banerjee S, Parsaramka MA, Paruthy SB. Garcinol: Preclinical Perspective. Asian Pac J Cancer Prev. 2020;21(5):1487–94.

2. Johnston WT, Erdmann F, Newton R, Steliarova-Foucher E, Schüz J, Roman E. Childhood cancer: estimating regional and global incidence. Cancer Epidemiol. 2021;2022(71):101662.

3. Namayandeh SM, Khazaei Z, Najafi ML, Goodarzi E, Moslem A. Global leukemia in children 0–14 statistics 2018, incidence and mortality and Human Development Index (HDI). GLOBOCAN sources and methods. Asian Pac J Cancer Prev. 2020;21(5):1487–94.

4. Memine ST, Habtemariam MK, Asefa M, Deressa BT, Abayneh G, Tegey B, Abraha MW, Ababi G, Jemal A, Rebbeck TR, Verguet S. Estimates of cancer incidence in Ethiopia in 2015 using population-based registry data. J Glob Oncol. 2018;4:1–11.

5. Yifu S, Muluye D. Childhood cancer in Gondar university hospital. North-west Ethiopia BMC Res Notes. 2015;8(1):1–5.

6. Walubita B, Sikateyo B, Zulu JM. Challenges for health care providers, patients and parents who face a childhood cancer diagnosis in Zambia. BMC Health Serv Res. 2018;18(1):1–7.

7. Ameringer S, Elswick RK Jr, Shockey DP, Dillon R. A pilot exploration of symptom trajectories in adolescents with cancer during chemotherapy. Cancer Nurs. 2013;36(1):60–7.

8. Li H, Chung OKJ, Chiu SY. The impact of cancer on children's physical, emotional, and psychosocial well-being. Cancer Nurs. 2010;33(1):47–54.

9. Lopez-Rodriguez MM, Fernandez-Millan A, Ruiz-Fernandez MD, Dobarro-Sanz I, Fernandez-Medina IM. New technologies to improve pain, anxiety and depression in children and adolescents with cancer: a systematic review. Int J Environ Res Public Health. 2020;17(10):3563.

10. Yardeni M, Campino GA, Hasson-Ohayon I, Basel D, Hertz-Palmor N, Bursztyn S, Weisman H, Pessach IM, Toren A, Gotthel D. Trajectories and risk factors for anxiety and depression in children and adolescents with cancer: A 1-year follow-up. Cancer Med. 2021;10(16):5653–60.

11. Fardell JE, Vetsch J, Trahair T, Mateos MK, Groothuis MA, Touyz LM, Marshall GM, Wakefield CE. Health-related quality of life of children on treatment for acute lymphoblastic leukemia: a systematic review. Pediatr Blood Cancer. 2017;64(9):e26489.

12. Kobayashi N, Nakagami-Yamaguchi E, Hayakawa A, Adachi S, Hara J, Tokimasa S, Ohta H, Hashii Y, Rikishi T, Sawada M, Kuroyama K, Kohdera U, Kanibeppu K, Kawauchi H, Oda M, Hon H. Health-related quality of life in Japanese children with acute lymphoblastic leukemia during and after chemotherapy. Pediatr Int. 2017;59(2):145–53.

13. Mitchell HR, Lu X, Myers RM, Sung L, Balsamo LM, Carroll WL, Raetz E, Loh ML, Mattano LA Jr, Winick NJ, Devidas M, Hunger SP, Maloney K, Kadan-Lottick NS. Prospective, longitudinal assessment of quality of life in children from diagnosis to 3 months off treatment for standard risk acute lymphoblastic leukemia: Results of Children's Oncology Group study AALL0331. Int J Cancer. 2016;138(2):332–9.

14. Nunes MDR, Jacob E, Bomfim EO, Lopes-Junior LC, de Lima RA, Floria-Santos M, Nascimento LC. Fatigue and health related quality of life in children and adolescents with cancer. Eur J Oncol Nurs. 2017;29:39–46.

15. Pan HT, Wu LM, Wen SH. Quality of life and its predictors among children and adolescents with cancer. Cancer Nurs. 2017;40(5):343–51.

16. Zahed G, Koohi F. Emotional and behavioral disorders in pediatric cancer patients. Iran J Child Neurol. 2020;14(1):113–21.

17. Lauer AL. Treatment of anxiety and depression in adolescents and young adults with cancer. J Pediatr Oncol Nurs. 2015;32(5):278–83.

18. Pitman A, Suleman S, Hyde N, Hodgskiss A. Depression and anxiety in patients with cancer. BMJ. 2018;361:k1415.

19. Kurtz BP, Abrams AN. Psychiatric aspects of pediatric cancer. Child Adolesc Psychiatr Clin N Am. 2010;19(2):401–21.

20. Kunin-Batson AS, Lu X, Balsamo L, Graber K, Devidas M, Hunger SP, Carroll WL, Winick NJ, Mattano LAM Jr, Maloney KW, Kadan-Lottick NS. Prevalence and predictors of anxiety and depression after completion of chemotherapy for childhood acute lymphoblastic leukemia: a prospective-longitudinal study. Cancer. 2016;122(10):1680–7.

21. Jaycox LH, Stein BD, Paddock S, Miles JMV, Chanda A, Meredith LS, Tanielian T, Hickey S, Burnam MA. Impact of teen depression on academic, social, and physical functioning. Pediatrics. 2009;124(4):e596-605.

22. Kondryn HJ, Edmondson CL, Hill J, Eden TO. Treatment non-adherence in teenage and young adult patients with cancer. Lancet Oncol. 2011;12(1):100–8.

23. Butow P, Palmer S, Pa I, Goodenough B, Luckett T, King M. Review of adherence-related issues in adolescents and young adults with cancer. J Clin Oncol. 2010;28(32):4800–8.

24. Gupta S, Bhata S. Optimizing medication adherence in children with cancer. Curr Opin Pediatr. 2017;29(1):41–5.

25. Leader A, Raanani P. Adherence-related issues in adolescents and young adults with hematological disorders. Acta Haematol. 2014;132(4):348–62.

26. Bansal M, Sharma KK, Vatsa M, Bakshi S. Comparison of health-related quality of life of children during maintenance therapy with acute
lymphoblastic leukemia versus siblings and healthy children in India. Leuk Lymphoma. 2013;54(5):1036–41.

27. Hyslop S, Davis H, Duong N, Loores R, Schechter T, Tomlinson GA, Dupuis LL, Sung L. Symptom documentation and intervention provision for symptom control in children receiving cancer treatments. Eur J Cancer. 2019;109:120–8.

28. da Silva Santa IN, Schweitzer MC, Dos Santos ML, Ghelman R, Odone FV. Music interventions in pediatric oncology: systematic review and meta-analysis. Complement Ther Med. 2021;59:102725.

29. González-Martín-Moreno M, Garrido-Ardila EM, Jiménez-Palomares M, González-Martín-Moreno M, Oliva-Ruiz R. Music-based interventions in paediatric and adolescents oncology patients: A systematic review. Children. 2021;8(2):73.

30. Silva LA, Baran FD, Mercêrs NN. Music in the care of children and adolescents with cancer: integrative review. Texto Contexto Enferm. 2016;25(04):E1720015.

31. Abdulah DM, Abdulla BM. Effectiveness of group art therapy on quality of life in paediatric patients with cancer: A randomized controlled trial. Complement Ther Med. 2018;41:180–5.

32. Aytan N, Kilicaslan-Toruner E, Sari Ç. The effect of drawing and writing technique on the anxiety level of children undergoing cancer treatment. Eur J Oncol Nurs. 2017;28:1–6.

33. Aguilar BA. The efficacy of art therapy in pediatric oncology patients: an integrative literature review. J Pediatr Nurs. 2017;36:173–8.

34. Tahmasebi Z, Maghsoudi J, Talakoub S. The effect of painting on depression in children with cancer undergoing chemotherapy. Iran J Nurs Midwifery Res. 2017;22(2):102–5.

35. Carrion-Plaza A, Jaen J, Montoya-Castilla I. HabitApp: New play Technologies in Pediatric Cancer to improve the psychosocial state of patients and caregivers. Front Psychol. 2020;11:157.

36. Ebrahimi E, Mirzae H, Borujeni MS, Ghasemi M, Mirzakhani N. The effect of filial therapy on depressive symptoms of children with cancer and their mother’s depression, anxiety, and stress: A randomized controlled trial. Asian Pac J Cancer Prev. 2019;20(10):2935–41.

37. Mohammadi A, Mehraban AH, Damavandi SA, Zarei MA, Haghihi H. The effect of play-based occupational therapy on symptoms and participation in daily life activities in children with cancer: A randomized controlled trial. Br J Occup Ther. 2021;84(7):400–9.

38. Flowers SR, Birnie KA. Procedural preparation and support as a standard of care in pediatric oncology. Pediatr Blood Cancer. 2015;62(5):S694–723.

39. Pao M, Kazak AE. Anxiety and depression. In: Wiener LS, Pao M, Kazak AE, editors. Caring for children and adolescents at the Uganda Cancer Institute. BMC Cancer. 2015;62(5):S585–618.

40. Wiener L, Kazak AE, Noll RR, Patenaude AF, Kupst MJ. Standards for the psychosocial care of children with cancer and their families: an introduction to the special issue. Pediatr Blood Cancer. 2015;62(5):S519–24.

41. Baredent K, Bardideh F, Kakabarae K. Study of the Effectiveness of the Cognitive Behavioral Therapy on Self Efficacy and Pain among Children Suffering from Cancer. Glob J Health Sci. 2017;9(5):33–41.

42. Hamed V, Hamid N, Beshlideh K, Marashi SA, Hashemi Sheikh Shabani SE. Effectiveness of Conventional Cognitive-Behavioral Therapy and Its Computerized Version on Reduction in Pain Intensity, Depression, Anger, and Anxiety in Children with Cancer: A Randomized, Controlled Trial. Iran J Psychiatry Behav Sci. 2020;14(4):e83110.

43. Hisao HJ, Chen SH, Jaing TH, Yang CP, Chang TY, Li MY, Chu CH, Huang JL. Psychosocial interventions for reduction of distress in children with leukemia during bone marrow aspiration and lumbar puncture. Pediatr Neonatol. 2019;60(3):278–84.

44. Mehrara M, Ghaffari Z, Ghezelghabr RM, Ghavasi F, Fatemizadeh M. The Effectiveness of Cognitive-Behavioral Play Therapy on Pain Tolerance and Trait State Anxiety Among Children with leukemia cancer in Isfahan City. Int J Appl Behav Sci. 2018;5(2):22–7.

45. Zhang P, Mo L, Torres J, Huang X. Effects of cognitive behavioral therapy on psychological adjustment in Chinese pediatric cancer patients receiving chemotherapy: A randomized trial. Medicine. 2019;98(27):e16319.

46. Fenn K, Byrne M. The key principles of cognitive behavioural therapy. InnovAit. 2013;6(9):579–85.

47. Stallard P. Think good, feel good: A cognitive behavioural therapy workbook for children and young people. 2nd ed. Hoboken, NJ: Wiley; 2019.

48. Craske MG. Cognitive-behavioral Therapy. 2nd ed. Washington, District of Columbia: American Psychological Association, 2017.

49. Beck JS, Beck AT. Cognitive behavior therapy: Basics and beyond. 2nd ed. New York: Guilford Press; 2011.

50. Kircanski K, Joormann J, Gottlib IH. Cognitive aspects of depression. Wiley Interdiscip Rev Cogn Sci. 2012;3(3):301–13.

51. Li R, Ma J, Chan Y, Yang Q, Zhang C. Symptom Clusters and Influencing Factors in Children With Acute Leukemia During Chemotherapy. Cancer Nurs. 2020;43(5):411–8.

52. Wu LM, Sheen JM, Shu HL, Chang SC, Hsiao CC. Predictors of anxiety and resilience in adolescents undergoing cancer treatment. J Adv Nurs. 2013;69(1):158–66.

53. Haileselassie W, Mulugeita T, Tigeneh W, Kaba M, Labioso WL. The situation of cancer treatment in Ethiopia: challenges and opportunities. J Cancer Prev. 2019;24(1):33–42.

54. Minutse MK, Tolla MT, Memirie ST, Palm MT, Hailu D, Abdi KA, Bula ED, Noostrum OF. The magnitude and perceived reasons for childhood cancer treatment abandonment in Ethiopia: from health care providers’ perspective. BMC Health Serv Res. 2022;22(1):1–3.

55. Powers MB, de Kleine RA, Smits JA. Core mechanisms of cognitive behavioral therapy for anxiety and depression: A review. Psychiatr Clin North Am. 2017;40(4):611–23.

56. Rasusberg J, Eversen J, Dammen T, Willberg T, Klungsøy O, Jones B, Eend E, Geerland R, Brevik R, Lavgren A, Ulberg R. Mechanisms of change and heterogeneous treatment effects in psychodynamic and cognitive behavioral therapy for patients with depressive disorder: a randomized controlled trial. BMC Psychol. 2021;9(1):1–14.

57. Friedman LM, Furberg CD, DeMets DL, Reboussin DM, Granger CB. Fundamentals of clinical trials. 5th ed. Springer, 2015.

58. Chan A-W, Tetlzaft JM, Gatzsche PC, Altman DG, Mann H, Berlin J, Dickerson K, Hrobjartsson A, Schulz CF, Paralekar WR, Krile-ženić K, Laupais A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586.

59. Zijie Z. Tuan ti ren zhi xing wei gan yu dui xiao er bai xue bing hua liao e16319.
68. Chorpita BF, Moffitt CE, Gray J. Psychometric properties of the Revised Child Anxiety and Depression Scale in a clinical sample. Behav Res Ther. 2005;43(3):309−22.
69. Chorpita BF, Ebesutani C, Spence SH. Revised children’s anxiety and depression scale: User’s guide. 2020. https://www.childfirst.ucla.edu/wp-content/uploads/sites/163/2020/12/RCADSUsersGuide20201201.pdf. Accessed 20 Oct 2021.
70. Varni JW, Seid M, Kurtin PS. PedsQL™ 4.0: Reliability and validity of the Pediatric Quality of Life Inventory™ Version 4.0 Generic Core Scales in healthy and patient populations. Med Care. 2001;39(8):800–12.
71. Varni JW. Scaling and scoring of the Pediatric Quality of Life Inventory™ PedsQL 2017. https://www.pedsqol.org/PedsQL-Scoring.pdf. Accessed 15 Oct 2021.
72. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. Trials. 2010;11(1):1−8.

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