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Title Page

The efficacy of interactive group psychoeducation for children with leukaemia: A randomised controlled trial

Running title: Psychoeducation for children with leukaemia

Authors:

Marianne Day, PhD[1*], Sally Harris, PhD[2], Deema Hussein, PhD[3], Mohamad Yassin Saka, PhD[3], Chris Stride, PhD[4], Myles Jones, PhD[1], Guy Makin, PhD[5], Richard Rowe, PhD[1]

Author emails:

Marianne.day@manchester.ac.uk, sally.harris13@nhs.net, deemah@hotmail.com, myassin3@hotmail.com, c.b.stride@sheffield.ac.uk, m.jones@sheffield.ac.uk, guy.makin@manchester.ac.uk, r.rowe@sheffield.ac.uk

Institutional affiliations:

[1] Department of Psychology, University of Sheffield, UK
[2] Royal Alexandra Children's Hospital, Eastern Road, Brighton, BN2 5BE
[3] King Fahd Medical research Center, Department of Medical Laboratory Technology, Faculty of Applied Medical Sciences King Abdulaziz University, Saudi Arabia
[4] Institute of Work Psychology, Management School, University of Sheffield, UK
[5] Division of Cancer Sciences, Faculty of Medicine, Biology and Health, University of Manchester and Royal Manchester Children's Hospital, Oxford Road, Manchester, M13 9WL

*Corresponding author at: Marianne Day, Manchester Centre for Audiology and Deafness, The University of Manchester, Oxford Road, Manchester, M13 9PL.

Tel: (+44) (0) 161 306 6000, email: marianne.day@manchester.ac.uk.

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Abbreviation	Full term
ALL	Acute Lymphoblastic Leukaemia
AML	Acute Myeloblastic Leukaemia
BCAMHS	British Child and Adolescent Mental Health Survey
ES	Effect Size
HRQoL	Health Related Quality of Life
MCID	Minimal clinically important difference
PACQLQ	Paediatric Asthma Caregiver's Quality of Life Questionnaire
PedsQL	Paediatric Quality of Life Inventory
RCT	Randomised Controlled Trial
SD	Standard Deviation
SDQ	Strengths and Difficulties Questionnaire
UK	United Kingdom

Abstract

Objective To evaluate an interactive group psychoeducation programme for children treated for leukaemia. **Methods** A longitudinal randomised controlled study across four UK hospitals with an immediate (N=26) and delay control group (N=32). The intervention covered the pathophysiology of leukaemia, its treatment, side effects and the importance of positive health behaviours. Primary outcomes were parent-reported child health related quality of life (HRQoL) and behavioural difficulties. Secondary outcomes were child-reported HRQoL, cancer-specific HRQoL, child confidence, caregiver burden, and treatment anxiety. Measures were completed pre- and immediately post-intervention, and at 13 and 26-weeks follow-up. Change over time was analysed using multilevel modelling. Acceptability questionnaires rated the intervention on benefits, recommendations, and barriers to participation. **Results** The intervention significantly improved parent-reported child HRQoL but did not have a significant effect on other outcomes. Acceptability of the intervention was high. **Conclusions** This study provides initial evidence that interactive group psychoeducation is acceptable to families and improves HRQoL in children with leukaemia. Difficulties with recruitment removed power to detect effect sizes that are plausible for psychoeducational interventions. **Practise implications** Further studies to explore the potential of psychoeducation to improve outcomes for children with leukaemia and an examination of barriers to participation within this population are warranted.

1. Introduction

Leukaemia is the most common childhood cancer, with approximately 500 cases diagnosed in the UK annually [1]. Acute Lymphoblastic Leukaemia (ALL) makes up approximately 78% of childhood cases, 15% are Acute Myeloid Leukaemia (AML), with the remainder representing chronic cases [2]. Treatment involves chemotherapy over 2-3 years for ALL and 6 months for AML. Five-year survival rates are approximately 90% for childhood ALL and 65% for AML [3,4].

Given the strong survival rates, Health Related Quality of Life (HRQoL) is widely recognised as a key outcome target in the treatment of paediatric leukaemia [5]. The World Health Organisation [6] specified that HRQoL measures should be multi-dimensional including physical, mental, social and emotional functioning. Assessments should include measures of parent and child generic and disease-specific HRQoL [5,7].

Many aspects of leukaemia treatment could compromise HRQoL. Families face a life-threatening illness, uncertain prognosis, and long-term disruption to family and school life [8]. Children undergo approximately 20 medical procedures during treatment (e.g. lumbar punctures, bone marrow aspirations) which can cause stress and anxiety [9,10], and chemotherapy can lead to side effects (e.g. hair loss, nausea) and late effects (e.g. cardiotoxicity, joint problems) [10]. Steroid treatment causes problems with weight, cognition and behaviour which can impact peer and family relations, and HRQoL [11].

Survivors have significantly higher risks for long-term depression and impaired HRQoL compared to healthy controls, particularly when living with long-term health conditions [12,13]. One or more adverse late effects have been reported in over 70% of children treated for leukaemia [14]. Survivors are at higher risk of

85 developing chronic health conditions and future cancers compared to the general
86 population, making positive health-related behaviours particularly important [14,15].
87 However, survivors may not be equipped to engage in healthy behaviours without
88 adequate information about their illness.

89 Psychoeducational interventions may mitigate the psychosocial impacts of
90 leukaemia treatment. Being prepared for medical procedures, understanding the
91 purpose of treatment and the ability to communicate with healthcare providers may
92 offer children a greater sense of empowerment and control [16]. Psychoeducation
93 may also contribute to preventing and managing late effects in survivors.

94 Systematic reviews of psychoeducational interventions have identified
95 improvements in symptoms, self-efficacy and self-management for children with
96 chronic conditions [17,18]. For children with cancer, improvements in positive
97 thinking and communication following a group cognitive behavioural intervention
98 have been reported [19]. Computer-delivered psychoeducational interventions have
99 improved treatment adherence in adolescents with cancer [20] and locus of control in
100 children with leukaemia [21]. Short interventions to familiarise children with medical
101 procedures and reduce distress during cancer treatment, have reduced negative
102 threat appraisal [22,23].

103 The study reported here evaluated a novel psychoeducational intervention for
104 children treated for leukaemia, delivered in an interactive, social context. We
105 hypothesized that receiving this intervention would lead to improvements in two
106 primary outcomes: parent-reported child generic HRQoL, and emotional and
107 behavioural difficulties. We also examined efficacy on a number of exploratory
108 secondary outcomes (child-reported generic HRQoL, illness-specific HRQoL, child
109 confidence, caregiver burden and treatment distress). It was hypothesised that

caregiver burden would reduce in line with improvements in child quality of life, behavioural issues and treatment-related anxiety. The UK Medical Research Council recommends that acceptability should be evaluated alongside efficacy to ensure interventions could be effectively integrated into clinical provision [24]. Therefore, we also assessed intervention acceptability by recording attendance during the intervention and collecting parent and child feedback at the end of the intervention.

2. Methods

2.1. Study Design

We used a longitudinal Randomised Controlled Trial (RCT) design. An immediate treatment group received the intervention in the week after receiving their first baseline questionnaire, while a delayed treatment group received the intervention 18 weeks later. The immediate group received the psycho-educational intervention for four weeks and provided data immediately post-intervention (week 5). The delay group acted as a control group before receiving the intervention at week 18, providing data at baseline and week 5; time points matched to assessments in the immediate group . At week 18 the delayed group provided pre-intervention data. They then received the intervention for four weeks, before providing post-intervention data in week 23. Both groups provided follow-up data at 13 and 26 weeks after their four-week intervention ended.

We powered our study to detect an effect size of 0.5 as meta-analyses have found medium to large effects for psychological interventions delivered to children with chronic conditions on a range of outcomes (e.g. adherence to treatment, symptoms, adjustment) [25: mean ES=0.71; 26: mean ES= 0.58). Eighty percent power to detect an effect size of 0.5 using a between-group comparison with a 1-

tailed hypothesis is provided by a design with 51 participants in each group. Therefore, we aimed to recruit 60 children in each group, allowing for 15% dropout.

A modified intention to treat design was used [27]. Children were analysed in their allocated treatment group, regardless of intervention attendance. However, only families providing baseline data and at least one follow-up timepoint were used to analyse change over time. The clinical protocol was registered with the International Standard Randomised Controlled Trials registry (ISRCTN: 3679062) and approved by the University of Sheffield's Psychology Ethics Committee, and the North-West Haydock National Research Ethics Service (10/H1010/45).

2.2. Participants and Procedure

The eligibility criteria for participation were children aged 7-12 years, on-treatment, and survivors, treated for leukaemia in one of four participating UK hospitals (Leeds General Infirmary, Manchester Children's Hospital, Sheffield Children's Hospital, Liverpool Alder Hey). A parent or caregiver was also recruited into the study to provide parent-reported outcome data for each child. Families were informed about the study by research nurses in each hospital. From a sample of 422 children, 74 families gave consent and were recruited by research nurses (see Supplementary Figure A.1: 78 declined, 2 excluded for comorbidities, 268 non-contactable), before they were randomised into intervention groups. Participants were randomly assigned into a delay or immediate group by the fifth author (CS), who was not involved in delivering the intervention or recruiting participants, using a random number generator. Randomisation was stratified by age (7-9 and 10-12 years) and gender. It was not possible to blind the participants or the deliverer of the intervention to group allocation due to the timing of the workshops.

Participants were assigned a unique number at randomisation which was used for data collection. Data was collected using paper questionnaires. Pre-intervention data was collected at the first intervention session. Additional questionnaires were sent and returned via mail. Data was provided by 58 families at baseline and 45 at follow-up.

2.3. Intervention

The intervention was initially developed and piloted by a clinical team at Manchester Children's Hospital (including authors DH, GM and MYS), following needs assessments from the academic literature [e.g., 9, 10] and clinical practise. These needs were identified in the study protocol (ISRCTN: 3679062). Feedback from parents and children following piloting were used to refine intervention content and delivery. The intervention consisted of four 2-hour sessions run on consecutive weeks in each hospital, following teaching plans laid out in the study protocol. Groups consisted of 2-6 children. Nine blocks of the intervention were run during the study period (June 2012-April 2016). All sessions were taught by the first author (a trained teacher) who was the research assistant on the project. Adherence to the research protocol and engagement with the learning materials was recorded using attendance records, monitoring, and assessment forms for delivery of activities and child understanding, and responses on the acceptability questionnaires.

Each session (shown in Supplementary Table B.1) included information, demonstrations, games, and activities, addressing basic anatomy, leukaemia pathophysiology, understanding treatment and its side effects and the importance of maintaining a healthy lifestyle. Supplementary Table B.2 describes the components of the intervention in relation to modifiable targets and secondary outcomes. Group

sessions were interactive to engage children and to provide a supportive peer social context. As the emphasis was on education rather than therapy, children chose the extent to which they disclosed their own experiences.

2.4. Outcomes

2.4.1. Primary outcomes

Primary outcomes tested the efficacy of the intervention in relation to the main hypothesis that it would improve child quality of life and behavioural issues. Generic parent-reported child HRQoL was measured using the Paediatric Quality of Life Inventory (PedsQL) generic scale for 8-12-year-olds [28] which measures physical, emotional, social, and school functioning. For example, 'In the past 4 weeks, how much of a problem has your child had with walking down the road a little bit?' Responses used a 5-point scale (0=never a problem to 4= almost always a problem). Items were reverse-scored so higher scores indicate better HRQoL. Reliability and validity of the PedsQl in cancer studies has been demonstrated (α=.93) [28]. A minimal clinically important difference (MCID) of 4.5 has been estimated for this scale [29] which represents the minimum amount of change required for patient benefit [30].

Child behaviour difficulties were measured using the parent-reported Strengths and Difficulties questionnaire (SDQ) for children aged 4-16 years [31], which addresses conduct, emotional difficulties, hyperactivity, and peer functioning. For example, 'Often has temper tantrums or hot tantrums'. The SDQ uses a 3-point scale (1=not true, 2=somewhat true, 3=certainly true) with higher scores reflecting greater difficulties. The SDQ satisfactorily discriminates samples of young people

with and without mental health problems [32] and demonstrates satisfactory internal consistency (α=.73) [31].

2.4.2. Secondary outcomes

Secondary outcomes measured intervention efficacy on a number of exploratory measures. Cancer-specific parent-reported child HRQoL was measured using the cancer-specific module of the PedsQL [28]. This assesses pain and hurt, nausea, procedural anxiety, treatment anxiety, worry, cognitive problems, perceived physical appearance and communication. For example, 'In the past 4 weeks, how much of a problem has your child had with having a lot of pain?', scored as with the generic PedsQL scale. Child-reported HRQoL was measured using child versions of the generic and cancer-specific scales. These PedsQl scales have satisfactory internal consistency (parent-report cancer-specific: α=.87, child-report generic α=.88, cancer-specific: α=.72) [28].

Caregiver burden was measured using a modified version of the Paediatric Asthma Caregiver's Quality of Life Questionnaire (PACQLQ) [33], measuring activity limitations and emotional burdens modified to be specific to caring for a child with cancer. For example, 'During the past 4 weeks how often did you feel helpless or frightened when your child had a temperature?' Responses used a 7-point scale (1=all of the time to 7= none of the time) and were reverse-scored with higher scores indicating greater caregiver burden. This modified scale has demonstrated satisfactory internal consistency (α=.87-.92) [34].

Parent-reported child confidence was measured using seven items modified from the Self-Efficacy Questionnaire for Children [35] for this study, which addressed leukaemia treatment. For example, 'How confident is your child that he/she can ask

your doctor about matters of concern?' (shown in Appendix C). Responses used a 5-point scale (0= not at all confident to 4= totally confident). Satisfactory internal consistency was demonstrated in the current study (α=.89).

Parent and child treatment-related anxiety were measured using 6 items developed for the study (shown in Appendix C). For example, 'thinking about coming to clinic appointments, I have felt…' with responses recorded on a 7-point scale (1= much less anxious than usual to 7= much more anxious than usual). Internal consistency was satisfactory in this study (α=.85 to.91).

Parents and children completed acceptability questionnaires after the final intervention session (shown in Appendix C) which included open and closed questions. Closed questions rated the intervention on a range of properties (e.g. friendly, interesting, fun). Open questions recorded satisfaction with the intervention, perceived benefits, barriers to participation and recommendations for improvement. Participant attendance was also recorded for each intervention session.

2.5. Analysis

To check for baseline imbalances between study groups, baseline differences were assessed using t-tests and Fisher's exact tests. We checked whether our sample faced greater (parent-reported) emotional and behavioural problems than the general population by comparing our observed SDQ scores with those from the British Child and Adolescent Mental Health Survey [36] using the immediate form of the t-test in Stata 13 [37]. Analysis of the acceptability data used descriptive statistics for the closed questions and simple thematic coding for the open questions.

The principal hypothesis, that intervention participation would affect the outcome variables, was tested using a series of multilevel models, with repeated

measurements (lower level units) nested within children (higher level units). A between-subject dichotomous variable distinguished study group (0= delay, 1= immediate). A within-subject dichotomous variable distinguished whether children had received the intervention at each timepoint (0= not received, 1= received). Time was coded as weeks since baseline.

Seven models were tested for each outcome. Model 1 was an unconditional model with no predictors which partitioned total variance into within-child (variation across time) and between-child components. Model 2 introduced time from diagnosis to baseline (measured in days) to control for stage of treatment. Model 3 added study week to measure change over time during the study. Model 4 introduced the main effect of the intervention and Model 5 introduced the main effect of study group (immediate, delay). Model 6 tested whether intervention efficacy varied between children by treating it as a random effect. Model 7 added an interaction term for study group x intervention to test whether differential intervention effects were due to variation in time of intervention delivery. Model improvement was measured using reduction in the model deviance statistic (-2Log-Likelihood [-2LL]) resulting from adding additional parameter(s). Model parameters were reported using p-values and confidence intervals. These analyses were carried out using SPSS v25 [38].

3. Results

Table 1 shows baseline characteristics and outcome measurements for the immediate and delay groups. There were no significant baseline differences. Numbers of children on-treatment were 9 in the immediate group (17 survivors) and 14 in the delay group (18 survivors). Our sample showed significantly higher SDQ

283 total scores (mean=12.45, SD=7.02) than the BCAMHS sample [36] (mean=8.4,
284 SD=5.8) (t=4.97, df=10347, p<0.001).
285
286 3.1. Intervention efficacy
287 It was hypothesised that the intervention would lead to improvements on the
288 primary outcome measures, parent-reported child HRQoL and behaviour difficulties.
289 Figure 1 plots changes in these outcomes over the study. Plots for the secondary
290 outcomes are shown in Supplementary Figure A.2.
291
292 3.1.1. Parent-reported child generic HRQoL
293 Figure 1 shows that parent-reported generic child HRQoL scores were similar
294 in the immediate and delay groups at baseline. Scores improved in the immediate
295 group after receiving the intervention (week 5), with no simultaneous increase in the
296 delay group. The immediate group's scores continued to improve 13 weeks post-
297 intervention before falling slightly at 26 weeks post-intervention. The delay group's
298 scores improved before and after receiving the intervention (weeks 18 and 23) and
299 the improvement was maintained at 13 and 26-weeks post-intervention.
300
301 3.1.2. Emotional and behavioural difficulties
302 SDQ total difficulties decreased in the immediate group after receiving the
303 workshops (week 5) while difficulties increased slightly in the delay group over the
304 same period (Figure 1). The immediate group's scores continued to decrease at 13
305 weeks post-intervention but increased at 26 weeks post-intervention. Difficulties in
306 the delay group decreased before receiving the intervention (week 18), increased

slightly after the intervention (week 23), decreased at 13 weeks post-intervention, and increased at 26 weeks post-intervention.

3.2. Multi-level modelling

3.2.1. Parent-reported child generic HRQoL

Multi-level modelling of the data (reported in Table 2), showed that time between diagnosis and baseline (Model 2) significantly improved model fit in comparison to the baseline model. This demonstrates improvements in HRQoL as time from diagnosis increased. Model 3 showed change over time during the study was a significant addition, meaning that HRQoL scores improved during the study. Adding the main effect of the intervention (Model 4) significantly improved model fit, demonstrating that HRQoL improved as a result of the intervention. Further additions to the model; adding the main effect of group (Model 5), random effect of the intervention (Model 6) and interaction term (study group x intervention) (Model 7), did not significantly improve model fit. Model 4 was the most parsimonious model (model parameter estimates are shown in Table 3). Mean parent-reported PedsQl had improved from 62.21 (SD: 19.59) at baseline to 71.25 (SD: 17.96) at 6 months.

3.2.2. Emotional and Behavioural difficulties

Table 2 shows that Model 3, including change over time, was the most parsimonious model (Table 3 reports parameter estimates). Increasing study week was associated with decreasing SDQ difficulties. Time elapsed between diagnosis and baseline (Model 2) did not significantly predict SDQ scores and there was no evidence that SDQ improvements resulted from the intervention (Model 4).

3.3. Secondary Outcomes

Supplementary tables B.3 and B.4 show the modelling and parameter estimates for the secondary outcomes. Time between diagnosis and baseline significantly improved model fit in all secondary outcomes, demonstrating improvements with increasing time since diagnosis. The main effect of the intervention was not a significant predictor for any secondary outcome measure. Parsimonious models for parent-reported PedsQl (cancer) and child-reported PedsQl (generic) modelled the intervention as a random effect (Model 6), indicating that intervention efficacy varied between children. Parent-reported caregiver burden, child confidence, treatment anxiety and child-reported HrQoL (cancer) and treatment anxiety were best explained by change over time (Model 3).

3.4. Acceptability

Acceptability was high in the families who participated in the intervention. Children rated the intervention as very enjoyable (95%) and very interesting (92.5%). All parents said they would recommend the intervention to other families. Families highlighted benefits including filling in gaps in the child's knowledge, reducing child anxiety and improving the ability of children to communicate about their illness. Full attendance of the intervention for children who started the programme was 85%, with 90% attending three or more sessions. Barriers to participation included scheduling around work, school and family commitments, travel issues and child illness.

4. Discussion and conclusion

4.1. Discussion

356 This study evaluated a novel, small-group psychoeducational intervention for
357 children with leukaemia. Acceptability testing showed that both children and parents
358 found the intervention appropriate, suggesting that families would find this approach
359 beneficial if included in healthcare provision. The acceptability assessment
360 highlighted perceived benefits of the intervention (increasing child knowledge and
361 communication and reducing anxiety). However, recruitment levels were
362 substantially lower than expected, suggesting that intervention uptake might be
363 problematic. Scheduling around work and family commitments, and travel issues,
364 were commonly identified as barriers to participation. Similar barriers have been
365 described in other healthcare interventions [39,40] which emphasises the importance
366 of considering the burdens associated with intervention delivery.
367 Lower recruitment to the study reduced the power to detect intervention
368 effects. Despite this, we detected an intervention effect on one of the primary
369 outcomes (child HRQoL), suggesting that this approach is worthy of further
370 development and evaluation. HRQoL increased by more than twice the MCID [28]
371 during the study. This includes the significant effect of the intervention as well as
372 other improvements over time. No effects were detected on the other primary
373 outcome (emotional and behavioural difficulties) or the secondary outcomes.
374 The intervention might improve HRQoL through providing information about
375 the disease and treatment, healthy lifestyle advice and through access to peers with
376 shared experiences. Reducing illness uncertainty has been shown to reduce stress
377 and anxiety [41], while improving the ability to communicate with doctors and families
378 enables children to make choices and utilise social support [16]. Survivors may have
379 been too young or distressed during treatment to fully assimilate illness information
380 and will have less contact with healthcare providers once their treatment ends. Our

intervention provided opportunities to address questions and misunderstandings. Lack of knowledge about health vulnerabilities is common in survivors of childhood leukaemia and survivors sometimes fail to practise health protective behaviours (e.g. healthy eating, exercise, avoiding sun exposure) despite their higher risk for long-term health conditions [41,42]. Psychoeducational interventions highlighting positive health behaviours have the potential to address these on-going health needs. Future work is needed to explore how far positive health messages are incorporated into behaviour and maintained over time and how this impacts long-term HRQoL.

Our sample showed more emotional and behavioural problems than the general population. Behavioural difficulties are a substantial burden during leukaemia treatment, particularly associated with steroid treatment [11]. SDQ was the only outcome not associated with time since diagnosis suggesting that issues remain stable. We found no evidence of improvements in behavioural difficulties associated with the intervention. In addition to psychoeducation, families might benefit from targeted interventions addressing the effects of steroids and long-term behavioural issues (e.g. parenting programmes, coping skills training, family teamwork).

Plots of scores of the HRQoL measures (child and parent-reported generic and cancer-specific QoL) showed that HRQoL improved in the immediate group after receiving the intervention, with no similar improvement in the delay group. This suggests a positive effect of the intervention. However, we also found improvements in the delay group immediately prior to beginning the workshop programme. It is possible that preparing for the intervention and completing measures might have improved family communication about leukaemia prior to the intervention, leading to improvements in HRQoL. Increased involvement with healthcare and open

406 communication in families has been associated with improved adjustment to illness
407 [16,43]. Likewise, HRQoL monitoring has been used in paediatric diabetes care to
408 address problematic issues [44]. The delay group also improved in HRQoL following
409 the intervention (parent reported generic, parent and child-reported cancer-specific
410 HRQoL). However, improvements before the workshops may have obscured some
411 of the effects of the intervention identified in the multilevel modelling. Improvements
412 in HRQoL scores tended to plateau at the 3 and 6-month follow-ups for the delay
413 and immediate groups but were also largely maintained.

414 The intervention included a number of different components and potentially
415 active ingredients (see Supplementary Table B.2). The focus was on delivering
416 psychoeducation to reduce illness uncertainty and anxiety, and to improve illness-
417 related communication and coping. However, it is possible that the social delivery of
418 the intervention improved HRQoL. Further evaluation of the intervention with an
419 active control group, rather than a delay control group would be helpful in evaluating
420 the relative contributions of these components.

421 A number of limitations must be considered in interpreting these findings. Our
422 sample size was limited, removing the power to detect intervention effects that are
423 plausible for psychoeducational interventions. This also prevented the examination
424 of potential moderators of effect, such as treatment status and leukaemia type
425 (ALL/AML). Some intervention components were more relevant for families receiving
426 treatment, so effects may have been larger in this sub-group. Various methods were
427 used to improve recruitment, including repeated attempts to contact families,
428 involvement of family support groups and flexible arrangements for sessions. Much
429 of the eligible sample (63.5%) were not contactable during recruitment. This reflected
430 increased difficulties in recruiting survivors, who often had non-current contact

details. Some outcome measures, such as treatment-related anxiety and cancer-specific HRQoL, may also have been more sensitive to changes in the on-treatment group.

4.2. Conclusion

We found HRQoL improvements following group psychoeducation for children treated for leukaemia which provides encouragement for the development of this interactive group approach to providing illness information, despite recruiting a smaller sample than targeted.

4.3. Practice implications

Replication of our findings in larger samples would be a useful goal for future research. Difficulties with uptake and retention are common in interventions for paediatric chronic conditions. Therefore, it is vital that future studies examine barriers to participation in intervention studies, both to improve sample sizes and to increase access to psychosocial support for this population. The acceptability assessment suggested a number of barriers to participation in our study (scheduling around work, school and family commitments, travel issues and child illness) which reflect particular difficulties in recruiting into group interventions. This might prompt an exploration of different methods for delivering group psychoeducation (e.g., remote delivery), particularly for rarer conditions such as leukaemia.

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Conflict of interest statement:

The authors report no conflicts of interest.

Data availability statement:

The data that support the findings of this study is not publically available as it contains potentially identifiable and sensitive information about participants. Data is available from the corresponding author upon request.

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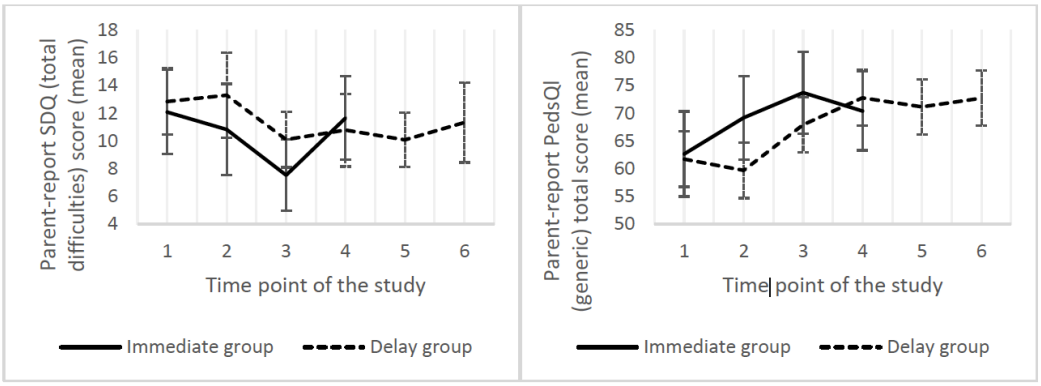
Figure 1: Parent-reported PedsQl (generic) and SDQ (total difficulties) mean scores plotted over time for the immediate and delay groups.



Time point	Immediate group	Delay group
1	Pre (Week 1)	Mc (Week 1)
2	Post (Week 5)	Mc (Week 5)
3	Follow-up 1 (Week 18)	Pre (Week 18)
4	Follow-up (Week 31)	Post (Week 23)
5		Follow-up 1 (Week 36)
6		Follow-up 2 (Week 49)

Key shows outcome measurement for study groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, Follow-up 1: 13 weeks post-intervention, Follow-up 2: 26 weeks post-intervention. PedsQl: Pediatric Quality of Life Inventory. SDQ: Strengths and Difficulties Questionnaire. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

TABLE 1: *Baseline characteristics and measures for the immediate and delay groups*

	Immediate group (N=26)	Delay group (N=32)	Test on group difference †
	Means (SD)	Means (SD)	t-test (df)
Age (years)	8.81 (1.79)	9.41 (1.81)	1.262 (56)
Time since diagnosis (years)	4.35 (2.63)	4.71 (3.31)	0.451 (56)
Parent reported outcomes:			
PedsQL (generic)	62.65 (19.58)	61.74 (20.04)	-.164 (56)
PedsQL (cancer module)	73.25 (18.26)	71.17 (19.99)	-.388 (56)
SDQ (total)	12.08 (7.88)	12.84 (6.14)	.383 (56)
Caregiver burden	4.76 (1.64)	4.16 (1.65)	-1.302 (56)
Child treatment anxiety	4.07 (1.19)	3.62 (2.01)	-.977 (56)
Parent treatment anxiety	3.79 (1.52)	3.95 (1.56)	.371 (56)
Child self-efficacy	2.4 (1.06)	2.57 (.79)	.647 (56)
Child reported outcomes:			
PedsQL (generic)	63.79 (17.41)	61.94 (22.29)	-.331 (56)
PedsQL (cancer module)	78.55 (10.75)	78.14 (12.98)	-.123 (56)
Child treatment anxiety	.71 (.52)	.74 (.6)	.191 (56)
	Number	Number	Fisher's exact test
Male	13	21	.288
ALL Regimen: A	15	16	
B	5	0	
C	5	14	
AML	1	2	Nc
On-treatment (number)	9	14	.592
Attrition	9	17	.145

SD: standard deviation, df: degrees of freedom, Nc: test not calculable on treatment regimen (zero value), ALL: Acute Lymphoblastic Leukaemia, Regimen A= low risk treatment, Regimen B= moderate risk treatment, Regimen C= high risk treatment, AML: Acute Myeloid Leukaemia, PedsQL: Pediatric Quality of Life Inventory, SDQ: Strengths and Difficulties Questionnaire.

† No t-tests or Fishers exact tests on differences between the study groups were statistically significant.

TABLE 2: *Multilevel model-fit for the primary outcomes*

Model	Deviance (-2LL)	Change in Deviance, change in df	Residual variance	Child level intercept variance	Child level slope co-variance	Intercept slope covariance
Parent-report PedsQL (generic)						
Unconditional	1583.376		71.947	274.915		
Control model	1565.661	17.715*, 1df	71.526	197.893		
Change over time	1528.106	37.555*, 1df	55.634	199.350		
Main effect of intervention	**1522.355**	**5.751*, 1df**	**53.444**	**200.445**		
Main effect of group	1521.605	.75, 1df	53.436	197.645		
Intervention as random effect	1519.294	2.311, 2df	49.892	198.754	12.547	-20.811
Group*Int interaction	1519.205	.089, 1df	49.892	198.754	12.547	-20.811
Strengths and Difficulties Questionnaire (SDQ) (total difficulties)						
Unconditional	1243.678		13.140	34.493		
Control model	1241.670	2.01, 1df	13.135	33.175		
Change over time	**1237.586**	**4.084*, 1df**	**12.852**	**32.722**		
Main effect of intervention	1237.084	.502, 1df	12.778	32.986		
Main effect of group	1236.730	.354, 1df	12.778	32.753		
Intervention as random effect	1231.497	5.233, 2df	11.099	33.602	5.983	-6.192
Group*Int interaction	1231.449	.048, 1df	11.101	33.580	5.942	-6.112

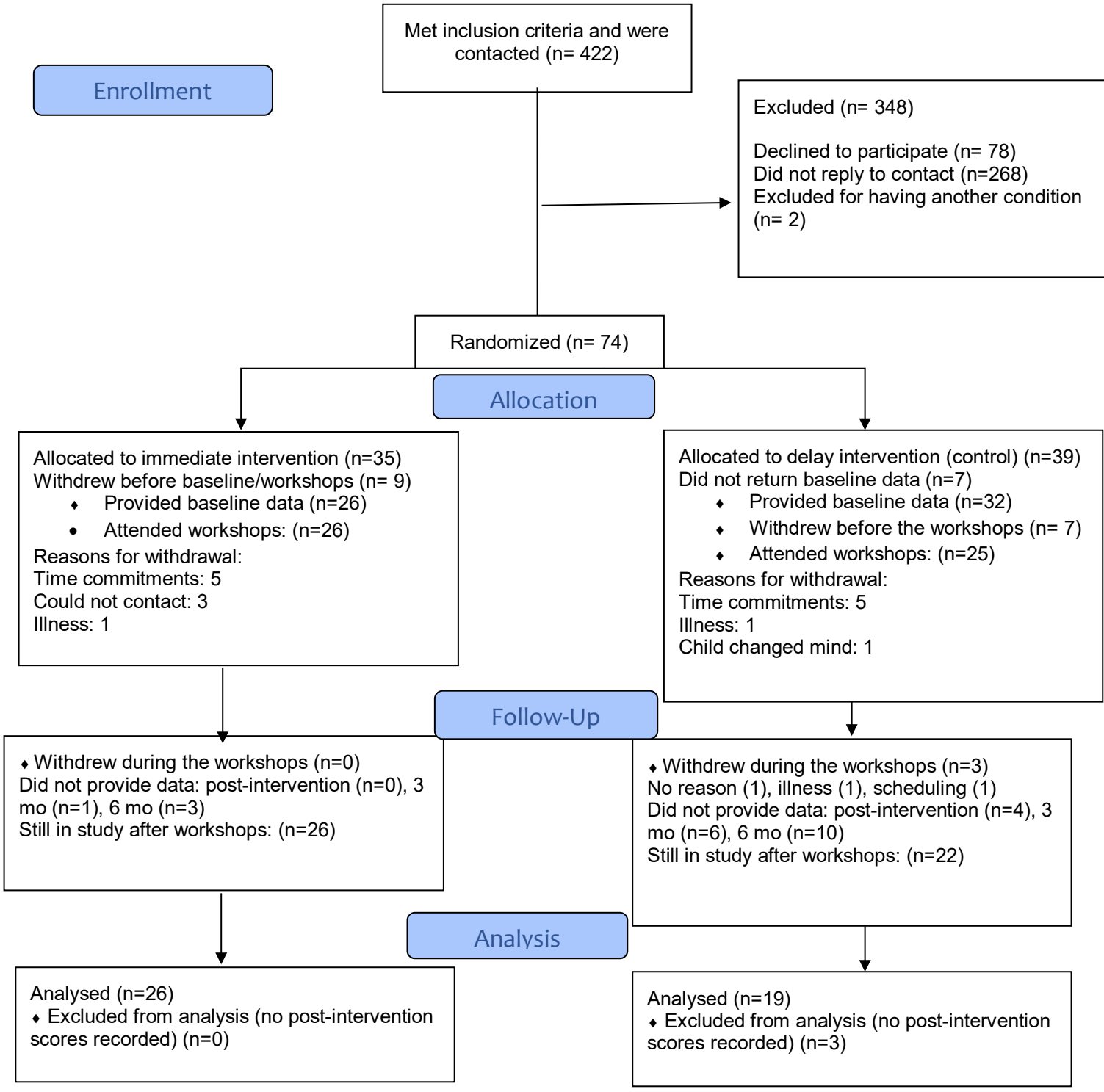
-2LL: -2 log likelihood, df: degrees of freedom.
Bolded model is the model with the best fit to the data. * indicates a significant improvement in the model, tested using Chi-square distribution on reduction in -2LL deviance

TABLE 3: *Parameter estimates for the best fit models for the primary outcomes*

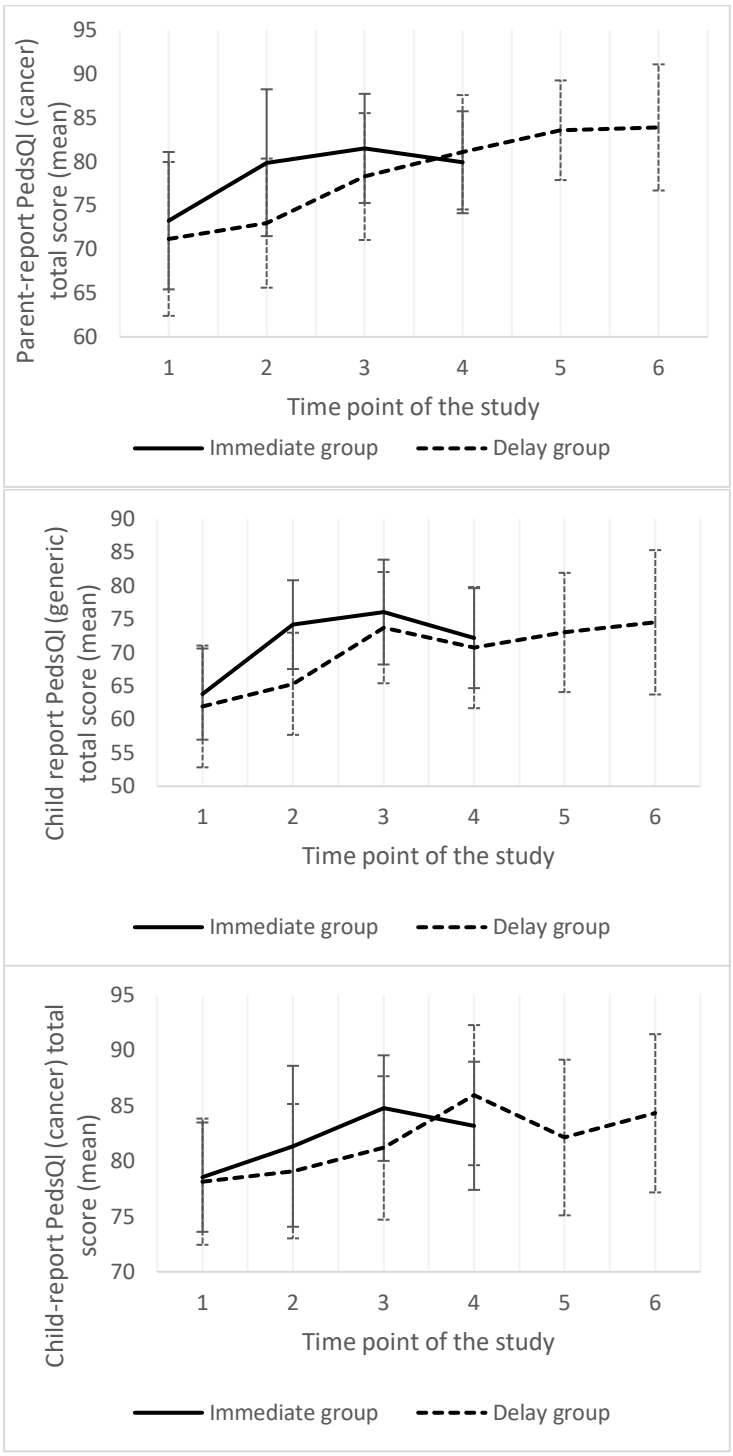
Parameter	Estimate	SE	Df	T	Significance (p value)	95% CI (lower bound)	95% CI (upper bound)
Outcome= Parent-report PedsQL (generic)							
Intercept	50.481	3.734	63.891	13.518	0.001*	43.020	57.941
Time since diagnosis	3.047	0.666	58.552	4.576	0.001*	1.714	4.380
Change over time	0.151	0.060	155.566	2.539	0.012*	0.034	0.269
Intervention	4.222	1.742	151.581	2.423	0.017*	0.779	7.665
Outcome= Strengths and Difficulties Questionnaire total difficulties							
Intercept	13.864	1.499	57.125	9.250	<0.001*	10.863	16.866
Time since diagnosis	-0.385	0.271	54.504	-1.419	0.162	-0.928	0.159
Change over time	-0.038	0.019	152.199	-2.031	0.044	-0.076	-0.001

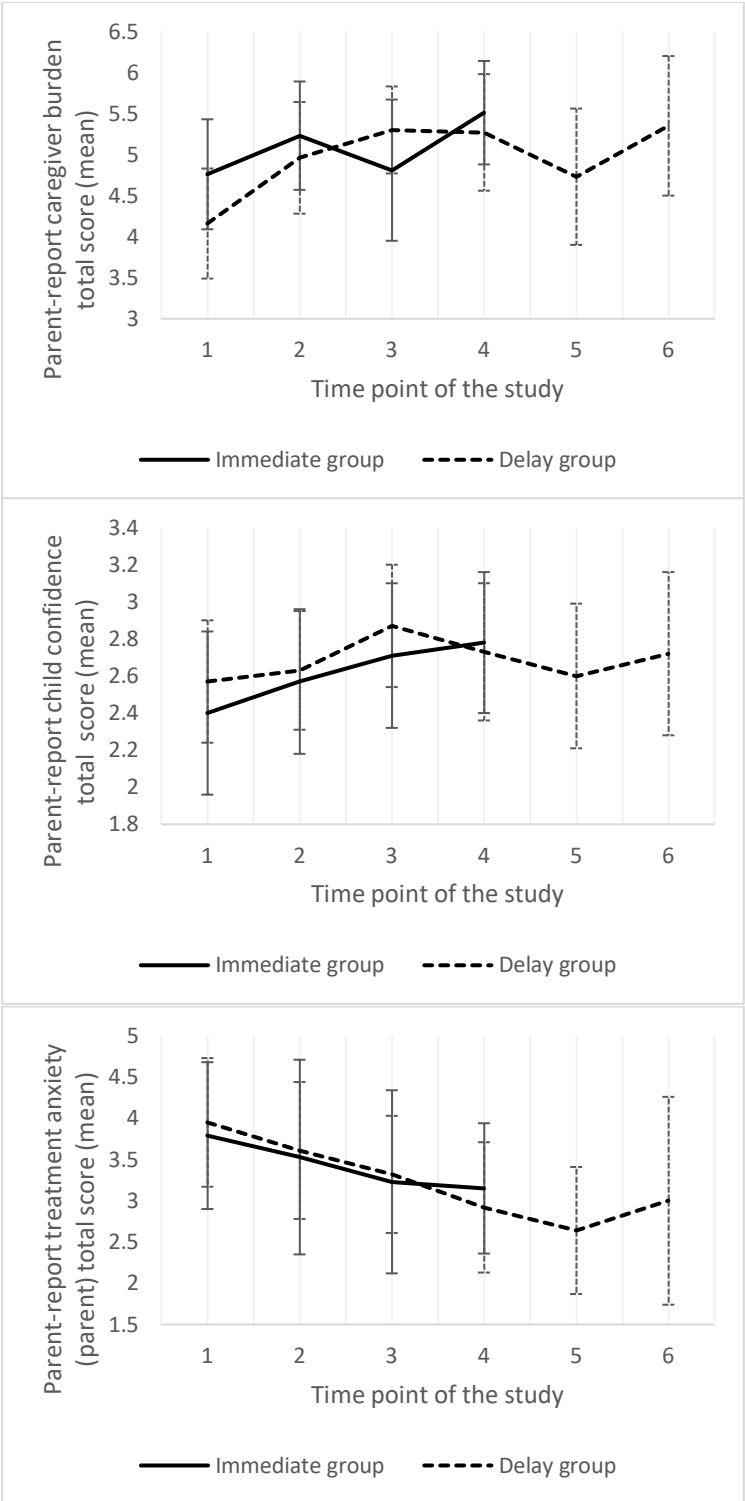
SE: Standard Error, df: degrees of freedom, T: t test. * indicates a significant predictor of the outcome measure.

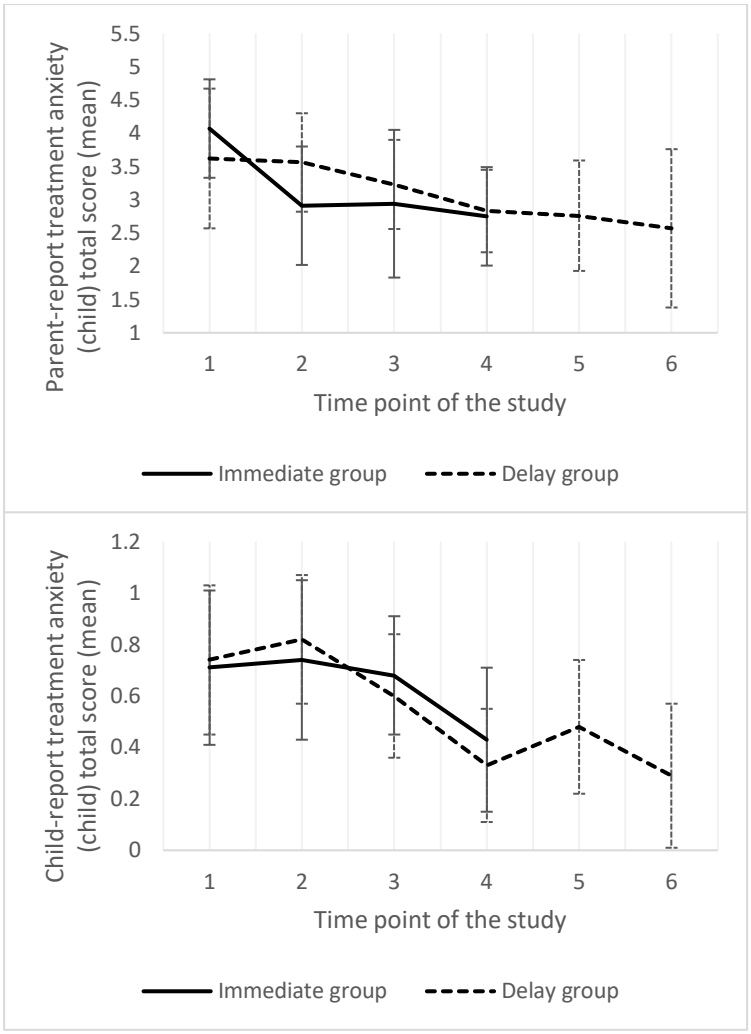
Figure A.1: CONSORT Flow Diagram showing flow of participants through the study.



Supplementary Figure A.2: Mean scores plotted over time for the immediate and delay groups for the secondary outcomes.




Parent-report caregiver burden total score (mean)
6.5
6
5.5
5
4.5
4
3.5
3
1
2
3
4
5
6
Time point of the study
Immediate group
Delay group
Parent-report child confidence total score (mean)
3.4
3.2
3
2.8
2.6
2.4
2.2
2
1.8
1
2
3
4
5
6
Time point of the study
Immediate group
Delay group
Parent-report treatment anxiety (parent) total score (mean)
5
4.5
4
3.5
3
2.5
2
1.5
1
2
3
4
5
6
Time point of the study
Immediate group
Delay group



Time point	Immediate group	Delay group
1	Pre (Week 1)	Mc (Week 1)
2	Post (Week 5)	Mc (Week 5)
3	Follow-up 1 (Week 18)	Pre (Week 18)
4	Follow-up (Week 31)	Post (Week 23)
5		Follow-up 1 (Week 36)
6		Follow-up 2 (Week 49)

Key shows outcome measurement for study groups at each time point. Pre: pre-intervention, Post: post-intervention, Mc: Matched control, Follow-up 1: 13 weeks post-intervention, Follow-up 2: 26 weeks post-intervention. PedsQl: Pediatric Quality of Life Inventory. Error bars represent 95% confidence intervals for group means (solid line for immediate group, dashed line for delay group).

Supplementary TABLE B.1: *Content of the four intervention workshops*

Workshop	Exploratory activity	Activity One	Activity Two
Workshop One: The human body and the effects of chemotherapy.	Constructing 3-D models of the human body: skeletons and organs.	Let's Bowl Game: skittles labelled with parts of the body are knocked down with balls representing chemotherapy drugs. Discussion of side effects and managing symptoms.	Changing body image: drawing activity using cards to draw and reconstruct bodies with different body shapes, hair and faces. Discussion of temporary changes in physical appearance due to chemotherapy.
Workshop Two: Blood and leukaemia	Models of the heart and circulatory system. Using stethoscopes to listen to heartbeat.	'Put it together' blood activity: models representing the different blood cells: red blood cells, platelets and white blood cells in a blood vessel. Demonstration of what happens with the proliferation of blasts and with chemotherapy to remove blasts.	'Spot the difference': looking at pictures of 'normal' blood and blood from a leukaemia patient to spot the differences between them.
Workshop Three: Cell biology, DNA, leukaemia caused by change in DNA	Looking at slides of blood from leukaemia patient under the microscope. Compared to 'normal' blood cell slides. Cell models.	'Cell factory' game: Making a model of the cell and matching the function of organelles to parts of a factory. Role of the nucleus and DNA.	'DNA chain' activity: demonstrate the structure of DNA using a model. Using beads with letters show that a change in sequence means that the sequence no longer makes sense.
Workshop Four: The sensory system and pain. Healthy living for the future.	'Exploring the senses' activities: touch, smell Models of the eye and ear.	'Rope and donut' exercise: demonstrate how messages are sent by nerves to the brain using normal and painful messages. How you respond affects the pain you feel. Discussion of coping strategies during procedures.	Discussion of the importance of staying healthy. 'Healthy living' exercise: identify components of a healthy lifestyle. Choose 3 changes to improve future health.

This is a brief summary of the workshop programme. Further details and lesson plans are available by request from the first author.

Supplementary TABLE B.2: *Components of the intervention and modifiable targets*

Component	Target
Understanding the pathophysiology of leukaemia (changes to blood cells, DNA)	• Increase illness-related communication skills and confidence • Reduce illness uncertainty
Understanding what treatment does and why it is important (chemotherapy, steroids, tests)	• Increase familiarity with treatment and procedures • Increase illness-related communication skills • Increase treatment adherence and compliance • Reduce threat appraisal (e.g. chemotherapy, blood tests)
Understanding the side effects of treatment	• Managing symptoms (e.g. coping with effects of steroids, nausea) • Increase illness-related communication skills and confidence • Reduce stress related to changes in appearance
Coping with painful procedures	• Reduce threat appraisal/ anticipatory anxiety • Promote positive coping strategies
Healthy living	• Increase adherence to treatment (survivors) • Promote positive health behaviours • Perceive vulnerability to late effects • Promote positive coping through health behaviours • Future orientation/motivation
Small group setting	• Increase illness-related communication skills and confidence • Social support
Interactive	• 'Hands-on' learning • Information-seeking • Address misunderstandings • Age-appropriate explanations

Supplementary TABLE B.3: *Results of the multilevel modelling analysis on the secondary outcomes*

Model	Deviance (-2LL)	Change in Deviance, change in df	Residual variance	Child level intercept variance	Child level slope covariance	Intercept slope covariance
Parent-reported PedsQl (cancer module)						
Unconditional	1438.168		78.941	203.539		
Control model	1419.298	18.87*, 1df	78.116	140.662		
Change over time	1394.359	24.939*,1df	64.387	144.931		
Main effect of intervention	1393.408	.951, 1df	63.947	144.866		
Main effect of group	1392.867	.541, 1df	63.987	142.970		
Intervention as random effect	**1385.141**	**7.726*,2df**	**56.477**	**146.317**	**29.740**	**-46.587**
Group*Intervention interaction	1384.943	.198, 1df	56.500	146.193	29.408	-46.721
Child-reported PedsQl (generic)						
Unconditional	1621.855		113.355	243.968		
Control model	1608.018	13.837*, 1df	112.476	186.564		
Change over time	1592.293	15.725*, 1df	101.570	185.838		
Main effect of intervention	1590.574	1.719. 1df	100.366	186.212		
Main effect of group	1589.907	.667, 1df	100.405	183.353		
Intervention as random effect	**1583.790**	**6.117*, 2df**	**87.727**	**186.918**	**44.477**	**-45.237**
Group*Intervention interaction	1582.121	1.669, 1df	87.393	186.370	40.705	-43.341
Child-reported PedsQl (cancer)						
Unconditional	1298.107		59.451	114.114		
Control model	1288.188	9.919*, 1df	58.667	94.629		
Change over time	**1278.602**	**9.586*, 1df**	**54.237**	**95.902**		
Main effect of intervention	1277.054	1.548, 1df	53.652	95.582		
Main effect of group	1277.033	.021, 1df	53.661	95.488		
Intervention as random effect	1273.890	3.143, 2df	48.914	96.309	17.387	-15.278
Group*Intervention interaction	1273.269	.621, 1df	48.951	96.323	15.905	-15.035
Caregiver burden						
Unconditional	641.216		.946	1.626		
Control model	624.737	16.479*, 1df	.942	1.146		
Change over time	**618.733**	**6.004*, 1df**	**.900**	**1.167**		
Main effect of intervention	618.731	.002, 1df	.900	1.167		
Main effect of group	617.100	1.631, 1df	.898	1.132		
Intervention as random effect	616.033	1.067, 2df	.831	1.152	.248	-.042
Group*Intervention interaction	614.856	1.177, 1df	.830	1.154	.217	-.043
Parent-reported child confidence						
Unconditional	418.452		.279	.499		
Control model	411.899	6.553*, 1df	.278	.438		
Change over time	**407.712**	**4.187*, 1df**	**.270**	**.442**		
Main effect of intervention	407.592	.12, 1df	.270	.443		
Main effect of group	407.526	.066, 1df	.270	.443		

Intervention as random effect	405.094	2.432, 2df	.235	.454	.129	.013
Group*Intervention interaction	402.562	2.532, 1df	.236	.458	.099	.070
Parent-reported parent treatment-related anxiety						
Unconditional	430.243		1.226	1.300		
Control model	419.415	10.828*, 1df	1.201	.957		
Change over time	**414.876**	**4.539*, 1df**	**1.148**	**.948**		
Main effect of intervention	414.840	.036, 1df	1.148	.949		
Main effect of group	414.835	.005, 1df	1.148	.949		
Intervention as random effect	414.196	.639, 2df	1.190	.986	.097	.309
Group*Intervention interaction	414.034	.162, 1df	1.181	.989	.089	.297
Parent-reported child treatment-related anxiety						
Unconditional	429.389		1.606	.698		
Control model	423.702	5.687*, 1df	1.575	.583		
Change over time	**417.869**	**5.833*, 1df**	**1.497**	**.561**		
Main effect of intervention	417.550	0.319, 1df	1.487	.572		
Main effect of group	417.372	.178, 1df	1.486	.567		
Intervention as random effect	416.548	.824, 2df	1.410	.578	.287	.201
Group*Intervention interaction	414.739	1.809, 1df	1.407	.567	.209	.226
Child-reported treatment-related anxiety						
Unconditional	161.064		.113	.160		
Control model	154.588	6.476*, 1df	.112	.140		
Change over time	**145.432**	**9.156*, 1df**	**.103**	**.134**		
Main effect of intervention	144.838	.594, 1df	.103	.134		
Main effect of group	144.692	.146, 1df	.103	.134		
Intervention as random effect	144.655	.037, 2df	.103	.135	.000	-.007
Group*Intervention interaction	143.996	.659, 1df	.103	.135	.000	-.006

PedsQl: Pediatric Quality of Life Inventory. * indicates a significant improvement in the model, tested using Chi-square distribution on reduction in -2LL deviance.

Supplementary TABLE 4: *Parameter estimates from the best fit models for the secondary outcomes*

Parameter	Estimate	SE	Df	T-test	Significance
Parent-reported PedsQl (cancer module)					
Intercept	63.920	3.508	60.200	18.220	<.001*
Time since diagnosis	2.554	.551	52.360	4.639	<.001*
Change over time	.183	.066	123.559	2.776	.006*
Main effect of intervention	2.531	2.154	107.429	1.175	.243
Main effect of group	-1.962	3.298	53.665	-.595	.554
Child-reported PedsQl (generic)					
Intercept	57.101	4.102	62.639	13.920	<.001*
Time since diagnosis	2.847	.651	57.535	4.376	<.001*
Change over time	.140	.078	135.538	1.793	.075
Intervention	3.191	2.498	118.041	1.277	.204
Group	-4.471	3.878	57.238	-1.153	.254
Child-reported PedsQl (cancer)					
Intercept	71.763	2.790	60.191	25.721	<.001*
Time since diagnosis	1.595	.494	57.110	3.227	.002*
Change over time	.136	.043	131.613	3.158	.002*
Caregiver burden					
Intercept	3.760	.302	61.182	12.458	<.001*
Time since diagnosis	.235	.056	56.736	4.204	<.001*
Change over time	.013	.005	147.753	2.480	.014*
Parent-reported child confidence					
Intercept	2.194	.180	59.644	12.178	<.001*
Time since diagnosis	.084	.033	56.168	2.585	.012*
Change over time	.006	.003	150.342	2.060	.041*
Parent-reported parent treatment-related anxiety					
Intercept	4.450	.332	45.865	13.386	<.001*
Time since diagnosis	-.228	.069	43.497	-3.314	.002*
Change over time	-.016	.008	94.932	94.932	.034*
Parent-reported child treatment-related anxiety					
Intercept	4.055	.309	44.326	13.127	<.001*
Time since diagnosis	-.141	.062	37.292	-2.264	.029*
Change over time	-.021	.009	96.742	-2.445	.016*
Child-reported treatment-related anxiety					
Intercept	.973	.113	54.804	8.640	<.001*
Time since diagnosis	-.054	.021	50.588	-2.540	.014*
Change over time	-.007	.002	106.122	-3.080	.003*

PedsQl: Pediatric Quality of Life Inventory, SE: standard error, df: degrees of freedom. * indicates a significant predictor ($p<0.05$).