CHAPTER 5

Factors influencing childhood cancer patients to participate in a combined physical and psychosocial intervention program: Quality of Life in Motion

Elisabeth M. van Dijk-Lokkart, Katja I. Braam, Jaap huisman, Gert-Jan J.L. Kaspers, Tim Takken, Margreet A. Veening, Marc B. Bierings, Johannes H.M. Merks, Martha A. Grootenhuis, Marry M. van den Heuvel-Eibrink, Isabelle Streng, Eline van Dulmen-den Broeder

Psycho-oncology 2014, 24:465-471

ABSTRACT

For a multi-center randomized trial investigating the effects of a 12-week physical and psychosocial intervention program for children with cancer, we invited 174 patients (8-18 years) on treatment or within one year after treatment; about 40% participated. Reasons for non-participation were investigated.

Eligible patients received written and verbal information about the study. Those declining to participate were asked to complete questionnaires concerning: reasons for non-participation, daily physical activity, health-related quality of life (HrQoL) and behavioral problems. Participants completed the same questionnaires at baseline (excluding 'Reasons for non-participation').

Of 174 eligible patients 106 did not participate; of these, 61 (57.5%) completed the one-time survey. Main reasons for non-participation as reported by the parents were 'Too time-consuming' and 'Participation is too demanding for my child', while children most frequently reported 'Too time-consuming' and 'Already frequently engaged in sports'.
No differences between participants and non-participants were found for age, HrQoL, parental-reported behavior problems, sport participation, school type, BMI and perceived health. A greater distance from home to hospital resulted in reduced participation (β: -0.02; p=0.01). Non-participants rated their fitness level higher (p=0.03). Participating children (11-18 years) reported more behavioral problems (p=0.02), in particular internalising problems (p=0.06).
Participation of childhood cancer patients in an intensive physical and psychosocial intervention program seems related to the burden of the intervention and the travel distance from home to hospital. In general, non-participants rated their fitness level higher compared with participants. Patients with more (internalising) behavioral problems seem more likely to participate in the study.

BACKGROUND

Due to advances in techniques for diagnosis and treatment, survival rate of childhood cancer patients (CCP) has increased substantially over the last decades. However, childhood cancer survivors (CCS) suffer significant adverse long-term side-effects due to the disease and its treatment. Geenen et al. (2007) concluded that about 75% of CCS has at least one late adverse health effect after median follow-up of 17 years.[17] Impaired physical fitness has been reported during and after childhood cancer treatment[29,45,138,214,240] which may lead to fatigue, obesity and poor skeletal and/or mental health.[19,166,216–220] These adverse health outcomes may negatively impact perceived health-related quality of life (HrQoL).[19,219,220] Therefore, prevention of inactivity-related health problems by increasing physical fitness, both during and after treatment, is essential.
Rehabilitation programs in adult cancer patients, including physical exercise and psychosocial support, report positive effects on physical fitness and HrQoL.[221,222] In CCP, few studies have examined the effects of physical exercise training during and after treatment. Moreover, those available had small study groups and did not include a psychosocial support program to increase wellbeing, self-belief and compliance with the intervention.[63–65,92,93] However, they did show that it is safe for children with acute lymphoblastic leukemia to engage in exercise interventions.
Therefore, the Quality of Life in Motion (QLIM) study was set up. A randomized controlled trial (RCT) to evaluate the feasibility and effects of an intensive 12-week intervention program, combining physical exercise (twice a week in a physical therapy center close to home) and psychosocial training (six sessions, once every 2 weeks in the treating hospital). Improved wellbeing is hypothesized to increase willingness and motivation to engage in sport activities and, as a result, to enhance the efficacy of the exercise program and to prevent dropouts. Vice versa, improved physical fitness is expected to enhance patient's wellbeing and HrQoL. The design of this RCT has been described in detail elsewhere.[148]

During the inclusion period for the QLIM-RCT many patients declined to participate, despite that most of them experienced mild to severe deficits in physical activity. Of the 174 eligible patients only 68 (39.1%) participated, a low number compared with reported participation rates of ≥ 80% in other physical intervention studies in CCP.[63,65] In psychosocial intervention studies both lower and higher participation rates have been described.[241–244] No studies are available, to our knowledge, reporting on participation rate in a combined intervention study.

The present study examines reasons for limited participation rate in the QLIM study, barriers that are related to non-participation, and consequently which factors might

be influenced to improve participation rates in future studies. Little is known about psychosocial functioning of participants/non-participants in earlier childhood exercise studies and whether or not this is related to participation. We hypothesised that non-participants had a better quality of life and showed less behavior problems than participants and therefore could be less prone to participate in an intervention program. It was also hypothesised that non-participants had a less positive attitude towards sports and came from families with a less physically active background.

METHODS

Study population

The inclusion period was March 2009 to July 2013. Eligible participants for the QLIM-RCT were aged 8-18 years, diagnosed with any type of childhood malignancy, treated with chemotherapy and/or radiotherapy and on or no longer than 12 months off treatment. Exclusion criteria were: stem cell transplantation, growth hormone therapy, wheelchair-dependency, unability to 'ride a bike', and unability to read, write, self-reflect, and/or follow instructions for whatever reason.
Patients were recruited from VU University Medical Center (Amsterdam), Wilhelmina Children's Hospital UMC (Utrecht), Emma Children's Hospital/Academic Medical Center (Amsterdam), and Erasmus Medical Center (Rotterdam). Patients and parents individually received written and verbal information about the study, an informed consent form, and an addressed return envelope. In two centers the information was given by a member of the QLIM research team, in the other two centers this was done by a research nurse of that center, because due to privacy regulations they were not allowed to give patient information to the QLIM research team before approval. Written informed consent was obtained from the parents or legal guardian, and also separately from each patient aged ≥ 12 years. Patient inclusion started after approval of the Medical Ethics Committee (number 2008/208).

Data collection and instruments

Participants of the QLIM-RCT were asked to complete questionnaires on topics described below on four occasions (at baseline and after 3-4 months, 6-9 months and 12 months post-baseline). Data obtained from the questionnaires completed at baseline were used for the present cross-sectional study. Patients and parents declining to participate in the study were asked to complete the same questionnaires once. In addition, they were asked to complete a questionnaire evaluating reasons for non-

participation. In contrast to the participants, non-participants completed the questionnaires on their own at home.

Health-related quality of life (HrQoL)

Dutch version of the 23-item PedsQL 4.0 Generic Core scale was used; self-report and parent-proxy report. It consists of 4 multi-items subscales: physical functioning (8 items), emotional functioning (5 items), social functioning (5 items) and school functioning (5 items). Psychosocial health status was derived from the last three subscales. Per item, child or parent indicated on a 5-point Likert scale to what extent the child had difficulties with the stated problem in the past month: never (0), almost never (1), sometimes (2), often (3), and almost always (4). Each answer was reversed, scored and rescaled to a 0-100 scale (0=100, 1=75, 2=50, 3=25, 4=0). Items on each subscale were summarized and divided by the amount of items in the subscale to get a total score between 0 and 100 for each subscale, with higher scores indicating higher levels of functioning or quality of life.[57] The Dutch version has adequate psychometric properties and normative scores of the Dutch population are available [131].

Behavioral problems

Dutch version of Child Behavior Checklist (CBCL) was used to assess parental perception of behavioral problems in children aged 6-18 years.[245] All participants and non-participants aged ≥ 11 years also completed the Youth Self-Report (YSR) designed to assess behavioral problems in adolescents aged 11-18 years. In the present study the total problem scale, as well as internalising and externalising scales were used. Scores of the subscales are computerized to the Aseba program (ADM) and converted to T-scores, with higher scores indicating more behavioral problems.[245] T-scores ≤ 60 are in the normal range, scores of 60-63 are in the borderline range (84th to 90th percentile) indicating problems of concern, and scores ≥ 63 (≥ 90th percentile) are in the clinical range and indicate problems of clinically relevant deviance. Both CBCL and YSR are useful, valid and reliable instruments to assess evaluation of internalizing and externalising behavioral problems.[245]

Daily physical activity questionnaire

In this questionnaire patients are asked to answer questions about sport participation before their illness, sport participation rate of their families, co-existing morbidity, attitude towards sports, current health and fitness score (on a 10-point rating scale), transport methods to school, and present physical activity compared with healthy peers. Some information on general characteristics was also collected, e.g. type of school and (ages of) siblings.

General and medical characteristics

Information about sex, date of birth, diagnosis, during or after treatment, weight, height, and travel distance from home to the hospital, were obtained from the patients' medical records.

Additional questionnaire for non-participants

Non-participants and their parents were asked to complete a short additional questionnaire concerning their main reasons for non-participation (parents and child separately). They could choose one or more of the following reasons: study not important; due to 'bad' memories not wanting to engage in new or extra activities in the hospital; participation too demanding (for my child); scary to (allow my child to) sport while being ill; already frequently engaged in sports; participation too time demanding; already involved in several other studies; already having physiotherapy; already having psychological treatment; and 'other reasons' - which they could indicate themselves in an open field. This questionnaire was not validated and the answer categories were based on author's assumptions of possible reasons for non-participation. Therefore, authors may have overlooked some additional reasons due to which an open field question was added.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) for Windows version 20 was used for the analyses. Data were checked for normality and log-transformed when skewed. Independent sample t-tests, Mann-Whitney U tests and chi-square tests for independence were used for group comparison (participants/non-participants). Logistic regression analyses were used to assess which factors could predict the likelihood of the patients to participate in the intervention program. Potential predictors were determined using univariate logistic regression analyses. For multivariate regression modeling, factors associated with participation at a level of $p \leq 0.20$ (2-sided) were entered into a backward selection procedure.

RESULTS

Participant and general (medical) characteristics

A total of 174 patients were eligible for participation in the QLIM-RCT and 68 (39.1%) participated. Of the 106 patients who did not wish to participate, 61 (57.5%) completed the one-time survey and were included in the non-participants' analyses. Demo-

graphic and medical characteristics of each group are provided in Table 5.1. No general and medical information about the non-participants who also declined to fill in the one-time survey is available due to Dutch privacy regulations.

Table 5.1: Demographic and medical characteristics

	Participants (n=68)	Non-participants (n=61)
Males (n [%])	**36 (52.9)**	**32 (52.2)**
Center		
VU University Medical Center, Amsterdam	34 (50.0)	27 (44.3)
Wilhelmina's Childrens Hospital/UMC Utrecht	9 (13.2)	12 (19.7)
Emma's Childrens Hospital/AMC, Amsterdam	16 (23.5)	17 (27.9)
Erasmus Medical Center, Rotterdam	9 (13.2)	5 (8.2)
Diagnosis (n [%])		
Leukemia/lymphoma	46 (67.6)	43 (70.5)
Brain tumors/central nervous tumors	7 (10.3)	5 (8.2)
Solid tumors	15 (22.1)	13 (21.3)
When eligible for study (n [%])		
during treatment	21 (30.9)	20 (32.8)
within the first year after treatment	47 (69.1)	41 67.2)
Families with multiple children (yes) * (n [%])	55 (93.2)[1]	39 (76.5)[2]
Other illnesses (yes) (n [%])	11 (17.7)	13 (21.3)
Age at study (years) (mean [SD])	13.2 (3.1)	13.4 (3.0)
Height (cm) (mean [SD])	156.8 (17.6)	157.7 (16.8)
Weight (kg) (mean [SD])	50.3 (16.8)	51.0 (17.6)
BMI z-score (mean [SD])	0.15 (1.02)	0.17 (1.00)
Distance home-hospital (km) (mean [SD]) **	32.7 (19.9)	50.4 (42.1)

Abbreviation: SD: standard deviation; n: number
* p=0.03 difference between the two groups (chi-square tests)
* * p=0.01 difference between the two groups (independent sample t-test)
[1] Based on self-reported answers of only 59 participants.
[2] Based on self-reported answers of only 51 non-participants

No differences between participants and non-participants were found for sex, age, diagnosis group, on or off treatment, type of school, co-existing morbidities, height, weight, BMI (z-score), treating hospital, and travel distance from home to school. For non-participants distance from home to hospital was longer (p=0.01) than for participants. Participants more often came from families with multiple children than did non-participants (93.2% of participants had siblings vs. 76.5% of non-participants) (p=0.03).

Reasons for non-participation

Main reasons for not participating in the study as reported by the parents were 'too time consuming' (24.8%) and 'participation too demanding for the child' (12.8%) and the children reported 'too time consuming' (20.6%) and 'already frequently engaged in sports' (14.4%) (Table 5.2).

Table 5.2: Reasons for non-participation

Reasons for non-participation by parents (total N=117)	N	%
Too time consuming	29	24.8
Participation is too heavy for my child	15	12.8
My child already sports weekly	14	12.0
My child already has physiotherapy	13	11.1
My child is already involved in other research and this is enough	7	6.0
Travel distance from home to hospital	6	5.1
Too much school absence	6	5.1
Due to bad memories I want no new or extra activities for my child in the hospital	5	4.3
My child must live a normal life without hospital visits	3	2.6
Participation only if with certainty my child will get the intervention	3	2.6
We do not want to come to the hospital on extra occasions	3	2.6
My child already has psychological treatment	2	1.7
Other reasons (mentioned only once)	11	9.3
Reasons for non-participation by children (total N=97)	**N**	**%**
Too time consuming	20	20.6
I am already frequently engaged in sports	14	14.4
Due to bad memories I want no new or extra activities in the hospital	11	11.3
Participation is too heavy for me	11	11.3
I already have physiotherapy	7	7.2
Travel distance from home to hospital	5	5.2
I do not want psychological treatment	5	5.2
Too much school absence	5	5.2
I do not want to come to the hospital on extra occasions	4	4.1
I am already involved in other research and this is enough	3	3.1
I already have psychological treatment	2	2.1
I do not like the study	2	2.1
Too much sports takes away time to play with my friends	2	2.1
Other reasons (mentioned only once)	6	6.1

Health-related quality of life

No significant differences were found between both groups for HrQoL; quality of life of the non-participating children, as assessed by both the parents and the children, was similar to that of the participating children

Behavioral problems

As perceived by their parents, no significant differences in behavioral problems were found between the two subgroups of CCP. Only a trend towards a lower parental-reported total behavior problem score of the participant group was seen (p=0.06). Participating older children (aged 11-18 years) self-reported more behavioral problems (total behavior problem score; p=0.02), in particular internalizing problems (p=0.06). In the subgroup of parents of participating children aged 11-18 years there was a trend towards reporting more externalizing problems (p=0.05). When analyzing percentages of children with behavior problems scores in the normal, borderline and clinical range, no differences were found between the two subgroups.

Physical activity

No differences between participants and non-participants were found regarding current and pre-illness sport participation, sport participation of parents (before illness and present state), methods of transportation to get to school (active vs. passive transportation) and perceived physical activity over the past year (school days/weekends/holidays). In addition no difference was found in how patients perceived their condition compared with their peer group, how they perceived themselves as an athlete, and whether they found that intensive sport activities positively contributed to their health. Both groups equally rated their own health; however non-participants gave a higher score on their perceived physical fitness than the participants (6.1 versus 5.4 on a 10-pointscale; p=0.03).

Predictors of participation

The only independent factor associated with participation was shorter travel distance from home to hospital; with increasing distance to the hospital the participation decreased (OR: 0.98; 95% CI: 0.97 - 0.99; P=0.01). Model: Participation (yes/no) = 0.962 - 0.02 x kilometers from the hospital.

DISCUSSION

The main outcome of this cross-sectional study evaluating barriers to participate in a combined physical and psychosocial intervention program for CCP, is that participation seems to be mainly related to the burden of the intervention (too time consum-

ing, too demanding) according to non-participants and their parents. Travel distance from home to hospital was found to be the only significant mediator of participation with a shorter travel distance to the hospital predicting a higher participation rate. In addition, patients with a less positive view regarding their own physical fitness and adolescents with more (internalizing) behavioral problems were more motivated to participate while children who declined participation mentioned already frequently engaged in sports as reason for non-participation.

Research on other types of intervention programs for different pediatric populations have also shown that time demands are main barriers for parents to participate.[24,6] Perhaps participation rates drop as time consumption and burden of the intervention increase. The participation rate in a study by Hartman et al. (2009), including ALL patients (N=51) offered a (preventive) physiotherapy intervention once every 6 weeks in the hospital during the entire treatment period in combination with a medical check-up, was 82.1%.[65] In the intervention sessions children were offered exercises to perform independently at home. Marchese et al. (2004) included 28 ALL patients on maintenance treatment in a study (participation rate: 87.8%) and offered them five physiotherapy intervention sessions at weeks 0, 2, 4, 8 and 12 after baseline testing.[63] Children also received home exercises. Both studies included ALL patients only and had a considerably less intensive and time consuming physical intervention compared to the QLIM-RCT with no psychosocial intervention.[63,65,148] There is a possibility that this resulted in higher participation rates. This seems plausible since participation rates seem to drop when intensity and time-effort, of the physical intervention, increases as seen in a study by Takken et al. (2009).[92] Their intervention offered to ALL patients who were more than 6 months off treatment, included a physical training twice a week, during 12 weeks at a local physical therapy clinic close to home. Participation rate was 56.3% (N=9). This study by Takken et al. (2009) resembles our study when considering its time-consuming nature.[92] However, in our QLIM-RCT participation rates were even lower (39.1%). The fact that the QLIM intervention, in contrast to the studies mentioned above, also included a psychosocial program might have contributed to this. However, only 5% of the children, and none of the parents, reported the psychosocial part of the intervention to be a main reason for non-participation; thus, additional travel distance associated with the psychosocial intervention increasing time effort, seems more important than the psychosocial intervention itself. However, due to lack of similar studies this cannot be substantiated.

Since shorter travel distance to the hospital could motivate patients and parents to participate in an intervention program, such program located closer to home might enhance participation. Although exercise training was performed in physical therapy centers close to home, the children in our study had to travel to the hospital on six occasions for the psychosocial part of the intervention (and an additional three times for the assessment of outcome measures). In future, more convenient options for the

psychosocial part should be explored. Psychologists in primary healthcare settings could be trained to perform the intervention to reduce children's travel time and expended energy; however, a disadvantage of this approach is that these psychologists are not likely to be specialized in childhood psycho-oncology. Another option is to consider adapting the program to an online intervention.

Sport participation rate among both participants and non-participants in general was very high (approximately 70%) compared to the general Dutch population aged 4-18 years (47.6% takes part in sport activities outside school.[247] This is surprising since the patients in our study just had cancer treatment. Therefore, one would expect the opposite. However this information is self-reported so response shift could have been an issue and the children could have said that they participate in sports, just when they were member of a sports club. Children were instructed to report only those sports which they performed on a frequent basis; excluding sports performed at school or on the street. It is however possible that children reported otherwise. So maybe this could also be a factor explaining the difference with the Dutch norm.

Surprisingly, participants rated their physical fitness as lower than the non-participants and nearly 15% of the non-participants stated 'already frequently engaged in sports' as reason for non-participation. So although we thought to include more sportive children, we seem to have reached the children most in need of a physical intervention.

This study also has some limitations. Since only 57.5% completed the one-time survey, we lack full insight into the characteristics of the total group of non-participants. This might have biased our results in either direction. Comparing general and medical information between the participants and non-participants to the survey could shed some light on possible bias. However, due to local hospital privacy regulations, these data are not available. For the same reason we also did not have any information available on how many patients were excluded for this study based on the exclusion criteria.

A second limitation is the heterogeneity of the study population, a well-considered choice in order to provide as much patients as possible the opportunity to participate in this program. In addition, since childhood cancer is rare, we needed to include as many patients as possible to meet the required patient numbers. This heterogeneity, however, and the relatively small sample size limits subgroup analyses, for instance according to diagnosis. Striking is also the low number of brain tumor patients in our study. This could be due to the fact that brain tumor patients who had received surgery only, were excluded from the QLIM-RCT. Lack of willingness to participate did not seem to be an issue for brain tumor patients considering the same percentages of this diagnosis group in both participant and non-participant group.

A third limitation, in retrospect, is the fact that the fixed answer categories in the questionnaire for 'reasons for non-participation' did not cover all possible options.

Although an open field was added providing the opportunity to fill in every other reason for non-participation, the possibility exists that patients and parents do not think of all possible options and are inclined to pick one of the fixed categories. For example, study recruiters and staff performing the intervention are in most cases unfamiliar to the families and this may influence participation rate. However, it is unlikely that patients and parents themselves would pick up on this reason by themselves as they may find it easier to choose one of the fixed options. In addition 'too time-consuming' and 'too demanding' are not specific enough. They can be interpreted in different ways. For instance, the intervention itself or the travel distance to the hospital can be too time consuming, but unfortunately we do not have any information available which specifies these categories more accurately.

The results of this study did not lead to any changes in the ongoing QLIM-intervention protocol and recruitment strategies since the current analysis occurred after the inclusion period. However, taking the results of this study into account, when designing future intervention studies, might increase participation rates. In addition, in future studies, the use of focus groups of parents and/or patients could add valuable input in the study design. For example above-mentioned limitations in answer categories on the questionnaire could have been avoidable. In addition, asking participants in future studies for their reasons to participate could add valuable information. Although in the present study the number of patients on or off treatment did not differ between the participants and non-participants, it is important to more specifically assess in future studies, at which point in time participants would be most inclined to participate. Again focus groups among patients and parents could be helpful.

Further study of the effectiveness of the QLIM intervention to improve physical fitness, and comparing its effect with the outcome data of available studies with less intensive physical interventions, is required. If a less demanding and time consuming intervention yields comparable (or better) results, application of that intervention should be considered; this might also improve the participation rate. However, if the results of the intensive intervention are better, the increased supporting evidence may help to increase patients' and parents motivation to participate in such an intervention. In general, proof of effectiveness of the intervention can be the strongest motivational argument for future patients to put effort (time, energy) in such a program. The benefits will then outweigh the 'costs'.

CONCLUSION

In conclusion, this explorative study shows that participation of CCP in an intensive physical and psychosocial intervention program seems to be related to the burden of the intervention and travel distance from home to hospital. In general, participants rated their physical fitness as lower than non-participants, and reported more (internalizing) behavior problems. We cautiously conclude that, with this intervention program, patients most in need of it were probably reached. More insight into the effectiveness of the QLIM intervention is necessary before adapting the program. However, if proven effective, participation rates might increase if the intervention is less time consuming and travel distances are reduced. In this way, more patients could benefit from the program and it could perhaps also serve as an intervention aimed at prevention.