Fatigue in children and adolescents with cancer during early clinical remission

Masterthesis

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"ONDERGETEKENDE

Wies Johanneke Petronella van Aalst,

bevestigt hierbij dat de onderhavige verhandeling mag worden geraadpleegd en vrij mag worden gefotokopieerd. Bij het citeren moet steeds de titel en de auteur van de verhandeling worden vermeld."

Examiner

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ABSTRACT

Background: Due to the growing and relatively high survival rate in childhood cancer, more emphasis is put on the long-term effects of the disease and its treatment. One of the most common and distressing symptoms experienced by children with cancer, both during treatment and into adulthood, is fatigue. An extreme amount of fatigue can result in reduced quality of life. Strikingly, merely a few studies actually applied a validated instrument to assess fatigue. From the few studies that assess fatigue after treatment of childhood cancer, there is hardly any report on fatigue during early clinical remission.

Aim: To assess the level of perceived fatigue in children and adolescents with cancer during the early remission phase after treatment.

Methods: For this cross-sectional study, children and adolescents diagnosed with cancer at ages between 2-18 years, entering their remission phase from the outpatient clinic of the Princess Maxima Centrum (PMC) for pediatric oncology were included. The primary study parameter for this study is perceived fatigue, assessed with the Pediatric Quality of Life Inventory Multidimensional Fatigue Scale (PedsQL MFS). The PedsQL MFS is an instrument designed to measure child and parent proxy perceptions of fatigue in pediatric patients.

Results: A total of 71 patients were included in this study. No significant differences in perceived fatigue were found in children with cancer during early clinical remission compared to healthy controls($p=0.155$). Only 6.8% of the total fatigue can be explained by patient characteristics such as age, gender, type of cancer, type of treatment and disease duration.

Conclusion: Post-cancer fatigue in children and adolescents is not more common than fatigue in a healthy population.

Implications of key findings: As subjective fatigue seems not lowered during the early remission phase in pediatric survivors of cancer, future research should assess fatigue with a longer observation time. The high prevalence of chronic fatigue in adult cancer survivors and the coherent impact of the fatigue, illustrates the relevance of additional research to allow for early detection, preventing chronic fatigue at a later stage and simultaneously establishing improved interventions, in pediatric cohorts.

Keywords: Fatigue, children, adolescents, cancer, clinical remission**.**

INTRODUCTION

While cancer is relatively rare in children, pediatric cancer still is the most common cause of death due to a disease in children over the age of 1 year; with 160.000 new cases annually worldwide.[1] In the Netherlands approximately 550 children under the age of 18 years are diagnosed with malignancies every year.[2] The most common malignancies in children are leukaemia's and lymphomas, followed by central nervous system tumours and other various solid tumours.[1] Intensive treatment, including combined treatment modalities such as chemotherapy, surgery and radiotherapy is frequently necessary in children with cancer. As a result of improved treatment regimens in the last decades, currently eighty percent of the children diagnosed with cancer will eventually be considered cured.[4-5] Due to this emergent and relatively high survival rate, the focus of research has shifted towards the long-term effects of disease and treatment.[6-8]

One of the most common and distressing symptoms experienced by children with cancer, both during treatment and into adulthood, is fatigue.[8] An extreme amount of fatigue can result in reduced quality of life, reduced school participation, depression and lowered levels of self-esteem.[9-10] Fatigue is an inconvenient symptom for children with cancer that may have impact on both their cognitive and psychosocial well-being.[11] The impact and side effects caused by both the type of cancer and the specific type of treatment can influence the extent of fatigue.[12] Fatigue does not only occur during treatment, it also represents a problem among long-term survivors of childhood cancer.[6,8-12] Descriptions of fatigue can include tiredness, weakness, lack of energy and an inability to concentrate.[13] When these descriptions of tiredness are persistent for longer than 6 months, it is diagnosed as chronic fatigue.[13, 22-24]

Even though fatigue is one of the most frequently clinical described complications in children with cancer, most studies lack validated measurements of fatigue. Merely a few studies [15-18] actually applied an instrument to assess fatigue in children with cancer. From the few studies that assess fatigue after treatment for cancer, there is hardly any report on fatigue (directly) after treatment for childhood cancer. [19-25] Furthermore, the findings in these studies reveal a wide range of reported fatigue, partly because of differences in patients age limits and methods used in various studies.[18-23] Studies in long-term survivors of adult cancers have shown increased fatigue levels, compared to the general and healthy population. [13,23-25] Also a two to three times higher prevalence of chronic fatigue was found amongst long-term adult survivors. [13,21-23]

This high prevalence of chronic fatigue in adult cancer survivors and the coherent impact of the fatigue, illustrates the relevance of additional research in pediatric cohorts to allow for early detection, preventing chronic fatigue at a later stage and simultaneously establishing improved interventions. Therefore, the aim of the current study is to assess the level of perceived fatigue with validated questionnaires in children and adolescents during their early

remission phase after treatment. A secondary objective is to assess the potential associations between patient characteristics and the level of perceived fatigue.

METHODS

Design, study population and domain

A cross-sectional design was considered to answer the research question. All children under care at the Princess Maxima Medical Center Utrecht, aged between two and 18 years and entering their remission phase after treatment for pediatric cancer, were approached to fill in questionnaires as part of their usual care. Patients were included from June 2014 till May 2017, during their first year of clinical remission. The inclusion criteria were: (1) age between 2 and 18 years old, (2) in clinical remission phase after treatment for cancer (≤1 year after treatment), and (3) patients were under medical control in the outpatient clinic of the Princess Maxima Centre. Patients without an e-mail address, and those who did not have sufficient Dutch language skills were excluded. The study was approved by the medical ethics committee of the University Medical Center Utrecht (UMCU)(protocol no: 16-707/C).

Data Collection

Medical history and information regarding time of diagnosis, disease duration, type of pediatric cancer and treatment regimens were collected from medical records. Disease duration and treatment regimens were established based on type of cancer and severity according to the specified protocols compiled by the Dutch Childhood Oncology Group (DCOG) which can be found on their website (www.skion.nl). Furthermore, general clinical patient characteristics needed for this study, such as age and gender, were also retrieved from their medical records.

Multiple patient reported outcome measurements (PROMS) were assessed (including perceived fatigue) at home using the KLIK method. The KLIK (Dutch acronym for Quality of Life in Clinical Practice) method is an online system that enables monitoring and discussion of electronic PROMs regarding quality of life (www.hetklikt.nu). Parents of eligible patients were approached by the KLIK coordinators (2 research psychologists) within 1 to 3 weeks after diagnosis. Verbal and written information regarding this study were given during either inpatient hospitalization, outpatient clinical visits, or by phone. Patients and/or parents gave consent on the website (www.hetklikt.nu) as to whether they agree to their data being used for scientific purposes(appendix I). Parents gave consent if the child was younger than 12 years old, when older than 12 years the children (also) gave permission. After registration, patients and/or parents received an e-mail with their unique password and self-chosen username. All data were extracted from medical records under supervision of the principle investigator of this study (S.L. Nijhof) and an independent researcher (A. van Eijndhoven).

Outcome Measures

The primary outcome measure in this study was perceived fatigue, as measured with the PedsQL Multidimensional Fatigue Scale (PedsQL MFS) (appendix II). The PedsQL MFS is an instrument designed to measure child and parent perceptions of fatigue in pediatric patients.[26,27] The questionnaire consists of 18 items with three subscales; general fatigue (6 items), sleep/rest fatigue (6 items) and cognitive fatigue (6 items). A 5-point Likert response scale (0 = never a problem - 4 = almost always a problem) is utilized across child self-report for ages between 8 and 18 years, parent proxy-report is used for children with ages between two and seven years. Items are reverse scored and linearly transformed to a 0 to 100 scale; 0=100, 1=75, 2=50, 3=25 and 4=0. A higher the score on the PedsQL MFS indicates a lower level of fatigue and smaller consequences of fatigue. The internal consistency reliability for the PedsQL MFS is α=0.88 for children and α=0.93 for parent proxy.[26] Norm values of healthy children were used to determine whether the outcomes of the PedsQL MFS of pediatric cancer cohort differed compared to normal fatigue levels. Norm values regarding the PedsQL MFS were assessed by Gordijn et al.[27]

Data analysis

Participants could not complete the questionnaire unless all the items were answered completely, therefore missing data was not possible. Normality of the data was tested using histograms, QQ plots and the Shapiro Wilk test. Differences in patient characteristics were assessed with a t-test in case of a normal distributed continuous variable, a Mann Whitney U test in case of a not normally distributed continuous variable and a Chi-Square test in case of a categorical variable. Non-parametrical tests were used to analyse the primary outcome as the data was not normally distributed. Effects with a P-value below 0.05 (two-tailed) were regarded as significant. Norm values of healthy children assessed by Gordijn et al [27] were compared to the mean scores on the PedsQL- MFS of the participants using a Mann Whitney U test. A Mann Whitney U test was also applied to calculated differences between the subscales of PedsQL-MFS.

Hierarchical regression analysis

Hierarchical regression model analysis was used to explain variance of fatigue. The following patient characteristics were included one by one based on their clinical and theoretical importance: 1) Gender, as women are more likely to experience fatigue in various chronic diseases with a peak of perceived fatigue in adolescence[28-29], and 2) The type of cancer and the sort treatment, as they can both influence the experience of fatigue, due to the impact and side effects caused by the type of cancer and the treatment module [28]. The models were composed as follows: (1) age, (2) gender (3) type of cancer, (4) type of treatment, (5) disease duration and (6) age, gender, type of cancer, type of treatment and disease duration. All statistical tests were two-sided and considered significant when $p < 0.05$. Statistical Package

for Social Sciences (SPSS version 22, Inc., Chicago, Illinois, USA) was used for analysing the data.

Sample Size

The sample size calculation was based on the primary objective, to assess the perceived level of fatigue in children and adolescents with cancer during clinical remission compared to norm values. The calculation was performed using G*power version 3.1.9.2..[30] The type 1 error was set at 0.05 (two-tailed) and for the type 2 error, a power of 80% was chosen. As no effect size is known from the aforementioned outcome measures in children with cancer, the effect size of 0.5 was applied, based on the standard medium effect of Cohen in order to ensure sound sample size. [31] A sample size of 64 patients with cancer was needed to provide sufficient power to answer the primary objective(appendix III).

RESULTS

Demographic and Medical Characteristics

A total of 71 Dutch pediatric cancer survivors were approached, assessed for eligibility to participate, and all were included and completed the study (no drop-outs). A total of 504 healthy controls were used as reference values. Age at assessment ranged from 2-18 years (with a mean age (SD) of 8.73 years (5) for the pediatric cancer survivors and a mean age (SD) of 9.5 years (4.8) for the healthy controls). All patients were in their first year of clinical remission. The distribution of diagnoses, age group and treatment variables are displayed in Table 1.

Group differences

No significant differences were found between children and adolescents in early clinical remission of cancer and the age- and gender-matched healthy controls, as shown in Table 1.

Perceived fatigue

No significant differences of perceived fatigue were found between children and adolescents in early clinical remission of cancer compared to the age- and gender-matched healthy controls ($p=0.155$). Calculations for the different subscales of the PedsQL MFS were performed. A significant difference was found between patients in clinical remission compared to healthy controls (Table 2). Healthy controls score significantly lower on subscale cognitive fatigue than children and adolescents in early clinical remission of cancer ($p=0.011$).

Hierarchical regression analysis

The explained variances from the different models ranged from 0.001 to 0.049 (Table 3). Model 6 indicates that the total explained variance for fatigue is 6.8%; however this is not significant ($p>0.05$). The only variable, with tendency towards significance, is type of cancer, which explains 4.9% of the variance in fatigue ($p=0.062$)(Table 3).

Table 1. Descriptive statistics and clinical characteristics of pediatric and adolescent patients in clinical remission of cancer compared to healthy age and gender matched controls.

Variable	Pediatric cancer patients (N = 71) N (%)	Healthy pediatric controls [27] (N =504) N (%)	P-value
Gender			0.344
- **Male**	33 (46.5%)	240 (47.6%)	
- **Female**	38 (53.5%)	264 (52.4%)	
Age at assessment in years, Mean (SD)	8.73 (5)	9.5 (4.8)	0.202
Age at assessment			0.052
- **2-4 year**	22 (31%)	104 (20.6%)	
- **5-7 year**	12 (16.9%)	83 (16.5%)	
- **8-12 year**	19 (26.7%)	152 (30.2%)	
- **13-18 year**	18 (25.4%)	165 (32.7%)	
Type of cancer			
- **Neuroblastoma**	12 (16.9%)	NA	
- **ALL/AML**	15 (21.1%)		
- **Wilms tumor**	15 (21.1%)		
- **Hodgkin lymphoma**	10 (14.1%)		
- **Other type of cancer**	19 (26.8%)		
Type of treatment			
- **Chemotherapy**	27 (38%)	NA	
- **Chemotherapy and operation**	16 (22.5%)		
- **Chemotherapy, operation and radiotherapy**	12 (17%)		
- **Other therapies**	16 (22.5%)		
Disease duration(months), Mean (SD)	13.2 (9.2)	NA	
Disease duration			
- **0-6 months**	18 (25.4%)	NA	
- **6-12 months**	16 (22.5%)		
- **12-24 months**	20 (28.2%)		
- **>24 months**	17 (23.9%)		

*N = number of individuals, M = mean, SD = standard deviation, NA = not applicable

Table 2. Perceived fatigue scores on the different subscales of the PedsQL MFS; pediatric and adolescent cancer survivors in clinical remission compared to healthy age and gender matched controls.

	Pediatric cancer patients (N=71) Mean scores (SD)	**Healthy pediatric controls [27] (N=504) Mean scores (SD)**	**p- value**
Total fatigue score	79,85 (15,35)	79,25 (12,17)	0,373
- **General fatigue**	78,23 (19,87)	81,11 (13,38)	0,853
- **Sleep fatigue**	79,23 (16,63)	78,64 (15,00)	0,556
- **Cognitive fatigue**	82,10 (19,05)	77,92 (16,96)	0,011

*N = number of individuals, SD = standard deviation,

Table 3. R square changes for hierarchical regression analysis evaluating the explained variances of fatigue with different patient characteristics.

	R Square change	**p-value**
Model 1: Age	0.001	0.757
Model 2: Gender	0.002	0.689
Model 3: Type of cancer	0.049	0.062
Model 4: Type of treatment	0.007	0.489
Model 5: Disease duration	0.023	0.204
Model 6: Age, gender, type of cancer, type of treatment, disease duration	0.068	0.455

DISCUSSION

The current study is the first to examine the level of perceived fatigue in Dutch survivors of pediatric cancer as the assessments were performed during their early clinical remission phase. Data indicated that children in early clinical remission of cancer did not differ significantly from the age- and gender-matched healthy controls on the level of perceived fatigue, except for the subscale cognitive fatigue. Healthy controls score significantly lower on subscale cognitive fatigue than children in early clinical remission of cancer ($p=0.011$), but this is regarded not to be a clinically important difference. These findings are in line with earlier studies on fatigue in childhood cancer survivors.[18] Meeske et al. (2005) estimated the prevalence of fatigue in 161 acute lymphocytic leukaemia (ALL) survivors. The prevalence of fatigue (30%) fell within normal limits of the general population.[18]
Others studies have shown significant differences between survivors and controls. [25,26] Varni et al. (2002) studied 2645 childhood cancer survivors and found significant differences between cancer survivors and the sibling control group.[26] Fatigue was assessed with the Functional Assessment of Chronic Illness Therapy-Fatigue (40.8 vs 42.0, $p<0.02$), Pittsburgh Sleep Quality Index (6.1 vs 5.5, $p<0.004$), and Epworth Sleepiness Scale (6.2 vs 5.4, $p<0.001$).[26] All questionnaires were answered by the cancer survivors or their siblings, parents did not answer any questionnaires. On the basis of the results in this study, we concluded that fatigue falls within the general population normal limits. Compared to post-cancer fatigue in adults and young adults, the post-cancer fatigue in children and adolescents seems less common.

Some issues require further consideration. First, the lack of differences between the childhood cancer survivors and the controls may be due to the 'response-shift'. Response shift is based on a theory that, as a result of changes in a person's health state, a person may undergo changes in internal standards and values.[33,34] In this study, it could imply that the experience of fatigue after treatment (early remission phase) compared to how the children felt during their treatment could have changed a fatigued survivor's standard of measurement concerning fatigue. As a result fatigue may have been underreported. Previous studies have documented that response shift may adversely affect the result of self-reported outcomes in clinical trials and other types of studies.[35]
Secondly, in this study, the exact type of fatigue in combination with the intensity of activity, and the characteristics of fatigue has not been assessed. In the qualitative study of Langeveld et al. (2000), the childhood cancer survivors gave many examples of how fatigue limited their daily activities or how they had to limit their activities to the essentials.[29] Therefore, it is possible that survivors who experience fatigue limit their activities to such a degree that as a result, their fatigue score does not differ from the level found in the comparison group. Differences in study samples and measurements may also explain some of the variance.

This study showed that only 6.8% (not significant) of the amount of perceived fatigue can be explained with patient characteristics such as age, gender, type of cancer, type of treatment

and disease duration. This is not in line with possible associations that were found in previous studies. [35,36] Armstrong et al. reported that female childhood cancer survivors have a higher risk of long-term fatigue compared to male survivors. Other studies in chronic diseases also showed that women are more likely to experience fatigue and there is a peak of perceived fatigue in adolescents.[34,35] Explanations for this fatigue in female adolescents may be hormonal changes during puberty, psychosocial struggles and new educational and social demands.[35] Half of the population of this study consisted of relatively young males, which might explain some of the results that have been found in this study.[34-37]
Previous studies showed that fatigue is experienced more in children with brain tumours and solid tumours.[3,38] A large part of this study population consisted of hematologic type of cancers where fatigue is less prevalent. This may explain the fact that no significant differences were found.[38] Also the relatively small subgroups may camouflage potential differences and may become more pronounced with a longer observation time.

The strength of this study is the completeness of the cohort. This is the first study to measure fatigue with a validated questionnaire in children in early remission phase after treatment for cancer. However, a limitation is that many of the participants were very young when diagnosed with cancer. Langeveld et al.(2003) stated that survivors who were toddlers or pre-schoolers at the time of cancer treatment reported, as far as they could recall, that they were fatigued their entire life. So it is possible that the children in this study have adapted their view on 'normal' fatigue, and therefore consider (severe) fatigue as normal.[20] In this light, a combination of assessments regarding both the psychosocial and physiological aspects of fatigue is recommended, so the full spectrum of fatigue can be displayed.

The pediatric cancer survivors were recruited from a specialist oncology hospital in the Netherlands, so it may not be possible to generalise results to other settings. Furthermore, in future research, differences in treatment protocols between centres and countries should be taken in account. Certainly as not all different types of cancer, such as brain tumours, were included in this study. In literature a high prevalence of fatigue was found in children diagnosed with brain cancer.[3] Future research regarding fatigue in remission should include all types of pediatric cancer and increase the number with international collaboration to generalise these results even more.

The parents completed the questionnaires if the child was between two and seven years old, and the child did so itself when he/she was between 8 and 18 years old. The different perspectives might have influenced the results. Johnston et al.(2003) indicate that parents of children with cancer tend to rate their children's quality of life poorer than children report themselves.[37] This could not be determined in this study since only one of them completed the questionnaire, however differences in parental and self-reports of children were observed in the study of Gordijn et al. (2011). Parents rated the ALL survivors in this study as having more disturbed sleep, more fatigue and poorer physical quality of life compared to the Dutch norm.[27] The authors concluded that differences in parental and self-reports, including worse

parental ratings, might be explained by worried parents and/or the adaptive style of children. Future research should take into account that both parents and children might have different perceptions on perceived fatigue, and it might be interesting to compare these different perceptions.
Finally, an important remark regarding the possible consequences of the assessed fatigue is that whether fatigue leads to disabilities or whether disabilities could be related to fatigue could not be assessed in the current study, since the applied questionnaires are only aimed at measuring perceived fatigue.

Future studies should be aimed at including all centres to more precisely assess fatigue among survivors of all forms of childhood cancer. For the fatigued survivors, the nature and extent of their disabilities should be further addressed. Lastly, if these disabilities are proven to be severe, a treatment aimed at severe disabling fatigue in adolescents cancer survivors should be initiated.

CONCLUSION

In conclusion, self-reported and post-cancer fatigue in children and adolescents is not more common than fatigue in a healthy population. In addition, only 6.8% of the total fatigue can be explained by patient characteristics such as gender, type of cancer, type of treatment and disease duration.

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APPENDIX I Informed consent - Dutch

Akkoordverklaring voor op KLIK site

Wanneer? Zodra ouders zich hebben aangemeld, en voor de eerste keer inloggen met het wachtwoord, komen ze eerst op deze akkoordverklaring pagina. Eenmalig

Akkoordverklaring

Beste ouder(s)/verzorger(s),

Welkom op de KLIK website. Voor deelname aan KLIK is het van belang dat u de voorwaarden heeft gelezen en begrepen. Voor meer informatie, zie onder de knop voorwaarden onderaan deze pagina. U heeft eerder uw e-mailadres doorgegeven op de site. Uw e-mailadres wordt uitsluitend gebruikt in het kader van het KLIK project. Informatie hierover vindt u onder de kopjes 'vertrouwelijkheid' en 'privacy'.

☐ Ik verklaar dat ik de voorwaarden op de KLIK website heb gelezen en begrepen.

U kunt toestemming geven voor het gebruik van uw gegevens, verzameld via KLIK, voor wetenschappelijk onderzoek binnen het ziekenhuis. Uw behandelcentrum wil graag te weten komen hoe het met kinderen met een (chronische) ziekte of aandoening gaat en hoe ze zich voelen. Daarom wordt gevraagd of de informatie die u invult op de KLIK website gebruikt mag worden voor wetenschappelijk onderzoek naar de Kwaliteit van Leven en het psychosociaal functioneren van kinderen en eventueel hun ouders binnen het ziekenhuis of binnen multicenter onderzoek van Nederlandse zorginstellingen. Dit is geheel vrijwillig. Uw beslissing zal geen enkele invloed hebben op de gebruikelijke begeleiding of medische zorg. Wij zouden alleen wel willen benadrukken dat het doen van wetenschappelijk onderzoek met gegevens van grote groepen kinderen en ouders voor ons van groot belang is om de toekomstige zorg voor kinderen met een chronische ziekte te verbeteren. Wij hopen dan ook van harte dat u hiervoor toestemming geeft. Voor meer informatie over het gebruik van de gegevens voor wetenschappelijk onderzoek klikt u hier. De gegevens zullen vertrouwelijk en anoniem worden behandeld.

☐ Ik ga akkoord met het gebruik van de door mij ingevulde antwoorden op de vragenlijsten voor wetenschappelijk onderzoek.

Met vriendelijke groet,

Lotte Haverman
Psycholoog / projectleider KLIK

Aanmelding versturen

Mensen kunnen alleen de aanmelding versturen als ze het eerste vinkje hebben aangevinkt. Het tweede vinkje is optioneel.

APPENDIX II 'PedsQL- MFS Dutch version'

PedsQL Multidimensionele Vermoeidheid Schaal

VRAGENLIJST voor TIENERS (leeftijd **12-18**)

Instructies
Op de volgende bladzijde staat een lijst van dingen die een probleem voor jou kunnen zijn. Kunt je ons vertellen **hoezeer je** in de **AFGELOPEN MAAND** met elk van deze dingen **een probleem** hebt gehad? Omcirkel het antwoord dat het beste bij jou past. Je kunt kiezen uit: **0** als het **nooit** een probleem is **1** als het **bijna nooit** een probleem is **2** als het **soms** een probleem is **3** als het **vaak** een probleem is **4** als het **bijna altijd** een probleem is Er zijn geen goede of foute antwoorden. Als je een vraag niet begrijpt, vraag dan om hulp.

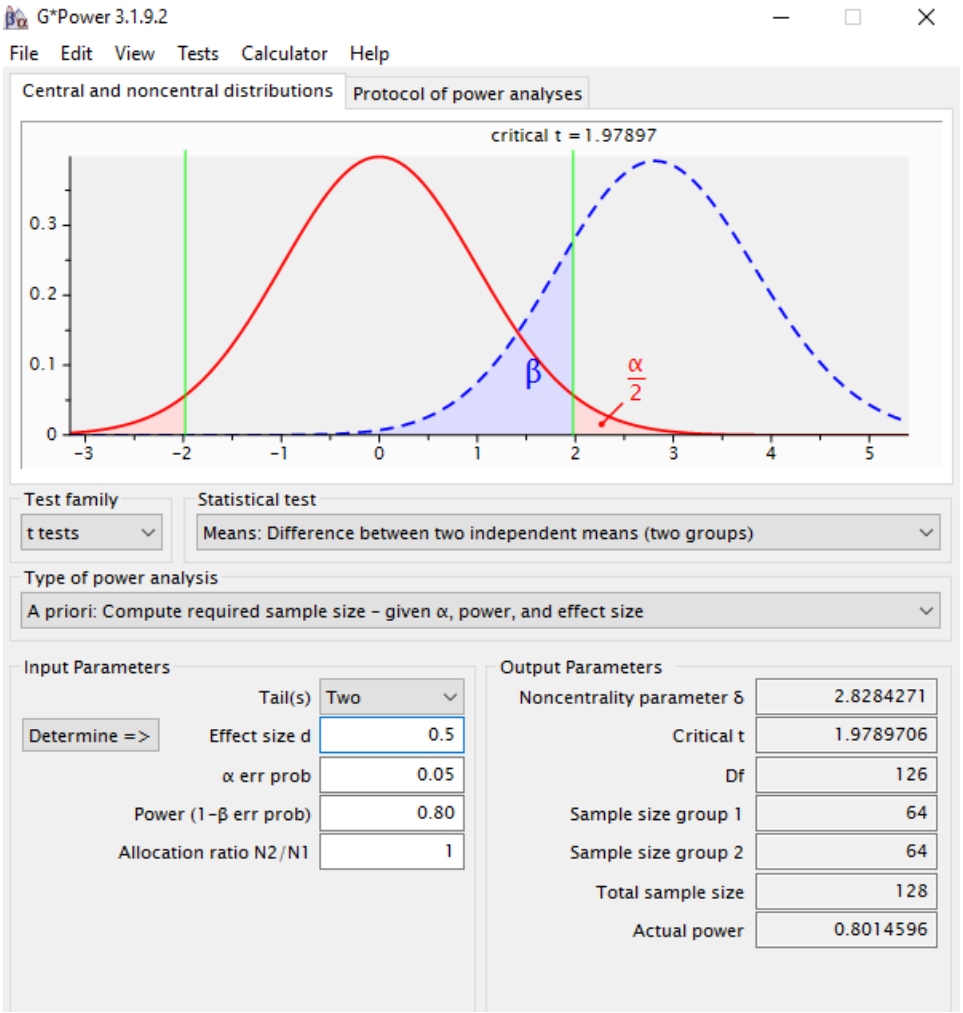
*Hoezeer is dit voor jou in de **AFGELOPEN MAAND** een **probleem** gehad geweest ...*

Algemene vermoeidheid *(problemen met…)*	**Nooit**	**Bijna Nooit**	**Soms**	**Vaak**	**Bijna Altijd**
1. Ik voel me moe	0	1	2	3	4
2. Ik voel me lichamelijk zwak (niet sterk)	0	1	2	3	4
3. Ik voel me te moe om dingen te doen die ik leuk vind	0	1	2	3	4
4 Ik voel me te moe om tijd met mijn vrienden door te brengen	0	1	2	3	4
5. Ik vind het lastig dingen af te maken	0	1	2	3	4
6. Ik vind het lastig dingen te beginnen	0	1	2	3	4

Slaap/rust vermoeidheid *(problemen met…)*	**Nooit**	**Bijna Nooit**	**Soms**	**Vaak**	**Bijna Altijd**
1. Ik slaap veel	0	1	2	3	4
2. Het is moeilijk voor me om 's nachts door te slapen	0	1	2	3	4
3. Ik voel me moe wanneer ik 's ochtends wakker word	0	1	2	3	4
4. Ik rust veel	0	1	2	3	4
5. Ik doe veel dutjes	0	1	2	3	4
6. Ik breng veel tijd in bed door	0	1	2	3	4

Geestelijke vermoeidheid *(problemen met…)*	**Nooit**	**Bijna Nooit**	**Soms**	**Vaak**	**Bijna Altijd**
1. Ik heb moeite mijn aandacht bij dingen te houden	0	1	2	3	4
2. Het is moeilijk voor me te onthouden wat mensen me vertellen	0	1	2	3	4
3. Het is moeilijk voor me te onthouden wat ik net gehoord heb	0	1	2	3	4
4. Het is moeilijk voor me om snel te denken	0	1	2	3	4
5. Ik vind het lastig om te onthouden waar ik net aan dacht	0	1	2	3	4
6. Ik vind het lastig om meer dan één ding tegelijk te onthouden	0	1	2	3	4

APPENDIX III Sample size calculation



SAMENVATTING

Achtergrond: *Door de groeiende en steeds groter wordende overlevingskans voor kinderen gediagnostiseerd met kanker wordt meer nadruk gelegd op de langetermijneffecten van ziekte en de behandeling ervan. Een van de meest voorkomende en ontstellende symptomen die patiënten met pediatrische kanker hebben, zowel tijdens de behandeling als na einde behandeling, zijn vermoeidheid. Vermoeidheid heeft ook een impact op hun cognitieve en psychosociale welzijn. Opvallend dat maar een paar studies een meetinstrument toegepast hebben om de vermoeidheid in deze populaties objectief te beoordelen. Bovendien zijn de bevindingen in deze studies inconsistent in resultaten en onthullen een breed scala aan variatie.*

Doelstelling: *Om de mate van ervaren vermoeidheid bij pediatrische oncologie patiënten met hun remissiefase(0 tot 5 jaar na einde behandeling) te beoordelen.*

Methode: *De primaire studieparameter voor deze studie is waargenomen vermoeidheid, beoordeeld met de Pediatric Quality of Life Inventory Multidimensional Fatigue Scale(PedsQL MFS). De PedsQL MFS is een instrument dat is ontworpen om de perceptie van vermoeidheid van kinderen en ouders in kaart te brengen.*

Resultaten: *In deze studie zijn geen verschillen aangetroffen in ervaren vermoeidheid bij pediatrische oncologie patiënten tijdens klinische remissie in vergelijking met gezonde leeftijdgenoten. Slechts 6,8% van de totale vermoeidheid kan worden verklaard door eigenschappen van de patiënt, zoals leeftijd, geslacht, type kanker, behandelingstype en ziekteduur.*

Conclusie: *Vermoeidheid bij kinderen en na behandeling voor kanker is niet meer gebruikelijk dan vermoeidheid in een gezonde populatie.*

Klinische relevantie: *Aangezien er geen sprake van subjectieve vermoeidheid lijkt te zijn tijdens de vroege remissiefase bij kinderen na behandeling voor kanker, zou toekomstig onderzoek meer gericht moeten zijn op een langere observatie tijd om de vermoeidheid in kaart te brengen. De hoge prevalentie van chronische vermoeidheid bij volwassen overlevenden van kanker en de impact van de vermoeidheid illustreert de relevantie van aanvullend onderzoek om vroegtijdige detectie mogelijk te maken, chronische vermoeidheid te voorkomen en tegelijkertijd verbeterde interventies in pediatrische cohorten te ontwikkelen.*