BMJ Paediatrics Open

Role of parents in fatigue of children with a chronic disease: a cross-sectional study

Niels Kramer,[1] Sanne L Nijhof,[1] Elise M van de Putte,[1] Marjolijn Ketelaar,[2] Martha A Grootenhuis,[3] Kors van der Ent,[4] Joost F Swart,[5] Martine van Grotel,[6] Geertje W Dalmeijer,[7] Merel M Nap-van der Vlist [1]

To cite: Kramer N, Nijhof SL, van de Putte EM, *et al*. Role of parents in fatigue of children with a chronic disease: a cross-sectional study. *BMJ Paediatrics Open* 2021;**5**:e001055. doi:10.1136/bmjpo-2021-001055

Received 9 February 2021
Revised 23 March 2021
Accepted 9 April 2021

For numbered affiliations see end of article.

Correspondence to
Merel M Nap-van der Vlist; m.m.vandervlist-3@umcutrecht.nl

ABSTRACT

Objective As parents majorly impact their child's well-being, and as fatigue is a highly prevalent threat to the well-being of children with a chronic disease, we aimed to explore the association between parental factors and fatigue in children with a chronic disease.

Design Cross-sectional study

Setting Two Dutch children's hospitals.

Population Children 2–18 years of age with either an autoimmune disease, cystic fibrosis or post-cancer treatment, and one of their parents.

Main outcome measures Paediatric fatigue was measured using the PedsQL Multidimensional Fatigue Scale. Parental factors included parental pain, fatigue and physical symptoms, parental distress, catastrophising thoughts about their child's pain and family empowerment. Multiple linear regressions were used to study associations with paediatric fatigue. A multivariable regression model was used to assess the effect of the different parental factors on paediatric fatigue. All analyses were adjusted for the age and sex of the child.

Results 204 families participated (mean age 11.0±4.3 and 43.5±6.3 years for children and parents, respectively; 69% participation rate). More parental pain, fatigue and physical symptoms, and more parental distress and pain catastrophising were associated with more paediatric fatigue. More parental empowerment was associated with less paediatric fatigue on both subscales. In the multivariable model, only paediatric age remained significantly associated with fatigue. In a separate multivariable model for children 8–18 years old, more parental distress (β=−1.9, 95% CI −3.7 to −0.1) was also significantly associated with more paediatric fatigue.

Conclusions In a population of children with a chronic disease, parental factors, both physical and psychosocial, were associated with paediatric fatigue. Our study provides evidence that more family empowerment is associated with less paediatric fatigue. This exploratory study adds to our knowledge of associated factors with fatigue in paediatric chronic disease, providing starting points for targeted interventions.

What is known about the subject?

- Fatigue is highly prevalent among children with chronic disease and can have a significant impact on their quality of life.
- Fatigue is multidimensional, with various predisposing, precipitating and perpetuating factors that are both biological and psychosocial in nature.
- Knowledge regarding the effect of parental factors on fatigue in children with chronic disease is limited but could benefit the child and the parents.

What this study adds?

- We provide new evidence that several parental factors, both physical and psychosocial, are associated with paediatric fatigue in children with chronic disease.
- More family empowerment is associated with less paediatric fatigue.
- This exploratory study adds to our knowledge of associated factors with fatigue in paediatric chronic disease, providing starting points for targeted interventions.

INTRODUCTION

An increasing number of children with a serious chronic disease reaches adulthood.[1] Unfortunately, this does not go without obstacles. Paediatric chronic disease affects the health and well-being of both children and their families.[2 3] One of the most common health issues among children with chronic disease is fatigue.[4–6] Several child factors, both somatic and psychosocial, have been associated with fatigue.[5 7–12] Although child factors explain a considerable amount of variance in fatigue, part of the variance of fatigue cannot be explained by child factors.[7] Interpersonal factors, family environment and parental functioning are important contributors to how the child functions with his or her disease, especially for younger children.[3 13]

As parents have a major impact on their child's well-being, we hypothesise that parental factors, both physical and

psychosocial, influence paediatric fatigue in paediatric chronic disease, in line with the biopsychosocial model.[12] Several parental physical factors, such as parental pain, fatigue and a focus on bodily symptoms, have been shown to negatively influence paediatric outcomes in children with chronic pain or chronic fatigue syndrome (CFS).[14–18] Regarding parental psychosocial factors, parents of children with a chronic disease experience more psychological distress.[19 20] Several factors, such as parental distress or catastrophising thoughts, have been shown to negatively influence paediatric health outcomes, such as fatigue or pain, across paediatric chronic diseases.[14 15 19–21] However, in line with the concept of positive health, there may also be potentially protective factors, such as family empowerment.[22 23] Empowerment can be described as a sense of being able to influence your social environment to mobilise the resources you need and to feel in control over the situation.[23 24] Family empowerment has been associated with fewer somatic and psychological symptoms in children, although no studies have focused on fatigue yet.[25]

Parental physical and psychosocial factors have been associated with poor paediatric outcomes but have not yet been investigated in the context of fatigue in children with a chronic disease. Examining the association between parental factors and paediatric fatigue across different paediatric chronic diseases may help us understand more of the perpetuating factors of fatigue across paediatric chronic disease and may open the door for targeted interventions.[26] Therefore, we aimed to explore the association between parental physical and psychosocial factors and fatigue in children with a chronic disease aged 2–18 years old. Second, as older age is associated with more fatigue and as children of 8 years and older can self-report their fatigue, we zoom in on the associations between parental factors and paediatric fatigue in this age group.[27]

METHODS

Study design

This is a cross-sectional study in which parents and children filled out questionnaires prior to an outpatient visit. This study was part of a larger cohort study on fatigue and associated factors across paediatric chronic diseases at the Wilhelmina Children's Hospital and the Princess Máxima Centre for Paediatric Oncology in the Netherlands: the PROactive cohort.[4] The data used for this study were collected from January 2018 through February 2020 and were based on an extended follow-up assessment of patients included in the PROactive cohort. Informed consent for the use of questionnaires for scientific purposes was obtained from children 12 years of age and older and from one of the parents.

Patient and public involvement

Patient organisations were involved in setting the priorities for this research. Several choices in the design were reviewed by patient representatives. Patients and the public were not involved in the conduct of the study. We added qualitative research methods to our research line in order to stress the patient's and parent's perspective. Patient organisations and societal partners were involved in the dissemination of our research.

Participants

Families with a child 2–18 years of age with cystic fibrosis (CF), autoimmune disease or previous treatment for cancer were included. The group of children with an autoimmune disease included children with an immunodeficiency disorder, an auto inflammatory condition or an autoimmune disease in the strictest sense. We included children who were at least 1 year postdiagnosis (the CF and autoimmune disease groups) or who were within 1 year after completing their cancer treatment. This latter inclusion criterion was chosen since disease activity (generally highest in the first year after diagnosis), receiving the diagnosis, starting treatment and the disease itself can cause significant fatigue in the first year postdiagnosis or during cancer treatment. One parent filled out the questionnaires. The primary outcome measure, paediatric fatigue, was child-reported when the child was between 8 and 18 years of age and parent-reported for younger children (2–7 years of age). All other measures were parent-reported questionnaires.

Study procedures

Before an outpatient visit, the researchers approached families via email to take part in the study. They then completed the questionnaires via a web-based tool (www.hetklikt.nu).[28] All participants received one reminder to participate in the study via email and one via telephone. A research team was available to answer questions via mail and telephone.

Measurements

Paediatric fatigue was the primary outcome measure, which was measured using the General Fatigue Subscale of the PedsQL Multidimensional Fatigue Scale (PedsQL MFS), which has good internal consistency.[29] As the primary outcome was the perception of fatigue, we used only the General Fatigue Subscale, instead of the other subscales of the PedsQL MFS, namely, sleep/rest and cognitive fatigue. The General Fatigue Subscale contains questions about the perception of fatigue and whether the child has enough energy to perform activities.

For all questionnaires and tools used in our study, the number of items, range, interpretation and Cronbach's alpha are provided in table 1.

Physical factors

The measured parental physical factors included parental pain, fatigue and physical symptoms. A Visual Analogue Scale ranging from 0 to 10 was used to measure last week's average parental pain.[30] Parental fatigue was assessed using the well-validated Eight-Item Checklist Individual Strength, which has good psychometric properties.[31] To

Table 1 Summary of the factors assessed in this study and features of the corresponding questionnaires/tools

Assessed factor	Questionnaire	Items	Range/replies	Cronbach's alpha
Paediatric fatigue	PedsQL MFS	6	0–100: higher score=less paediatric fatigue	0.92
Parental pain	VAS	1	0–10: higher score=more parental pain	N/A
Parental fatigue	CIS-8	8	8–56: higher score=more parental fatigue	0.93
Parental physical symptoms	CDC criteria for CFS-related symptoms	8	0–8: higher score=more parental physical symptoms	0.79
Parental pain catastrophising	PCS-P	13	0–52: higher score=more parental pain catastrophising	0.93
Parental distress	DT-P	1	0–10: higher score=more parental distress	N/A
Family empowerment family subscale	FES	12	1–5: higher score=more parental empowerment. The score is calculated as the mean of the items.	0.89
Family empowerment service system subscale	FES	12	1–5: higher score=more parental empowerment. The score is calculated as the mean of the items.	0.91

CDC, Centers for Disease Control and Prevention; CFS, chronic fatigue syndrome; CIS-8, Eight-Item Checklist Individual Strength; DT-P, Distress Thermometer for Parents; FES, Family Empowerment Scale; PCS-P, Pain Catastrophising Scale for Parents; PedsQL MFS, PedsQL Multidimensional Fatigue Scale; VAS, Visual Analogue Scale.

assess physical symptoms, the eight CFS-related symptoms of the US Centers for Disease Control and Prevention criteria were used.[32]

Psychosocial factors

The Pain Catastrophising Scale for Parents was used to determine the degree of catastrophising thoughts parents have regarding their child's pain. This scale has high internal consistency.[33] Parental distress was measured using the Distress Thermometer for Parents, assessing overall parental distress over the past week. This scale has good internal consistency.[20] Family empowerment was measured using two subscales of the Family Empowerment Scale.[23 34] The family subscale assesses the parents' management of everyday situations, for example, 'I feel my family life is under control'. The service system subscale assesses how parents relate to the service system; for example, 'I know what services my child needs'.

Data analyses

Descriptive statistics were used to summarise characteristics of all participants. Normally distributed continuous variables were presented as mean±SD; otherwise, median and IQR were provided. Categorical variables were presented as frequencies. Differences between participants and non-participants and between disease groups were analysed using Student's t-test, Kruskal-Wallis test or χ^2 test.

We applied an exploratory aetiological research design. Multiple linear regression analyses were performed for each parental factor to assess its association with the outcome variable paediatric fatigue. As age and sex of the child are important determinants of fatigue, these factors were used as covariates in all analyses.[27] The associations were described using the unstandardised beta (β), effect size (standardised beta) and 95% CI. The unstandardised beta is how much the paediatric fatigue score (Y) changes if the parental factor (X) changes by one point. For example, for every point that parents score higher on parental pain, the paediatric fatigue score goes up with beta points. The assumptions for linear regression analysis were tested, including linearity between the dependent and independent variables, homoscedasticity and normality of the residuals. Minimal differences were found between SEs and robust SEs. Bootstrapping was performed on the regression analyses and the results were in line with the initial results from the regression analyses. Multicollinearity between the separate parental factors was investigated. Second, to investigate whether associations differed between disease groups, we added an interaction variable of the interaction between disease group and the tested parental factor to the regression analyses. Third, we build a full model with all parental factors and the covariates entered together to describe the variance in paediatric fatigue explained by parental factors. This full model was performed for the full age range (2–18 years) and separately for children 8–18 years old. We used these models to describe the explained variance of the parental factors in fatigue. In this explorative study, $p<0.05$ was considered statistically significant. Effect sizes of <0.5 were considered small, ≥0.5 was moderate and ≥0.8 was large.[35]

Table 2 Descriptive characteristics of the children and parents included in this study

	Entire group (N=204)	Disease groups		
		Autoimmune disease (n=105)	Cystic fibrosis (n=51)	Postcancer treatment (n=48)
Child characteristics				
Age (years), mean±SD	11.1±4.4	12.2±3.9	11.3±4.8	8.4±3.9
Sex (male), n (%)	83 (41)	35 (33)	24 (47)	25 (50)
Fatigue,* median (IQR)	83.3 (62.5–95.8)	79.2 (58.3–93.8)	79.2 (58.3–95.8)	91.7 (68.8–100)
Parent characteristics				
Age (years), mean±SD	43.6±6.4	44.9±5.8	43.2±6.9	41.1±6.3
Sex (male), n (%)	49 (24)	22 (21)	15 (29)	12 (25)

*Measured with the General Fatigue Scale of the PedsQL Multidimensional Fatigue Scale, range 0–100; higher scores indicate less fatigue.

RESULTS

Demographics of the study population

Of the 296 families who were approached for this study, 204 participated (69%). Non-participating children were significantly older compared with participating children (13.5±4.3 vs 11.0±4.3 years). The most commonly cited reasons for not participating were personal circumstances and current participation in other research. table 2 summarises the general characteristics of the participants and table 3 summarises the parental factors. There were significant differences in age and sex of the child between disease groups, which supports our decision to control for children's sex and age in the main analyses. In this sample, the sex of the child did not significantly influence fatigue scores (p=0.48, β=–2.2, 95% CI –8.3 to 3.9). The median paediatric fatigue score was 83.3 (IQR 62.5–95.8) on the General Fatigue Scale. Paediatric fatigue was self-reported by children aged 8–18 years old (69.8%) and parent-reported for children 2–7 years old (30.2%).

Parental factors and paediatric fatigue

All parental physical and psychosocial factors were significantly associated with paediatric fatigue, although with small effect sizes (table 4). More parental pain (β=–1.62, 95% CI –2.90 to –0.34), more parental fatigue (β=–0.50, 95% CI –0.73 to –0.27) and more parental physical symptoms (β=–2.77, 95% CI –4.33 to –1.21) were significantly associated with more paediatric fatigue. Also, more pain catastrophising (β=–0.36, 95% CI –0.67 to –0.05) and more parental distress (β=–2.07, 95% CI –3.06 to –1.08) were also associated with more paediatric fatigue. More parental empowerment was associated with less paediatric fatigue, both on the family subscale (β=10.14, 95% CI 3.74 to 16.53) and the service system subscale (β=7.21, 95% CI 1.55 to 12.86). We found no significant differences between disease groups on any of the physical or psychological parental associations with paediatric fatigue.

Multivariable regression models

All parental factors were entered in a regression model, together with the covariates age and sex of the child. This model explained 20.2% of the variance in fatigue (table 5). A separate model for children aged 8–18 years old (n=142) explained 20.3% of the variance in paediatric fatigue. Besides age, more parental distress was

Table 3 Parent-reported outcomes

Parental factor	Parents (n=204)
Physical factors	
Pain	
Experienced pain in VAS, median (IQR)	0 (0–2)
Fatigue	
Score (CIS-8) fatigue subscale, median (IQR)	24.0 (15.0–33.0)
Percentage of severely fatigued (CIS-8≥35)	21.5
Physical symptoms	
Number of CFS-related symptoms, median (IQR)	1.0 (0–2)
Psychosocial factors	
Pain catastrophising	
PCS-P total score, median (IQR)	9.0 (4.0–14.5)
Distress	
DT-P stress thermometer, median (IQR)	2.0 (1.0–5.0)
Percentage of clinically elevated distress (≥4)	34.8
Family empowerment	
FES family subscale, median (IQR)	4.4 (4.1–4.8)
FES service system subscale, median (IQR)	4.3 (4.0–4.8)

VAS: range 0–10, FES: range 1–5, PCS-P: range 0–52, DT-P: range 0–10, CIS-8: range 8–56; CFS: range 0–8.
CFS, chronic fatigue syndrome; CIS-8, Eight-Item Checklist Individual Strength; DT-P, Distress Thermometer for Parents; FES, Family Empowerment Scale; PCS-P, Pain Catastrophising Scale for Parents; VAS, Visual Analogue Scale.

Table 4 Linear regression per factor with dependent variable paediatric fatigue (PedsQL MFS General Fatigue Scale) for the entire group of children with chronic diseases, adjusted for age and sex of the child

	Unstandardised β	Effect size	95% CI
Physical factors			
Parental Pain			
VAS (range 0–10)	−1.62	−0.16	**−2.90 to −0.34**
Parental fatigue			
CIS-8 (range 0–56)	−0.50	−0.27	**−0.73 to −0.27**
Reported CDC CFS symptoms			
Number of symptoms (0–8)	−2.77	−0.23	**−4.33 to −1.21**
Psychosocial factors			
Pain catastrophising			
PCS-P total score (0–52)	−0.36	−0.15	**−0.67 to −0.05**
Parental distress			
DT-P stress thermometer (range 0–10)	−2.07	−0.26	**−3.06 to −1.08**
Family empowerment			
FES family subscale (1–5)	10.14	0.20	**3.74 to 16.53**
FES service system subscale (1–5)	7.21	0.17	**1.55 to 12.86**

On the PedsQL MFS General Fatigue Scale, a higher score indicates less fatigue.
Significant results in bold.
CDC, Centers for Disease Control and Prevention; CFS, chronic fatigue syndrome; CIS-8, Eight-Item Checklist Individual Strength; DT-P, Distress Thermometer for Parents; FES, Family Empowerment Scale; PCS-P, Pain Catastrophising Scale for Parents; PedsQL MFS, PedsQL Multidimensional Fatigue Scale; VAS, Visual Analogue Scale.

Table 5 Complete model with all parental factors, covariates age and sex of the child and dependent variable fatigue (PedsQL MFS General Fatigue Scale) for the entire group of children with chronic disease

Associated factors	Unstandardised β	Effect size	95% CI
Confounders			
Age of the child	−1.5	−0.3	**−2.2 to −0.9**
Sex of the child (0=female)	2.2	0.1	−3.4 to 7.8
Physical parental factors			
Parental pain (VAS, range 0–10)	−0.2	−0.0	−1.8 to 1.4
Parental fatigue (CIS-8, range 8–56)	−0.1	−0.0	−0.5 to 0.3
Number of CDC CFS symptoms (0–8)	−0.5	−0.0	−2.6 to 1.7
Psychosocial parental factors			
Parental pain catastrophising (PCS-P, range 0–52)	−0.2	−0.1	−0.5 to 0.1
Parental distress (DT-P, range 0–10)	−1.3	−0.2	−2.7 to 0.2
Family empowerment			
FES family subscale (1–5)	5.9	0.1	−2.4 to 14.2
FES service system subscale (1–5)	2.4	0.1	−4.8 to 9.6

The PedsQL MFS is scored on a scale from 0 to 100, with a lower score indicating more severe fatigue. Thus, a negative correlation indicates a lower score, indicating more fatigue.
Significant results in bold.
CDC, Centers for Disease Control and Prevention; CFS, chronic fatigue syndrome; CIS-8, Eight-Item Checklist Individual Strength; DT-P, Distress Thermometer for Parents; FES, Family Empowerment Scale; PCS-P, Pain Catastrophising Scale for Parents; PedsQL MFS, PedsQL Multidimensional Fatigue Scale; PedsQL MFS, PedsQL Multidimensional Fatigue Scale; VAS, Visual Analogue Scale.

Table 6 Complete model with all parental factors and fatigue (PedsQL MFS General Fatigue Scale) as dependent variables for the group of children 8–18 years of age with chronic disease

Associated factors	Unstandardised β	Effect size	95% CI
Confounders			
Age of the child	−2.5	−0.4	**−3.5 to −1.4**
Sex of the child (0=female)	3.5	0.1	−3.5 to 10.4
Physical parental factors			
Parental pain (VAS, range 0–10)	−0.6	−0.1	−2.5 to 1.4
Parental fatigue (CIS-8, range 8–56)	0.2	0.1	−0.3 to 0.6
Number of CDC CFS symptoms (0–8)	0.5	0.0	−2.0 to 3.0
Psychosocial parental factors			
Parental pain catastrophising (PCS-P, range 0–52)	−0.4	−0.1	−0.8 to 0.1
Parental distress (DT-P, range 0–10)	−1.9	−0.2	**−3.7 to −0.1**
Family empowerment			
FES family subscale (1–5)	9.6	0.2	−0.2 to 19.5
FES service system subscale (1–5)	2.1	0.1	−6.5 to 10.6

The PedsQL MFS is scored on a scale from 0 to 100, with a lower score indicating more severe fatigue. Thus, a negative correlation indicates a lower score, indicating more fatigue.
Significant results in bold.
CDC, Centers for Disease Control and Prevention; CFS, chronic fatigue syndrome; CIS-8, Eight-Item Checklist Individual Strength; DT-P, Distress Thermometer for Parents; FES, Family Empowerment Scale; PCS-P, Pain Catastrophising Scale for Parents; PedsQL MFS, PedsQL Multidimensional Fatigue Scale; VAS, Visual Analogue Scale.

significantly associated with more paediatric fatigue in this model (table 6).

DISCUSSION

The aim of this study was to explore the associations between parental factors, both physical and psychosocial, with paediatric fatigue in children with a chronic disease. All parental physical and psychosocial factors were associated with paediatric fatigue. Our study provided evidence that more family empowerment is associated with less paediatric fatigue. Nevertheless, all these parental factors were associated with paediatric fatigue when assessed individually, but when adjusted for each other, they did not hold their significance in a full model. Although parental factors did not explain as much of the variance in paediatric fatigue as child factors, this exploratory study adds to our knowledge of associated factors with fatigue in paediatric chronic disease.[7]

Fatigue is highly prevalent in paediatric chronic disease and associated with various factors on the biological, psychological and social domains.[7] As parents form a major part of the child's social environment, our finding that both physical and psychosocial parental factors are associated with paediatric fatigue is in line with our hypothesis. First, for physical parental factors, an association between more parental fatigue or bodily symptoms and more paediatric fatigue was also found in children with CFS.[16 17] Also in line with our findings, more parental pain and catastrophising were often associated with worse child outcomes in healthy children or children with chronic conditions.[14 36] Second, for psychosocial parental factors, the significant correlation between parental distress and paediatric fatigue is consistent with the findings reported by Carroll *et al*, who found a similar correlation in children with multiple sclerosis.[21]

Concerning family empowerment, previous research provided evidence suggesting that parental family empowerment is correlated with fewer somatic and psychological symptoms in children with chronic disease.[25] In line with these results, our study provides evidence that more family empowerment is correlated with less fatigue in children with chronic disease. Important elements of empowerment include the acquisition of knowledge, skills, attitudes and self-awareness.[24] Possible ways to support parents may be providing information and education, interventions supporting family function, and interventions supporting parent's own needs.[24 37] Information needs of families differ between families and vary over time, but in general, information needs go beyond information about the diagnosis.[38] It also concerns issues such as how to make use of available services, how to find information about suitable leisure activities, how to deal with financial issues, how to manage daily care tasks in the family and how to raise a child with a chronic condition and his/her siblings. Parent peers can play an important role in information provision and are regarded more and more as an important source of experience-based knowledge and support.[38] A good example of providing information/education as well as peer support for parents may be an online group course, such as *On Track*.[39] A good example of helping parents to gain more control over the service system may be by making the conversations with healthcare providers more family-centred, for example, by letting parents fill out parent-reported outcome measures on beforehand or using tools to help parents explore their

needs.[40 41] The effect of such interventions on family empowerment is of interest for future studies.

Interestingly, almost all parental factors were not significantly associated with fatigue in the full model when adjusted for each other. The age of the child was significantly associated with paediatric fatigue, but this is not a modifiable factor. In children aged 8–18 years old, more parental distress was associated with more paediatric fatigue. We already know that fatigue is more prevalent in older children.[27] Especially for older children, parents of a child with a chronic disease face extra challenges, such as balancing their wish to care for and protect the child and their wish to let the child become autonomous.[42 43] We also know that these challenges may lead to significant parental distress, which can have substantial negative effects for the child and the family.[44] Therefore, in clinical practice, it is important to detect parental distress, for example, through a simple validated questionnaire.[20] Being aware of the well-being of parents may be beneficial for both the parent and the child and could be a starting point for targeted interventions.

A strength of our study is that we examined parental factors across several paediatric chronic diseases, rather than focusing on one specific disease, so our results may be applicable to a wider range of paediatric chronic diseases. We found no significant differences between disease groups on any of the physical or psychological parental associations with paediatric fatigue, which may reflect the general nature of fatigue across all chronic diseases. Another strength is that we included children ranging from 2 to 18 years of age. Most studies focused on adolescents, but fatigue is also prevalent among younger children.[4] Given that current treatment options for fatigue in younger children are limited, and given the important role that parents play in these early years, identifying parental factors that can be targeted is particularly important in this age group.

A possible limitation is that, although the participation rate was relatively high (69%), the age of the child was lower for participants than for non-participants. As we already found correlations in our relatively young study population, and as the prevalence of fatigue increases with age, the actual correlations between parental factors and paediatric fatigue may be even stronger.[27] Second, the group of patients with autoimmune disease contained a relatively high percentage of girls; however, this reflects the epidemiology of those diseases.[45] Another limitation is that most of the participating parents were mothers; thus, it is possible that certain associations may be more applicable to mothers than fathers. In this study, parents had the choice which parent would participate. It would be of interest to know whether there are differences in representation of symptoms between parents for future studies, as gender differences may influence the outcomes of parental factors and parent-reported child outcomes.[46] Nevertheless, we compared parental outcomes and found no difference between mothers and fathers, with the exception of a difference in amount of parental physical symptoms. Given the cross-sectional nature of this study, the causal relation between parental factors and paediatric fatigue could not be examined. Within this aetiological, exploratory study design, we chose to analyse the data using linear regressions containing a risk factor (parental factor) and potential confounders (age and sex of the child), and we added an interaction variable (parental factor×disease group) to best answer the research question. Furthermore, we presented a full model to show how these parental factors jointly influence fatigue and how much of the variance in paediatric fatigue is explained by these parental factors. Our goal was not to best predict paediatric fatigue, although that may be of interest for future (preferably longitudinal) studies. This study shows which factors co-occur and possibly perpetuate fatigue, in line with the cognitive behavioural model.[26]

In this exploratory study, we found several physical and psychosocial parental factors that are associated with paediatric fatigue, but all with small effect sizes. For future research, longitudinal studies investigating causal relationships are needed. Also, studies that investigate which parental factors can be used as effective therapeutic targets for treating fatigue in children with chronic disease are of interest.

CONCLUSIONS

In a population of children with a chronic disease, more parental pain, fatigue and physical symptoms, and more parental distress and pain catastrophising are associated with more paediatric fatigue. Our study also provides evidence that more family empowerment is associated with less paediatric fatigue. This exploratory study adds to our knowledge of associated factors with fatigue in paediatric chronic disease, providing starting points for targeted interventions.

Author affiliations
[1]Social Paediatrics, Wilhelmina Children's Hospital University Medical Centre, Utrecht, The Netherlands
[2]Centre of Excellence for Rehabilitation Medicine, UMC Utrecht Brain Centre, University Medical Centre Utrecht and De Hoogstraat Rehabilitation, Utrecht, The Netherlands
[3]Psycho-Oncology, Princess Maxima Center for Paediatric Oncology, Utrecht, The Netherlands
[4]Cystic Fibrosis Center and Department of Paediatric Respiratory Medicine, University Medical Center, Utrecht, The Netherlands
[5]Paediatric Rheumatology, Wilhelmina Children's Hospital University Medical Centre, Utrecht, The Netherlands
[6]Oncology, Princess Máxima Center for Paediatric Oncology, Utrecht, The Netherlands
[7]Division management, Julius Center for Health Sciences and Primary Care, Utrecht, The Netherlands

Acknowledgements The authors acknowledge the contribution of the patients and parents who participated in this study and the involved caregivers who included patients and discussed the outcomes of the questionnaires with them. The authors also thank Emma Berkelbach van der Sprenkel, Lotte Meijerink, Pleun Terpstra and Eline Albers for their help with the data collection. The authors also thank Dr C F Barrett for his assistance with English language editing. The authors thank Dr Peter Zuithoff for his advice regarding the statistics of this study.

Contributors NK analysed and interpreted the data and drafted the paper. MMN-vdV collected the data and contributed in the analysis and interpretation of the data and in drafting the paper. SLN, GWD, MAG and EMvdP designed the study and coordinated and supervised data collection and interpretation and reviewed the manuscript. KvdE, MK, JFS and MvG critically reviewed the data analyses and reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, conduct, reporting or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not required.

Ethics approval The study was classified by the institutional review board of the University Medical Centre Utrecht as exempt from the Medical Research Involving Human Subjects Act (16–707/C).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Please contact the corresponding author.

ORCID iD

Merel M Nap-van der Vlist http://orcid.org/0000-0002-7911-8516

REFERENCES

1 Perrin JM, Bloom SR, Gortmaker SL. The increase of childhood chronic conditions in the United States. *JAMA* 2007;297:2755.
2 Maurice-Stam H, Nijhof SL, Monninkhof AS, *et al*. Review about the impact of growing up with a chronic disease showed delays achieving psychosocial milestones. *Acta Paediatr* 2019;108:apa.14918
3 Christin A, Akre C, Berchtold A, *et al*. Parent-adolescent relationship in youths with a chronic condition. *Child Care Health Dev* 2016;42:36–41.
4 Nap-van der Vlist MM, Dalmeijer GW, Grootenhuis MA, *et al*. Fatigue in childhood chronic disease. *Arch Dis Child*. 2019;104:archdischild-2019-316782
5 Nijhof LN, van de Putte EM, Wulffraat NM. Prevalence of severe fatigue among adolescents with pediatric rheumatic diseases. arthritis care Res (Hoboken) 2015.
6 van Deuren S, Boonstra A, van Dulmen-den Broeder E, *et al*. Severe fatigue after treatment for childhood cancer. *Cochrane Database Syst Rev* 2020;3:CD012681.
7 Nap-van der Vlist MM, Dalmeijer GW, Grootenhuis MA, *et al*. Fatigue among children with a chronic disease: a cross-sectional study. *BMJ Paediatr Open* 2021;5:e000958.
8 Nap-van der Vlist MM, Burghard M, Hulzebos HJ, *et al*. Prevalence of severe fatigue among adults with cystic fibrosis: a single center study. *J Cyst Fibros* 2018;17:368–74.
9 Van de Vijver E, Van Gils A, Beckers L, *et al*. Fatigue in children and adolescents with inflammatory bowel disease. *World J Gastroenterol* 2019;25:632–43.
10 Armbrust W, Siers NE, Lelieveld OTHM, *et al*. Fatigue in patients with juvenile idiopathic arthritis: a systematic review of the literature. *Semin Arthritis Rheum* 2016;45:587–95.
11 Langeveld NE, Grootenhuis MA, Voûte PA, *et al*. No excess fatigue in young adult survivors of childhood cancer. *Eur J Cancer* 2003;39:204–14.
12 Engel GL. The need for a new medical model: a challenge for biomedicine. *Science* 1977;196:129–36.
13 Wallander JL, Varni JW. Effects of pediatric chronic physical disorders on child and family adjustment. *J Child Psychol Psychiatry* 1998;39:29–46.
14 Wilson AC, Moss A, Palermo TM, *et al*. Parent pain and catastrophizing are associated with pain, somatic symptoms, and pain-related disability among early adolescents. *J Pediatr Psychol* 2014;39:418–26.
15 Palermo TM, Valrie CR, Karlson CW. Family and parent influences on pediatric chronic pain: a developmental perspective. *Am Psychol* 2014;69:142–52.
16 Smith MS, Buchwald DS, Bogart A, *et al*. Adolescent offspring of mothers with chronic fatigue syndrome. *J Adolesc Health* 2010;46:284–91.
17 van de Putte EM, van Doornen LJP, Engelbert RHH, *et al*. Mirrored symptoms in mother and child with chronic fatigue syndrome. *Pediatrics* 2006;117:2074–9.
18 Nijhof SL, Priesterbach LP, Uiterwaal CSPM, *et al*. Internet-Based therapy for adolescents with chronic fatigue syndrome: long-term follow-up. *Pediatrics* 2013;131:e1788–95.
19 Cousino MK, Hazen RA. Parenting stress among caregivers of children with chronic illness: a systematic review. *J Pediatr Psychol* 2013;38:809–28.
20 van Oers HA, Schepers SA, Grootenhuis MA, *et al*. Dutch normative data and psychometric properties for the distress thermometer for parents. *Qual Life Res* 2017;26:177–82.
21 Carroll S, Chalder T, Hemingway C, *et al*. Adolescent and parent factors related to fatigue in paediatric multiple sclerosis and chronic fatigue syndrome: a comparative study. *Eur J Paediatr Neurol* 2019;23:70–80.
22 Huber M, van Vliet M, Giezenberg M, *et al*. Towards a 'patient-centred' operationalisation of the new dynamic concept of health: a mixed methods study. *BMJ Open* 2016;6:e010091.
23 Koren PE, DeChillo N, Friesen BJ. Measuring empowerment in families whose children have emotional disabilities: a brief questionnaire. *Rehabil Psychol* 1992;37:305–21.
24 Fumagalli LP, Radaelli G, Lettieri E, *et al*. Patient Empowerment and its neighbours: Clarifying the boundaries and their mutual relationships. *Health Policy* 2015;119:384–94.
25 Ashcraft LE, Asato M, Houtrow AJ, *et al*. Parent Empowerment in pediatric healthcare settings: a systematic review of observational studies. *Patient* 2019;12:199–212.
26 Deary V, Chalder T, Sharpe M. The cognitive behavioural model of medically unexplained symptoms: a theoretical and empirical review. *Clin Psychol Rev* 2007;27:781–97.
27 ter Wolbeek M, van Doornen LJP, Kavelaars A, *et al*. Severe fatigue in adolescents: a common phenomenon? *Pediatrics* 2006;117:e1078–86.
28 Haverman L, van Rossum MAJ, van Veenendaal M, *et al*. Effectiveness of a web-based application to monitor health-related quality of life. *Pediatrics* 2013;131:e533–43.
29 Gordijn MS, Suzanne Gordijn M, Cremers EMP, *et al*. Fatigue in children: reliability and validity of the Dutch PedsQL™ multidimensional fatigue scale. *Qual Life Res* 2011;20:1103–8.
30 Price DD, McGrath PA, Rafii A, *et al*. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. *Pain* 1983;17:45–56.
31 Worm-Smeitink M, Gielissen M, Bloot L, *et al*. The assessment of fatigue: psychometric qualities and norms for the checklist individual strength. *J Psychosom Res* 2017;98:40–6.
32 Fukuda K, Straus SE, Hickie I, *et al*. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International chronic fatigue syndrome Study Group. *Ann Intern Med* 1994;121:953–9.
33 Goubert L, Eccleston C, Vervoort T, *et al*. Parental catastrophizing about their child's pain. The parent version of the pain Catastrophizing scale (PCS-P): a preliminary validation. *Pain* 2006;123:254–63.
34 Segers EW, van den Hoogen A, van Eerden IC, *et al*. Perspectives of parents and nurses on the content validity of the family Empowerment scale for parents of children with a chronic condition: a mixed-methods study. *Child Care Health Dev* 2019;45:111–20.
35 Cohen J. Statistical Power Analysis for the Behavioural Science. In: *Statistical power Anaylsis for the behavioural science*. 2nd ed. Lawrence Erlbaum, 1988: 79–80.
36 Lynch-Jordan AM, Kashikar-Zuck S, Szabova A, *et al*. The interplay of parent and adolescent catastrophizing and its impact on adolescents' pain, functioning, and pain behavior. *Clin J Pain* 2013;29:681–8.
37 King G, Williams L, Hahn Goldberg S. Family-oriented services in pediatric rehabilitation: a scoping review and framework to promote parent and family wellness. *Child Care Health Dev* 2017;43:334–47.
38 Alsem MW, Ausems F, Verhoef M, *et al*. Information seeking by parents of children with physical disabilities: an exploratory qualitative study. *Res Dev Disabil* 2017;60:125–34.
39 Douma M, Maurice-Stam H, Gorter B. Online psychosocial group intervention for parents: positive effects on anxiety and depression. *J Pediatr Psychol* 2020.
40 Greenhalgh J, Gooding K, Gibbons E, *et al*. How do patient reported outcome measures (PROMs) support clinician-patient communication and patient care? A realist synthesis. *J Patient Rep Outcomes* 2018;2:42.
41 Alsem MW, Verhoef M, Braakman J, *et al*. Parental empowerment in paediatric rehabilitation: exploring the role of a digital tool to help parents prepare for consultation with a physician. *Child Care Health Dev* 2019;45:623–36.

42 Peeters MAC, Hilberink SR, van Staa A. The road to independence: lived experiences of youth with chronic conditions and their parents compared. *J Pediatr Rehabil Med* 2014;7:33–42.
43 Schmidt S, Petersen C, Bullinger M. Coping with chronic disease from the perspective of children and adolescents--a conceptual framework and its implications for participation. *Child Care Health Dev* 2003;29:63–75.
44 Grootenhuis MA, Bronner MB. Paediatric illness! family matters. *Acta Paediatr* 2009;98:940–1.
45 Armbrust W, Lelieveld OHTM, Tuinstra J, *et al*. Fatigue in patients with juvenile idiopathic arthritis: relationship to perceived health, physical health, self-efficacy, and participation. *Pediatr Rheumatol Online J* 2016;14:65.
46 Waters E, Doyle J, Wolfe R, *et al*. Influence of parental gender and self-reported health and illness on parent-reported child health. *Pediatrics* 2000;106:1422–8.