Fatigue and chronic fatigue syndrome-like complaints in the general population*

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Background: Most knowledge on chronic fatigue (CF) and chronic fatigue syndrome (CFS) is based on clinical studies, not representative of the general population. This study aimed to assess the prevalence of fatique in an adult general population and to identify associations with lifestyle factors. Methods: Total 22500 residents of Nijmegen were selected at random and interviewed by questionnaire. Data on 9062 respondents (43% response) were analysed, taken into account age, gender and concomitant disease. Subjects were classified into four groups: not fatigued (NF, reference group), short-term fatigue (SF, <6 months), chronic fatigue (CF, \geq 6 months) and CFS-like fatigue (in accordance with the Center for Disease Control criteria for CFS, without clinical confirmation). Results: Our study population showed the following breakdown: NF 64.4% (95% CI 63.6–65.6%), SF 4.9% (95% CI 4.5–5.4%), CF 30.5% (95% CI 29.5–31.4%) and CFS-like fatigue 1.0% (95% CI 0.8–1.2%). Compared with the NF group, more of the CFS respondents were female [odds ratio (OR) = 1.9], obese (OR = 4.1), using analgesics (OR = 7.8), had a low alcohol intake (OR = 0.4), were eating less healthy food (OR = 0.5) and were physically less active (OR = 0.1). These associations largely applied to the SF and CF group. The fatigue could have been due to a concomitant disease in 34 and 55.5% of the SF and CF cases, respectively. Conclusion: The prevalence of CF in the general population appears to be much higher than previously indicated. Even with strict criteria for CFS, it is estimated that $\sim 1\%$ of the adult population experiences this condition. Interestingly, a large part of this group remains unrecognized by the general practitioner. A striking similarity in lifestyle pattern between SF, CF and CFS calls for further research.

Keywords: chronic fatigue, epidemiology, lifestyle.

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Introduction

F^{atigue} is a common problem with varying severity. According to international studies in general practice, 25-30% of the complaints were found to concern fatigue, while in the population at large, 30-50% reported symptoms of fatigue.¹⁻⁷ Substantial limitations in mental, physical and social functioning occur, with considerable social and economic impact because of increased medical consumption and absenteeism from work. Severe, incapacitating, chronic fatigue that is not caused by a pre-existing (chronic) disease and meets the internationally accepted operational criteria is worthy of the diagnosis of the chronic fatigue syndrome (CFS).⁸ Recently, the Dutch Health Council estimated that 30 000-40 000 people fit the diagnosis of CFS in the Netherlands, based on prevalence studies in general practices.^{5,9} If CFS is left untreated, <10% of the patients will recover.^{10–13} Therefore, CFS is a considerable health problem.

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Correspondence: Prof. GA Zielhuis, Department of Epidemiology, Biostatistics and HTA, Radboud University Nijmegen Medical Centre, 133, PO Box 9101, 6500 HB Nijmegen, the Netherlands, tel: +31 24 3616975, fax: +31 24 3613505, e-mail: g.zielhuis@ebh.umcn.nl Literature suggests that potentially amendable life style factors are relevant in explaining the occurrence of chronic fatigue.¹⁴⁻¹⁷ People with CFS seem to have less healthy life styles,^{5,18-24} including higher use of analgesics, antidepressants, sleeping-pills and tranquillizers.^{25,26}

Because most studies are based on small, selected samples and varying definitions of fatigue, the actual occurrence of fatigue and the associated risk factor pattern in the general population remains unknown.

To investigate the prevalence of fatigue in the general population and to identify possible risk factors, we analysed data from the Nijmegen Biomedical Study (NBS) in which information was obtained from a large unselected sample of the Nijmegen population in 2003. The following specific questions were addressed:

- (1) What is the prevalence of fatigue in the adult general population? What are the proportions of short-term fatigue, chronic fatigue and chronic fatigue syndromelike fatigue? Are the outcomes affected by the presence of a (chronic) disease that might be causing the fatigue?
- (2) Are there differences in lifestyle between subjects who are not fatigued and persons who have short-term, chronic or CFS-like fatigue? Are there differences between these groups regarding the use of analgesics, antidepressants or sedatives?
- (3) Are there differences in the degree that persons with short-term, chronic and CFS-like fatigue consult their GP because of fatigue?

Methods

In 2003, our department conducted a cross-sectional survey on a random sample of the adult population of Nijmegen (stratified for age and gender; the NBS). We selected 750 persons of each gender in 15 5-year age groups. A total of

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Table 1 Demographic aspects of NBS-population 2003(N = 9375)

Subjects	(%)
Sex	
Male	46
Female	54
Marital Status	
Married	64
Single	32
Other	4
Educational	
Primary education	12
Primary vocational education	15
Secondary education	15
Secondary vocational education	13
Higher secondary education	12
Higher vocational educational	19
University	15
Age, years	
18–29	13
30–39	4
40–49	15
50–59	16
60–69	17
70–79	16
≥80	9
Socioeconomic	
Employed	49
Unemployed	6
Pension	28
Housewife/man \pm job	18
Students \pm job	6

22 500 inhabitants aged \geq 18 years were invited for a blood sample and an additional questionnaire addressing demographic characteristics (table 1), lifestyle, occupation, medical history and family diseases.

The following instruments were used:

- Shortened fatigue questionnaire (SFQ), with good internal reliability (Cronbach-α: 0.88) and discriminating validity.²⁷ A cut-off score of ≥18 was considered as severe fatigue; in the remaining text this will be referred to as 'fatigue'.
- Rand 36 Physical functioning (Cronbach's- α : 0.92):^{28,29} A 10-item subscale, transformed to a 0–100 score, where higher scores mean better physical function. A cut-off of ≤ 65 was considered to reflect severe problems with physical functioning.
- Symptom criteria for CFS according to the CDC-94.⁸ Four of the eight symptoms (memory or concentration problems; sore throat; tender cervical or axillary lymph modes; muscle pain; pain in several joints; new headaches; non-refreshing sleep; malaise after exertion) had to be present for at least 6 months to comply with the diagnosis of CFS.
- A list of (chronic) disorders that might cause fatigue was composed by a panel of experts on CFS. This list was based on questionnaire data: cardiac infarction and/or medication for cardiac and vascular diseases; (medication used for) rheumatic disorders; asthma/chronic obstructive pulmonary disease requiring medication; renal pathology (kidney stones not included); cancer; stroke; thyroid disorders; liver disorders (<2 years); diabetes (<2 years); anaemia (<2 years).

Based on self-reported data, subjects were classified into one of the following four groups:

 (1) 'CFS-like': meets the operational definition of CFS according to the CDC-94 criteria, excluding alcohol abuse (>5 units daily), BMI>40 and concomitant disease, serious mental problems (bipolar affective disorders, schizophrenia, delusional disorders) and/or eating disorders, measured by either a medication list and items on social functioning, health and medical history in the questionnaire.⁸ For reasons of convenience, the term 'CFS' is used to describe the results of this study, although CFS was not medically confirmed.

- (2) 'Short-term fatigue': fatigue present for less than 6 months (SF), with or without (chronic) disease that may cause fatigue (SF+ and SF-, respectively).
- (3) 'Chronic fatigue': fatigue present for longer than 6 months (CF), not meeting the operational criteria for CFS, with or without (chronic) disease that may cause fatigue (CF+ and CF-, respectively).
- (4) 'No fatigue': no complaints of fatigue (NF). This group served as a reference group. No fatigue with or without fatigue-related (chronic) disease.

The following variables were used (questionnaire): gender and age (10-year strata, starting at 18 years); food intake: vegetables, fruit, cereals, meat, fish, milk (never/1-2 days a week/3–5 days a week/almost every day; with score 0/1/2/3); use of supplements (multivitamins, folic acid, vitamins B and C, iron); medication (analgesics, sleeping pills, tranquillizers and antidepressants); non-smoker/smoker/ stopped and number of pack years (< or >10); coffee (< or >6 cups a day); alcohol intake (none/<2 units a day/2-5 units a day/>5 units a day); physical activity (inactive/averagely active/active; based on the average of five activity items, each with three levels); education level (primary (vocational) education/secondary (vocational or higher) education/higher vocational education or university); children (yes/no). Body Mass Index was calculated by height and weight $(<19.5/19.5-25/25-30/30-40/>40 \text{ kg m}^{-2})$. 'Healthy food intake' was constructed by the sum of fruit, vegetables and cereals intake (score at least 3).

Proportions with 95% confidence intervals (CI) were used to estimate the prevalence of fatigue.

First, relations were studied between the three types of fatigue (NF = reference group) and several variables using univariate analysis (cross tables). This provided odds ratios (ORs) with 95% CI. The same analysis was carried out after the groups had been split up according to the presence or absence of a (chronic) disease. This included the reference group.

Secondly, the number of variables in each of the following sets of coherent variables were reduced by means of multiple logistic regression: food/supplements; use of medication; smoking. Variables that caused at least 10% change in the sum score and/or 10% shift in the coefficients in the multiple logistic regression analysis were retained (likelihood technique).

Thirdly, for each of the three types of fatigue (NF = reference group) a multiple logistic regression model was created with a reduced set of variables. By means of 'stepwise forward' and 'stepwise backward' techniques (likelihood technique), we searched for the smallest model in which all the variables contributed at least 10% to the model (sum score and betas). In the final model, the relations were estimated by expressing the regression coefficients in ORs with 95% CI.

All the analyses were carried out with SPSS 12.0.1.

Results

The questionnaire was returned by 9375 out of the 22 500 persons approached (43%). A small-scale non-responder survey (n = 200) revealed that most non-responders 'were not interested' or 'had no time' (57%). Another subgroup of non-responders was 'too old', 'too il', dead or moved (24%). The sample of nonresponders was similar to the responders with

Step NBS population

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9375]
<u> </u>	(313 miss)
9062	
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1. Yes/no fatigue & duration fatigue

Chronic fatigue (≥ 6 months) CFS & CF	Short term fatigue (< 6 months SF)	No fatigue NF
2763 ↓ 320 miss	$\begin{array}{c} 447 \\ \downarrow \\ 41 \text{ miss} \end{array}$	5852 ↓ 635 miss
(chronic) disorder (medical condit	ion explaining fatigue)	
Without With	Without With	Without With
CFS&CF- CF+	SF- SF+	NF- NF+
$ \begin{array}{c c} \downarrow & \downarrow \\ \hline 1086 \\ \downarrow & 37 \text{ miss} \end{array} $	↓ ↓ 267 139	↓ ↓ 3686 1531
Severity fatigue (SFQ> 18) 426 \downarrow 14 miss		
Severity physical impairment (Rat	nd 36, physical functioning ≤ 65)	

- ↓ 0 miss
 5. <u>CDC-criteria</u> (4 of 8 symptoms ≥ 6 months, Fukuda et al)
- 6. BMI > 40 excluded 95

96 1

- Alcohol intake > 5 units daily excluded
 89
 ↓
 - Severe mental problems or eating disorders excluded
 89
 Meets CFS criteria

Figure 1 Flow diagram NBS. Breakdown of the surveyed population of the NBS study based on appearance of fatigue. The steps follow the criteria for CFS

regard to age and gender, but more of the responders had higher education, employment and better health perception. Of the responders, 313 were excluded because of missing fatigue data. This left 9062 responders for analysis. Figure 1 shows a flowchart of the study population, broken down into fatigue categories.

Most responders did not have fatigue (64.6% CI 63.6– 65.6%); 4.9% (CI 4.5–5.4%) were considered to have shortterm fatigue (SF; n=447); 30.5% (CI 29.5–31.4%) were considered to have chronic fatigue (CF; n=2763); 89 persons (1%; CI 0.8–1.2%) met the operational criteria for CFS. A concomitant (chronic) disease that may explain the fatigue was present in 34% of the responders with short-term fatigue (n=139) and in 55.5% with chronic fatigue (n=1357).

Relations between the different variables and fatigue are shown in tables 2 and 3. As our study focused on CFS, this group was analysed first (table 3); Significant relations found in univariate analysis of this group were used in the multiple logistic regression analysis. Milk, coffee, present smoking behaviour, children and education level did not contribute to the model. Thus, the following remained in the analysis: gender, age, healthy food (vegetables, fruit and cereals), smoking pack years, alcohol intake, vitamins, iron, sedatives, tranquillizers, sleeping pills and antidepressants, overweight and physical activity. None of the analyses showed a relation between CFS and age, although there seemed to be more cases in the age group 40–60 years (OR = 1.7). Age was retained in the model, because pack years of smoking depended strongly upon age. A clear relation with gender was found: more women had CFS (OR = 1.9). Besides a strong relationship with the use of analgesics (OR = 7.8), persons with CFS drank less alcohol (OR = 0.4) and ate less healthy food (OR = 0.5). As expected, they were less physically active (OR = 0.1/0.2) and there was a strong relationship with overweight (BMI > 30) (OR = 4.1). Although iron intake was not associated with CFS, we included this variable, because it was strongly interdependent with other variables; omission would have led to distortion of the model.

Univariate analyses on the SF and CF group show the same relationships as in the CFS group. After multiple logistic regression analysis (tables 2 and 3) the final SF and CF models were very similar to the CFS model. The only differences were clear relationships in the SF and CF groups with age (younger than 40–60 years and >60 years) and greater intake of iron. Antidepressants and sedatives did not contribute to the SF model.

Overall, SF and CF groups comprised more women, less older respondents (>60 years of age), more obese (BMI > 30), more respondents with low-alcohol intake (2–5 units) and more smokers (>10 pack years).

Yes/no	SF ^a compared with NF ^b		SF- ^c compar	red with NF- ^d	SF+ ^e compared with NF+ ^f		
	OR	95% CI	OR	95% CI	OR	95% CI	
Female	2.2	1.71–2.93	2.5	1.77–3.45	1.9	1.13–3.22	
40–60 years	0.5	0.39-1.71	0.5	0.36-0.73	0.5	0.23-0.89	
>60 years	0.3	0.21-0.42	0.2	0.12-0.36	0.3	0.16-0.50	
Analgesics	1.7	1.14-2.48	1.3	0.75-2.37	2.1	1.18–3.90	
Activity, average ^g	0.7	0.49-1.00	0.6	0.38-0.91	1.1	0.52-2.13	
hysically active ^g	0.6	0.38-0.83	0.4	0.25-0.66	1.0	0.48-2.22	
lealthy food ^h	1.1	0.73-1.61	1.1	0.68-1.76	1.3	0.54-2.97	
/itamins	1.3	0.95-1.70	1.2	0.84-1.74	1.2	0.69-2.03	
ron intake	1.6	0.66-3.70	2.1	0.67-6.88	1.0	0.24-4.25	
Pack years <10 ⁱ	1.2	0.88-1.54	1.3	0.92-1.78	0.7	0.39–1.35	
Pack years >10 ⁱ	1.4	1.03-1.97	1.5	0.98-2.31	1.0	0.57-1.76	
Alcohol ^j 0 <units<2< td=""><td>0.9</td><td>0.63-1.20</td><td>0.8</td><td>0.52-1.18</td><td>1.0</td><td>0.56-1.82</td></units<2<>	0.9	0.63-1.20	0.8	0.52-1.18	1.0	0.56-1.82	
Alcohol ^j 2 <units<5< td=""><td>0.6</td><td>0.40-1.00</td><td>0.6</td><td>0.37-1.15</td><td>0.5</td><td>0.21-1.29</td></units<5<>	0.6	0.40-1.00	0.6	0.37-1.15	0.5	0.21-1.29	
Alcohol ^j >5 units	1.6	0.76-3.41	1.8	0.76-4.39	0.7	0.09-6.06	
BMI 25–30	1.4	1.03-1.79	1.4	0.94-1.97	1.1	0.67-1.97	
3MI >30	2.1	1.46-3.14	2.1	1.29-3.53	2.2	1.15-4.39	
ntercept	B = -3.302		B=-3.319		B = -2.940		

Table 2 Determinants	of short-term fatigue	e (SF) based on	a multiple logistic	regression model

a: n=447

b: *n* = 5852

c: n=267

d: n = 3686

e: *n* = 139

f: n=1531

g: Reference category: physically inactive to less than averagely active

h: Sufficient vegetables, fruit, cereals in meals

i: Pack years = 10 is similar to smoking one packet of cigarettes per day for 10 years

j: Alcohol intake in units of one glass

Estimates with CI <1 had a significant lower proportion of positive responders

Estimates with Cl >1 had a significantly higher proportion of positive responses

	CFS-like ^a compared with NF- ^b		CF ^c compared with NF ^d		CF- ^e compared with NF- ^b		CF+ ^f compared with NF+ ^g	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Female	1.9	1.05–3.44	1.6	1.36–1.78	1.6	1.31–1.87	1.5	1.16–1.84
40–60 years	1.7	0.85-3.38	1.0	0.82-1.13	0.8	0.70-1.03	0.8	0.56-1.19
>60 years	1.3	0.60-2.82	0.8	0.67-0.93	0.4	0.34-0.57	0.6	0.41-0.82
Analgesics	7.8	4.11-14.79	2.5	2.08-3.05	1.9	1.38-2.59	2.6	1.97-3.45
Antidepressives	2.0	0.60-6.35	3.1	2.32-4.20	3.7	2.44-5.61	2.2	1.43-3.54
Sedatives	2.7	0.93-7.91	3.0	2.31-3.94	4.0	2.49-6.32	2.2	1.57-3.16
Activity, average ^h	0.2	0.11-0.37	0.6	0.47-0.67	0.8	0.62-1.06	0.5	0.35-0.60
Physically active ^h	0.1	0.04-0.22	0.3	0.26-0.39	0.5	0.35-0.64	0.3	0.23-0.43
Healthy food ⁱ	0.4	0.22-0.91	0.8	0.66-0.98	0.7	0.52-0.85	1.1	0.74-1.55
Vitamins	1.1	0.57-2.23	1.5	1.26-1.69	1.6	1.32-1.97	1.2	0.97-1.59
Iron intake	0.0	0->>	1.6	0.96-2.53	0.6	0.20-1.60	2.0	1.03-3.71
Pack years <10 ^j	1.2	0.59-2.01	1.2	1.01-1.36	1.3	1.08-1.58	0.9	0.68-1.18
Pack years >10 ^j	1.7	0.85-3.31	1.3	1.13–1.57	1.3	1.06-1.71	1.1	0.85-1.42
Alcohol 0 $<$ units $<2^{k}$	0.4	0.22-0.79	0.9	0.75-1.05	1.1	0.83-1.41	0.8	0.63-1.08
Alcohol 2 <units <5<sup="">k</units>	0.4	0.17-0.97	0.7	0.52-0.82	0.9	0.62-1.20	0.5	0.37-0.76
Alcohol >5 units ^k			1.0	0.66-1.51	1.5	0.87-2.55	0.8	0.39-1.66
BMI 25-30	1.4	0.76-2.74	1.1	1–1.32	1.2	0.96-1.41	1.1	0.89-1.42
BMI >30 (CFS <40)	4.1	2.03-8.45	1.4	1.14-1.76	1.3	0.93-1.81	1.5	1.09-2.11
Intercept	B = -3.258		B = -1.	079	B = -1.6	516	B = -0.1	109

Table 3 Determinants of chronic fatigue syndrome (CFS) and chronic fatigue (CF) based on a multiple logistic regression model

Estimates with CI <1 had a significant lower proportion of positive responders; estimates with CI >1 had a significantly higher proportion of positive responders

a: n=89

b: *n* = 3686

c: *n* = 2674

d: *n* = 5852

e: *n*=997

f: n=1357

g: *n* = 1531

h: Reference category: physically inactive to less than averagely active

i: Sufficient vegetables, fruit, cereals in meals

j: Pack years = 10 is similar to smoking one packet of cigarettes per day for 10 years

k: Alcohol intake in units of one glass

More SF+ subjects had a healthy food intake (OR = 1.3) and were as physically active as the reference group. More CF+ subjects were using sedatives and antidepressants (both OR = 2.2). More CF+ subjects used iron (OR = 2.0) and were less physically active (OR = 0.5/OR = 0.3).

SF– and CF– subjects were less physically active (OR = 0.4/ OR = 0.5), More of them were smokers (>10 pack years) (OR = 1.8/OR = 1.5), more of them drank >5 units of alcohol per day (OR = 1.8/OR = 1.5). The CF– group consumed more antidepressants and sedatives (OR = 3.7 and OR = 4.0, respectively). The SF– group used more iron (OR = 2.1) and more of them were obese (BMI >30) (OR = 2.1).

In the SF group, 29% of the respondents had consulted their general practitioner (GP) because of fatigue. In the CF and CFS groups, this applied to 55 and 71%, respectively. After stratification for concomitant (chronic) disease, these percentages were 21 (SF), 47 (CF) and 71% (CFS) in the absence of (chronic) disease, versus 40 (SF) and 63.5% (CF) when a chronic disease was present.

In each of the fatigue groups, the only difference between the subjects who consulted their GP because of fatigue and those who did not was that the former were using more prescribed medication.

Discussion

This study showed that one-third of the adult population had complaints of fatigue, including 1% reporting CFS-like complaints. This rate was identified using a strict definition of CFS and was considerably higher than previously assumed in the Dutch population. Two physician-based surveys showed a much lower prevalence of 0.1-0.2%.4,5 When adjusted for the stratified sampling and extrapolated to the adult population of the Netherlands, this 1% would imply that ~128 500 Dutch adults have a CFS-like disorder.³⁰ In a study in Kansas using similar operational criteria for 'CFSlike' complaints, an initial prevalence of 6.4% was found, but clinical evaluation dropped this rate to 0.6%.³¹ Unlike the initial part of the Kansas study (detailed telephone interviews followed only for the cases with fatigue >1 month), the detailed questionnaire of our study allowed us to pay close attention to concomitant diseases, for which we used a strict selection. Although we actually do not know how many CFS subjects would have been clinically confirmed, it is unlikely that clinical evaluation would exclude as many cases as in the Kansas study. Assuming that half of the persons with CFS-like complaints in our study would receive a definite diagnosis of CFS after clinical evaluation (i.e. a prevalence rate of 0.5%, about the same as in the Kansas study), then this would still imply doubling of the estimate made by the Dutch Health Council.¹²

Given the large number of people who apparently have CF or CFS, the question arises as to why the diagnosis of CFS is underestimated? More than 70% of our CFS group consulted their GP because of complaints of fatigue, only 6.7% (6 out of 89) reported to be diagnosed as having CFS. Although we did not check these answers in the medical files, we infer that physician-related factors (e.g. ignorance, no confidence with the diagnosis, scepticism towards CFS) need to be taken into account.^{5,9,32–35}

Fatigue is a relative nonspecific symptom, compared with other symptoms of the CFS definition like problems with memory/concentration, unrefreshing sleep or muscle/joint pain. Besides, if people feel their problem will not be taken seriously by a GP, they will be discouraged to present it.

Half of the subjects in our study who were suffering from fatigue had a concomitant disease that could explain the complaints. Stratification for concomitant disease revealed relevant differences in risk factors. More of the CF subjects without concomitant disease were obese, had an unhealthy lifestyle, were smokers, ate less healthy food, were physically less active and made more use of analgesics, antidepressants and sedatives. The lifestyle of the SF subjects without concomitant disease largely showed the same unhealthy pattern.

Demographically, our group of CFS-like subjects was strikingly different from the clinical populations described in the literature. First, the male/female ratio of 1:2 in this study deviated from the 1:3 or greater ratios reported in clinical studies.^{3,5,18} An explanation could be that stratification and correction for other variables diminished the gender differences.³⁶ Secondly, the prevalence of CFS in the age group of 40–60 years was higher than reported in the literature. Younger adults were probably overrepresented in the clinical populations because they sought help at an earlier stage.^{5,18–21}

As the group with concomitant disease was very heterogeneous, inferences based on the relationships found in this study are less straightforward.

The strong relationship with the use of analgesics in the CFS group supports the notion that pain, especially in the muscles, is a component of CFS.⁸

Antidepressant use by subjects with fatigue may indicate a relation with depression, but it may also be explained by the prescription behaviour of GPs in the case of unexplained fatigue.²⁵ Conversely, fatigue may be a side effect of drug use. Sedatives may also cause fatigue, but on the other hand, people with CFS often use sedatives because of disturbed sleep patterns.²⁵

A remarkable finding in our study was that the CFS group tended to eat less healthy food. This might be explained by the findings reported by Smith and Cohen that CFS patients were more inclined to eat ready-made meals because they lacked the energy to prepare fresh ingredients.¹⁹

The lower intake of alcohol in the CFS group is intriguing. Part of the explanation may be alcohol intolerance, which has been reported before in relation with CFS.²¹

Physical inactivity and obesity appeared to be an important relationship not only in CFS, but also in SF and CF groups.

Our study had some limitations. Firstly, the subjects in our CFS group were classified according to self-reported symptoms, without any confirmation by means of clinical evaluation. Thus, only an approximation can be given of the real number of CFS cases, as was also the case in previous studies.^{3,4}

Secondly, the cross-sectional design of this study makes it impossible to determinate the direction of any relationships. Combining worldwide research on fatigue and CFS should contribute to a more efficient investigation on this subject; it will strengthen evidence and speed up the insight in fatigue and CFS.

Thirdly, less than half of the original population responded to the study. This is not exceptional in a public health survey and indeed may lead to quantitative bias in the estimates. The main reason for nonresponse was 'not interested', or 'no time'. Assuming that 'busy' people (who are less likely to report fatigue) are overrepresented among non-respondents, we cannot exclude that some selection bias (leading to overestimation of the presence of fatigue) has occurred. The low response may have partly been due to the simultaneous request to undergo blood tests, because in a similar study without this request in Boxmeer, the Netherlands, the response rate was 70%.³⁷

Finally, as a university town, the population of Nijmegen is slightly more educated than the Dutch population in general. Combined with our survey on the non-responders, which gave the impression that the responders had a higher socio-economic status, they make up for a bias away from the group with a lower education. The univariate analysis on education level in our study showed no difference with the general population, as you can see in other studies as well.^{6,7,31} Literature suggests fatigue is related with lower socio-economic groups³⁶, so an underestimation of the real prevalence of CFS, SF and CF is more likely than overestimation.

Any of these factors may have led to biased estimates of the real prevalence of fatigue (underestimation in all cases except for selective response), but it is unlikely that any type of bias would have disturbed the relations we found between certain variables and fatigue.

In conclusion, the results of this study strongly suggest that CFS is much more common than was previously assumed on the basis of physician-based research. The majority of our CFS cases had consulted their GP because of specific complaints of fatigue, but apparently, for various reasons the diagnosis had not been made.

This similarity in lifestyle pattern suggests that SF, CF and CFS probably are not so much different types of disorders, but more likely different manifestations on a continuum for fatigue. Literature so far does not provide support for this notion, nor for the contrary. It is worthwhile to study the association between lifestyle and different forms of fatigue in other databases. Such studies should find out whether an (un)healthy lifestyle is a cause, a consequence or a correlate of some underlying predisposing factor for SF, CF and CSF.

Conflicts of interest: None declared.

Key points

- No population-based prevalences of chronic fatigue syndrome (CFS) have been published so far.
- Nearly one-third of the adult population experience CF of 6 months or more. Of these half is comorbidity.
- About 1% fulfils the CDC criteria for CFS which is much higher than estimated before.
- More than 70% of the CFS cases have presented the complaints to their GP. Yet, most of the cases remain undetected. Training of GPs to recognize CFS in an early stage is advocated.

References

- Cullen W, Kearny Y, Bury G. Prevalence of fatigue in general practice. Ir J Med Sci 2002;171:10–2.
- 2 Wessely S, Chalder T, Hirsch S, et al. The prevalence and morbidity of chronic fatigue and chronic fatigue syndrome: a prospective primary care study. *Am J Public Health* 1997;87:1449–55.
- 3 Buchwald D, Umali P, Umali J, et al. Chronic fatigue and the chronic fatigue syndrome: prevalence in a Pacific Northwest health care system. Ann Intern Med 1995;123:81–8.
- 4 Versluis RG, de Waal MW, Opmeer C, et al. Prevalence of chronic fatigue syndrome in four general practices in Leyden region. *Ned Tijdschr Geneeskd* 1997;141:1523–6.
- 5 Bazelmans E, Vercoulen JHMM, Swanink CMA, et al. The prevalence of Chronic Fatigue Syndrome and Primary Fibromyalgia Syndrome in the Netherlands. *Family Pract* 1999;16:602–4.
- 6 Lloyd AR, Hickie I, Boughton CR, Spencer O, Wakefield D. Prevalence of the chronic fatigue syndrome in an Australian population. *Med J Aust* 1990;153:522–8.

- 7 Lawrie SM, Manders DN, Geddes JR, Pelosi AJ. A population-based incidence study of chronic fatigue. *Psychol Med* 1997;27:343.
- 8 Fukuda K, Straus SE, Hickie I, et al. The chronic fatigue syndrom: a comprehensive approach to its definition and study. *Ann Intern Med* 1994;121:953–9.
- 9 The Health Care Insurance Board (CVZ). *Cognitive behaviour therapy for chronic fatigue syndrome*. Diemen: CVZ, 2002; Publ. No. 02/111.
- 10 Van der Werf SP, De Vree B, Van der Meer JWM, Bleijenberg G. Natural course and predicting selfreported improvement in patients with a relatively short illness duration. J Psychosom Res 2002;53:749–53.
- 11 Nisenbaum R, Jones JF, Unger ER, et al. A population-based study of the clinical course of chronic fatigue syndrome. *Health Qual Life Outcomes* 2003;1:49.
- 12 Health Council of the Netherlands. *Chronic fatigue syndrome*. The Hague: Health Council of the Netherlands, 2005; Publ. no. 2005/02.
- 13 Cairns R, Hotoph M. A systematic review describing the prognosis of chronic fatigue syndrome. *Occup Med C* 2005;55:20–31.
- 14 Alcohol report: report on intensifying the policy against alcohol use. Ministry of Health, Welfare and Sport. VWS, 2003.
- 15 Foundation for Public Health and Smoking. For a smoke free future. Annual report 2002. The Hague: STIVORO, 2003.
- 16 Health Council Commission on trends in nutritional consumption. Some important developments in the nutritional consumption. The Hague: Health Council, 2002; Publ. no. 2002/12.
- 17 Hildebrandt VH, Ooijendijk WTM, Stiggelbout M, Hopman-Rock M. Trend report activity and health 2002/2003. Leiden: TNO, 2004.
- 18 Prins JB, Bleijenberg G, Bazelmans E, et al. Cognitive behaviour therapy for chronic fatigue syndrome: a multicentre randomised controlled trial. *Lancet* 2001;357:841–8.
- 19 Smith BA, Cohen MJ. Dietary intake of patients with chronic fatigue syndrome. J Am Dietetic Assoc 1998;98(Suppl 1):A87.
- 20 Jay SJ. Tobacco use and chronic fatigue syndrome, fibromyalgia, and temporomandibular disorder. Arch Intern Med 2000;160:2398–401.
- 21 Woolley J, Allen R, Wessely S. Alcohol use in chronic fatigue syndrome. *J Psychosom Res* 2004;56:203–6.
- 22 Bazelmans E, Bleijenberg G, Van der Meer JWM, Folgering H. Is physical deconditioning a perpetuating factor in chronic fatigue syndrome? A controlled study on maximal exercise performance and relations with fatigue, impairment and physical activity. *Psychol Med* 2001;31:107–14.
- 23 Bultmann U, Kant I, Kasi SV, et al. Lifestyle factors as risk factors for fatigue and psychological distress in the working population: prospective results from the Maastricht Cohort Study. J Occup Environ Med 2002;44:116–24.
- 24 Laaksonen M, Luoto R, Helakorpi S, Uutela A. Associations between health-related behaviors: a 7-year follow-up of adults. *Prev Med* 2002;34:162–70.
- 25 Wessely S, Chalder T, Hirsch S, et al. Psychological symptoms, somatic symptoms, and psychiatric disorder in chronic fatigue and chronic fatigue syndrome: a prospective study in the primary care setting. *Am J Psychiatry* 1996;153:1050–9.
- 26 Lawrie SM, Pelosi AJ. Chronic fatigue syndrome in the community. Prevalence and associations. Br J Psychiatry 1995;141:793–7.
- 27 Alberts M, Vercoulen JHMM, Bleijenberg G. Assessment of fatigue the practical utility of the subjective feeling of fatigue in research and clinical practice. In: Vingerhoets A, editor. Assessment in behavioral medicine. London: Routledge, 2001, 301–27.
- 28 Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). Conceptual framework and item selection. *Med Care* 1992;30:473–83.
- 29 Aaronson NK, Muller M, Cohen PD, et al. Translation, validation, and norming of the Dutch Language version of the SF-36 Health Survey in community and chronic disease populations. J. Clin Epidemiol 1998;51:1055–68.
- 30 Central Bureau for Statistics (CBS): http://statline.cbs.nl/StatWeb/ publication/?DM=SLNL&PA=03743&D1=1-2&D2=0,97-116,127-129&D3= 0-7,129,l&D4=12&HDR=T,G1&STB=G2,G3&VW=T.

- 31 Solomon L, Nisenbaum R, Reyes M, et al. Functional status of persons with chronic fatigue syndrome in the Wichita, Kansas, population. *Health Qual Life Outcomes* 2003;1:48.
- 32 Torres-Harding SR, Jason LA, Taylor RR. Fatigue severity, attributions, medical utilization and symptoms in persons with chronic fatigue. J Behav Med 2002;25:99–113.
- 33 Bowen J, Pheby D, Charlett A, Mc Nulty C. Chronic Fatigue Syndrome: a survey of Gps' attitudes and knowledge. *Family Pract* 2005;22:389–93.
- 34 Prins JB, Bleijenberg G, Klein Rouweler E, et al. Doctor-patient relationship in primary care of chronic fatigue syndrome: perspectives of the doctor and the patient. J Chronic Fatigue Syndr 2000;7:3–15.
- 35 Solomon L, Reeves C. Factors influencing the diagnosis of chronic fatigue syndrome. *Arch Intern Med* 2004;164:2241–5.
- 36 Van Mens-Verhulst J, Bensing J. Distinguishing between chronic and nonchronic fatigue, the role of gender and age. *Soc Sci Med* 1998;47:621–34.
- 37 Meuleman EJH, Donkers LHC, Robertson C, et al. Erectile dysfunction: prevalence and influence on the quality of life: the Boxmeer study. Ned Tijdschr Geneeskd 2001;145:120–24.

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