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Diagnosing chronic fatigue syndrome: comparison of a protocol and computerised questionnaires

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ABSTRACT

Background: In the context of outpatient care and within the framework of scientific research, guidelines and measuring instruments have been developed to help improve CFS diagnostics. The purpose of this study was to measure the agreement between the evaluations of chronically fatigued patients by physicians using a CFS protocol and by researchers using computerised questionnaires.

Methods: The sample consisted of 516 patients referred to an internal medicine outpatient clinic with complaints of chronic fatigue. Retrospectively the medical records and the computerised questionnaires were checked separately and compared to see whether the criteria for diagnosis of CFS had been met. In addition, the reasons for not diagnosing CFS were evaluated.

Results: Agreement between the physicians' and the researchers' evaluations was 84%. Disagreement mostly concerned severity of fatigue and functional impairment, or premorbid exclusion criteria. A physical cause for the chronic fatigue was only found in 3% of the cases.

Conclusions: For physicians, questionnaire assessment may be complementary to the CFS protocol in optimising the process of diagnosing CFS.

INTRODUCTION

In recent years we have seen a rise in the diagnosis of chronic fatigue syndrome (CFS). A comparison of studies investigating the prevalence of CFS has revealed that general practitioners diagnose CFS more often than a decade ago. In 1993, 27% of GPs never diagnosed CFS.[1] In a similar study in 1999 this percentage had dropped to 13%. However, despite this increase in diagnosing CFS, many clinicians still have difficulty in making this diagnosis, partly because there is no known organic substrate. The international criteria that have facilitated scientific research[2] have not been validated for individual patients and are thus less appropriate for use in clinical practice. There is a debate among medical professionals, for instance, as to which medical investigations are needed to exclude physical causes of the symptoms of fatigue. Also, the criteria on the basis of which the physician can establish the severity of the fatigue and functional impairment are a matter of discussion. During the last decade our outpatient clinic has seen large numbers of patients suffering from chronic fatigue, both in the context of outpatient care and within the framework of scientific research. In both settings guidelines and measuring instruments have been developed to help improve CFS diagnostics.[3,4] At our outpatient clinic a chronic fatigue protocol is applied.[5] In our scientific studies, patients fill in several computerised questionnaires to establish whether they meet the operational and centres for disease control (CDC) criteria for CFS.[6]
In this paper we report a retrospective study aimed at establishing the extent to which there is agreement on the diagnosis of CFS between physicians using the chronic fatigue protocol and researchers evaluating the computerised questionnaires.

**** J.W.M. van der Meer was not involved in the handling and review of this paper.**

METHODS

Patients and procedure

The sample consisted of all patients referred to the general internal medicine outpatient clinic of the University Medical Centre St Radboud in Nijmegen with complaints of chronic fatigue between October 1996 and January 1998. These patients were screened according to the CFS protocol. The protocol included an extensive anamnesis administered by the attending physician, frequently a resident in internal medicine, followed by a medical examination and a restricted number of laboratory tests. This consultation lasted approximately one hour. Subsequently, after a trained nurse had instructed the patient on how to operate the computer, the patient was requested to fill in the questionnaires on a computer in a separate consulting room, which took about 30 minutes. The nurse remained available throughout the procedure for any questions. After four weeks the patient was called in for a second consultation during which the physician explained the findings of the clinical examination. The diagnosis of CFS was based solely on the physician's judgement of these clinical findings. The outcome of the questionnaire assessment was used later to select CFS patients eligible for a randomised controlled trial[6] and was not taken into account in the clinical judgement.

CFS protocol

To streamline and facilitate CFS diagnostics in patients referred with complaints of chronic fatigue, a CFS protocol for outpatients was developed containing guidelines for both the anamnesis and physical examinations as well as supplementary diagnostics.

CFS is defined as a self-reported fatigue that has lasted more than six months, is irrespective of physical exertion, leads to severe functional impairment, and where there is no medical explanation for the symptoms. For a diagnosis of CFS to be made, the physician needs to answer the following questions: Can a somatic explanation for the symptoms be excluded? Is this a case of severe fatigue associated with serious limitations in the patient's professional, social and/or personal functioning? Have the symptoms and impairments been present for at least six months? Do any of the exclusion criteria as formulated by the CDC concerning depression, psychosis, eating disorders or alcohol abuse apply?

Anamnesis

The first step in the symptom-specific anamnesis is to try and gain insight into the patient's expectations and objectives with respect to this consultation and this doctor. Frequently, CFS patients attribute their symptoms to a variety of factors, which cause them to have high expectations for the diagnostics. Also, there may be a hidden agenda involving insurance issues and invalidity benefit claims. It is essential to identify these issues and expectations at an early stage to make communication more transparent and to prevent both sides from digging in.[7] When it has been established what the patient may or may not expect from his or her visit to the clinic, the severity and extent of the functional impairment is investigated. A suitable technique is to have the patient describe what a normal, average day looks like, for instance the day before. Important details that should be discussed are: At what time does the patient get up? Does he or she take a shower, have breakfast, get dressed? Also issues such as who does the shopping, or the cooking, whether he/she goes to work, plays sports, etc. should be addressed. It is recommended to literally go through the patient's day, hour by hour.[8] Subsequently, the duration and the course of the symptoms are discussed. It is essential to try and establish whether the patient has been fatigued his/her entire life or whether the onset of the symptoms can be more or less clearly defined. This is assessed both from the physician's and the patient's perspective. Next, any concomitant complaints are investigated, which are often abundant. It is important to determine whether fatigue is indeed the principal complaint. In principle, the interview continues with a full internal anamnesis, use of medication (including alternative medication) and stimulants, and the patient's case history, specifically with respect to psychiatric symptoms and eating disorders. Finally, any previous diagnoses and treatment(s) are discussed.

Physical examination

The patient is given a full physical examination during which specific attention is paid to the detection of so-called stigmata indicating possible endocrine causes for the fatigue symptoms, such as orthostatic hypotension, pigmentations, pattern of body hair, etc.

Supplementary diagnostics

Laboratory tests are restricted to erythrocyte sedimentation rate (ESR), haematological parameters, minerals, liver and renal functions, protein spectrum, thyroid stimulating hormone (TSH), ferritin and creatine phosphokinase (CPK). In rare cases this range of tests may be extended on the basis of the findings of the anamnesis and/or physical examination.

Computerised questionnaires

A total of four questionnaires were administered to verify whether patients fulfilled the international criteria for CFS as used in scientific research.[2] The fundamental criterion, i.e. exclusion of physical causes, could not be included in this part of the study since a medical practitioner can only evaluate this aspect. The remaining criteria were all assessed by means of the various questionnaires, which

were administered on a personal computer. Patients completed the following five questionnaires: 1) a general questionnaire on the patient's personal data, and the nature, duration and onset of the complaints, 2) the validated fatigue inventory checklist individual strength (CIS),[3,9] 3) a functional impairment questionnaire consisting of eight subscales of the sickness impact profile (SIP-8): sleep/rest, housekeeping, mobility, social interaction, walking, alertness/intellectual functioning, work, recreational and leisure activities,[10] 4) a questionnaire scoring premorbid functioning and finally 5) a questionnaire assessing additional CFS-related physical complaints. For the diagnosis of CFS as commonly applied in research, the following criteria needed to be met:

- Fatigue is the principal complaint
- The fatigue symptoms have been present for at least six months, excluding lifelong incidence
- A score of 35 or higher on the CIS subscale fatigue severity
- A score of 800 or higher on the eight subscales of the SIP
- Absence of premorbid eating disorders, alcohol-related problems in the two years prior to the assessment, premorbid depressive disorders or psychotic episodes.

The concomitant physical complaints were not included in the diagnosis since it has already been established that these are not contributing factors.[4]

Analysis

A researcher from the department of general internal medicine (H. Koning) retrospectively evaluated the medical files of all the patients examined in the above-mentioned period. A researcher from the department of medical psychology (J.B. Prins) evaluated the computerised questionnaire data. Both evaluations were aimed at establishing whether a diagnosis of CFS had been made. In the absence of a CFS diagnosis, the rationale behind the judgement was determined. Next, the two datasets were linked and compared to determine statistically the agreement with respect to the CFS diagnosis for each patient. Concordance between the physician's diagnosis and the researcher's evaluation of the computerised questionnaires was evaluated by Cohen's kappa, which is a measure of concordance between two dichotomous variables corrected for chance. A value of Cohen's kappa of .40 or lower is considered moderate, between .40 and .70 satisfactory, and above .70 good.

RESULTS

Patient characteristics

In the period investigated, 567 patients were referred to our outpatient clinic because of complaints of chronic fatigue. Fifty patients were not included in the study. Their symptoms could be explained on the basis of existing data and a consultation was not expected to reveal any additional information. Of the remaining 517 patients, 212 were referred by their GPs, 46 by a medical specialist and 259 patients had contacted the clinic of their own accord. Nearly 75% of the patients attended the outpatient clinic in the expectation that they would be diagnosed with CFS, 16% mentioned participating in scientific research as their main reason for requesting the consultation and 10% reported both these motives. In one patient a full assessment proved to be impossible. Thus, the data of 516 patients could be analysed and compared. Of the patients included in the analyses 78% were female, 22% male, and their mean age was 36 years and 9 months (range 14-69 years).

CFS protocol

Figure 1 shows the results of the physical assessment of all 516 patients. Based on the protocol, the clinicians diagnosed 409 patients (79%) as suffering from CFS. In the remaining 107 patients CFS was not diagnosed on various grounds. In half of these patients (n=54) the fatigue-related symptoms or functional impairment were not judged sufficiently severe to justify a diagnosis of CFS. In 40 patients comorbidity, possibly explaining the fatigue, was diagnosed. The comorbidity included somatic illnesses (n=17), psychosocial problems (n=9), alcohol-related problems or eating disorders (n=4), and other principal complaints (n=10). Thirteen patients met the exclusion criteria for CFS relating to the premorbid condition, viz. eating disorders, depression or lifelong fatigue.

Computerised questionnaires

The results of the questionnaire-based assessment of all 516 patients referred are also listed in *Figure 1*. According to the outcome of the questionnaires, 369 patients (71%) met the CFS criteria investigated. The reasons why the remaining 147 patients were not diagnosed as suffering from CFS included insufficient scores on the CIS and/or SIP-8 (n=59), fatigue proved not to be the principal complaint (n=29) and the presence of premorbid eating disorders or alcohol-related problems, depression, psychoses or lifelong fatigue (n=59).

Comparison of the two assessments

Table 1 indicates that in 84% of the cases there was agreement between the clinicians' assessments and the researchers' evaluations of the questionnaires as regards the presence or absence of a CFS diagnosis. The degree of agreement was analysed using Cohen's kappa and was .58 (SE .04), a correspondence that is common in scientific research in a clinical setting[11] and is generally regarded as satisfactory.[12]

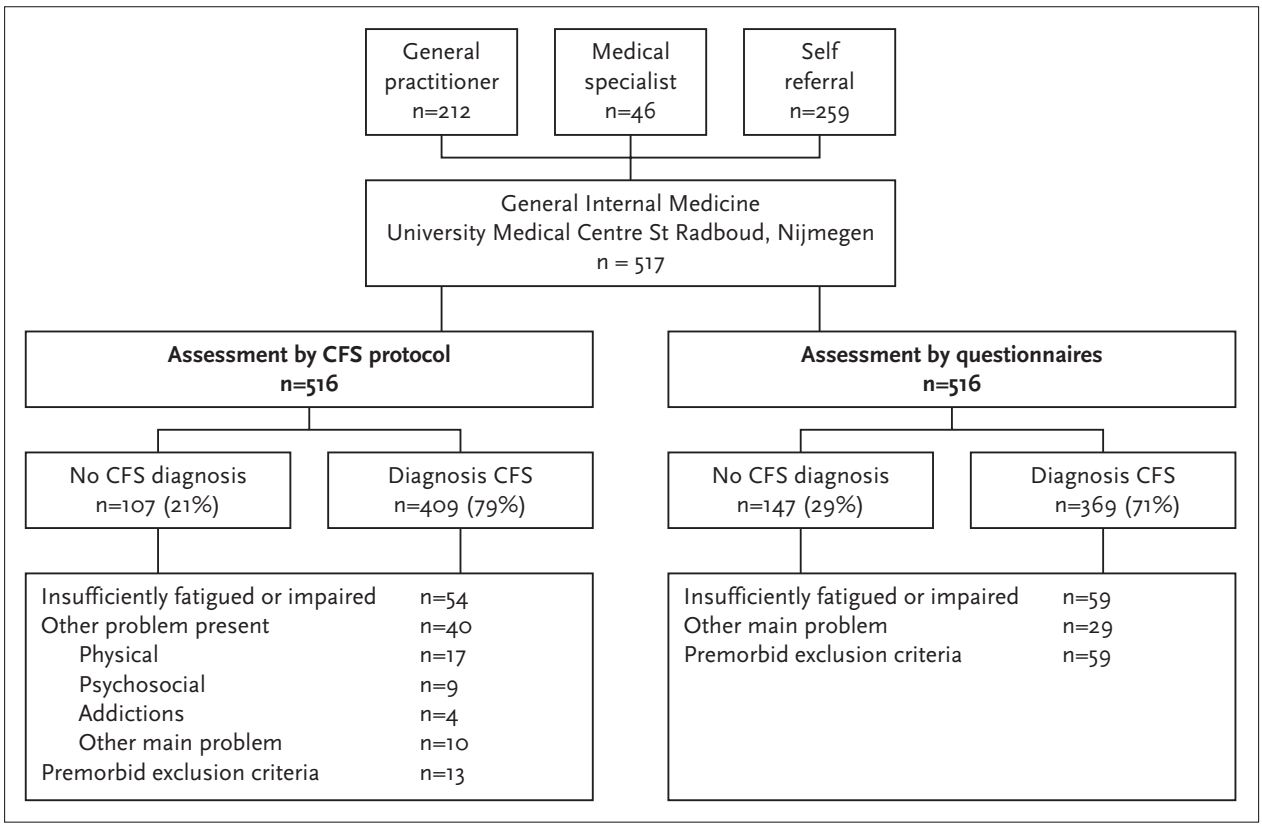

Figure 1
Number of patients referred for fatigue-related symptoms and the results of the protocol-based physicians' and questionnaire-based computerised assessments

Table 1
Numbers and percentages of patients evaluated for the diagnosis of CFS by physician's use of CFS protocol and researcher's evaluation of computerised questionnaires

		QUESTIONNAIRES		
		CFS	**NO CFS**	**TOTAL**
CFS PROTOCOL	**CFS**	348 (67%)	61 (12%)	409 (79%)
	No CFS	21 (4%)	86 (17%)	107 (21%)
	Total	369 (71%)	147 (29%)	516

Of all 516 patients examined, 21 (4%) were diagnosed as suffering from CFS on the basis of the computerised questionnaires whereas the internist excluded CFS. In these 21 patients, a different diagnosis was made in six of them: either somatic (n=3) or psychiatric (n=3). In the remaining 15 patients the physician found insufficient complaints and/or impairments for a diagnosis.
In 61 (12%) of the patients the inclusion criteria for CFS were not met according to the questionnaire-based assessment, whereas the specialist did diagnose CFS. The scores on the CIS or SIP were found to be too low in 40% of the patients concerned, while the physician judged the complaints and impairments as sufficiently severe. In the computer assessment 29% of the patients had not indicated fatigue as their main complaint and 31% had reported premorbid eating disorders or alcohol-related problems, depression or lifelong fatigue, aspects that had not come to light during the physician's consultation.

DISCUSSION

It goes without saying that the diagnosis of CFS can and should never be solely based on an assessment using computerised questionnaires. First and foremost, any physical cause for the symptoms should be excluded, a criterion that always requires the judgement of a physician. In this study a physical cause for the fatigue symptoms could only be found in a few cases. Apparently, prior to their referral, the majority of patients had been screened in such a way that further diagnostics did not yield any additional information. We concluded that referral of CFS patients to our internal medicine outpatient clinic seldom

Table 2

Shortened fatigue questionnaire (SFQ) medical psychology, University Medical Centre St Radboud, Nijmegen, the Netherlands

Name: ..... Gender: male/female .....
Date of birth: ..... Today's date: .....

On this page you will find four statements indicating how you have been feeling during the past two weeks.
You can answer each question by placing a cross in one of the seven boxes. The position of the marking indicates to what extent you feel the statement applies to you.
For example: if you think the statement is completely true, you should place a cross in the left box, like this:

Yes, that is true [X] [ ] [ ] [ ] [ ] [ ] [ ] No, that is not true

If you think the answer is not 'yes, that is true' but also not 'no, that is not true', you should mark the box that best corresponds with your feeling, for example like this:

Yes, that is true [ ] [ ] [ ] [ ] [X] [ ] [ ] No, that is not true

Please answer all the statements and place only one cross for each statement.

1. I feel tired — Yes, that is true [ ] [ ] [ ] [ ] [ ] [ ] [ ] No, that is not true
2. I tire very quickly — Yes, that is true [ ] [ ] [ ] [ ] [ ] [ ] [ ] No, that is not true
3. I feel fit — Yes, that is true [ ] [ ] [ ] [ ] [ ] [ ] [ ] No, that is not true
4. Physically I feel exhausted — Yes, that is true [ ] [ ] [ ] [ ] [ ] [ ] [ ] No, that is not true

Score form SFQ

Chief complaint: ..... Date of origin: ..... (month) ..... (year) .....
Diagnosis: .....

GROUPS	AVERAGE AGE	<< LOW	< AVERAGE	= AVERAGE	> AVERAGE	>> HIGH
HEALTHY GROUPS						
Healthy adults	37	4	4	5-8	9-14	≥15
Students, normal circumstances	22	4	5-7	8-14	15-21	≥22
Students, demanding circumstances	21	≤5	6-9	10-17	18-23	≥24
Servicemen at rest (normal)	21	4	5-6	7-14	15-22	≥23
Servicemen in field exercise	21	≤5	6-11	12-18	19-24	≥25
PATIENT GROUPS						
Cancer	61	4	5-12	13-21	22-27	28
Functional bowel disease	41	≤6	7-12	13-21	22-27	28
Multiple sclerosis	36	≤12	13-19	20-26	27	28
Chronic fatigue syndrome	38	≤22	23-25	26-27	28	28

1. I feel tired — Yes, that is true [7] [6] [5] [4] [3] [2] [1] No, that is not true
2. I tire very quickly — Yes, that is true [7] [6] [5] [4] [3] [2] [1] No, that is not true
3. I feel fit — Yes, that is true [1] [2] [3] [4] [5] [6] [7] No, that is not true
4. Physically I feel exhausted — Yes, that is true [7] [6] [5] [4] [3] [2] [1] No, that is not true

Total score SFQ:

lead to new medical insights. Therefore, referrals could be limited to those patients for whom the expertise of a specialist is required to exclude any physical causes, for instance in cases of suspected adverse effects of medication, slightly deviating laboratory test results or somatic comorbidity. According to a recent unpublished survey among general practitioners, currently 78% of fatigued patients are still being referred to a medical specialist. It is our view that administration of the presented protocol for chronic fatigue complaints by GPs would not only lead to substantial reductions in public spending, but would also prevent undue expectations in patients about new or additional medical diagnoses.

When retrospectively comparing the diagnoses based on the CFS protocol with the diagnoses on the basis of the computerised questionnaires, agreement between both assessments was found in the majority of the cases. In 16% of the cases the clinicians' and the researchers' conclusions were contradictory. In quite a few instances, there was ambiguity about the severity of the fatigue and functional impairment. When a physician is having doubts about symptom severity, questionnaire assessment might be considered. Supplementary to the protocol, the shortened version of the fatigue questionnaire[13,14] could be administered to assess fatigue severity or the physical functioning subscale of the SF-36 questionnaire (MOS-Short Form-36)[15-17] to measure functional impairment (*tables 2* and *3*).

Physicians using the CFS protocol more often diagnosed CFS than researchers evaluating the computerised questionnaires (79 and 71% respectively). Premorbid exclusion criteria for the diagnosis CFS, such as alcohol dependency, eating disorders or depressive disorders, were found more often in the computerised questionnaires than in the physician's consultation. Obviously, it is difficult to establish the patient's case history or current situation with respect to psychological problems or psychiatric disorders. Questionnaire assessment might lead to additional information.

At our outpatient clinic, after consulting the internist patients with chronic fatigue routinely fill in computerised questionnaires to establish whether they meet the operational criteria for CFS. The physician is able to consider the questionnaire data concerning fatigue severity, functional impairment and actual and premorbid functioning before the second consultation. In this way the questionnaire assessment is complementary to the CFS protocol and the process of diagnosing CFS is optimised.

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Table 3
SF 36 questionnaire, subscale physical functioning[15]

The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	YES, LIMITED A LOT	YES, LIMITED A LITTLE	NO, NOT LIMITED AT ALL
Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	1	2	3
Lifting or carrying groceries	1	2	3
Climbing several flights of stairs	1	2	3
Climbing one flight of stairs	1	2	3
Bending, kneeling or stooping	1	2	3
Walking more than a mile	1	2	3
Walking several blocks	1	2	3
Walking one block	1	2	3
Bathing or dressing yourself	1	2	3

Score range 10-30. Score <25 indicative of severe impairment in physical functioning.

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