Once tired, always tired? Limitations in function over time of tired patients in Dutch general practice

E. G. H. Kenter, I. M. Okkes, S. K. Oskam & H. Lamberts

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E. G. H. KENTER, I. M. OKKES, S. K. OSKAM & H. LAMBERTS

Department of General Practice, Division of Clinical Methods & Public Health, Academic Medical Centre, University of Amsterdam, Amsterdam, the Netherlands

Abstract

Objective: To gain insight into limitations in function over time of general-practice patients who presented and were diagnosed with "tiredness". *Methods:* In a routine family-practice electronic register based on use of the International Classification of Primary Care (ICPC), 684 patients were identified who presented (in 1997 or 1998) with the complaint tiredness, who were given the same symptom diagnosis, and who still had this diagnosis on 1 August 1999. A questionnaire (WONCA/COOP charts, HAD Scale, recent medical care, tiredness and attribution) was sent to these 684 "cases" and 858 controls. In a logistic regression analysis (16 dichotomous variables), we constructed five models for optimizing sensitivity and specificity for the detection of patients with an episode of care for "tiredness". *Results:* We received 385 fully completed questionnaires of cases, on average 19 (7–31) months after the start of their episode of care for "tiredness". The results of the 1997 and 1998 cases were similar. Cases did considerably worse than did the 385 optimally matched controls: e.g., seriously limited by tiredness: 52% of cases vs 32% of controls; poor overall health: 35% of cases vs 20% of controls; HAD Scale scores indicating anxiety or depression: about 20% of cases vs about 10% of controls. Highest sensitivity (70%) was reached by including poor overall health, recent medical care and HAD Scale depression score >10 in the model; and highest specificity (65%) by including poor overall health and a HAD Scale anxiety score >7.
Conclusion: Patients who present with tiredness and receive the same diagnosis have a high probability of suffering from substantial limitations in function in the years following diagnosis. Their limitations are more serious than those of controls, but no indication is found for a specific limitation. The indicators are strongly related and concentrate around "poor overall health".

Key words: *Comorbidity, fatigue, general/family practice, limitations in function, tiredness*

Introduction

Tiredness is a frequent complaint in the population, and also, although less frequently, a reason for an encounter with a general practitioner (GP) (1–7). Over the last decade, many studies have been undertaken concerning tiredness, quite often focused on the existence and treatment of chronic fatigue syndrome (CFS). CFS has now been established as a nosological entity without a proven aetiology other than patients' behavioural change, which at the same time forms the basis for effective therapies such as cognitive behavioural therapy (CBT) and graded exercise therapy (GES) (8–14).

In general practice, brief episodes of care for "tiredness" are much more common than chronic ones: in an earlier study, we reported that 72% of episodes of "tiredness" required only one GP encounter, while only 10% lasted over 6 months (5,6,10). In a 4-year period, 21% of all listed patients presented with tiredness, and 12% were diagnosed with the symptom diagnosis tiredness; both groups were strongly skewed towards elderly women. Patients with a new episode of tiredness had to deal with a variety of other diagnoses (comorbidity): their comorbidity was 61% higher than that of other visiting patients. This difference was mainly accounted for by high rates of potential tiredness-related comorbid conditions: depressed or anxious feelings, mood disorders, and sleeping disturbance, but also side effects of medication and ischaemic heart disease; these findings were in accordance with other studies (15,16).

Obviously, the fact that most episodes of care for tiredness required only one GP encounter does not necessarily mean that the episode of illness as perceived by the patient has ended. In fact, episodes of illness may last far longer than the related episode of care (both before and after). People may for a

variety of reasons decide not to seek (further) medical care for their symptoms or complaints (14–16). In this study, we examined how "tired" general-practice patients cope over time, regardless of whether or not they still see their GP because of it.

Methods

We performed a questionnaire study aimed at comparing limitations in function of "cases" (patients identified in the Transition Project's database who presented and were diagnosed with "tiredness") and controls.

Description of the database

Since 1985, members of the Transition Project of the Amsterdam University Department of General Practice have been contributing to the episode-oriented epidemiology of general practice. In the Dutch healthcare system, all inhabitants are listed (registered) with a GP, and cannot, in principle, seek specialist care without their GP's referral. Therefore, Dutch GPs document a close approximation of all episodes of care in the population (5,6,10).

GPs participated for at least 1 year; the registration period ranged from 1 to 20 years. The unit of data collection was the episode of care: "a health problem in an individual from the first encounter until the completion of the last encounter with a healthcare provider". For all episodes of care, the patient's reason(s) for encounter (RFE), the diagnosis (episode title) and the GP's intervention(s) were coded according to the International Classification of Primary Care (ICPC), the classification designated by the World Organization of Family Doctors (WONCA) as the ordering principle of the general practice domain (5,17). Also, for each episode of care, GPs indicated its status: "new" (start) or "old" (follow-up). Obviously, episodes of care only reflect problems that led to a demand for care (consulting the GP), and the episode of illness (the patient's illness experience) may last considerably longer than the episode of care, both before and after its presentation. The episode title (the diagnosis) could be modified; if that occurred, the final diagnosis was used in the analysis. The average yearly practice population served as the denominator.

Between 1985 and 2000, 58 GPs routinely coded data on 504 145 episodes of care in 168 550 patient years. Until 1995, coding occurred on self-copying encounter forms, for all face-to-face encounters. Since 1995, an electronic patient record (EPR), Transhis, has replaced this system and was used (1995–ongoing) by 10 GPs in five practices with a total listed population of 21 003 patients (80 244 patient years), for all direct and indirect encounters. The database includes, in a 1-year observation period, all combinations of RFEs, diagnoses and interventions for 14 standard sex/age groups, at the start of episodes and during follow-up, and comorbidity data.

The 1985–1994 reference database is available in Dutch on a CD-ROM included in a family-practice textbook (18). The database collected with the EPR Transhis (1995–2004) is available online (www.transitieproject.nl) and on CD-ROM (5,7).

Selection of cases and controls

From this database, all patients over age 15 who had started an episode of care with an RFE of tiredness, who received the diagnosis "tiredness" in 1997 or 1998, and in whose EPR this diagnosis was unchanged by 1 August 1999 were included in the study ("cases", $n = 684$). Each case was matched for sex and age with 1.4 controls from the same practice: patients who in the same year had had at least one GP encounter, and, until July 1999, none related to tiredness either as an RFE or as a diagnosis ($n = 858$). The over-sampling occurred in order to be able to optimally match for sex, age and practice.

Questionnaire

In order to assess functional status, we selected the COOP/WONCA Functional Status Indicators, which are designed for use in general practice, especially together with the ICPC (19–21). This instrument, widely tested and used in the Netherlands, consists of six questions that are in themselves relevant for patient–physician communication, as opposed to questions from index measures, which often only serve the purpose of establishing a composite score with a predefined cut-off point. Questions concern physical fitness, feelings, daily activities, social activities, overall health and change in health, and limitations in function during the past 2 weeks. Each item is rated on a five-point ordinal scale; the scores have been used with a chosen cut-off point (scores > 3 indicate substantial limitations in function). When using the COOP/WONCA Functional Status Indicators, it has to be kept in mind that an indicator is not an index: the scales are not equidistant, and, consequently, the answers relate directly to the questions and do not have other psychometric properties (21).

Because of the well-known relation between tiredness and mood disorders, we added the Hospital Anxiety and Depressive Scale (HAD Scale), a diagnostic index particularly appropriate for use in general practice because it contains no questions

concerning physical symptoms that could be part of a mood disorder or physical disorder (22–25). The HAD Scale is self-administered and brief: 14 items (seven for depression, seven for anxiety), each with four response categories ordered by severity/frequency. HAD Scale scores are to be used with a chosen cut-off point; a score of >10 for a firm diagnosis of an anxiety/depressive disorder is generally accepted. Some studies have found that a cut-off point of >7 could also serve research objectives. No indications exist that, in general practice, the use of HAD Scale scores as a continuous variable serves a clinical purpose, and, for that reason, we used the HAD Scale as a dichotomous variable with two cut-off points.

A questionnaire was prepared containing the Dutch translations of both the WONCA/COOP questions and the HAD Scale, to which we added eight questions regarding sex/age, visit to a GP or prescribed medication use in the past month, to what extent and for how long the interviewee felt limited by tiredness, and whether this was attributed to psychological or physical factors (26). Because of privacy reasons, the questionnaires were anonymous to the researchers, and therefore no medical ethics committee had to be consulted for this study. However, we had to ask the project's GPs to send out the questionnaires, which they did. Each questionnaire was given a code indicating whether it was sent to a case or a control, and (for cases) whether the episode of care had started in 1997 or 1998.

Analysis

We compared cases who first presented with tiredness in 1997 and 1998, (chi-square, p values), assessing the influence of (an average of) 1 additional year. Similarly, we tested for differences between cases and controls, adding odds ratios (95% confidence interval). For a logistic regression, 16 dichotomous variables were established to construct five logistic regression models (SPSS 10.1: stepwise forward, conditional; iteration terminated when log-likelihood decreased by less than 0.01%): A) all variables ($n=16$); B) all variables, excluding information on current tiredness ($n=12$); C) all variables, excluding current tiredness and HAD Scale scores of >7 ($n=10$); D) only variables regarding utilization and current tiredness ($n=6$); E) only the variables WONCA/COOP scores and utilization ($n=8$).

Results

Questionnaires were returned by 64% of cases ($n=402$) and 66% of controls ($n=569$). The over-

sampling of controls allowed for an optimal matching of the 385 fully completed questionnaires of cases for practice, sex and age with the same number of controls. The results are shown in Table I.

A comparison of cases that first presented with tiredness in 1997 ($n=223$) and 1998 ($n=162$) showed no significant differences ($p<0.01$) for any variable; this allowed us to analyze both groups together as the "cases" group. The comparison between cases and controls, however, did show important differences. Cases did worse: approx. 20% had a firm diagnosis of anxiety/depressive disorder (HAD Scale >10), as compared to about 10% of controls, 52% were seriously limited by tiredness that lasted for >6 months (as compared to 20% of controls), and 35% considered their health as poor (compared to 20% of controls); they had received more medical care in the past month, and were, in the past 2 weeks, more limited in their daily and social activities, and more bothered by emotional problems. They attributed their tiredness more often to psychological causes than did controls (43% vs 32%). Variables without significant differences were the WONCA/COOP scores on physical activities (approx. 20% felt up to only very light/light physical activities), attribution of tiredness to a physical cause, and whether their health had changed in the past 2 weeks (most indicated no change). Although cases scored higher on almost all variables, a considerable proportion of controls also suffered from tiredness and serious limitations, and had high depression and anxiety scores.

In Table II, the results of the logistic regression are presented. In model A, including all variables, the maximum difference was reached with four variables: sensitivity and specificity were 56% and 66%, respectively. Leaving out information on current tiredness had practically no effect (model B). Leaving out information on current tiredness and low HAD Scale cut-off points (>7) resulted in a much higher sensitivity, but a low specificity (model C). Model D, excluding WONCA/COOP and HAD Scale scores, resulted in the lowest sensitivity of all models. Finally, in model E, with only WONCA/COOP scores and information about a recent visit and medication, the sensitivity increased, and the clinical utility of this model was practically the same as the more complicated model C.

Discussion

This study has several strengths and limitations. A strong point is its focus on all tired patients in routine general practice (as opposed to aiming at patients who would or would not qualify for CFS), and the fact that we were able to compare data on

Table I. Results of the postal questionnaire (n =770).

Variables for logistic regression	Start 1997 (n =223) vs 1998 (n =162), p value	Cases (n =385)		Start 1997 (n =223) vs 1998 (n =162), p value	Controls (n =385)		Cases vs controls, p value	Odds ratio (95% CI)
	Female (n =587)	(n =293)	76.2%	0.078	(n =293)	76.2%	—	—
	Age group:			0.503			0.643	
	15–24 years (n =104)	(n =59)	15.3%		(n =45)	11.7%		
	25–44 years (n =280)	(n =134)	34.8%		(n =146)	37.9%		
	45–64 years (n =220)	(n =108)	28.1%		(n =112)	29.1%		
	65–74 years (n =66)	(n =33)	8.6%		(n =33)	8.6%		
	75+ (n =100)	(n =51)	13.2%		(n =49)	12.7%		
	65+ (n =166)	(n =83)	21.6%	0.408	(n =82)	21.3%	0.930	1.03 (0.73–1.45)
1	Visit GP in last month (n =365)	(n =213)	55.3%	0.206	(n =164)	42.5%	0.000	1.83 (1.37–2.43)
2	Medication prescribed in last month (n =405)	(n =229)	59.5%	0.554	(n =181)	46.9%	0.000	1.67 (1.25–2.22)
	Daily activities limited by tiredness (last 2 wks):			0.157			0.000	
	Not at all (n =224)	(n =76)	19.8%		(n =148)	38.5%		
	Slightly (n =56)	(n =26)	266.8%		(n =30)	7.8%		
	Moderately (n =164)	(n =84)	21.9%		(n =80)	20.8%		
	Quite a bit (n =144)	(n =76)	19.8%		(n =68)	17.7%		
	Extremely (n =180)	(n =122)	31.8%		(n =58)	15.1%		
3	Limited quite a bit/extremely by tiredness (n =324)	(n =199)	51.6%	0.593	(n =126)	32.8%	0.000	2.15 (1.61–2.88)
	Duration of tiredness:			0.704			0.000	
	<1 month (n =43)	(n =18)	4.7%		(n =25)	6.5%		
	1–3 months (n =64)	(n =30)	7.9%		(n =34)	8.9%		
	3–6 months (n =69)	(n =37)	9.5%		(n =33)	8.6%		
	>6 months (n =358)	(n =220)	57.3%		(n =142)	36.8%		
	not applicable (n =228)	(n =79)	20.6%		(n =152)	39.2%		
4	Tired >6 months (n =358)	(n =221)	57.3%	0.604	(n =142)	36.8%	0.000	2.27 (1.70–3.04)
5	Tiredness experienced as physical (n =174)	(n =101)	26.2%	0.759	(n =76)	19.8%	0.058	1.41 (1.00–1.98)
6	Tiredness experienced as psychological (n =284)	(n =66)	43.2%	0.542	(n =124)	32.1%	0.002	1.61 (1.19–2.16)
	Overall health (last 2 wks):			0.188			0.000	
	Excellent (n =59)	(n =20)	5.2%		(n =39)	10.1%		
	Very good (n =113)	(n =40)	10.5%		(n =73)	19.0%		
	Good (n =386)	(n =191)	49.6%		(n =197)	51.2%		
	Fair (n =176)	(n =111)	28.9%		(n =66)	17.1%		
	Poor (n =32)	(n =22)	5.7%		(n =10)	2.6%		
7	Overall health fair or poor (n =208)	(n =133)	34.6%	0.506	(n =76)	19.7%	0.000	2.16 (1.53–2.99)
	Possible physical activities (last 2 wks):			0.671			0.762	
	Very heavy (n =157)	(n =77)	20.1%		(n =84)	21.9%		
	Heavy (n =200)	(n =99)	25.6%		(n =104)	27.9%		
	Moderate (n =243)	(n =126)	32.8%		(n =124)	32.3%		
	Light (n =114)	(n =646)	16.8%		(n =53)	13.8%		
	Very light (n =33)	(n =18)	4.7%		(n =16)	4.2%		

Table I (Continued)

Variables for logistic regression	Start 1997 (n=223) vs 1998 (n=162), p value	Cases (n=385)		Start 1997 (n=223) vs 1998 (n=162), p value	Controls (n=385)		Cases vs controls, p value	Odds ratio (95% CI)
8	Possible physical activities light/very light (n=147)	(n=82)	21.5%	0.442	(n=69)	18.0%	0.233	1.25 (0.87–1.79)
	Daily activities (last 2 wks):			0.868			0.000	
	No difficulty at all (n=194)	(n=65)	17.0%		(n=129)	33.5%		
	A little bit of difficulty (n=220)	(n=118)	30.6%		(n=103)	26.8%		
	Some difficulty (n=232)	(n=123)	31.9%		(n=110)	28.6%		
	Great difficulty (n=94)	(n=59)	15.4%		(n=35)	9.1%		
	Could not do (n=27)	(n=19)	5.0%		(n=8)	2.1%		
9	Daily activities great difficulty/could not do (n=121)	(n=79)	20.4%	0.328	(n=43)	11.2%	0.000	2.04 (1.36–3.05)
	Social activities limited (last 2 wks):			0.812			0.000	
	Not at all (n=347)	(n=152)	39.6%		(n=196)	50.9%		
	Slightly (n=207)	(n=96)	24.9%		(n=112)	29.1%		
	Moderately (n=94)	(n=60)	15.7%		(n=34)	8.8%		
	Quite a bit (n=85)	(n=55)	14.4%		(n=30)	7.8%		
	Extremely (n=33)	(n=20)	5.2%		(n=13)	3.4%		
10	Social activities limited quite a bit/extremely (n=118)	(n=76)	19.7%	0.914	(n=43)	11.2%	0.001	1.95 (1.30–2.92)
	Bothered by emotional problems (last 2 wks):			0.636			0.002	
	Not at all (n=268)	(n=112)	29.1%		(n=158)	40.8%		
	Slightly (n=236)	(n=118)	30.6%		(n=119)	30.9%		
	Moderately (n=128)	(n=70)	18.3%		(n=58)	15.1%		
	Quite a bit (n=108)	(n=69)	17.8%		(n=40)	10.4%		
	Extremely (n=27)	(n=16)	4.2%		(n=11)	2.9%		
11	Bothered by emotional problems quite a bit/extremely (n=135)	(n=85)	22.0%	0.903	(n=54)	13.3%	0.002	1.85 (1.27–2.70)
	Change in health (last 2 wks):			0.808			0.294	
	Much better (n=56)	(n=32)	8.4%		(n=24)	6.2%		
	A little better (n=61)	(n=32)	8.4%		(n=28)	7.5%		
	About the same (n=606)	(n=298)	77.4%		(n=312)	81.0%		
	A little worse (n=28)	(n=12)	3.2%		(n=16)	4.2%		
	Much worse (n=14)	(n=10)	2.6%		(n=4)	1.0%		
12	Health a little/much worse (n=42)	(n=22)	5.8%	0.936	(n=20)	5.2%	0.753	1.12 (0.60–2.09)
	HAD Scale anxiety score 0–7 (n=525)	(n=234)	60.8%	0.749	(n=290)	75.6%	0.000	
	8–10 (n=123)	(n=74)	19.2%		(n=49)	12.7%		
	11–21 (n=122)	(n=77)	20.0%		(n=45)	11.7%		
13	HAD Scale anxiety score >7 (n=245)	(n=151)	39.2%	0.127	(n=94)	24.4%	0.000	2.00 (1.47–2.72)
14	HAD Scale anxiety score >10 (n=122)	(n=77)	20.0%	0.735	(n=45)	11.7%	0.000	1.85 (1.24–2.75)
	HAD Scale depression score 0–7 (n=573)	(n=263)	68.3%	0.661	(n=309)	80.5%	0.000	
	8–10 (n=94)	(n=51)	13.3%		(n=43)	11.2%		
	11–21 (n=197)	(n=70)	18.4%		(n=32)	8.3%		
15	HAD Scale depression score >7 (n=291)	(n=122)	31.7%	0.790	(n=75)	19.5%	0.000	1.92 (1.38–2.67)
16	HAD Scale depression score >10 (n=197)	(n=70)	18.4%	0.493	(n=32)	8.3%	0.000	2.57 (1.65–4.01)

Table II. Five logistic regression models with selections of the dichotomous variables in Table I.

Model	Variables in analysis	Variables in model	B	SE	Exp. (B) with 95% CI	% true cases (sensitivity) ($n=385$)	% true controls (specificity) ($n=385$)
A	1–16	HAD Scale anxiety >7	0.41	0.17	1.50 (1.07–2.11)	56	66
		Recent medical care	0.43	0.15	1.54 (1.15–2.08)	($n=216$)	($n=254$)
		Overall health	0.42	0.18	1.52 (1.06–2.18)		
		Quite tired	0.43	0.17	1.54 (1.10–2.15)		
		Constant	−0.63	0.12			
B	1, 2, 7–16	HAD Scale anxiety >7	0.54	0.16	1.72 (1.20–2.17)	55	65
		Recent medical care	0.48	0.15	1.61 (1.25–2.38)	($n=212$)	($n=258$)
		Overall health	0.55	0.18	1.73 (1.22–2.44)		
		Constant	−0.54	0.12			
C	1, 2, 7–12, 14, 16	Recent medical care	0.46	0.15	1.59 (1.18–2.13)	70	50
		HAD Scale depression >10	0.67	0.24	1.96 (1.24–3.11)	($n=270$)	($n=193$)
		Overall health	0.56	0.18	1.76 (1.24–2.48)		
		Constant	−0.45	0.11			
D	1–6	Tired >6 months	0.56	0.16	1.75 (1.28–2.40)	52	64
		Quite tired	0.49	0.16	1.63 (1.19–2.25)	($n=200$)	($n=246$)
		Recent medical care	0.44	0.15	1.55 (1.15–2.08)		
		Constant	−0.67	0.12			
E	1, 2, 7–12	Overall health	0.68	0.17	1.97 (1.41–2.75)	66	52
		Recent medical care	0.49	0.15	1.63 (1.21–2.18)	($n=254$)	($n=200$)
		Constant	−0.41	0.11			

the functional status of patients who did and who did not present with tiredness. It is a limitation that elderly women were overrepresented in our sample; this finding is, however, in agreement with the epidemiological characteristics of "tiredness" as a reason for encounter and as a diagnosis. Further, the study is limited because of the sufficient, but admittedly relatively low response rates, as are to be expected in an anonymous questionnaire study.

We found that people who had presented and been diagnosed with tiredness, after an average of 19 months, do considerably worse than controls: their tiredness has lasted longer and results in more limitations, their overall health is worse, they have higher depression and anxiety scores, and a substantial proportion (still) suffers from limitations in function not unlike the disability level required for various CFS definitions (3,8–10). Since no difference exists in limitations in function between people who presented with tiredness 20–32 months and 7–19 months after first presentation, there does not seem to be a tendency to improve within an average period of 19 months.

Although controls generally do better, one in three suffers from serious tiredness-related limitations. The proportion of controls with a HAD Scale score >10 (depressive/anxiety disorder) is largely in line with the results of other studies (23–25).

The maximal discrimination that could be obtained with logistic regression (model A) is far better at predicting true controls than true cases, but the relatively high specificity (66%) and low sensitivity (56%) are rather disconcerting findings for GPs. In reality, the proportion of "cases" and "controls" is not equal (as it is in this study). In fact, of all patients starting a new episode of care, only one in 70 can be expected to be related to tiredness (5,6,10). Model B, containing variables representing information that is usually available in a GP encounter, is not very useful. When tiredness and low HAD Scale cut-off points (>7) are left out, recent medical care, a high depression score (>10) and poor overall health best predict cases (model C). Model E, including only two questions concerning overall health and recent medical care, appeared to be practically as useful as model C. It hardly makes a difference whether or not a depression score >10 is included.

The most important finding is that in both cases and controls, so many individuals (mainly elderly women) suffer from considerable limitations in function, and that no indication was found for specific limitations: e.g., a depressive or anxiety disorder established by the instrument did not contribute to better distinguishing cases from controls when the simpler and more mundane information from group D was available. The substantial overlap of tiredness with indications of mood disorders, however, does help the GP in deciding on management since the utility of treating tiredness, depression or anxiety (if the latter two diagnoses were generated by a screening instrument rather

than by a patient with specific demands and preferences) has proven to be rather non-specific and very limited (27–31). It is important to realize that serious comorbidity is far more frequent in patients with a long (>6 months) than in those with a brief episode of care for tiredness; this is, however, true for practically every "chronic" condition (7).

Since interventions in general practice, focused as they are on multi-morbidity, simply cannot be guided by the decision strategy implied by the HAD Scale indices for establishing a nosological diagnosis in a psychiatric context, quality assessment in family practice needs more complex criteria based on GPs' generic contributions to the well-being and health of patients (30–34). It seems crucial to adopt a stepped care approach which allows tired patients to decide for themselves whether or not they agree that they suffer from a well-defined mood disorder that would be the basis for psychological and/or pharmaceutical treatment (29–31). Many of the patients included in this study did in fact receive a substantial amount of attention from their GP in the context of their comorbidity, and it would seem difficult to delineate how this attention differs from a more targeted approach (5). Supervised cognitive behavioural therapy (CBT) is potentially helpful both in patients with CFS and those with mild to moderate anxiety and depression, but it is as yet unclear to what extent patients with brief episodes of tiredness would benefit from these treatments.

It can be concluded that a patient presenting with tiredness has a relatively high probability of suffering from relatively important limitations that will persist for quite some time, and could well result in sickness absenteeism (35). In the context of general practice in the Netherlands, where there is an accessible healthcare system and a high acceptance of illness behaviour based on tiredness, a red flag should be raised by the GP—and in the EPR as well—that this patient has a high probability of requiring long-term attention.

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