

Diagnoses during follow-up of patients presenting with fatigue in primary care

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ABSTRACT

Background: Little is known about the distribution of diagnoses that account for fatigue in patients in primary care. We evaluated the diagnoses established within 1 year after presentation with fatigue in primary care that were possibly associated with the fatigue.

Methods: We conducted a prospective observational cohort study with 1-year follow-up. We included adult patients who presented with a new episode of fatigue between June 2004 and January 2006. We extracted data on diagnoses during the follow-up period from the patients' medical records as well as data on pre-existing chronic diseases.

Results: Of the 571 patients for whom diagnostic data were available, 268 (46.9%) had received one or more diagnoses that could be associated with fatigue. The diagnoses were diverse and mostly included symptom diagnoses, with main categories being musculoskeletal (19.4%) and psychological problems (16.5%). Clear somatic pathology was diagnosed in 47 (8.2%) of the patients. Most diagnoses were not made during the consultation when fatigue was presented.

Interpretation: Only a minority of patients were diagnosed with serious pathology. Half of the patients did not receive any diagnosis that could explain their fatigue. Nevertheless, because of the wide range of conditions and symptoms that may explain or co-occur with the fatigue, fatigue is a complex problem that deserves attention not only as a symptom of underlying specific disease.

Fatigue is a common problem seen in primary care. It is reported as the main presenting symptom in 5% to 10% of patients.¹⁻³ Both its nonspecific nature and its high prevalence make fatigue a challenging problem for general practitioners to manage. The symptom may indicate a wide range of conditions, including respiratory, cardiovascular, endocrine, gastrointestinal, hematologic, infectious, neurologic and musculoskeletal diseases, mood disorders, sleep disorders and cancer.⁴⁻¹³ Patients with a chronic disease often report symptoms of fatigue,^{14,15} and the prevalence of chronic disease is higher among patients presenting with fatigue than among other patients.¹⁶ Regardless of the underlying pathology, fatigue is a phenomenon with social, physiologic and psychological dimensions.¹⁷⁻²⁰

Little is known about the distribution of diagnoses in popu-

lations of patients presenting with fatigue as a main symptom in primary care. A Dutch morbidity registration of episodes of care showed that fatigue was a symptom diagnosis in about 40% of patients.²¹ Previous studies involving patients presenting with fatigue as a main symptom either had small samples^{22,23} or reported diagnoses that were based on standardized laboratory testing at baseline.^{24,25} Because of the wide range of possible diagnoses, large observational studies are needed to determine the distribution of diagnoses in primary care.

We carried out a prospective study involving patients in primary care practices in whom fatigue was the main presenting symptom. The aim of our study was to describe the distribution of diagnoses established within 1 year after presentation that were possibly associated with the fatigue.

Methods

Study population

We conducted an observational cohort study in 147 general practices across the Netherlands involving adult patients who presented with a new episode of fatigue between June 2004 and January 2006. We defined a presenting symptom of fatigue as a report of tiredness or synonyms indicating fatigue such as exhaustion; we excluded more general reports of "malaise." We also excluded patients who were receiving or had received chemotherapy or radiation therapy within 3 months before presentation, as well as women who were pregnant or had had a baby within 3 months before presentation.

Eligible patients were informed about the study by their general practitioner and invited to participate. If interested, they were sent an information letter and baseline questionnaire. Patients were enrolled in the study when they returned a signed consent form and the baseline questionnaire. Participating patients completed several questionnaires during the follow-up year (at 1, 4, 8 and 12 months after baseline).

The study design was approved by the Medical Ethics Committee of the VU University Medical Center, the Netherlands.

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Data collection and analysis

We extracted data from the participants' patient files concerning diagnoses made during the follow-up period and selected diagnoses that could provide an explanation for the presented fatigue. We also extracted data on pre-existing chronic diseases at the time of presentation. We limited these chronic diseases to conditions that could be related to fatigue and that could be assumed to be current at the moment of presentation of fatigue, regardless of treatment. We used descriptive statistics to describe frequencies of diagnoses, comorbidities and patient characteristics.

Results

General practitioners enrolled 856 patients, of whom 642 consented to participate and returned the baseline questionnaire (Figure 1). All but 1 of these patients also consented to have data extracted from their general practitioner's medical records. In addition, 15 patients who did not complete the baseline questionnaire consented to have data extracted from their medical records. We were able to obtain data on diagnoses for 571 (87.0%) of these 656 patients. Characteristics of the 571 participants are shown in Table 1.

Diagnoses made in the year following consultation represented all categories of the International Classification of Primary Care (ICPC).^{29,30} In total, 268 (46.9%) of the 571 patients received one or more diagnoses (378 in total) that could be associated with fatigue (Table 2).

The most frequently recorded somatic diagnoses were musculoskeletal problems ($n = 111$ [19.4%]) and diseases or symptoms of the digestive system ($n = 46$ [8.1%]), nervous system ($n = 38$, [6.7%]) and respiratory tract ($n = 28$ [4.9%]).

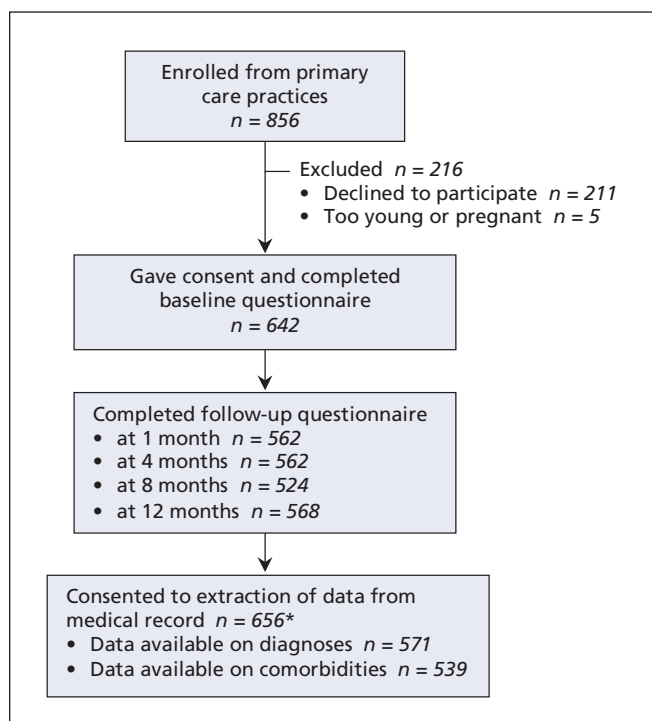


Figure 1: Selection of participants and collection of data. *Includes 15 patients who did not complete any of the questionnaires but who consented to extraction of data.

The majority of diagnoses reflected symptoms or signs only. A total of 47 patients (8.2%) received one or more diagnoses of clear somatic pathology (anemia, pulmonary pathology, thyroid dysfunction, diabetes mellitus, celiac disease, vitamin B₁₂ deficiency, heart failure, angina pectoris, malignant disease, rheumatoid arthritis, adverse drug effect). Infections were diagnosed in 104 (18.2%) of the patients. When we considered the time frame from the onset of fatigue to the diagnosis of infection, infection was a likely explanation for the fatigue in 2 cases.

A total of 94 patients (16.5%) received a diagnosis indicating psychological problems or social difficulties. Stress or neurasthenia was the diagnosis most frequently recorded during the initial consultation (Table 2).

Table 1: Characteristics of 571 patients in primary care practices who presented with fatigue as a main symptom

Characteristic	No. (%) of patients*
Age, yr, mean (SD)	43 (16)
Female sex ($n = 571$)	422 (73.9)
Duration of fatigue ($n = 546$)	
< 1 mo	44 (8.1)
1–3 mo	87 (15.9)
3–6 mo	98 (17.9)
6–12 mo	103 (18.9)
> 1 yr	214 (39.2)
Localization of fatigue ($n = 556$)	
Primarily head (mental fatigue)	91 (16.4)
Primarily extremities	46 (8.3)
Whole body, or head and extremities	362 (65.1)
Not clear	57 (10.3)
Psychological symptom† ($n = 556$)	
Distress	338 (60.8)
Depression	131 (23.6)
Anxiety	52 (9.4)
Sleep problem‡ ($n = 556$)	365 (65.6)
Other physical symptoms,§ mean no. (SD)	4.3 (2.7)
Fatigue attributed to stress or worry ($n = 551$)	307 (55.7)
Prolonged difficulties** ($n = 556$)	458 (82.4)
Score combining number and severity of difficulties (range 0–25), mean (SD)	4.3 (4.3)
Severe difficulties in at least 1 area ($n = 556$)	105 (18.9)
Expectation that general practitioner is able to find the cause of the fatigue ($n = 548$)	287 (52.4)
Satisfied with general practitioner's management of the fatigue during consultation ($n = 552$)	504 (91.3)

Note: SD = standard deviation.

*Unless stated otherwise.

†As indicated by elevated score on the Four-dimensional Symptom Questionnaire (4DSQ).²⁶

‡As indicated by elevated score on the Symptom Checklist-90 (SCL-90).²⁷

§From 13 physical symptoms listed on the Illness Perception Questionnaire-Revised.²⁸

**Long-term difficulties, including work-related, family, neighbourhood, housing and financial problems, experienced in the year before presentation.²⁸

The frequency of psychological symptoms reported in the patient questionnaires differed from the frequency in the medical records. Overall, 155 (24.1%) of the 642 patients who completed a baseline questionnaire reported having depressive symptoms; this diagnosis was recorded in 28 (4.9%) of the 571 medical records that had diagnostic data. Distress or worry was reported by 392 (61.1%) of the patients but was

recorded in 25 (4.4%) of the medical records. Sleep problems were reported by 417 (65.0%) of the patients but recorded in 11 (1.9%) of the patients' charts (see also reference 29).

Data on comorbidities were available for 539 of the patients. A total of 58 patients had a concurrent disease that could explain the fatigue. The most frequently recorded comorbid diseases were respiratory diseases ($n = 37$) and dia-

Table 2: Diagnoses during 1-year follow-up period among 571 patients in primary care practices who presented with fatigue as a main symptom

Diagnosis (code*)	No. (%) of patients	Diagnosis recorded during initial visit	Diagnosis (code*)	No. (%) of patients	Diagnosis recorded during initial visit
Musculoskeletal (L)	111 (19.4)		General (A)	28 (4.9)	
Rheumatoid arthritis or polymyalgia rheumatica	2	0	Anemia	9	3
Back problem	35	2	Adverse drug effect	6	1
Neck problem	20	1	Chronic fatigue syndrome	4	0
Joint problem in extremities	42	0	Chronic pain syndrome or widespread pain	3	1
Myalgia	21	2	Hay fever, rhinitis, allergy	6	2
Noncardiac chest symptoms	8	0	Infection (various)	104†	2
Osteoarthritis	7	0	Respiratory (R)	28 (4.9)	
Psychological or social (P or Z)	94 (16.5)		Asthma, chronic obstructive pulmonary disease, decreased pulmonary function or chronic bronchitis, including exacerbations	12	1
Depressive symptoms or depression	28	4	Chronic sinusitis	3	0
Strain, neurasthenia, burnout	31	15	Cough	9	1
Anxiety, tension, hyperventilation (R), distress or worry	25	4	Upper airway or throat symptoms	3	0
Sleeplessness or sleeping problem	11	1	Dyspnea	2	0
Family or relationship problem	9	1	Endocrine (T)	16 (2.8)	
Psychological problem	5	2	Hypothyroidism	7	1
Loss or mourning	4	1	Diabetes mellitus	4	0
Affective psychosis	1	0	Hyperthyroidism	3	0
Digestive (D)	46 (8.1)		Celiac disease	1	0
Abdominal pain or symptoms	23	0	Vitamin B ₁₂ deficiency	1	0
Diarrhea	8	1	Obesity	1	0
Constipation	5	0	Cardiovascular (K)	11 (1.9)	
Abnormal liver function	1	0	Heart failure	3	0
Irritable bowel syndrome	12	2	Angina pectoris	3	0
Neurologic (N)	38 (6.7)		Arrhythmia	3	0
Headache	13	2	Cardiac symptoms	2	1
Dizziness	11	1	Intermittent claudication	1	0
Chronic tension-type headache	8	2	Female genital organs (X)	6 (1.1)	
Migraine	3	0	Climacteric symptoms	6	0
Polyneuropathy	2	0	Malignant disease	4 (0.7)	
Concussion	2	1	Bladder (U)	1	0
			Leukemia (B)	1	0
			Melanoma (S)	1	0
			Colon (D)	1	0
			Skin (S)	3 (0.5)	
			Itch	3	0

*Diagnostic codes are from the International Classification of Primary Care.^{29,30}

†Of these patients, 2 had a diagnosis of infection that was considered to provide a likely explanation for the fatigue based on the time frame between the onset of fatigue and the diagnosis.

betes ($n = 17$). Fourteen patients were known to have a malignant disease in their medical history. For 20 patients, a functional syndrome, most often irritable bowel syndrome, had been recorded in their chart.

Interpretation

The participants in our study received a wide range of diagnoses in the year following consultation that could have been associated with the fatigue. Psychological and physical problems were diagnosed more frequently than somatic diseases. The variety of diagnoses reflects evidence from the literature and practical experience regarding the differential diagnosis of fatigue.

The small proportion of patients who received a diagnosis of somatic pathology corresponds with findings of previously published smaller studies in primary care.^{24,25,32} Those studies, however, used stricter inclusion criteria, excluded patients with existing chronic disease or reported on diagnoses based only on laboratory test results. Two studies, one of which included only 52 patients, reported higher prevalence rates of somatic disease (45% and 51%) than in our study.^{22,33} Of chronic diseases that were likely to be present at the time of consultation, respiratory conditions were more frequent in our cohort than in the general patient population in primary care in the Netherlands.¹⁵ Our study population had fewer older patients compared with those in a Dutch national morbidity registry,³⁴ which may explain the difference in prevalence of chronic respiratory conditions.

Of the patients in our study who received a symptom diagnosis during the follow-up year, one-fifth received a diagnosis of a musculoskeletal problem, mostly nonspecific. Virtually none of the symptom diagnoses were established during the consultation, which raises questions about the temporal association between fatigue and other symptoms. Because most symptoms may show a recurrent pattern over time, further research is needed to help clarify the association between fatigue and other nonspecific symptoms.

Although psychological or social problems were the second largest diagnostic category, the number may be an underestimation. Depressive symptoms and elevated distress scores were reported more frequently in the patient questionnaires than in the medical records. Furthermore, other studies have reported psychological symptoms in the majority of patients with fatigue.³⁵⁻³⁷ Because of the variation in how the general practitioners recorded or coded the diagnoses, psychological problems may have been identified but not explicitly recorded as diagnoses in the patients' charts.

Sleep problems were recorded in only 1.9% of the patients' charts. This number is in stark contrast to the number of sleep problems reported by the majority of patients in the questionnaires. As with psychological symptoms, problems with sleep might either not be recognized or not recorded.³⁸⁻⁴⁰ Because general practitioners may perceive a sleep problem as a lifestyle issue or evidently related to fatigue, they may not record it as a diagnosis.

At least half of the patients did not receive a diagnosis that could possibly explain their fatigue. This suggests that fatigue remains "medically unexplained" in many cases, which is consistent with previous findings.²¹ However, the lack of a medical

explanation does not always mean that there is no explanation. Given the data in the questionnaires, other psychosocial factors, although not registered in the patients' medical records, may have played a role in the fatigue of many patients.

Almost 50% of the patients did receive a diagnosis in the year following consultation that could explain their fatigue. However, for most of the diagnoses, we were unable to assess the potential association with fatigue more closely, even when considering the time frame from onset of the fatigue to the diagnosis. This would require more information both on the severity of the symptom or disorder diagnosed and on the severity of the fatigue at the time of diagnosis.

Limitations

One limitation of our study was that we did not use a standardized protocol for physical examination or diagnostic testing. The diagnoses represent those made and recorded in daily practice by individual general practitioners. Because general practitioners differ in their decision-making regarding diagnostic procedures and referrals, this will have resulted in variation in recorded diagnoses.

Data on existing comorbidities are important to provide when presenting an overview of diagnoses. We were able to show that respiratory conditions and diabetes were more often pre-existing than newly diagnosed conditions. Our data were not comprehensive, however, and we may have missed other conditions that could have been associated with the fatigue. Furthermore, patients presenting with fatigue may have several concurrent conditions.

Conclusion

The patients who presented with fatigue in primary care had a wide range of diagnoses. However, the prevalence of severe pathology was low. The number of psychosocial problems was relatively high and may explain in part the fatigue in this primary care population. In addition, the number of psychosocial symptoms, including sleep problems, differed between the patients' medical records and the self-reported data from the questionnaires. Practitioners need to address these problems in patients presenting with fatigue.

This article has been peer reviewed.

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