Introduction

Both chronic fatigue (CF) connected to a chronic or serious disease, and Chronic Fatigue Syndrome (CFS) form a serious problem in our Western society. It causes a lot of suffering for patients and may lead to disability to work. Doctors are frequently confronted with these patients, but it is unknown how many of these patients are suffering without help-seeking.

Most research has been done in CFS, and in specialised CFS clinics. Much less is known about other types of chronic fatigue, connected with a serious disabling disease, or with a psychiatric condition. There is hardly any knowledge about the prevalence and characteristics of these types of chronic fatigue and especially CFS, and the course of CFS in the general population. If we would know more about fatigue and chronic fatigue in the general population then, for example, the development of prevention programs would become nearer.

Both studies published in this Journal [1,2] give a lot of interesting information about CF and CFS and the course of CFS in the general population. It is interesting to look at the differences between these studies and the data found in studies with referred CFS patients and, looking at the course of CFS, to discuss the possible implications for the diagnostic criteria for CFS.

In the study of Solomon et al [1] a group of fatigued persons was compared with a group of about the same size of non-fatigued respondents, both from the general population. The fatigued group was subdivided in prolonged fatigue (fatigue between 1 and 6 months), chronic fatigue (fatigue longer than 6 months but with insufficient symptoms to meet the case definition of CFS) and CFS-like (respondents with self-reported sufficient fatigue severity and symptoms). Within all 4 groups the authors looked at the presence of medical or psychiatric conditions. Only those medical or psychiatric conditions were asked for that might explain the fatigue symptoms and thus exclude a diagnosis of CFS. So there emerged 8 groups.

Chronic fatigue in the general population

In several studies it was shown that more women suffer from CFS than men. One of the reasons could be that this has to do more with help seeking behaviour and referral bias than with gender. In that way of thinking one would expect that fatigue in the general population is equally divided in men and women. According to these two studies this seems not to be the case. Although the percentage of females in the 8 groups is not explicitly mentioned, with each level of fatigue, the preponderance of females increases, with CFS showing the highest percent of females (93%) [1]. In the other study the percentage of female CFS subjects was 83% [2]. So the proportion of females with CFS in the general population is not different from tertiary care CFS patients.

The proportion females in chronic fatigue with medical conditions is not explicitly mentioned, but seems higher than we found in our studies in neuromuscular diseases and in disease-free cancer patients, where we found no relationship between gender and fatigue severity [3,4].

The reported onset of symptoms in CFS seems different in the general population. More than 75% of the sample of 65 persons fulfilling the CFS criteria reported a gradual onset. In most CFS studies in tertiary care only a small
proportion of the patients (25%) report a gradual onset (see for example ref. [5]).

Impairment in explained and unexplained chronic fatigue
Patients with so-called Explained Syndromic Fatigue (people whose fatigue is associated with a known chronic disabling condition), appeared to be as severely impaired as CFS. But the unemployment rate in the ESF subjects is even higher, namely 40%, compared to 15% unemployment due to fatigue in the CFS subjects. This is in contrast with most CFS studies in tertiary care where higher percentages of unemployment are found. This means that CFS patients in the general population, diagnosed as CFS or not, are less severe impaired as far as employment is concerned. It would be interesting to know whether there is also a relationship with help seeking.

Fatigue as a continuum?
One cannot become chronic fatigued from one day to the other. Only after 6 months of suffering one can speak of CFS, if the other conditions are fulfilled. Does this mean that CFS is the end of a continuum, running from acute, short-term fatigue to long-term fatigue, and ultimately to chronic fatigue and chronic fatigue syndrome? Or is CFS a distinct disease entity not only quantitatively different (in degree of fatigue, functional impairment and additional symptoms) but also qualitatively different from the non-CFS conditions?

From the here presented studies one can hardly sustain the last option. The results in both studies seem to support the notion that fatigue and chronic fatigue can best be seen as a continuum, with CFS and Explained Syndromic Fatigue at one end of this continuum. For example, in general it is found that the more severe or the longer the fatigue the more impairment is reported. Also the finding that the CFS classification is not stable over time [2] fits the idea of a continuum.

The problem of CFS case finding
Another remarkable finding is that of the 256 persons with CFS-like characteristics who agreed to be clinically evaluated, only 43 (17%) fulfilled the criteria for CFS. This is a very low percentage. It is not commented by the authors. If the interpretation of misclassification of CFS in this study is less likely then it could be that CFS-like characteristics by self-report do not predict the clinical diagnosis of CFS. If this is true then the conclusion is inevitable that it is impossible to make estimations of CFS prevalence in epidemiological studies only 1 of CFS. This would mean that valid epidemiological studies of CFS in the general population without clinical evaluation of the subjects are impossible. Anyway there is a need for an epidemiological CFS case-finding definition that corresponds better with the clinical diagnosis of CFS.

Diagnosed CFS cases in the general population
One of the advantages of studies in the general population is that there can be no referral bias. In the study of Solomon et al [1] only 7 of the above mentioned 43 subjects (16%) who fulfilled the criteria of CFS after clinical evaluation, were ever diagnosed as CFS in the past by a practitioner. This is a very small number, asking for an explanation.

There are at least two possible explanations.
1) Most subjects with CFS in the general population do not seek help for their symptoms and are therefore never diagnosed as such. These data are not available in this study, so we also do not know why these subjects don’t seek help. It may be the same situation as in IBS patients. Many subjects in the general population have IBS symptoms, but only a small proportion (25–38%) seeks help for their complaints (e.g. ref. [6]).

2) CFS is too difficult to diagnose for most practitioners. If it is assumed that the subjects with CFS visited practitioners, it might be that the practitioner is not familiar with the criteria for CFS [7] or that they do not understand or accept their symptoms [8]. It is not mentioned in the study [1] how many patients were diagnosed as CFS by a doctor in the past, but do not fulfil the criteria for CFS anymore at the moment of the study. That this is very well possible is demonstrated the other study of the CDC group [2].

It is a pity that the authors do not really try to explain or analyse the low rate of CFS diagnosis in their study. We have to wait for their next publication. They suggest that persons with diagnosed CFS are quite different from the undiagnosed. They also say that clinic-based samples may not be generalizable to the CFS population. But that still has to be demonstrated.

Course of CFS classification in the general population
In the study of Nisenbaum et al [2] the course of CFS in the general population over a period of three years was investigated. Persons who fulfilled the criteria for CFS by self-report were asked to participate in a clinical evaluation.

The most remarkable finding is that only one third of the CFS subjects retained the classification of CFS at one year follow-up, and only 21% at 2 and 3 years follow-up. And, most striking, only 3 of the 40 (8%) subjects sustained the CFS classification over two consecutive follow-ups.
Again, several explanations are possible. The non-consistent CFS classification might mean that the course of CFS in the general population is much more favourable than CFS patients from tertiary care, considering the finding that 57% of the sample experienced a partial or total remission at the end of follow-up. Most subjects reported reduced fatigue after the first visit. The figure of 57% remission is higher than the 20–50% that is found in tertiary care [9]. At the other side, only one quarter sustained partial remission and 10% sustained total remission for two consecutive periods. This figure cannot be compared with tertiary care CFS patients, as sustained remission over time have never been investigated in referred CFS patients.

One could also interpret these results as a support of the notion that CFS (and perhaps the same is true for Explained Syndromic Fatigue) is the end of a continuum (see above). Subjects might fluctuate on this continuum. At one moment subjects are at the end of this continuum, fulfilling the criteria for CFS, and at other moments subjects are before the end of the continuum, so not fulfilling the CFS criteria. In this interpretation CFS, perhaps as a consequence of the chosen definition, is not a stable condition at all. Symptoms are fluctuating over time.

The authors interpret the low proportion of subject consistently fulfilling the CFS criteria as a consequence of their study design and suppose that clinical diagnosis is less conservative. They assume that practitioners will continue to consider such persons as having CFS despite their reduction in fatigue. This interpretation cannot be tested in this study because there were hardly any subjects diagnosed or treated as CFS cases. The authors seem to refer to a problem of the CFS case definition. They implicitly suggest that there may be a difference between a research definition of CFS (as the CDC-1994 definition is) and a clinical definition for CFS. However, the problem is that an empirical validation is lacking for all proposed definitions of CFS [10] including a clinical definition of CFS [11].

Remission not associated with any particular treatment

Currently only CBT and graded exercise therapy (GET) have demonstrated evidence for efficacy in CFS. There is no evidence of efficacy of complementary or alternative medicine [3]. In this study also no relation between fatigue reduction and the use of complementary or alternative medicine was found. This means that these types of treatment should not be encouraged. Remission was not associated with any particular treatment, which probably means that the improvement is not the result of a specific treatment.

According to the authors CBT or GET was not an available treatment for the subjects in this study, so no relationship could be found between CBT/GET and remission. Remission was also not associated with the report of being ever diagnosed as CFS. Although the number of CFS diagnosed subjects was very low, it may mean that the diagnosis of CFS cannot be seen as unfavourable for remission. This is contrary the idea of some family doctors who are reluctant to diagnose their patients as having CFS, as they are afraid that this will facilitate an unfavourable course of the condition.

This finding and the availability of a possible effective treatment, together with the finding that sustained remission was associated with a shorter illness duration, is a plea to diagnose CFS as early as possible. Hopefully, the interesting questions these two studies in the general population evoke will stimulate more studies of fatigue in the general population.

References