

- in university students: report of a postal survey. *Public Health* 103: 199-203 (1989).
32. Strader, M. K., and Beaman, M. L.: College students' knowledge about AIDS and attitudes toward condom use. *Public Health Nurs* 6: 62-66 (1989).
  33. Beaman, M. L., and Strader, M. K.: STD patients' knowledge about AIDS and attitudes toward condom use. *J Comm Health Nurs* 6: 155-164 (1989).
  34. Heterosexual behaviors and factors that influence condom use among patients attending a sexually transmitted disease clinic—San Francisco. *MMWR* 39: 685-689, Oct. 5, 1990.
  35. Keeter, S., and Bradford, J. B.: Knowledge of AIDS and related behavior change among unmarried adults in a low-prevalence city. *Am J Prev Med* 4: 146-152 (1988).
  36. Valdiserri, R. O., Arena, V. C., Proctor, D., and Bonati, F. A.: The relationship between women's attitudes about condoms and their use: implications for condom promotion programs. *Am J Public Health* 79: 499-501 (1989).
  37. Gottlieb, N. H., Vacalis, T. D., Palmer, D. R., and Conlon, R. T.: AIDS-related knowledge, attitudes, behaviors and intentions among Texas college students. *Health Educ Res* 3: 67-73 (1988).
  38. Katzman, E. M., Mulholland, M., and Sutherland, E. M.: College students and AIDS: a preliminary survey of knowledge, attitudes, and behavior. *J Am Coll Health* 37: 127-130 (1988).

## Estimating the Prevalence of Chronic Fatigue Syndrome and Associated Symptoms in the Community

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### Synopsis .....

*Chronic fatigue syndrome is a poorly understood disease characterized by debilitating fatigue and neuromuscular and neuropsychological symptoms. Despite numerous studies on the subject, the epidemiology of the syndrome in the community remains largely unexplored. An estimate of the prevalence*

*in the population is presented, approximating the Centers for Disease Control criteria as well as the prevalence estimates of the fatigue symptom complex that include fatigue, disability, and neuromuscular and neuropsychological symptoms.*

*The study population consisted of a very large, multicenter, stratified, and random sample of a general population health survey known as the Epidemiologic Catchment Area Program. Data used for this study were gathered between 1981 and 1984. The Diagnostic Interview Schedule, a highly structured mental health interview, was used to assess the lifetime prevalence of medical and psychological symptoms.*

*Chronic fatigue was common. A total of 23 percent of the subjects reported having experienced the symptom of persistent fatigue sometime during their lives. Chronic fatigue syndrome, however, as defined by the Centers for Disease Control, appeared to be quite rare in the general population. Only 1 of 13,538 people examined was found to meet a diagnosis of the syndrome with an approximation of the CDC criteria. Fatigue symptom complex was frequently related to medical or psychiatric illness or substance abuse; thus, persons meeting partial criteria of chronic fatigue syndrome were also found to be rare when psychiatric or medical exclusions were applied.*

SINCE THE PUBLICATION of two reports in 1985 that first connected a clinical syndrome of chronic fatigue with unusual serologic responses to Epstein-Barr virus antigens (1,2), the chronic fatigue syn-

drome (CFS) has captured the attention of the media, the public, and also of the medical and scientific communities (3-5).

Despite this recent attention, the syndrome of

persistent fatigue is not new. In the past, epidemics of fatigue and related symptoms have been called neurasthenia, neuromyasthenia, myalgic encephalomyelitis, atypical poliomyelitis, post-viral syndrome, chronic mononucleosis-like syndrome, chronic Epstein-Barr virus syndrome, Icelandic disease, Royal Free Epidemic, and "yuppie flu." The syndrome has also been attributed to a variety of causes including chronic brucellosis, chronic candidiasis, and allergies, but none of these theories have been substantiated scientifically (6,7).

The definitive cause of CFS is unknown, although for the past several years a viral etiology has remained the most common hypothesis. In the United States, herpes viruses, particularly Epstein-Barr virus, have been prime suspects. Efforts to pinpoint a specific viral etiology, however, have yielded unsatisfactory results (8,9), and recent articles have questioned the evidence relating chronic fatigue syndrome to Epstein-Barr virus infection (8,10,11). In Britain, the term myalgic encephalomyelitis reflects a view of chronic fatigue as due to neuromuscular dysfunction, and the causative infective agent is most commonly thought to be an enterovirus (12). Data documenting this link, however, are also limited.

Because persistent fatigue is a prominent symptom of psychiatric disorders such as depression (11,13), some attribute chronic fatigue syndrome to an underlying psychiatric disorder. Recent reports, using structured diagnostic assessment, revealed that between 50 percent and 80 percent of patients complaining of persistent and disabling fatigue in various clinical settings meet criteria for a psychiatric disorder, most commonly major depression or somatization disorder (14-16). The studies that examined the timing of fatigue and psychiatric symptoms showed that psychiatric or psychological symptoms frequently occurred before or at the same time as the onset of the chronic fatigue (17-19).

In the face of the uncertain etiology of chronic fatigue syndrome, and because there is no diagnostic test for CFS, symptomatic diagnostic criteria were proposed by the Centers for Disease Control (CDC) in 1988 (20). Such clear operational criteria lend useful guidance to epidemiologic studies of CFS. Currently, only one study from Australia estimated the prevalence of CFS in the population (21), and there has not been a population-based data base specifically designed to study CFS in the United States. Thus, the population prevalence of CFS as well as the rates of comorbid physical and psychiatric conditions in the United States still remain unknown.

*'Recent reports, using structured diagnostic assessment, revealed that between 50 percent and 80 percent of patients complaining of persistent and disabling fatigue in various clinical settings meet criteria for a psychiatric disorder, most commonly major depression or somatization disorder.'*

By using a large-scale community-based mental health survey known as the Epidemiologic Catchment Area (ECA) Program (22,23), we attempted to estimate the prevalence of CFS in the population, approximating the CDC criteria. We also attempted prevalence estimates of fatigue symptom complex—a symptom cluster of fatigue, disability, neuromuscular and neuropsychological symptoms and exclusion conditions, that represent a subset of the CDC criteria. This paper is the first attempt, to our knowledge, to estimate the prevalence of CFS and fatigue syndrome in the general population of the United States.

## Methods

**Sample characteristics.** The ECA has been described in detail elsewhere (22,23). Briefly, survey respondents were drawn from persons ages 18 or older, living in New Haven, CT, Baltimore, MD, St. Louis, MO, Durham, NC, and Los Angeles, CA. A multistage sampling procedure, combining random and stratified cluster sampling, was applied to ensure representativeness of the sample respondents within each site. In addition, to obtain sufficient numbers of subpopulations of special interest, the surveys oversampled the elderly in New Haven, Baltimore, and Durham, blacks in St. Louis, and Hispanics in Los Angeles. Data from institutional respondents were not included in our analysis, because our purpose was to estimate general population prevalence rates. Also, the data from New Haven were excluded, since some information on the CFS symptoms was not available from this site. Thus, the total number of people surveyed for this paper was 13,538. The response rate was 78 percent at the Baltimore site, 80 percent at the St. Louis site, 77 percent at the Durham site, and 68 percent at the Los Angeles site.

Table 1 shows demographic characteristics (sex, age, and race) of the respondents included in our analyses. The unweighted percentages are based on

Table 1. Demographic characteristics of persons in the household sample from 4 sites, Epidemiologic Catchment Area Project, 1981-84

Characteristic	5,556 Men			7,982 Women		
	Number of persons <sup>1</sup>	Unweighted percentage <sup>2</sup>	Weighted percentage <sup>2,3</sup>	Number of persons <sup>1</sup>	Unweighted percentage <sup>2</sup>	Weighted percentage <sup>2,3</sup>
Total sample.....	...	41.0	47.6	...	59.0	52.4
Age (years):						
18-24.....	789	14.2	19.5	1,041	13.1	17.7
25-34.....	1,465	26.4	23.8	1,851	23.2	22.1
35-49.....	1,109	20.0	23.4	1,530	19.2	22.5
50-64.....	1,051	18.9	20.4	1,567	19.6	20.5
65 and older.....	1,141	20.5	13.0	1,987	24.9	17.2
Race:						
White, other.....	3,489	63.8	84.5	4,629	58.6	83.8
Black.....	1,341	24.5	10.0	2,540	32.2	11.0
Hispanic.....	640	11.7	5.5	726	9.2	5.3
Site:						
Baltimore.....	1,322	23.8	28.4	2,159	27.0	29.9
St. Louis.....	1,203	21.7	18.5	1,801	22.6	18.4
Durham.....	1,550	27.9	25.0	2,371	29.7	25.7
Los Angeles.....	1,481	26.7	28.1	1,651	20.7	26.0

<sup>1</sup> Excludes those not responding to the question.

<sup>2</sup> Percentages may not add to 100 because of rounding.

<sup>3</sup> Weighted to represent the national distribution according to the 1980 census.

the actual numbers. To correct for the intentional oversampling and other sources of sampling bias, a weighting procedure, known as "downweighting," was necessary (24). This weighting procedure also adjusts the sample distribution to match the demographic distributions in the 1980 census. Thus, with the downweighting corrections, the prevalence rates of CFS and associated symptoms are considered reasonable approximations to those that would have been obtained through a simple random sample of households in the United States.

**Assessment of CFS symptoms.** For the sake of clarity, we defined "chronic fatigue syndrome" as a syndrome that meets the CDC criteria. "Fatigue symptom complex," on the other hand, we defined as a cluster of CFS symptoms. Thus, a patient could be considered to have fatigue symptom complex if he had a few symptoms of CFS. He must have fulfilled the CDC criteria, however, to be counted as a case of CFS.

The presence of CFS symptoms was assessed from responses to specific questions about fatigue and related symptoms contained in the Diagnostic Interview Schedule (DIS), a highly structured psychiatric assessment interview designed to be administered by trained nonclinician interviewers (25). The questions were asked to elicit the person's lifetime experience. The fatigue question, for example, was worded, "Has there ever been a period lasting 2 weeks or more when you felt tired out all the time?" If the respondent answered affirma-

tively, the interviewer was instructed to probe further for potential medical explanations of the symptom (medication, alcohol or drug use, physical illness, or injury). After these possibilities were eliminated, if the respondent still answered affirmatively, then the symptom was considered "unexplained."

While the DIS has been used for CFS studies for the purpose of assessing psychiatric comorbidity (9,15,16), it was not designed for a study of prevalence rates and symptom patterns of CFS. It has been, however, successfully used for studies of syndromes such as fibromyalgia and irritable bowel syndrome that are not considered primary psychiatric disorders (26,27).

**The CDC-defined symptoms in the ECA.** The box on page 517 lists the DIS questions available in the ECA, corresponding to the CDC criteria of CFS (20). We designed the analysis so that symptoms of CFS in our data would correspond as closely as possible to the CDC criteria symptoms. To accomplish this, some CDC criteria symptoms were assessed with a combination of responses to two or more questions in the DIS. For example, the symptom of sleep disturbances was determined by combining the questions about insomnia and hypersomnia. The symptom of neuropsychological complaints, as defined in the CDC criteria, contains a variety of disturbances. Accordingly, matched questions from the DIS were combined to assess this CDC criterion symptom.

**Symptoms in Centers for Disease Control (CDC) Chronic Fatigue Syndrome Criteria Available in the Epidemiologic Catchment Area (ECA) Program**

<b>CDC criteria</b>	<b>ECA symptoms, responses</b>
<i>Major criteria</i> (all of A and none of B)	
<b>A. Persistent debilitating fatigue</b>	
1. Persistent fatigue	Tired out for 2 weeks or more
2. No previous history	Symptom was not assessed in Diagnostic Interview Schedule (DIS)
3. 50 percent or more reduction in usual activities	Giving up usual activities for several weeks or more (approximation)
4. 6 months or more duration	Not assessed in DIS
<b>B. Exclusions</b>	
1. Physical illness	Fatigue or disability from medical illness or injury, or "sickly" most of life from a medical illness (a computed variable)
2. Psychiatric illness	Diagnosis of a DSM-III (13) major psychiatric disorder other than substance use disorders (computed variable)
3. Substance use, abuse	Diagnosis of DSM-III (13) alcohol or drug use disorders (computed variable)
4. Weight loss	Unintentional loss of weight, 2 lbs. or more per week for several weeks, or 10 lbs. or more altogether (approximation)
<i>Minor criteria</i> (6 or more from C and 2 or more from D, or 8 or more from C)	
<b>C. Symptom criteria</b>	
1. Mild fever	Symptom not assessed in DIS
2. Sore throat	Symptom not assessed in DIS
3. Painful lymph nodes	Symptom not assessed in DIS
4. General muscle weakness	Cannot lift or move things
5. Muscle discomfort	Arm or leg pain (excluding joint pain)
6. Prolonged fatigue, for 24 hours or more	Same as A.1
7. Generalized headache	Generalized headache
8. Pain in joints	Pain in joints
9. Neuropsychological complaints	One or more of transient vision problems, forgetfulness (15 or fewer correct answers on Mini-Mental States Examination), slow thinking, trouble concentrating or easily distracted, depressive mood (computed variable).
10. Sleep disturbances	Insomnia or hypersomnia (computed variable)
11. Symptom cluster develops in a short time	Not assessed in DIS
<b>D. Physical criteria</b>	
1. Low grade fever	Symptom not assessed in DIS
2. Nonexudative pharyngitis	Symptom not assessed in DIS
3. Tender lymph nodes	Symptom not assessed in DIS

The case definition of the CDC criteria is satisfied by meeting (a) the major criteria that consist of persistent and debilitating fatigue lasting 6 months or longer, while excluding concurring or preexisting physical or psychiatric illness, substance use or abuse, and significant weight loss and (b) the minor criteria that consist of six or more neuropsychological and neuromuscular symptoms and two or more physical findings or, alternatively, eight or more symptoms alone (box).

Not all symptoms included in the CDC criteria were available in the ECA data (box). In particu-

lar, the three physical signs, low grade fever, nonexudative pharyngitis, and tender lymph nodes were not available, since they required verification by a clinician. Nevertheless, the principal components of CFS (persistent fatigue and disability) were available, along with 7 out of 11 criterion symptoms (muscle weakness, muscle discomfort, prolonged fatigue, generalized headache, joint pain, neuropsychological complaints, and sleep disturbances). It was thus possible to estimate the prevalence of CFS in the population by using an approximated version of the CDC case definition.

Table 2. Lifetime symptom prevalence by percentage<sup>1</sup> of chronic fatigue syndrome according to CDC criteria (N = 13,538)

Symptom	Unexplained	Explained <sup>2</sup>	Total
<i>Major criteria</i>			
<b>A. Persistent debilitating fatigue:</b>			
Persistent fatigue.....	13.9	9.8	23.7
50 percent or more reduction in usual activities <sup>3</sup> .....	2.6	10.7	13.3
<b>B. Exclusions:</b>			
Physical illness <sup>4</sup> .....	...	...	18.4
Psychiatric illness <sup>4</sup> .....	...	...	17.9
Substance abuse <sup>4</sup> .....	...	...	17.2
Weight loss <sup>3</sup> .....	9.0	5.4	14.4
<i>Minor criteria</i>			
<b>C. Symptom criteria:</b>			
General muscle weakness....	2.1	6.5	8.7
Muscle discomfort.....	3.5	14.5	18.0
Prolonged fatigue, 24 hours or more.....	13.9	9.8	23.6
Generalized headache.....	10.9	9.6	20.5
Pain in joints.....	3.7	25.4	29.2
Neuropsychological complaints <sup>4</sup> .....	35.5	45.7	81.2
Sleep disturbances <sup>4</sup> .....	21.5	4.0	25.6

<sup>1</sup> Weighted percentage, the "unexplained" and "explained" may not add up to the total exactly because of rounding.

<sup>2</sup> Includes medical illness, injury, and alcohol or drug use.

<sup>3</sup> Approximation in ECA (see box).

<sup>4</sup> Computed variable (see box and text).

We could also estimate the prevalence of individual symptoms of CFS included in the CDC criteria.

**Prevalence estimation.** A computer program was developed to generate a diagnosis of CFS approximating the CDC criteria as well as to assess the individual symptoms from the CDC criteria. The four exclusions to the CDC criteria—physical illness, psychiatric illness, substance use or abuse, and weight loss—were also incorporated into this program. The exclusion criteria of physical illness and significant weight loss were assessed from responses to other single or combined questions. The prevalence estimates of the other two exclusion criteria, psychiatric illness and substance abuse, were derived using another computer program (28) that scored diagnoses of psychiatric disorders, including alcohol and drug use disorders, as defined in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM III) (13). Details of the second program, including its algorithm procedures, are described elsewhere (29). Both programs are available from Dr. Price.

Because the literature consistently suggests that women are at a much higher risk than men for chronic fatigue, we performed most analyses separately for the two sexes. The extent of sex differences was then assessed using Chi-square statistics.

## Results

**Lifetime prevalence of CFS symptoms.** Table 2 summarizes the lifetime prevalence rates of chronic fatigue and other symptoms in the CDC criteria, available in the ECA data. The percentages for each symptom or exclusion refer to the prevalence rates, independent of other symptoms, in the entire study sample of 13,538. In the first section (Criteria A), 23.7 percent of the entire sample reported that they had ever experienced fatigue lasting 2 weeks or more. In 59 percent of those with fatigue (13.9 percent of the entire sample), this symptom was unexplained by medical causes. In this study sample, 13.3 percent overall reported that they had ever experienced a significant reduction in their usual activities (that is, disability), and this was "unexplained" only in 2.6 percent of the entire sample.

Study subjects commonly experienced the conditions considered as exclusions to CFS in the CDC criteria: physical illness, psychiatric illness, substance use or abuse, or a history of weight loss (Criteria B). Between 14.4 percent (weight loss) and 18.4 percent (physical illness) of the entire sample experienced at least one of these problems. Psychiatric illness, as defined by DSM III, amounted to 17.9 percent and substance abuse to 17.2 percent. A significant portion of the sample met more than one exclusion conditions.

The most frequent symptom among the minor criteria grouping (Criteria C) of the CDC definition was a neuropsychological complaint (transient vision problems, forgetfulness, slow thinking, trouble concentrating, depressed mood), present in 81.2 percent of the entire sample. A total of 44 percent of these neuropsychological complaints (35.5 percent of the entire sample) were unexplained, making such complaints the most frequently reported unexplained symptom of the minor criteria. Sleep disturbances were experienced by 25.6 percent of the subjects, and 84 percent of these (21.5 percent of the whole sample) did not have a medical explanation associated with this criterion symptom, thus making it the second most common unexplained symptom. Arthralgia, or joint pains, was also common (29.2 percent), although 87 percent of the joint pains were explained by medical illness, injury, medication, or substance use. Half of the headaches reported by 20 percent of the study subjects were unexplained by medical illness, injury, medication, or substance use. Generalized muscle weakness was the least frequent symptom, acknowledged by 8.7 percent of the subjects. It was

Table 3. Major criteria (Criteria A) of fatigue and disability by explanation of persons in the household sample in 4 sites, Epidemiologic Catchment Area Project, 1981-84<sup>1</sup>

Criteria	5,410 Men		7,775 Women		13,185 Total	
	Number	Percent	Number	Percent	Number	Percent
<i>Negative</i>						
Absence of fatigue or disability .....	5,205	96.3	7,395	95.0	12,600	95.6
<i>Positive</i>						
Medical: fatigue and disability because of medical conditions .....	107	2.2	159	2.4	266	2.3
Indeterminate: fatigue and disability partially explained <sup>2</sup> .....	52	.9	70	.9	122	.9
Unexplained: fatigue and disability unexplained .....	46	.6	151	1.7	197	1.2
Total prevalence: presence of fatigue and disability .....	205	3.7	380	5.0	585	4.4

<sup>1</sup> Numbers are raw; percentages are weighted.

<sup>2</sup> Fatigue was medically explained but disability unexplained, or fatigue was

induced by substance use but disability was unexplained or medically explained.

also the least frequently occurring unexplained symptom; only 24 percent of the subjects (2.1 percent of the entire sample) did not have a medical explanation for this symptom.

**The CDC major and minor criteria.** Only 0.6 percent of men and 1.7 percent of women reported that they had ever experienced both unexplained (that is, not medically related or substance induced) persistent fatigue and unexplained diminished activity during their lives (table 3). Additionally, 2.2 percent of men and 2.4 percent of women had fatigue and diminished activity that were medically related or substance induced. Altogether, 3.7 percent of men and 5 percent of women had fatigue and diminished activity regardless of its explanation.

When all four exclusions (Criteria B) were applied to the fatigue and disability questions in the DIS, 90 percent of the cases reporting unexplained fatigue and disability were excluded because of physical or psychiatric illness, substance abuse, or weight loss (table 4). Thus, only 19 subjects (0.1 percent of the entire sample) met the approximated CDC major criteria for CFS. The prevalence rate of "excluded" cases was higher among women than men, but this was not statistically significant.

Assessment of the CDC minor criteria could be accomplished only from the symptom criteria (Criteria C), because information about the physical symptoms (Criteria D) was not available. Therefore, five of seven (71 percent) of the available criterion symptoms from the DIS were used as a cutoff to match the proportion of symptoms in the CDC criteria (8 out of 11, or 73 percent). If medically related or substance induced symptoms were included, 3.4 percent of men and 8.5 percent of women had ever had five or more of these symptoms (table 5). Only 0.4 percent of men and 1.7 percent of women, however, had five or more

Table 4. Major criteria with exclusions. Unexplained fatigue and disability (Criteria A) with exclusions (Criteria B) applied<sup>1</sup>

Subjects	Excluded due to exclusion conditions <sup>2</sup>		Positive without exclusion conditions		Total	
	Number	Percent	Number	Percent	Number	Percent
Men.....	39	0.5	7	0.1	46	0.6
Women.....	139	1.6	12	0.1	151	1.7
Total ..	178	1.1	19	0.1	197	1.2

<sup>1</sup> Percentages are weighted.

<sup>2</sup> Physical illness, psychiatric illness, substance abuse or weight loss. (See box under B. "Exclusions").

of the seven possible symptoms without a medical explanation. Thus, 81 percent of the cases that could have otherwise met the symptom criteria would be disallowed because of medical or substance use exclusions.

The women in the sample were more than twice as likely as the men (8.5 percent versus 3.4 percent) to have reported five or more symptoms among the minor criteria. In addition, the men who reported five or more symptoms were more likely to be excluded than were the women who reported the same level of symptoms (88 percent versus 79 percent), because at least one positive symptom was due to either medical reasons or substance use. As a result, women were more than six times as likely as men to meet the minor criteria when exclusions were applied (1.7 percent versus .4 percent,  $P < .01$ ).

Overall, no men and only one woman out of the entire sample of 13,538 subjects met both major and minor criteria of CFS when we applied the Criteria B exclusions (psychiatric or medical illness, substance abuse, or weight loss) (table 6). This is our closest approximation to the CDC case definition of CFS. If Criteria B exclusions were not

Table 5. Minor criteria (Criteria C). 5 or more out of 7 symptoms<sup>1</sup>

Criteria	5,400 Men		7,756 Women		13,156 Total	
	Number	Percent	Number	Percent	Number	Percent
<i>Negative</i>						
Fewer than 5 symptoms	5,217	96.6	7,069	91.5	12,286	93.9
<i>Positive</i>						
Medical or substance use <sup>2</sup>	10	.2	39	.4	49	.3
Indeterminate <sup>3</sup>	151	2.8	505	6.4	656	4.7
Unexplained <sup>4</sup>	22	.4	143	1.7	165	1.1
Total	183	3.4	687	8.5	870	6.1

<sup>1</sup> Percentages are weighted.

<sup>2</sup> The 5 or more positive symptoms are all due to physical illness or substance use.

<sup>3</sup> The 5 or more positive symptoms contain both those attributed to medical conditions (physical illness or substance use) and those unexplained for medical reasons.

<sup>4</sup> The 5 or more positive symptoms are all unexplained by medical reasons.

Table 6. Prevalence of chronic fatigue syndrome using approximated Centers for Disease Control criteria<sup>1</sup>

Criteria	Men		Women		Total	
	Number	Percent	Number	Percent	Number	Percent
<i>Major and minor:</i>						
Excluded <sup>2</sup>	61	1.0	158	1.7	219	1.4
Positive	0	0.0	1	0.003	1	.001
Total	61	1.0	159	1.7	220	1.4
<i>Major or minor:</i>						
Excluded <sup>2</sup>	298	5.5	754	10.0	1,052	7.8
Positive	29	0.5	154	1.9	183	1.2
Total	327	6.0	908	11.9	1,235	9.0

<sup>1</sup> Percentages are weighted.

<sup>2</sup> Cases excluded due to physical illness, psychiatric illness, substance abuse, or significant weight loss.

applied, however, 61 men and 159 women, or 1.4 percent of the entire sample, would have fulfilled the criteria for CFS. A less restrictive operational definition of fatigue symptom complex, on the other hand, might be to include everyone who met either major or minor criteria with or without exclusions (table 6). This would yield 327 men (6 percent) and 908 women (11.9 percent). Eighty-five percent of these 1,235 people, however, would still not be considered as having cases of fatigue symptom complex if exclusion criteria were applied.

## Discussion

This study suggests that cases of chronic fatigue syndrome as defined by the CDC criteria may be quite rare in the general population, even though

individual symptoms included in the criteria are quite common. Because the ECA data were not gathered specifically to estimate the prevalence of CFS, certain limitations should be addressed. First, not all of the symptoms in the CDC criteria were available for analysis in the ECA, and hence our case definition represents only the best approximation of the CDC criteria. Omissions include prior history, the duration of fatigue (the CDC criteria requires 6 months or longer, while the DIS asked 2 weeks or longer), the temporal sequence of the fatigue and the other minor criteria symptoms, simultaneous clustering of the minor criteria symptoms, and the physical signs and symptoms. Inclusion of data on these required items, however, would almost certainly *reduce* the rate of CFS in this sample even further.

There is potential bias that could have affected the percentage of people meeting the CFS minor criteria due to the lack of 4 of the 11 symptom criteria (fever, sore throat, painful lymph nodes, and simultaneous symptom clustering). Although the proportion of our approximated minor criteria symptoms required for a diagnosis was nearly the same as with the CDC criteria, it is still possible that the lack of data on these symptoms could have artificially lowered the prevalence rate, if these symptoms were much more common than those available in the ECA.

Another source of potential bias is our lifetime-based assessment. Because all symptoms were assessed on a lifetime basis, we could not examine the timing of the fatigue syndrome in relation to the conditions of the four exclusion criteria. We would have excluded a number of subjects with chronic fatigue that occurred at a different time from their exclusion criteria. On the other hand, the lifetime-based assessment would have introduced people who had various symptoms spread out over a long period rather than occurring together within a short period. Therefore, many of the "positive" subjects might not have met our criteria, if temporal information about symptoms had been available. The issue of timing, however, is a limitation of all cross-sectional studies that are dependent upon retrospective recalls.

Given these limitations, it still would appear that CFS is quite rare in the community, but that fatigue, disability, and the neuropsychological symptoms are all very common. A recent prospective study in primary care has indeed shown that while fatigue symptom complex is common, a discrete CFS is not (30). Our results support this relationship in the general population as well. Our

prevalence estimate of the CDC-defined CFS, 7.4 cases per 100,000, is lower than the only existing general population estimate from Australia, 31.1 cases per 100,000 (21). The disparity could be due to the difference in the time when data were collected, since the ECA was conducted in the 1981-84 period, whereas Australian data were collected in 1988. It may also reflect the different cultural risk factors in the two populations. Nevertheless, both estimates are still very low, considering the media's image of overwhelming numbers of people suffering from CFS.

One reason for the apparent disparity between fatigue symptom complex and the CFS lies in the exclusion criteria. The CDC criteria were made intentionally restrictive by excluding patients with any of the four concurring or preexisting conditions. The objective of the exclusion criteria was to identify CFS patients among all those with fatigue. Consequently, the prevalence rate of CFS using the CDC criteria has been low even among highly selected patients presenting prolonged fatigue. For example, a University of Connecticut group found that only 4 percent of 135 patients consecutively referred to their specialized clinic for persistent and disabling fatigue actually met the CDC criteria (15). In our study, the exclusions defined by CDC eliminated 90 percent of those who would otherwise meet the major criteria and 81 percent of those who would otherwise meet the minor criteria in this community sample, leaving the "true" positive cases of CFS virtually nonexistent.

It is of interest to note that in our cross-cultural epidemiologic comparison of chronic fatigue between the United States and the United Kingdom, the exclusion criteria were found to have significant odds ratios for fatigue syndrome, independent of demographic and other risk factors (physical illness, OR = 6.4 in the United States and 1.7 in the United Kingdom; psychiatric illness, 2.7 in the United States and 3.4 in the United Kingdom; weight loss, 3.6 in the United States; drug use, 1.5 in the United Kingdom) (31). Perhaps the exclusion criteria should instead be considered as comorbid conditions if they occur concurrently, or as predictors of CFS if they occur prior to the onset of persistent fatigue (32).

Another reason for the apparent disparity between the frequency of fatigue symptom complex and discrete CFS relates to the structure of the CDC criteria that combines major and minor criteria. The major criteria exclude psychiatric or medical illness and substance use or abuse, concurrent or preexisting with prolonged fatigue. Most of

*'This study suggests that cases of chronic fatigue syndrome as defined by the CDC criteria may be quite rare in the general population, even though individual symptoms included in the criteria are quite common.'*

the 11 minor criteria symptoms overlap with symptoms that are part of the exclusion conditions. Thus, it may not be surprising to find that the CDC criteria actually are nondiscriminative despite their restrictive nature. Indeed, Komaroff and Geiger (33) noted that the CDC criteria failed to identify adequately subtypes of fatigue patients; similarly, a related study by the Connecticut group found that the neuropsychological and neuromuscular symptoms of the CDC criteria had low sensitivities and specificities for the CDC case definition (34). In our analysis, we observed 183 cases (1.2 percent) meeting the minor or major criteria, but only one case (.001 percent) meeting both.

The high prevalence rates of the minor criteria symptoms in the general population may be a reason for high prevalence "guesstimates" seen in media reports (3), despite the low prevalence estimate of CFS we found in this study as well as the finding from Australia. An increasing number of patients with these symptoms, prompted by media information about CFS, may be seeking evaluation for CFS, even though definitive cases of CFS represent only a fraction of these patients.

The findings of this study need to be verified by future studies using full CDC criteria, including clinical assessment and standardized data collection methods in general population settings. Such studies would not only provide a more precise prevalence estimate of the CFS, but also help establish valid diagnostic criteria that can be evaluated by means of standard diagnostic analysis techniques (35,36). Further studies, in turn, will promote better understanding of the epidemiology of CFS.

## References.....

1. Jones, J. F., et al.: Evidence for active Epstein-Barr virus infection in patients with persistent, unexplained illnesses: elevated anti-early antigen antibodies. *Ann Intern Med* 102: 1-7 (1985).
2. Straus, S. E., et al.: Persisting illness and fatigue in adults with evidence of Epstein-Barr virus infection. *Ann Intern Med* 102: 7-16 (1985).



3. Chronic fatigue syndrome: a modern medical mystery. *Newsweek*, Nov. 12, 1990, pp. 62-70.
4. Chronic fatigue: all in the mind? *Consumer Reports*, October 1990, pp. 671-675.
5. Palca, J.: Does a retrovirus explain fatigue syndrome puzzle? *Science* 249: 1240-1241, Sept. 14, 1990.
6. Wessely, S.: Old wine in new bottles: neurasthenia and ME. *Psycho Med* 20: 35-53 (1990).
7. Abbey, S. E., and Garfinkel, P. E.: Neurasthenia and chronic fatigue syndrome: the role of culture in the making of a diagnosis. *Am J Psychiat* 148: 1638-1646 (1991).
8. Holmes, G. P., et al.: A cluster of patients with a chronic mononucleosis-like syndrome: is Epstein-Barr virus the cause? *JAMA* 257: 2297-2302, May 1, 1987.
9. Gold, D., et al.: Chronic fatigue: a prospective clinical and virologic study. *JAMA* 264: 48-53, July 4, 1990.
10. Horwitz, C. A., Henle, W., Rudnick, H., and Latts, E.: Long-term serological follow-up of patients for Epstein-Barr virus after recovery from infectious mononucleosis. *J Infect Dis* 151: 1150-53 (1985).
11. Greenberg, D. B.: Neurasthenia in the 1980s: chronic mononucleosis, chronic fatigue syndrome, and anxiety and depressive disorders. *Psychosomatics* 31: 129-137 (1990).
12. Yousef, G. E., et al.: Chronic enterovirus infection in patients with postviral fatigue syndrome. *Lancet* No. 8578: 146-150, Jan. 23, 1988.
13. Diagnostic and statistical manual of mental disorders. Ed. 3, revised. American Psychiatric Association, Washington, DC, 1987.
14. Wessely, S., and Powell, R.: Fatigue syndromes: a comparison of chronic 'postviral' fatigue with neuromuscular and affective disorders. *J Neurol Neurosurg Psychiatry* 52: 940-948, (1989).
15. Manu, P., Lane, T. J., and Matthews, D. A.: The frequency of the chronic fatigue syndrome in patients with symptoms of persistent fatigue. *Ann Intern Med* 109: 554-556 (1988).
16. Kruesi, M. J. P., Dale J., and Straus, S. E.: Psychiatric diagnoses in patients who have chronic fatigue syndrome. *J Clin Psychiatry* 50: 53-56 (1989).
17. Lane, T. J., Manu, P., and Matthews, D. A.: The clinical application and operating characteristics of the criteria for the chronic fatigue syndrome. Paper presented at the Fourth Annual NIMH International Research Conference on the Classification and Treatment of Mental Disorders in General Medical Settings. Bethesda, MD, 1990.
18. Taerk, G.S., et al.: Depression in patients with neuromyasthenia (benign myalgic encephalomyelitis). *Int J Psychiat Med* 17: 49-56 (1987).
19. Kroenke, K., et al.: Chronic fatigue in primary care: prevalence, patient characteristics and outcome. *JAMA* 260: 929-934, Aug. 19, 1988.
20. Holmes, G. P., et al.: Chronic fatigue syndrome: a working case definition. *Ann Intern Med* 108: 387-389 (1988).
21. Lloyed, A.R., et al.: Prevalence of chronic fatigue syndrome in an Australian population. *Med J Australia* 153: 522-528 (1990).
22. Regier, D. A., et al.: The NIMH Epidemiologic Catchment Area (ECA) Program: historical context, major objectives, and study population characteristics. *Arch Gen Psychiatry* 41: 934-941 (1984).
23. Robins, L. N., and Regier D. A.: *Psychiatric disorders in America*. Free Press, New York, NY, 1991.
24. Robins, L. N., and Price, R. K.: Adult disorders predicted by childhood conduct problems: results from the NIMH Epidemiologic Catchment Area Project. *Psychiatry* 54: 116-132 (1991).
25. Robins, L. N., et al.: The Diagnostic Interview Schedule. *In* *Epidemiologic field methods in psychiatry: the NIMH Epidemiologic Catchment Area Program*, edited by W.W. Eaton and L. G. Kessler. Academic Press, New York, 1985, pp. 143-170.
26. Escobar, J. I., et al.: Medically unexplained physical symptoms, somatization disorder and abridged somatization: studies with the Diagnostic Interview Schedule. *Psychiat Develop* 3: 235-245 (1989).
27. Robbins, J. N., Kirmayer, L. J., and Tepper, S.: Latent variable models of functional somatic distress. *McGill Working Papers in Social Behavior*, No. 90-1. McGill University, Montreal, Canada, 1990.
28. NIMH DSM-III scoring algorithm, National Institute of Mental Health, Rockville, MD, 1984.
29. Boyd, J. H., et al.: Making Diagnoses from DIS data. *In* *Epidemiologic field methods in psychiatry: the NIMH Epidemiologic Catchment Area Program*, edited by W.W. Eaton and L.G. Kessler. Academic Press, New York, NY, 1985, pp. 209-234.
30. David, A., et al.: Tired, weak, or in need of rest: fatigue among general practice attenders. *BMJ* 301: 1199-1202 (1990).
31. Wessely, S., Price, R. K., and Fraser, V. J.: Epidemiology of fatigue: evidence from the United States and the United Kingdom. 118th Annual Meeting of the American Public Health Association, Abstract No. 3121-5, New York, NY, 1990.
32. Abbey, S. E., and Garfinkel, P. E.: Chronic fatigue syndrome and depression: cause, effect, or covariate. *Rev Infect Dis* 13 (Suppl 1): S73-83 (1991).
33. Komaroff, A., and Geiger, A.: Does the CDC working case definition of chronic fatigue syndrome (CFS) identify a distinct group? *Clin Res* 37 (Abstract): 778A (1989).
34. Lane, T. J., Manu, P., and Matthews, D. A.: The predictive value of the chronic fatigue syndrome criteria. *Clin Res* 37 (Abstract): 317A (1989).
35. Weinstein, M. C., and Fineberg, H. V.: *Clinical decision analysis*. W.B. Saunders, Philadelphia, 1980.
36. Hsiao, J. K., Bartko, J. J., and Potter W. Z.: Diagnosing diagnoses: receiver operating characteristic methods and psychiatry. *Arch Gen Psychiatry* 46: 664-667 (1989).