

Prevalence and Incidence of Chronic Fatigue Syndrome in Wichita, Kansas

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Background: Chronic fatigue syndrome (CFS) is a debilitating illness with no known cause or effective therapy. Population-based epidemiologic data on CFS prevalence and incidence are critical to put CFS in a realistic context for public health officials and others responsible for allocating resources and for practicing physicians when examining and caring for patients.

Methods: We conducted a random digit-dialing survey and clinical examination to estimate the prevalence of CFS in the general population of Wichita, Kan, and a 1-year follow-up telephone interview and clinical examination to estimate the incidence of CFS. The survey included 33 997 households representing 90 316 residents. This report focuses on 7162 respondents aged 18 to 69 years. Fatigued (n=3528) and randomly selected nonfatigued (n=3634) respondents completed telephone questionnaires concerning fatigue, other symptoms, and medical history. The clinical examination included the Diagnostic Interview Schedule for *Diagnostic and Statistical Manual of Mental Disorders,*

Fourth Edition, laboratory testing, and a physical examination.

Results: The overall weighted point prevalence of CFS, adjusted for nonresponse, was 235 per 100 000 persons (95% confidence interval, 142-327 per 100 000 persons). The prevalence of CFS was higher among women, 373 per 100 000 persons (95% confidence interval, 210-536 per 100 000 persons), than among men, 83 per 100 000 persons (95% confidence interval, 15-150 per 100 000 persons). Among subjects nonfatigued and fatigued for less than 6 months, the 1-year incidence of CFS was 180 per 100 000 persons (95% confidence interval, 0-466 per 100 000 persons).

Conclusions: Chronic fatigue syndrome constitutes a major public health problem. Longitudinal follow-up of this cohort will be used to further evaluate the natural history of this illness.

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CHRONIC FATIGUE syndrome (CFS) is a complex medical and public health problem. Population-based descriptive epidemiologic prevalence and incidence data are critical to accurately estimate the burden of this illness for public health officials, health maintenance organizations, and other insurance providers who must allocate resources. Such data are also important to help practicing physicians put CFS in a realistic context when examining and caring for patients. Yet, accurately describing the prevalence of CFS has challenged the scientific community for more than a decade because of difficulties in achieving uniform case ascertainment by interview or simple laboratory tests. The current research case definition, based on international expert consensus in 1994, requires debilitating fatigue for at least 6 months, accompanying

characteristic symptoms, and a thorough clinical and psychological examination to exclude known causes of fatigue.¹

Previous studies²⁻¹⁰ have estimated a wide range of CFS prevalence, from 2.3 to 600 per 100 000 persons. Prevalence estimates from those studies cannot be directly compared because of the lack of or inconsistent use of a standard CFS case definition, varying degrees of rigor in examining subjects,¹¹ and differences in study populations,^{2,6,9,10,12} sampling strategies, and methods for estimating prevalence.^{1,9,13,14} Physician-based surveillance studies, although they reflect the burden of CFS to the health care system, underestimate the true prevalence of CFS in the population. Telephone surveys, which can reach many persons, often overestimate the occurrence of CFS because subjects are not clinically examined to identify exclusionary medical and psychiatric illnesses. The most recent community-based study¹⁰ of CFS, which incor-

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porated a clinical examination of subjects, reported prevalence rates ranging from 291 to 522 per 100 000 persons.

Few studies have addressed the incidence of CFS. A physician-based surveillance study² of 4 US cities reported a 4-year incidence of less than 1 per 100 000 persons. A nationwide survey¹² in Japan estimated that 0.46 per 100 000 persons developed CFS annually. A prospective study¹⁵ in England, of primary care patients who presented with glandular fever, estimated that 6 months after infection, 9% could develop a postinfective fatiguing illness that otherwise would be classified as CFS. Differences among these figures indicate heterogeneity of the populations being studied and possibly different definitions of an incident case.

The primary objective of the present study was to estimate the baseline prevalence and 1-year incidence of CFS in Wichita, Kan. We studied the Wichita population because it is demographically similar to that of the United States for age, sex, race, ethnicity, and income (based on 1990 US census data), and it represents a geographically discrete and stable community. Finally, we could directly compare CFS prevalence and incidence estimated by passive surveillance in Wichita² with active population-based surveillance.

METHODS

OVERVIEW OF THE STUDY DESIGN

This was a longitudinal study with a baseline and 3 years of follow-up. At baseline, the study had 3 components: a screening telephone interview, a detailed telephone interview, and a clinical examination. Telephone interviews were conducted in English. The screening interview asked a household informant (≥ 18 years) to report the age, sex, race, ethnicity, and fatigue status of each household member. All persons 18 years or older for whom fatigue of 1 month or longer was reported, and a random sample of non-fatigued individuals, were asked to complete a detailed telephone interview. The detailed interview covered fatigue status and duration, other symptoms, demographic characteristics, and medical history. Respondents whose interview responses fulfilled the criteria of the 1994 CFS case definition¹ were considered to have a "CFS-like" illness and were invited for a clinical examination for final classification. The follow-up attempted to recontact, by telephone, all subjects originally interviewed in detail and to conduct a detailed interview to update their fatigue status. Newly identified subjects with a CFS-like illness and those who had previously come to the clinic and did not have medical or psychiatric exclusionary conditions were invited for a clinical examination. The present study reports on the results of the baseline and 12-month follow-up. This study adhered to human experimentation guidelines of the US Department of Health and Human Services. All participants were volunteers who gave informed consent.

TELEPHONE SURVEY

We conducted a population-based random digit-dialing survey of residents of Sedgwick County, Kansas, which includes Wichita and unincorporated areas. At least 5 attempts were made (if necessary) to establish contact. Within the first few minutes of telephone contact, respondents were offered the option to reschedule the call at a more convenient time. A staff member, experienced in refusal conversion, contacted those who initially declined to participate. We used a computer-assisted telephone interviewing system. Interviewers read questions dis-

played on a computer screen to respondents and entered their responses directly into the database. Software automatically performed range and logic checks on the entered data and displayed the next appropriate question.

We classified subjects as having a CFS-like illness if they reported severe fatigue for at least 6 months that was not relieved by rest and the occurrence of at least 4 CFS-defining symptoms¹ for at least 6 months. Subjects were also asked about medical and psychiatric conditions. The following conditions excluded subjects from being classified as having a CFS-like illness: cancer within 5 years of the interview (except for basal cell and nonmelanoma skin cancer), emphysema, chronic hepatitis, rheumatoid arthritis, acquired immunodeficiency syndrome, lupus or Sjögren syndrome, multiple sclerosis, organ transplantation, pregnancy or major surgery within the past year, any previous medical condition whose resolution had not been documented, any major psychiatric disorder (eg, manic depressive disorder, schizophrenia, or bipolar disorder), bulimia or anorexia, and any history of alcohol or other substance abuse. Stroke, myocardial infarction, heart failure, and a heart condition limiting the ability to walk were also exclusionary if they occurred within 2 years of the interview.

CLINICAL EXAMINATION

Respondents with a CFS-like illness and a random sample of non-fatigued persons were invited to participate in a clinical examination. They were telephoned to schedule a clinic appointment, with financial compensation (\$35) for travel to the clinic. Clinic participants were mailed an informed consent form and a questionnaire asking about the onset of fatigue, the severity and duration of symptoms, current energy level, medical history, and current medications. At the clinic, a trained interviewer confirmed that the subject understood the nature of the study, witnessed the informed consent document, and reviewed the mailed questionnaire for completeness and consistency of responses. The interviewer then privately administered a questionnaire about fatigue¹⁶ and modules from the Diagnostic Interview Schedule for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*¹⁷ (modules included somatization, specific phobias, panic disorder, generalized anxiety disorder, major depressive episode and dysthymia, manic episode, schizophrenia, anorexia nervosa, and bulimia nervosa). A physician assistant then performed a standardized physical examination.¹⁸ Blood and urine specimens were obtained for laboratory screening tests to identify possible underlying or contributing medical conditions, as stipulated by the CFS case definition.¹ Laboratory tests administered to all participants included blood chemistry tests (to determine the levels of glucose, calcium, electrolytes, uric acid, serum urea nitrogen, and creatinine), liver function tests (to determine the levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, albumin, globulin, total protein, lactate dehydrogenase, and total bilirubin), thyroid function tests (to determine the levels of thyrotropin, thyroxine, and triiodothyronine), the determination of the sedimentation rate, an autoimmune screen (for antinuclear antibody and rheumatoid factor), a transferrin saturation test, and a urinalysis (including the determination of urine protein, glucose, and blood levels and a microscopic examination). Participants were offered human immunodeficiency virus testing. Participants or their physicians were notified by mail of any significant abnormalities identified by the laboratory testing or physical examination to ensure appropriate clinical follow-up.

CLASSIFICATION OF SUBJECTS

At least 3 physicians (E.R.U., J.A.S., J.F.J., N.G., or W.C.R.) and 2 psychiatrists (S.A. and S.M.) on a physician review committee independently reviewed each subject's clinical and laboratory data

and classified the individual. If classification was not unanimous, committee members conferred to reach a consensus. Subjects fully meeting the 1994 CFS case definition¹ (fatigue for ≥ 6 months; rest did not alleviate fatigue; fatigue interfered substantially with work, educational, social, or personal activities; ≥ 4 of 8 symptoms; and no medical or psychiatric exclusionary conditions) were classified as having CFS. Those with exclusionary conditions were classified as having exclusionary medical or psychiatric diagnoses. Participants with insufficient fatigue severity (rest alleviated their fatigue, or fatigue did not result in substantial reduction of activities) or too few (< 4) accompanying symptoms were classified as having insufficient symptoms or fatigue (ISF).

DEFINING THE 1-YEAR INCIDENCE OF CFS

The population at risk of developing CFS during the following year (incident cases) consisted of nonfatigued subjects and subjects fatigued for less than 6 months who had no medical or psychiatric exclusionary conditions at baseline. We used data from 12-month follow-up interviews and examinations to classify incident CFS cases. A case was considered incident if all CFS case-defining criteria were met and fatigue onset occurred within 6 months of baseline.

STATISTICAL ANALYSIS

Data from surveys often involve sampling weights, which are necessary to maintain the relation between the survey and the population. In our random digit-dialing survey, the weights arose from several sources, including differential selection (we selected all fatigued persons, but only a random subsample of nonfatigued persons) and adjustments for nonresponse in the process of identifying households, screening for fatigued individuals, and conducting interviews.¹⁹ Persons who completed a detailed interview received a base weight that reflected the probability of selection for the telephone screening interview and of selection for the detailed interview. Nonresponse adjustments were applied to the base weights to account for persons who did not complete telephone interviews, households that did not complete screening interviews, and telephone numbers whose residential status could not be determined. A further adjustment used poststratification to bring the weighted numbers of black and non-black persons in the sample into agreement with the corresponding numbers in the Sedgwick County population. Subjects who completed a clinical examination received an additional sample weight that reflected the probability of being selected and an adjustment for nonresponse. Poststratified weights and clinical weights were used to calculate prevalence. Data from the 12-month follow-up received separate weights that also accounted for mortality and nonresponses on the follow-up interview and clinical examination. Weighted data were used for prevalence, incidence, and other estimates of population characteristics. Weighted prevalence and incidence estimates and weighted χ^2 tests for comparing proportions were calculated using computer software (SUDAAN; Research Triangle Institute, Research Triangle Park, NC). All other analyses were performed using SAS statistical software (SAS Institute Inc, Cary, NC).

RESULTS

CHARACTERISTICS OF THE SAMPLE

Interview Sample

The **Figure** illustrates the study's overall interview, classification, and examination process. Between February 1 and September 30, 1997, 116 000 telephone numbers

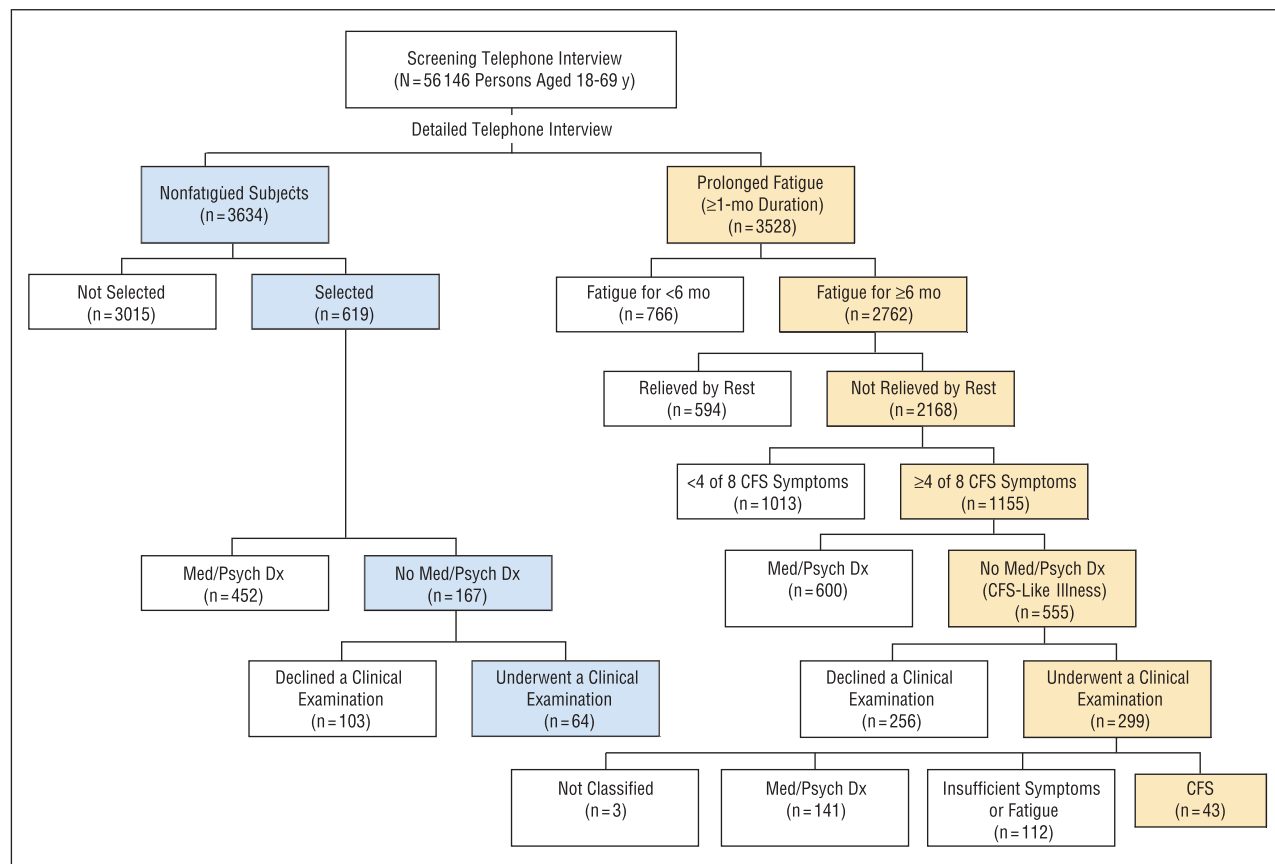
were selected for a screening interview; of these numbers, 53 509 (46.1%) were ineligible (eg, nonresidential, nonworking, facsimile, modem, or beeper or no contact). Of the 62 491 residential numbers contacted, screening interviews were completed for 33 997 households (54.4%). These households contained 90 316 persons, approximately one fifth of the Wichita population. Of these persons, 56 146 were adults aged 18 to 69 years, and 5295 (9.4%) were identified as having fatigue for 1 month or longer. These fatigued adults and a random sample of 6269 nonfatigued adults were asked to participate in detailed telephone interviews. Ultimately, 7162 adult respondents (3528 fatigued persons and 3634 nonfatigued persons) aged 18 to 69 years completed a detailed telephone interview. **Table 1** displays the distribution of exclusionary medical and psychiatric illnesses identified during the telephone interview among nonfatigued subjects and fatigued subjects who, in the absence of the exclusionary condition, would be classified as having a CFS-like illness.

Clinic Sample

At baseline, 555 fatigued subjects classified as having a CFS-like illness and 167 of 619 randomly selected nonfatigued respondents were invited for a clinical examination. Of those invited for a clinical examination, 299 (53.9%) of the subjects with a CFS-like illness and 64 (38.3%) of the nonfatigued respondents completed the examination. The subjects with a CFS-like illness who did not come for a clinical examination were similar to those who did in terms of age, sex, income, and duration of illness, although those who did not participate had less education (χ^2 test, $P = .002$) and were more likely to be nonwhite (13.3% vs 7.7%; χ^2 test, $P = .03$).

The physician review committee classified 43 participants as having CFS at baseline. Only 3 (7%) could not recall the type of onset, and most (34, or 79%) described a gradual onset of illness. The median time since the onset of illness was 7.3 years (range, 8 months to 44 years). Only a fraction (7 [16]) were diagnosed as having CFS or were treated for CFS by a physician. Subjects who had been diagnosed as having CFS were similar to those who had not been previously diagnosed as having CFS in age and duration of illness. However, subjects with CFS with a sudden onset were more likely to have been diagnosed as having the disorder than those with a gradual onset (4 [66.7%] of 6 vs 2 [5.9%] of 34; Fisher exact test, $P = .002$).

Of the 299 clinically examined subjects with a CFS-like illness, 112 (37.5%) were classified as having ISF. An additional 141 subjects (47.2%) had exclusionary medical or psychiatric conditions. The exclusionary conditions identified in the clinic differed from those previously identified through the telephone interview. Abnormalities in laboratory test or physical examination results were the most frequent reasons for medical exclusion (identified in 34 subjects), followed by obesity (15 subjects had a body mass index [calculated as weight in kilograms divided by the square of height in meters] of ≥ 45) and self-identified sleep disorders (9 subjects). Major depressive disorder with melancholia (identified in 18 subjects) was the most frequent exclusionary psy-



Flowchart for the classification of subjects in Wichita, Kan. CFS indicates chronic fatigue syndrome; Med/Psych Dx, medical or psychiatric diagnosis.

chiatric diagnosis, followed by bipolar disorder (identified in 12 subjects). Three patients could not be classified because their Diagnostic Interview Schedule for *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, data were missing.

POPULATION CHARACTERISTICS

Fatigue Groups

Table 2 presents the unweighted and weighted sample sizes for the study subjects, grouped by fatigue status. The 7162 respondents in our study represent, after weighting, 272838 adults in the Wichita population, and the 43 CFS cases identified at the clinical examination represent 641 CFS cases in the population. The demographic characteristics of the overall weighted sample (**Table 3**) were similar to data reported in the 1990 census for the Wichita population. Women composed more fatigued (those with a CFS-like illness and those with CFS) than nonfatigued respondents (weighted χ^2 test, $P < .001$). The ages of the group with a CFS-like illness and the group with CFS were more likely to be between 40 and 59 years, whereas the nonfatigued group was younger (weighted χ^2 test, $P < .001$). The median yearly incomes were the same for all groups.

Prevalence Estimates

Table 4 presents prevalence estimates for CFS and a CFS-like illness. The overall prevalence of CFS was 235 per

100 000 persons. Prevalence estimates for women were significantly higher than those for men in both fatigue categories. The prevalence ratio of women-men increased with illness severity: 0.9 for nonfatigued subjects, 2.3 for subjects with a CFS-like illness, and 4.5 for subjects with CFS. However, the prevalence ratio of white-nonwhite subjects did not increase with illness severity.

Among white women, prevalence of CFS increased steadily with age, reaching a maximum for those aged 50 to 59 years (863 per 100 000 persons; 95% confidence interval [CI], 280-1446 per 100 000 persons), and decreased in those aged 60 to 69 years (275 per 100 000 persons; 95% CI, 4-546 per 100 000 persons). For yearly income stratified into 3 categories (\leq \$20 000, \$20 001-\$40 000, and $>$ \$40 000), CFS prevalence estimates for white women were 485 per 100 000 persons (95% CI, 160-809 per 100 000 persons), 465 per 100 000 persons (95% CI, 119-812 per 100 000 persons), and 263 per 100 000 persons (95% CI, 118-408 per 100 000 persons), respectively.

Incidence Estimates

Only 4 of 2727 subjects who were at risk at baseline (2 nonfatigued subjects and 2 subjects fatigued for $<$ 6 months) developed CFS in the following 12 months. All were white, and they included 3 women and 1 man. The weighted 1-year CFS incidence was 180 per 100 000 persons (95% CI, 0-466 per 100 000 persons). The sample sizes were too small to yield useful estimates of male and female incidence.

Table 1. Exclusionary Medical and Psychiatric Illnesses Identified in the Telephone Interview

Illness	Fatigued Subjects (n = 600), %*†	Nonfatigued Subjects (n = 452), %*
Any medical exclusion	80.7	71.2
Rheumatoid arthritis	30.0	24.1
Lupus or Sjögren syndrome	8.7	2.1
Pregnancy	7.0	35.0
Heart failure or fluid in the lungs	6.0	0.7
Hepatitis or cirrhosis	5.5	5.5
Immunodeficiency disease	3.8	1.1
Multiple sclerosis	3.7	1.3
Heart condition limiting walking	3.3	0.4
Myocardial infarction	2.8	0.7
Organ transplantation	1.5	2.0
Stroke	1.2	0
Other exclusions‡	19.3	2.4
Any psychiatric exclusion	30.2	31.4
Alcohol or other drug dependency	18.2	21.2
Manic depressive disorder	13.2	6.2
Anorexia or bulimia	5.2	4.4
Schizophrenia	1.0	0.9

*Subjects could have more than one exclusionary condition.

†Screened to meet the fatigue and symptom criteria for chronic fatigue syndrome.

‡Includes malignancies, Crohn disease, sleep apnea, and Parkinson disease.

Table 2. Comparison of Unweighted and Weighted Sample Sizes for Adult Survey Respondents by Fatigue Group*

Variable	Unweighted Sample	Weighted Sample
Total respondents	7162	272 838
Nonfatigued respondents	3634	243 272
Respondents fatigued for ≥1 mo	3528	29 566
Respondents with a CFS-like illness†	555	4384
Respondents with CFS‡	43	641

Abbreviation: CFS, chronic fatigue syndrome.

*Weights account for the probability of selection and include adjustments that compensate for nonresponse and bring sample totals into agreement with population totals with respect to race.

†Includes patients with CFS.

‡Additional weight adjustments account for the probability of selection and for nonresponse in the clinical examination.

COMMENT

This study documents the magnitude of the public health problem posed by CFS in the general population, particularly among women. Our prevalence estimate of CFS among women (373 per 100 000 women) is about one third of the Kansas State Health Department's estimate for statewide breast cancer prevalence (1000 per 100 000 women) and is 3 times higher than their estimate for cervical cancer (100 per 100 000 persons). Our overall CFS prevalence estimate (235 per 100 000 persons) is much higher than the prevalence of tuberculosis (4 per 100 000 persons),²⁰ but much lower than the prevalence reported for diabetes mellitus (3900 per 100 000 persons) or asthma (6200 per 100 000 persons).

Our overall CFS prevalence was somewhat less than the estimate reported from a community-based study of 8 Chicago, Ill, neighborhoods (422 per 100 000 persons).¹⁰ While differences in prevalence estimates between Wichita and Chicago could reflect important differences in the occurrence of CFS in urban and metropolitan populations, other factors could also account for the discrepancy. Although the Wichita and Chicago studies both used random digit dialing, the studies differed with respect to sample design (simple vs stratified random sampling) and statistical methods (weighted estimates adjusted for non-response vs unweighted analyses). Differences in the questionnaires and fatigue classification algorithms may also have affected the findings. For example, in the Chicago study, only 35% of subjects initially screened as having fatigue for 1 month or longer had chronic fatigue (≥6 months), whereas in our study, this figure was 78.3% (2762/3528). The Chicago study classified slightly more than 50% of subjects with chronic fatigue as having a CFS-like illness, whereas only 20.1% (555/2762) of the subjects reporting chronic fatigue in our study were classified as having a CFS-like illness. Finally, the median duration of CFS in Chicago was 2.9 years, compared with 7.3 years in our study. Although both studies applied the 1994 CFS case definition, variations in the method of application (eg, different instruments to measure case-defining criteria) limit the reproducibility of findings. Standardization of questionnaires and algorithms for subject classification is needed to improve the precision of disease ascertainment in future studies. Despite the differences between these 2 studies, the similarities in their findings are striking. The prevalence of CFS is similar within the limits of error. In addition, both studies estimate the prevalence to be highest among women aged 40 to 59 years.

The higher prevalence of CFS and a CFS-like illness among women supports previous findings.^{3,7,8,21-23} The stratification of prevalence by income category also supports previous findings³ that CFS and CFS-like illnesses are not simply conditions of affluence. However, in contrast to other studies,^{2,12,21} the prevalence of CFS among women in Wichita peaked in the 50- to 59-year age group instead of the 30- to 39-year age group. Because the median duration of illness among the 50- to 59-year-old female patients with CFS was 7.3 years (data not shown), the same as the median duration overall, this observation is not likely to be the result of a cohort aging effect. We observed trends similar to those reported in findings of the San Francisco, Calif,³ and Chicago¹⁰ studies, showing that CFS was elevated (although not statistically significantly) in non-white persons (black, Hispanic, and Native American persons). Additional studies of metropolitan, urban, and rural communities that include more racial or ethnic minorities are needed to determine a more precise measure of the magnitude of CFS in these populations.

The 1-year incidence estimate of CFS (180 per 100 000 persons; 95% CI, 0-466 per 100 000 persons) is similar to previous estimates from a physician-based study in the United States² and a nationwide study in Japan.¹² Compared with prevalence, our incidence estimate might seem too high. However, several factors preclude making a simple and direct link between incidence and preva-

Table 3. Characteristics of the Weighted Sample by Fatigue Group and Overall Total*

Characteristic	Nonfatigued Subjects	Subjects With a CFS-Like Illness†	Subjects With CFS	Total
Female sex	50.7	72.1	83.2	52.4
White race	85.8	88.6	81.7	85.7
Hispanic ethnicity	4.8	5.4	2.2	4.9
Age, y				
18-29	25.8	9.3	5.3	24.9
30-39	24.4	24.3	19.0	24.4
40-49	22.6	34.7	35.8	23.0
50-59	15.0	23.0	33.2	15.6
60-69	12.1	8.7	6.7	12.1
Mean	40.5	44.4	47.0	40.7
Household income (1996), \$				
≤20 000	17.7	23.7	16.6	19.3
20 001-40 000	27.3	30.7	32.8	27.5
>40 000	44.3	38.9	42.5	42.9
Educational level				
≤High school graduate	39.7	47.3	51.9	40.9
College (1-4 y)	49.7	45.7	45.1	48.8
≥College graduate	8.9	4.7	3.0	8.6

Abbreviation: CFS, chronic fatigue syndrome.

*Data are given as percentage of each group. Some percentages may not total 100 because of rounding or missing data.

†Includes subjects with CFS.

lence in our study. First, prevalence estimates considered the probability of CFS in the entire population (all subjects with and without exclusionary conditions), while incidence reflected the yearly rate of developing CFS among the population at risk (baseline subjects who were nonfatigued and fatigued for <6 months, without medical or psychiatric exclusions). Second, even if the denominators for incidence and prevalence were the same, the classic formula relating incidence and prevalence cannot be applied because it assumes a uniform duration of illness. In the case of CFS, disease heterogeneity makes it likely that duration of illness (ie, time to recovery) is heterogeneous. This suggestion is supported by findings from a longitudinal study²⁴ that reported higher recovery rates for subjects with CFS who were ill for less than 5 years compared with those who were ill for a longer duration. Further studies on the clinical course of CFS and the occurrence of new cases are necessary.

Our findings are limited by difficulties associated with studying CFS in the general population. First, the study relied on telephone interviews to identify subjects for referral to the clinic, and this was based on self-reported information. As indicated in the 1994 CFS case definition, we used medical and psychiatric conditions known to cause fatigue to exclude subjects from being classified as having CFS. However, because the exclusionary conditions do not always cause fatigue, as indicated by the detection of these conditions in some nonfatigued subjects (Table 1), we are potentially excluding subjects from an examination for CFS. In clinical settings, the nature of fatigue in relation to concomitant illness can be more accurately determined. Finally, follow-up demonstrated that some subjects with ISF (ie, those with unexplained fatigue who do not meet all case definition criteria) eventually meet the criteria and some subjects with CFS at baseline subsequently become classified as having ISF. This indicates that the ISF pool includes prevalent cases that are missed because of fluctuations in dis-

ease severity. These factors indicate that our prevalence figures represent a lower estimate of the disease burden in the population.

Some persons with a CFS-like illness did not undergo a clinical examination, and this should be considered when interpreting our findings. Subjects with a CFS-like illness who came to the clinic were more likely to be white, which led to underestimation of CFS prevalence among nonwhite persons. However, because the sample was mostly white, the modest difference in percentage nonwhite between the subjects examined clinically and those not examined clinically (7.7% vs 13.3%) is unlikely to have biased the overall or white estimates to a noticeable extent. Likewise, because subjects with a CFS-like illness who came to the clinic were more likely to have a higher education than those who did not, the CFS prevalence among subjects who had less than a college education may be underestimated.

The 95% CIs are also quite wide, which complicates interpretation of the findings. The overall estimate of the prevalence of CFS, 235 per 100 000 persons, had a 95% CI of 142 to 327 per 100 000 persons, a width of 185. In relative terms, of course, the half-width of this 95% CI is a substantial fraction (roughly 40%) of the estimate. This situation reflects the challenge of obtaining precise estimates of prevalence for relatively rare conditions, even from a large sample. Thus, it is appropriate to interpret findings with caution. At the same time, we were also interested in the relation of the prevalence of CFS to such variables as sex, race, and age, even though creating a subset of the data in this way produced smaller (often quite small) sample sizes and correspondingly wider 95% CIs. However, by reporting those 95% CIs, we at least made the limitations clear.

In addition to documenting the high prevalence and, therefore, the public health importance of CFS, this study highlights limitations in the accuracy of case ascertainment with the current CFS case definition. Standardiza-

Table 4. Point Prevalence Estimates per 100 000 Persons by Fatigue Group

Characteristic	Persons With a CFS-Like Illness*	Persons With CFS†
Overall	1607	235 (142-327)
Sex		
Female	2211	373 (210-536)
Male	943	83 (15-150)
Race		
White	1661	224 (145-303)
Nonwhite	1280	300 (0-742)
Age, y		
18-29	600	50 (0-120)
30-39	1601	183 (54-311)
40-49	2424	365 (65-666)
50-59	2375	501 (196-806)
60-69	1149	130 (2-258)
Household income (1996), \$		
≤20 000	1980	202 (67-336)
20 001-40 000	1793	280 (97-463)
>40 000	1457	233 (69-397)
Race-sex specific		
White		
Females	2230	352 (221-483)
Males	1040	84 (9-158)
Nonwhite		
Females	2097	495 (0-1310)
Males	344	77 (0-228)

Abbreviation: CFS, chronic fatigue syndrome.

*Includes persons with CFS.

†Data in parentheses are 95% confidence intervals.

tion of criteria for exclusionary diagnoses and of instruments for measuring fatigue and other symptoms could improve comparability among studies. In addition, standardized measurements in multiple populations will be required for an empirically derived case definition. Molecular analyses of idiopathic fatiguing illnesses may yield diagnostic markers, provide evidence for disease stratification (ie, subtypes of CFS), and shed light on pathogenesis. Gene expression profiling of peripheral blood samples from this population is under way to begin construction of a molecular portrait of CFS.

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