Overlapping Conditions Among Patients With Chronic Fatigue Syndrome, Fibromyalgia, and Temporomandibular Disorder

Leslie A. Aaron, PhD, MPH; Mary M. Burke, MD; Dedra Buchwald, MD

Background: Patients with chronic fatigue syndrome (CFS), fibromyalgia (FM), and temporomandibular disorder (TMD) share many clinical illness features such as myalgia, fatigue, sleep disturbances, and impairment in ability to perform activities of daily living as a consequence of these symptoms. A growing literature suggests that a variety of comorbid illnesses also may commonly coexist in these patients, including irritable bowel syndrome, chronic tension-type headache, and interstitial cystitis.

Objective: To describe the frequency of 10 clinical conditions among patients with CFS, FM, and TMD compared with healthy controls with respect to past diagnoses, degree to which they manifested symptoms for each condition as determined by expert-based criteria, and published diagnostic criteria.

Methods: Patients diagnosed as having CFS, FM, and TMD by their physicians were recruited from hospital-based clinics. Healthy control subjects from a dermatology clinic were enrolled as a comparison group. All subjects completed a 138-item symptom checklist and underwent a brief physical examination performed by the project physicians.

Results: With little exception, patients reported few past diagnoses of the 10 clinical conditions beyond their referring diagnosis of CFS, FM, or TMD. In contrast, patients were more likely than controls to meet lifetime symptom and diagnostic criteria for many of the conditions, including CFS, FM, irritable bowel syndrome, multiple chemical sensitivities, and headache. Lifetime rates of irritable bowel syndrome were particularly striking in the patient groups (CFS, 92%; FM, 77%; TMD, 64%) compared with controls (18%) (P < .001). Individual symptom analysis revealed that patients with CFS, FM, and TMD share common symptoms, including generalized pain sensitivity, sleep and concentration difficulties, bowel complaints, and headache. However, several symptoms also distinguished the patient groups.

Conclusions: This study provides preliminary evidence that patients with CFS, FM, and TMD share key symptoms. It also is apparent that other localized and systemic conditions may frequently co-occur with CFS, FM, and TMD. Future research that seeks to identify the temporal relationships and other pathophysiologic mechanism(s) linking CFS, FM, and TMD will likely advance our understanding and treatment of these chronic, recurrent conditions.

Arch Intern Med. 2000;160:221-227
SUBJECTS AND METHODS

SUBJECTS AND SETTING

The sample consisted of 25 patients with CFS, 22 patients with FM, 25 patients with TMD, and 22 healthy control subjects. All subjects were new or established patients recruited from hospital-based clinics affiliated with the University of Washington and Pacific Medical Center in Seattle between January 1993 and September 1994. Patients with CFS were attending the Chronic Fatigue Clinic, a tertiary care referral practice. Patients with FM and TMD were seeking care at an academic rheumatology and oral medicine clinic, respectively. Control subjects included individuals from 2 dermatology clinics who were being evaluated for conditions other than CFS, FM, or TMD. Control subjects were healthy (ie, without major, chronic medical problems) and were typically being seen for minor, non-systemic, skin conditions (eg, warts).

In each of the clinics, a single, designated participating physician was asked to approach patients diagnosed as having CFS, FM, or TMD. In the case of the control subjects, the physician selected only patients who were healthy with the exception of their dermatologic condition. Treating physicians were well-versed in the application of published research criteria for the 3 conditions under study. Patients with CFS were diagnosed using the 1988 Centers for Disease Control case definition and a tender point sites as described by the American College of Rheumatology; and manual palpation of the 18 mandibular, anterior cervical, posterior cervical, and axillary lymphadenopathy; and chronic pelvic pain, and chronic low back pain. Characteristic symptoms were derived from 2 additional sources: (1) consultations with university faculty who had established expertise in the diagnosis and treatment of a given disorder ("experts"), and (2) searches of the extant literature for characteristic symptoms. Thus, the final items compiled for each disorder in the symptom checklist included both criteria-based symptoms and well-recognized features used in clinical practice in the diagnosis of the study conditions. Prior to the administration to subjects, the questions contained in the checklist for each individual disorder were approved by the appropriate expert.

To score the symptom checklist, the total number of symptoms endorsed for each syndrome were summed to obtain a subject's score for the relevant clinical condition. This score was intended to approximate the degree to which subjects reported characteristics of a particular syndrome as determined by our experts. All reported diagnoses and symptoms represent lifetime occurrence rates.

Finally, we were interested in common and distinguishing symptoms among the patient groups. "Common symptoms" were those for which there was both a clinical (defined as >25% difference in frequency) and a statistically significant (P ≤ .01) difference between the CFS, FM, TMD patient groups and controls. To be designated as a "distinguishing symptom," the symptom must have differentiated the specified group(s) of interest from the other(s) by these same criteria. For example, a distinguishing symptom of TMD was considered to differentiate patients with TMD from those with CFS, those with FM, and controls if a greater than 25% difference in frequency and P ≤ .01 statistical difference existed between the TMD group and each of the other groups' mean scores on that symptom.

DATA COLLECTION

Subjects were approached to participate in the study during routine clinic visits or by mailed letters to patients deemed eligible by the designated clinic physician. Information was gathered from interested subjects at their convenience, either following a regularly scheduled appointment or during a separate study appointment scheduled at another time. Patients who were unable to complete the lengthy questionnaire at the time of the study evaluation were asked to complete it at home and mail it to the investigators. After describing the study and obtaining informed consent, all patients underwent a physical examination by a physician (M.M.B. or D.B.) and completed a 138-item symptom checklist. The physical examination included an assessment of pharyngeal inflammation; submandibular, anterior cervical, posterior cervical, and axillary lymphadenopathy; and manual palpation of the 18 tender point sites as described by the American College of Rheumatology.

The symptom checklist included 138 items assessing demographic and clinical information (eg, age, education, sex, and duration of illness) as well as self-report of previous diagnoses and the presence of relevant symptoms of the following 10 overlapping conditions: CFS, TMD, FM, chronic tension-type headache, IBS, interstitial cystitis, post-concussive syndrome, multiple chemical sensitivities, chronic pelvic pain, and chronic low back pain. For the self-reported overlapping conditions, subjects were asked "Have you ever been told by a health care provider that you have . . . .". Symptoms for the 10 conditions of interest were derived from several sources. For CFS, FM, IBS, and chronic tension-type headache we used published criteria. For TMD, interstitial cystitis, post-concussive syndrome, multiple chemical sensitivities, chronic pelvic pain, and chronic low back pain, characteristic symptoms were derived from 2 additional sources: (1) consultations with university faculty who had established expertise in the diagnosis and treatment of a given disorder ("experts"), and (2) searches of the extant literature for characteristic symptoms. Thus, the final items compiled for each disorder in the symptom checklist included both criteria-based symptoms and well-recognized features used in clinical practice in the diagnosis of the study conditions. Prior to the administration to subjects, the questions contained in the checklist for each individual disorder were approved by the appropriate expert.

STATISTICAL ANALYSES

We used χ² analyses to compare the 4 groups (CFS, FM, TMD, controls) on all dichotomous variables. In the event of significant overall group differences, individual χ² analyses then assessed associations between patient status (CFS, FM, TMD) and controls on the dichotomous variable. Next, a series of 1-way analyses of covariance controlling for age and sex were performed for the summation of scores from each of the continuous ("expert-based") variables. When overall effects or trends were detected (P ≤ .05), each patient group was compared with control subjects in follow-up univariate analyses (1-tailed). All P values are shown in the tables. However, to decrease the likelihood of a type I error, only P values of .01 or less are considered significant; values of P ≤ .05 are described as trends.
TMD with other clinical conditions such as IBS, chronic headache, interstitial cystitis, multiple chemical sensitivities, and others have been systematically studied. For example, investigations using standardized criteria have reported 42% to 70% of patients with FM concurrently met criteria for IBS compared with only 10% to 16% of healthy control subjects.

No previous study has examined the co-occurrence of a comprehensive array of overlapping symptoms and conditions among patients diagnosed as having CFS, FM, or TMD. We hypothesized that, given the similarities between CFS, FM, and TMD, symptoms consistent with overlapping conditions such as IBS and interstitial cystitis and others would likewise be commonly observed. We therefore compared these 3 patient groups with a healthy control group with respect to these questions: (1) Do patients with CFS, FM, or TMD more often receive diagnoses of other overlapping conditions? (2) Do patients with CFS, FM, or TMD more frequently report the symptoms characteristic of 10 overlapping conditions than healthy persons? (3) Which symptoms do the CFS, FM, and TMD patient groups share and which distinguish the groups from each other? and (4) If published case definitions for CFS, multiple chemical sensitivities, chronic tension-type headache, and which distinguish the groups from each other?

TMD, chronic tension-type headache, and chronic low back pain); patients with FM reported symptoms consistent with 7 conditions (CFS, FM, IBS, interstitial cystitis, multiple chemical sensitivities, chronic tension-type headache. Of interest is the variability in the pattern of overlapping diagnoses. For instance, although only 18% of patients with FM had been diagnosed with CFS, 80% of those with chronic tension-type headache reported a diagnosis of FM. Patients with TMD more frequently had a history of chronic tension-type headache compared with control subjects. Overall, relatively few patients had histories of interstitial cystitis, post–concussive syndrome, or chronic pelvic pain.

Table 2 shows the mean number of expert-based symptoms for each clinical condition by group status. All patients reported significantly more symptoms consistent with CFS, FM, IBS, and chronic tension-type headache compared with control subjects, even after controlling for the effects of age and sex. Interestingly, patients with CFS were no more likely to control subjects to endorse symptoms characteristic of TMD, although patients with FM tended to report a greater number of the features characteristic of TMD. In striking comparison with the infrequent physician diagnosis of multiple chemical sensitivity syndrome observed in Table 1, Table 2 shows that patients with CFS, FM, and TMD all tended to have more symptoms of multiple chemical sensitivity compared with control subjects. In total, patients with CFS exhibited significantly more symptoms than controls for 5 conditions (CFS, FM, IBS, multiple chemical sensitivities, and chronic tension-type headache); patients with FM reported symptoms consistent with 7 conditions (CFS, FM, IBS, interstitial cystitis, multiple chemical sensitivities, chronic tension-type headache, and chronic low back pain); and patients with TMD reported more symptoms than controls for 5, including TMD, of the conditions (CFS, FM, IBS, and chronic tension-type headache). Patient groups did not differ from the control group with regard to the frequencies for post–concussive syndrome or chronic pelvic pain.

Table 1. Self-reported Diagnoses by Group Status*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. (%) of Subjects</th>
<th>CFS</th>
<th>FM</th>
<th>TMD</th>
<th>Controls</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFS</td>
<td>25 (100)</td>
<td>4 (18)</td>
<td>0</td>
<td>0</td>
<td>&lt;.001†‖</td>
<td></td>
</tr>
<tr>
<td>FM</td>
<td>20 (80)</td>
<td>22 (100)</td>
<td>2 (9)</td>
<td>0</td>
<td>&lt;.001§§</td>
<td></td>
</tr>
<tr>
<td>TMD</td>
<td>7 (28)</td>
<td>5 (24)</td>
<td>21 (88)</td>
<td>3 (14)</td>
<td>&lt;.001¶¶</td>
<td></td>
</tr>
<tr>
<td>IBS</td>
<td>9 (36)</td>
<td>13 (59)</td>
<td>4 (16)</td>
<td>0</td>
<td>&lt;.001§§</td>
<td></td>
</tr>
<tr>
<td>Interstitial cystitis</td>
<td>2 (8)</td>
<td>2 (8)</td>
<td>4 (17)</td>
<td>0</td>
<td>.22</td>
<td></td>
</tr>
<tr>
<td>Post-concussive syndrome</td>
<td>2 (8)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>.13</td>
<td></td>
</tr>
<tr>
<td>Multiple chemical sensitivities</td>
<td>1 (4)</td>
<td>4 (18)</td>
<td>0</td>
<td>0</td>
<td>.02†</td>
<td></td>
</tr>
<tr>
<td>Chronic tension-type headache</td>
<td>1 (4)</td>
<td>5 (23)</td>
<td>9 (36)</td>
<td>0</td>
<td>.002‡</td>
<td></td>
</tr>
<tr>
<td>Chronic pelvic pain</td>
<td>2 (8)</td>
<td>4 (18)</td>
<td>2 (8)</td>
<td>0</td>
<td>.21</td>
<td></td>
</tr>
<tr>
<td>Chronic low back pain</td>
<td>8 (32)</td>
<td>14 (67)</td>
<td>4 (16)</td>
<td>4 (18)</td>
<td>&lt;.001§</td>
<td></td>
</tr>
</tbody>
</table>

*Total number of subjects in each group may vary due to missing values. CFS indicates chronic fatigue syndrome; FM, fibromyalgia; TMD, temporomandibular disorder; and IBS, irritable bowel syndrome.
†CFS > controls, P = .01.
‡FM > controls, P = .05.
§FM > controls, P = .01.
¶TMD > controls, P = .15.
‖TMD > controls, P = .05.

Patients with FM were significantly older than those with TMD (48.5 vs 38.0 years; P = .01). The CFS, FM, TMD, and control groups did not differ with respect to sex (range, 73%-96% female; P = .06) or educational level (most having attended college, P = .18). Moreover, the patient groups were not different with respect to duration of illness (FM, 8.2 years; CFS, 4.3 years; and TMD, 8.1 years; P = .15).

Table 1 compares the percentage of subjects in each group who reported a prior diagnosis made by a health care provider for the 10 clinical conditions. Compared with control subjects, patients with CFS received diagnoses of CFS, FM, and IBS significantly more often. Patients with FM were significantly more likely to report diagnoses of FM, IBS, and chronic low back pain. They also tended to report diagnoses of CFS, multiple chemical sensitivities, and chronic tension-type headache. Of interest is the variability in the pattern of overlapping diagnoses. For instance, although only 18% of patients with FM had been diagnosed with CFS, 80% of those with chronic tension-type headache had received a diagnosis of FM. Patients with TMD more frequently had a history of chronic tension-type headache compared with control subjects. Overall, relatively few patients had histories of interstitial cystitis, post–concussive syndrome, or chronic pelvic pain.
characteristic of migraine-type headaches. In a typical headache, symptoms that are considered more endorserance of both sensitivity to lights and noise during patients for failing to meet the research criteria was the most common reason among the CFS, FM, and TMD patients for failing to meet the Research Diagnostic Criteria for CFS, FM, and TMD patients included those characteristic of CFS, FM, and IBS. Especially prominent among these were muscle and abdominal pain and sleep and concentration difficulties. Patients with CFS and FM were distinguished from patients with TMD and control subjects by symptoms of fatigue, joint aches, and burning or shooting muscle pain. Unique features for CFS included fever or sore throat; for FM, a more frequent history of low back pain that was made better by heat or massage and was exacerbated with sitting or standing; and patients with TMD were best distinguished by a history of facial ache or pain in jaw muscles or joints.

Table 3 presents the percentage of subjects in each group who met Research Diagnostic Criteria for CFS, FM, IBS, and chronic tension-type headache. Not surprisingly, patients with CFS and FM were significantly more likely than control subjects to meet stringent criteria for their respective disorders. A greater percentage of patients with TMD also tended to meet criteria for CFS (20%) and FM (13%) compared with healthy subjects, none of whom met criteria for these diagnoses. Most striking, the large majority of all patients met lifetime criteria for IBS according to the Manning criteria, in contrast to only 18% of controls (all P values ≤.001). There were no significant differences among the groups with respect to percentage of subjects meeting the 1988 International Headache Society definition for chronic tension-type headache. The most common reason among the CFS, FM, and TMD patients for failing to meet the research criteria was the endorsement of both sensitivity to lights and noise during a typical headache, symptoms that are considered more characteristic of migraine-type headaches.

Table 4 displays both common and distinguishing individual symptoms derived from 138 items contained on the symptom checklist encompassing the 10 conditions. Consistent with the results shown in Table 2, symptoms common to CFS, FM, and TMD patients included those characteristic of CFS, FM, and IBS. Especially prominent among these were muscle and abdominal pain and sleep and concentration difficulties. Patients with CFS and FM were distinguished from patients with TMD and control subjects by symptoms of fatigue, joint aches, and burning or shooting muscle pain. Unique features for CFS included fever or sore throat; for FM, a more frequent history of low back pain that was made better by heat or massage and was exacerbated with sitting or standing; and patients with TMD were best distinguished by a history of facial ache or pain in jaw muscles or joints.

Finally, differences were found in the mean number of tender points on the physical examination among control subjects (0.9) compared with patients with CFS (7.4, P <.001), FM (11.0, P <.001), and TMD (5.2, P =.001). Patients with FM also were found to have more tender points than either CFS or TMD patients (both P ≤.001). However, patient groups did not differ from the control group with respect to the total number of swollen and/or tender lymph nodes present on physical examination (P values, .18-.78).
In this study we assessed the degree of overlap of 10 clinical conditions among patients with CFS, FM, and TMD, and healthy control subjects using several complementary approaches. We examined the lifetime occurrence of each syndrome as diagnosed by a health care provider, as well as patients' endorsement of individual symptoms comprising these conditions as determined by experts in the field and the existing literature. Published diagnostic criteria were also applied for a subset of overlapping conditions. Finally, symptoms common to CFS, FM, and TMD, as well as those that distinguish them from each other were described. With the exception of TMD, interstitial cystitis, post–concussive syndrome, and chronic pelvic pain, all patient-reported health care provider diagnoses were more commonly reported by CFS and FM patients compared with controls. Differences between patients with TMD and controls were less striking. In contrast, using the symptom checklist, patients in the 3 groups generally scored much higher than healthy control subjects with regard to the total number of symptoms comprising each condition. Application of the published case definitions yielded similar findings. Thus, by investigating the clinical syndromes from a variety of perspectives, differences in the types of information obtained, discrepancies, probable missed diagnoses, and variable rates of illness could be observed.

In the case of CFS, 80% of patients reported a history of clinician-diagnosed FM, the FM symptom score was high, yet on examination only 20% met American College of Rheumatology criteria for FM. An opposite trend was observed for IBS, multiple chemical sensitivities, post–concussive syndrome, and chronic tension-type headaches in relation to CFS where we found low rates of clinician diagnoses and moderate symptom scores. When published criteria were applied, the apparent rate of missed diagnoses was relatively high for IBS (92%) and chronic tension-type headaches (12%) among patients with CFS. A similar situation existed for FM with respect to these disorders. However, in contrast to patients with CFS and concurrent FM, only 18% of FM patients carried a diagnosis of CFS, although 64% actually met the Centers for Disease Control criteria. These findings are surprising given the substantial overlap between CFS and FM in studies that have used both symptom-based and diagnostic criteria for the disorders.5,7 The reason for discrepancies in rates of clinician diagnoses and symptom reporting compared with the application of diagnostic criteria is unclear. Explanations might include the requirement of tender points in the FM case definition vs the symptom-based criteria for CFS, and clinicians' tendency to focus on particular conditions depending on the presenting symptom(s) and/or familiarity with alternative conditions.

Among patients with TMD, 0% and 9% had received a health care provider diagnosis of CFS and FM, respectively. Nevertheless, patients with TMD had many symptoms in common with CFS and FM, such as muscle pain, sleep problems, difficulty concentrating, and debilitating headaches. Thirteen percent of our TMD patients satisfied the American College of Rheumatology criteria for FM, which is comparable to the rate of 18% recently reported.7 The mean number of tender points for patients...
with TMD found in this study also was similar to previ- 
ously published values (5.2 vs 6.3). In comparing our re-
sults with epidemiological data on pain, it is interesting
to note that these values approximate the number of ten-
der points found in community residents with wide-
spread pain (6.2). Although TMD is believed to rep- 
resent a localized pain syndrome, this relatively high number of
tender points suggests that TMD may represent one manifes-
tation of a more global pain sensitivity disorder.

Regardless of the method of inquiry, the lifetime rate of IBS was common in the 3 patient groups relative to con-
trol subjects. In the medical literature, IBS has most fre-
quently been reported to co-occur with FM. In the pre-
sent study, however, patients with CFS and TMD also were more likely than control subjects to report a previous di-
agnosis of IBS, meet diagnostic criteria for IBS, and expe-
rience IBS-related symptoms. The rates of IBS among pa-
tients with CFS, FM, and TMD (92%, 77%, and 64%, re-
spectively) were well above the frequency both in our con-
trol group (18%) and in the general population (9%- 
21%) as estimated using the Manning criteria. The only study examining the overlap of IBS and chronic fatigue used identical standard diagnostic criteria and similarly re-
ported a high prevalence of IBS among patients with chronic fatigue over a 1-year retrospective evaluation period (73%). It should be noted that the prevalence of IBS in community surveys is typically assessed using a 3-month 
time frame, whereas this study ascertained lifetime preva-
ience. However, when we examined whether subjects cur-
rently met criteria for IBS (ie, >2 Manning symptoms en-
dorsed on the day of questionnaire completion), we also found significantly higher rates of IBS among patients (17%- 
40%) compared with control subjects (5%). Thus, while IBS is certainly common in the general population, our pa-
tient groups were disproportionately affected with IBS. 
These results suggest that a common pathogenic mecha-
nism related to bowel dysfunction may underlie CFS, FM, 
and TMD disorders. In this regard, some investigators have specu-
lated that the serotonin abnormalities observed in patients with FM may be the result of defective absorp-
tion of the precursor amino acid tryptophan from the gut.

The rates of several other clinical conditions of in-
terest were found to occur more frequently in the 3 pa-
tient groups. Patients with FM had a significantly greater number of symptoms characteristic of interstitial cystitis compared with patients with CFS or TMD or control sub-
jects but were no more likely to report a past diagnosis of 
this disorder than any other group. These results are con-
sistent with a survey of 2682 patients with interstitial cysti-
tis, 25% of whom reported having comorbid FM. Additional support for clinical similarities comes from a recent study demonstrating that patients with interstitial cysti-
tis and patients with FM were more similar to each other 
than to controls with regard to decreased pain thresholds 
and comparability of symptoms. Few patients in the pre-
sent study reported a past diagnosis of multiple chemical 
sensitivity syndrome, although their symptom checklist 
scores were high for this diagnosis. Previous studies have 
indicated that 55% of patients with FM reported symp-
toms consistent with multiple chemical sensitivities and 
30% of patients with multiple chemical sensitivities met the Centers for Disease Control criteria for CFS. To our

Collectively, the findings of this study provide addi-
tional evidence that patients with CFS, FM, and TMD share 
symptoms including generalized pain sensitivity, sleep and 
concentration difficulties, and bowel complaints. It also is 
apparent that other localized and systemic conditions, par-
ticularly IBS, interstitial cystitis, and multiple chemical sen-
sitivities may frequently co-occur with CFS, FM, and TMD. 
Although this study was not designed to assess either the 
temporal relationships among these conditions or poten-
tial mechanism(s) that link them, these are among the most 
intriguing questions that arise. In this regard, prospective 
studies that examine the onset of these disorders could im-
prove our understanding of the underlying pathophys-
iological mechanisms. For example, a localized injury might 
trigger a sensitization of the central nervous system to af-
ferent pain signals leading to decreased pain thresholds at 
other body sites. A similar process, known as neurogenic 
inflammation, occurs when an exogenous agent combines 
with chemical irritant receptors on sensory nerves, and the subsequent release of inflammatory neuropep-
tides sensitizes local and central structures.

While such mechanisms have been proposed to account 
for the development of both multiple chemical sensitivities 
and FM, they cannot alone account for illness in patients 
whose onset did not follow a physical injury or chemical ex-
posure. Indeed, many patients report a gradual onset, on-
set in conjunction with acute or chronic emotionally stress-
ful events, or a combination of physical and emotional events 
that appear to have precipitated their illness. These events 
may initiate perturbations in the hypothalamic-pituitary-
adrenal axis and the autonomic system and result in sensi-
tization of the central nervous system via neuropeptides, 
ultimately altering the processing of nociceptive signals as has 
been suggested in the case of FM. However, such theories 
as applied to the development of other related conditions 
require further testing as key differences in hypothalamic-
pituitary-adrenal axis and neuromodulatory functioning have 
been reported only for CFS and FM. In light of the pre-
sent study’s findings, it may be important in future studies 
investigating underlying pathophysiological mechanisms to 
identify patients who also meet criteria for comorbid related 
conditions and to either screen them out or subgroup pa-
tients with similar comorbidities. Otherwise, shared vs dis-
similar pathophysiological features among these conditions 
may be obscured due to illness confounding.

The present study has several limitations. First, we re-
lied on physician referrals for the identification of sub-
jects. Thus, we did not independently confirm the diag-
noses of FM and TMD prior to study participation (eg, TMD 
requires a specialized examination) nor were subjects guar-
anteed to meet criteria on the day of the study examina-
tion. This methodological point likely explains why only 
77% of previously diagnosed FM patients fulfilled the case 
definition upon enrollment. Second, we relied on the sub-
jects’ self-report of previous diagnoses of overlapping con-
ditions and did not confirm these with review of medical 
records. However, in most cases, the frequency of past di-
agnoses were lower than one might expect given the scores 
on the symptom checklist, consistent with underdiagno-
ses of these illnesses. Third, the nonblinded methodology
of the physical examinations might have influenced the examiner's findings. However, the examination represented only a small portion of the overall data presented. Fourth, the results from this study may not be generalizable to patients with CFS, FM, and TMD who do not seek treatment for their disorder as persons with multiple comorbidities may be overrepresented in tertiary care clinics. Last, our study design relied primarily on patients' subjective complaints and not on objective clinical or laboratory findings, which, for the most part, are not yet available for the conditions of interest. Thus, as noted by others, this approach is heavily influenced by patients' perceptions and symptom appraisals rather than representing functional impairment or other more objective outcomes.32

In summary, we investigated the degree of overlap for a variety of conditions believed to commonly occur among patients with CFS, FM, and TMD in a case-control study. We found that patients were more likely than control subjects to meet lifetime symptom and/or diagnostic criteria for many of these conditions including CFS, FM, IBS, multiple chemical sensitivities, and chronic tension-type headache, among others. Given the association of CFS, FM, and TMD with poor functional status13,26,33 and psychiatric illness,2,7,27,34,35 future research should evaluate physical impairments, potential mechanisms, and psychiatric comorbidities among patients with overlapping conditions. In addition, clinical trials might examine whether systematically identifying and targeting comorbid conditions for treatment produces superior outcomes compared with usual care or to a more general type of intervention (eg, education, stress management). The evaluation of such interventions seems particularly important in light of recent findings demonstrating that higher health care costs and utilization were independently associated with the number of self-reported comorbid conditions in patients with FM,22 and patients diagnosed as having both CFS and FM were significantly more likely to be unemployed and to use more health care services than those with only one disorder.32

Accepted for publication April 8, 1999.

This study was supported in part by a Department of Veterans Affairs General Internal Medicine/Ambulatory Care Fellowship (Dr Burke) and grant U19 AI38429 from the National Institute of Allergy and Infectious Diseases, Bethesda, Md (Dr Buchwald).

We gratefully acknowledge the cooperation and contributions of the following individuals: Tamara G. Bavendam, MD, Richard Berger, MD, Richard Deyo, MD, Kelley Egan, PhD, Peter Esselman, MD, Bradley Galer, MD, Greg Gardner, MD, Mark P. Jensen, PhD, Eric Sasso, MD, Gregory Simon, MD, Edmond Truelove, DDS, MSD, and Richard Willson, MD.

Corresponding author: Leslie A. Aaron, PhD, MPH, Department of Medicine, Division of General Internal Medicine, Harborview Medical Center, 325 Ninth Ave, Box 359780, Seattle, WA 98104 (e-mail: laaron@u.washington.edu).

REFERENCES