Development and Validation of a Structured Diagnostic Interview for Functional Somatic Syndromes

Final Report

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SUMMARY

Medical specialists and primary care physicians are often presented with symptoms and syndromes that are 'functional'—that is, due to disturbances in function rather than biological structure. The three most common functional somatic syndromes (FSS) are fibromyalgia (chronic widespread musculoskeletal aches and pains and tenderness), irritable bowel (abdominal discomfort, distension and alteration of bowel habits), and chronic fatigue (easy fatigability and cognitive impairment). Health conditions such as fibromyalgia, irritable bowel and chronic fatigue often receive unclear or contradictory medical explanations. This puts patients in a social and psychological quandary that may lead to excessive illness worry, 'doctor-shopping,' use of non-conventional practitioners, increased social stigma and disability. Because diagnostic criteria have relied on extensive medical investigations to rule out organic disease, there are few studies of these conditions in the general population that adequately address their personal and social consequences. Recent refinements in the diagnostic criteria for fibromyalgia, irritable bowel and chronic fatigue make it possible to approximate the diagnosis of these syndromes on the basis of specific symptom clusters and a few simple physical signs. Further, evidence that these putatively discrete syndromes share many common features suggests the value of a common research approach.

In this research program, we developed a structured diagnostic interview for functional somatic syndromes (the DIFS) based on the consensual diagnostic criteria of recent international working groups. This interview was then tested against known groups of patients with fibromyalgia, irritable bowel and chronic fatigue syndromes from specialty clinics and private practices. Patients with each functional syndrome were matched with patients with a disease with similar symptomatology: rheumatoid arthritis, inflammatory bowel disease and multiple sclerosis, respectively. There was moderate diagnostic agreement between clinician and interview-based diagnoses (kappa = .37 to .58). The DIFS showed good specificity but low sensitivity to the functional somatic syndromes.

The sample collected to validate the DIFS also allowed us to study the co-occurrence, psychological characteristics and health impact of FSS. We found high levels of co-occurrence of the syndromes, ranging from 33% of irritable bowel patients and 53% of fibromyalgia patients to 89% of chronic fatigue patients meeting criteria for at least one other syndrome. Most clinicians did not recognize this high degree of syndrome co-occurrence in their patients.

To examine psychological characteristics and illness impact we compared patients grouped according to referral diagnosis. We also aggregated functional syndrome patients and non-functional syndrome patients into two groups for some comparisons. On a measure of the five-factor theory of personality, there were no differences between functional syndrome patients taken as a group and the aggregate control group. There was some tendency for fibromyalgia patients to score higher on Neuroticism. Functional syndrome patients (chronic fatigue syndrome patients in particular) had higher levels of hypochondriacal worry than other groups. There were few significant differences among groups in symptom attributional style. While fibromyalgia patients acknowledged emotional distress as an important contributor to their illness, chronic

fatigue patients tended to reject this explanation, emphasizing infectious and immune causes instead.

Functional syndromes were highly disabling and were associated with higher degrees of social and emotional distress-related disability compared to other illnesses. Chronic fatigue syndrome was associated with the highest levels of self-perceived burden on the family and social stigma. In general, compared to the non-functional disease groups, functional syndromes were associated with higher levels of help-seeking and utilization of both conventional and alternative health care. This high utilization was associated with lower rates of perception of care as helpful and practitioners as understanding. This pattern was especially marked for patients with chronic fatigue syndrome and suggested that patients may keep seeking help until they find someone who understands them and something that works. If so, then the high rates of utilization by functional somatic syndrome patients should not be interpreted as 'abnormal illness behaviour', excessive help-seeking or over-utilization of services but as a pragmatic search for an effective response to poorly understood and managed conditions.

The development of the Diagnostic Interview for Functional Syndromes (DIFS) will allow researchers to conduct community epidemiological studies to trace the evolution and social consequences of these disorders before and after they are labeled by practitioners. This will enable the study of health coping and stigmatization of non-validated illness. In the clinic, improved diagnosis of functional somatic syndromes and their early recognition may reduce needless laboratory investigations with their excess cost and risk of iatrogenic morbidity. Future epidemiological applications will include reliable estimates of the prevalence and co-occurrence of functional somatic syndromes in the community, estimates of their co-occurrence with psychiatric disorders and tracking of changes in the prevalence of these conditions over time.

RÉSUMÉ

Les médecins spécialistes ainsi que les médecins de soins de première ligne sont souvent confrontés à des symptômes et à des syndromes dits 'fonctionnels'- c'est à dire qui sont causés par un problème de fonctionnement plutôt que par un problème au niveau de la structure biologique. Les trois syndromes somatiques fonctionnels (SSF) les plus répandus sont la fibromyalgia (douleurs musculaires et squelettiques répandues et chroniques, et sensibilité), l'intestin irritable (inconfort abdominal, ballonnement et changement au niveau des selles) et la fatigue chronique (fatigue facile et détérioration cognitive). Des conditions telles que la fibromyalgia, l'intestin irritable et la fatigue chronique reçoivent fréquemment des explications médicales confuses ou contradictoires. Ceci met les patients dans une situation sociale et psychologique problématique qui peut engendrée des soucis associés à la maladie, un 'magasinage médical' accru, l'utilisation de spécialistes non traditionnels, une augmentation des stigma sociaux et de l'invalidité. Compte tenu du fait que les critères diagnostiques dépendent d'une investigation médicale approfondie afin d'éliminer les maladies de type organique, il existe très peu d'études de ces conditions dans la population générale qui examinent avec justesse les conséquences personnelles et sociales qui y sont rattachées. Les récentes améliorations au niveau des critères diagnostiques de la fibromyalgia, des intestins irritables et de la fatigue chronique rendent possible l'approximation du diagnostic de ces syndromes en se basant sur des regroupements de symptômes spécifiques et sur quelques signes physiques particuliers. De plus, la preuve que ces supposés syndromes indépendants aient plusieurs choses en commun suggèrent l'utilisation d'une méthode de recherche commune.

Dans le cadre de ce projet de recherche, nous avons développé une Entrevue Diagnostique Structurée pour les Syndromes Somatiques Fonctionnels (le EDSS) basée sur des critères diagnostiques faisant l'unanimité de groupes de travail internationaux. Cette entrevue fut alors testée auprès de groupes de patients connus comme souffrant de fibromyalgia, d'intestin irritable et de fatigue chronique, provenant de cliniques spécialisées et de pratiques privées. Des patients souffrant de chacun des syndromes ont été appariés à des patients souffrant d'une symptomatologie similaire: arthrite rhumatoïde, maladie inflammatoire de l'intestin et sclérose en plaques, respectivement. L'entente entre le diagnostic des cliniciens et le diagnostic basé sur l'entrevue est moyenne (kappa=.37 à .58). Le EDSS a démontré une bonne spécificité mais une sensibilité basse aux syndromes somatiques fonctionnels.

L'échantillonnage afin de valider le EDDS nous permet également d'étudier la cooccurrence, les caractéristiques personnelles et l'impact sur la santé associés aux SSF. Nous avons trouvé une niveau élevé de cooccurrence des syndromes, variant de 33% des patients souffrant d'intestin irritable et 53% des patients souffrant de fibromyalgia à 89% des patients souffrant de fatigue chronique satisfaisaient les critères d'au moins un autre syndrome. La plupart des cliniciens n'ont pas reconnu le degré élevé de cooccurrence chez leurs patients.

Afin d'examiner les caractéristiques psychologiques et l'impact de la maladie, nous avons comparé les patients regroupés selon le diagnostic au moment de la référence. Nous avons également comparé tous les patients souffrant d'un syndrome à tous ceux

ne souffrant pas d'un syndrome. Les résultats de l'échelle de la personnalité basée sur la théorie des cinq facteurs indiquent aucunes différences entre les syndromes somatiques fonctionnels et les groupes contrôles. Seuls les patients souffrant de Fibromyalgia ont tendance à obtenir un score supérieur sur l'échelle de "*Neuroticism.*" Les patients souffrant de syndromes fonctionnels (et plus particulièrement ceux souffrant de fatigue chronique) ont un taux supérieur de soucis d'ordre hypochon-driaque comparativement aux autres groupes. Il y a quelques différences significatives entre les groupes au niveau du style d'attribution des symptômes. Les patients souffrant de Fibromyalgia ont reconnu la détresse émotionnelle comme ayant contribué de façon importante à la maladie, tandis que les patients souffrant de fatigue chronique ont rejeté cette explication, mettant plutôt l'emphase sur les infections et sur des causes immunitaires.

Les syndromes fonctionnels sont la cause d'une grande incapacité et sont associés à des degrés supérieurs de détresse sociale et émotionnelle et ce, comparativement aux autres groupes. Le syndrome de fatigue chronique est associé au taux le plus élevé de fardeau sur la famille perçu par le patient et de stigma sociaux. En général, comparativement aux groupes souffrant de troubles non fonctionnels, les syndromes fonctionnels sont associés à un taux supérieur de consultation et d'utilisation des soins de santé à la fois traditionnels et alternatifs. Ce taux élevé d'utilisation est associé à un taux inférieur de perception des soins comme étant utiles et des praticiens comme étant compréhensifs. Ceci est particulièrement marqué chez les patients souffrant du syndrome de fatigue chronique et suggère que les patients persistent à chercher de l'aide jusqu'à ce qu'ils trouvent quelqu'un qui les comprennent et quelque chose qui fonctionne. Si ceci est le cas, le taux élevé de consultations observé chez les patients souffrant de syndromes fonctionnels ne devrait pas être interprété comme un "*abnormal illness behaviour*", comme une recherche excessive d'aide ou comme une surutilisation des services de santé, mais plutôt comme une recherche pragmatique d'une réponse efficace à des conditions incomprises et mal diagnostiquées.

Le développement de l'Entrevue Diagnostique Structurée pour les Syndromes Somatiques Fonctionnels (EDSS) permettra aux chercheurs d'entreprendre des études épidémiologiques communautaires afin de retracer l'évolution et les conséquences sociales de ces troubles avant et après que ceux-ci soient catégorisés par les praticiens. Ceci contribuera à aider l'étude des mécanismes de coping et de stigmatisation des maladies non validées. En clinique, un meilleur diagnostique des syndromes somatiques fonctionnels et une identification plus rapide de ceux-ci peuvent éviter des investigations inutiles et coûteuses en laboratoire et tout ce qui en découle. Les applications épidémiologiques futures incluront un estimé digne de confiance de la prédominance et de la cooccurrence des syndromes somatiques fonctionnels dans la communauté, un estimé de leur cooccurrence avec des troubles psychiatriques et une façon de suivre l'évolution des changements dans la prédominance de ces conditions aux cours des années.

1. INTRODUCTION

This report concerns the development of a structured interview to approximate the clinical diagnosis of three common functional somatic syndromes (FSS): fibromyalgia, irritable bowel and chronic fatigue. In ordinary clinical practice, functional symptoms and syndromes are often diagnoses of exclusion—made only after physical examination and laboratory tests have ruled out organic disease. However, recent clarification of the diagnostic features of some common FSS suggest that it might be possible to approximate the clinical diagnosis through patient reports of specific symptom clusters.

Using the NIMH Diagnostic Interview Schedule as a conceptual model, we designed an instrument to be administered by lay interviewers. This new instrument was then validated against known groups drawn from specialty medical clinics. In the course of validation we also collected data which allowed us to study the co-occurrence of distinct FSS as well as some of their social and psychological correlates and relationship to patterns of health care utilization, disability and self-perceived stigmatization.

Specifically, in this study our goals were to:

1. Develop a structured diagnostic interview for functional somatic syndromes based on a comprehensive review of literature and expert opinion;

2. Validate the instrument against known clinical groups diagnosed by expert clinicians according to contemporary standards of care;

3. Determine the overlap or co-occurrence of these syndromes in selected clinical samples drawn from specialty medical practices;

4. Compare the psychological and social characteristics of patients with FSS to matched groups of patients with corresponding medical diseases with definite diagnoses and known pathobiology.

Functional somatic syndromes, including fibromyalgia syndrome (FMS), irritable bowel syndrome (IBS) and chronic fatigue syndrome (CFS) are common and costly health care problems (Cathey et al., 1986; Sandler, 1990; Wessely, 1990). While these syndromes are viewed as discrete conditions by the medical specialties that treat them, there is increasing evidence for a high degree of overlap in symptomatology, suggesting the value of a unified research approach (Kirmayer & Robbins, 1991a). Data on clinic-based samples and community surveys of symptomatology suggest the great burden of these conditions, yet few studies provide accurate estimates of their prevalence in the general population, examine their co-occurrence or address their personal and social consequences. We selected these three conditions from among myriad FSS as those likely to be of greatest public health concern because of their high prevalence and associated disability and because of recent improvements in their diagnostic criteria. These new diagnostic criteria make it possible for the first time to approximate the diagnosis of these syndromes on the basis of specific symptoms and a few simple physical signs without the need for extensive investigations to rule out organic disease (Holmes et al., 1988; Thompson et al., 1989; Wolfe et al., 1990).

FSS are poorly understood and diagnostic practices vary widely; many sufferers of FSS receive unclear or contradictory diagnoses and ineffective treatments. The ambiguity of their condition may lead to increased illness worry, doctor-shopping, use of alternative health care practitioners and ultimately to disability (Escobar et al., 1987; Verhoef et al., 1990). Lack of validation of their illness by physicians may lead to increased social stigma as friends and relatives come to doubt the reality of their affliction (Lennon et al., 1989). As well, repeated unsatisfactory responses from their physicians may lead FSS sufferers to believe that they are somehow personally responsible for their condition and/or make them more likely to seek additional care (Kirmayer, 1988). These research issues were addressed with questions on personality, cognitive and social factors in illness, disability, self-perceived burden on family and social stigma.

To advance the study of FSS, we used the NIMH Diagnostic Interview Schedule structured interview (DIS; Robins et al., 1991) format as a model to produce a new instrument that can approximate diagnoses of the common FSS. This instrument can diagnose current and lifetime FMS, IBS, CFS and incorporates measures of hypochondriacal worry, negative affectivity, symptom attribution, perception and management of social stigma, utilization of biomedical and alternative health care, disability and uncertainty about the diagnosis. These measures enabled us to examine some psychological and social correlates of FSS and their impact.

2. REVIEW OF LITERATURE

Patients with physical symptoms unexplained by organic disease are common in medical practice. Many of these symptoms may be due to disorders of physiological regulation without structural lesions. Such symptoms are commonly termed "functional"—that is, due to a disturbance in function rather than structure (Kellner, 1985). It is commonly assumed that psychosocial stress or emotional distress provoke functional somatic symptoms (Kirmayer & Robbins, 1991a). Whether or not they are causal factors in the genesis of FSS, it is likely that psychological factors can exacerbate FSS and affect individuals' ability to cope with symptoms.

Functional somatic syndromes (FSS) are clusters of regularly co-occurring functional symptoms. In clinical practice, FSS have been defined largely on the basis of exclusion making it necessary to conduct extensive investigations to rule out organic disease. Current research suggests the value of defining these syndromes descriptively as distinctive clusters of symptoms which may occur independently or in concert with organic disease (Talley et al., 1990; Wessely, 1990; Wolfe et al., 1990). In the sections below we review the symptomatology, current diagnostic criteria, evidence for co-occurrence and psychosocial correlates of three of the most common functional somatic syndromes: fibromyalgia, irritable bowel and chronic fatigue syndromes.

2.1 Fibromyalgia Syndrome (FMS)

Fibromyalgia or fibrositis is a syndrome of chronic musculoskeletal pains and stiffness of unknown etiology (Bennett, 1987). While patients with FMS may present with either localized or diffuse muscular pain, history and physical examination reveal multiple sites of pain. In an effort to characterize fibromyalgia as a distinct syndrome, rheumatologists have emphasized the presence of acute sensitivity to pressure over specific anatomical locations, termed tender points (Smythe, 1986). Variant diagnostic criteria have been proposed that differ chiefly in the number of tender points they require and in the significance of associated symptoms (Wolfe et al., 1985; Yunus et al., 1981). A recent intensive multicenter study of diagnostic criteria by the American College of Rheumatology evaluated many alternate sets of criteria and derived consensus criteria that discriminated well between FMS patients and other rheumatologic patients at 16 different clinics (Wolfe et al., 1985). The proposed criteria require: (1) a history of widespread musculoskeletal pain; (2) pain in 11 of 18 tender point sites on digital palpation. These criteria yielded a sensitivity of 88% and a specificity of 81% measured against rheumatologists' standard diagnostic practice as a gold standard. There was no difference in symptomatology between primary fibromyalgia (without accompanying organic illness) and secondary fibromyalgia (attributed to a pre-existing rheumatologic or systemic condition, e.g. rheumatoid arthritis, RA). The committee therefore suggested abolishing the distinction. Further, with these criteria, exclusionary tests for organic disease are not necessary to make a positive diagnosis of FMS. The criteria lend themselves to a two-stage method of diagnosis for epidemiological screening: only patients with a history of widespread musculoskeletal pain need be tested for tender points. Using this method in a rheumatology clinic setting only, 1.7% of patients who meet the tender point criterion would be misclassified by the generalized pain criterion (Wolfe et al., 1985: 171). There was no increase in diagnostic accuracy with the use of a

pressure dolorimeter provided examiners were instructed to apply adequate digital pressure at tender point sites (> 4 kg) and to count only actual pain responses.

2.1.1 *Prevalence and Comorbidity*

Fibromyalgia is the third most common disorder in rheumatologic practice following osteoarthritis and rheumatoid arthritis (RA). In a sample of all patients (N= 1,473) seen in a private rheumatic disease clinic over a two and one half year period, Wolfe and Cathey (1983) found a prevalence of 3.7% for primary FMS and 12.2% for FMS secondary to other rheumatologic conditions. FMS symptoms are also common, though under-recognized, in primary care with an estimated prevalence of 6% (Campbell et al., 1983). There are no reliable estimates of the prevalence of FMS in the community.

FMS patients report associated symptoms of fatigue, sleep disturbance (non-restorative sleep), headache, and irritable bowel syndrome and some authors include these as diagnostic criteria (Wolfe, 1986; Yunus et al., 1981). A recent study reported a high incidence of symptoms of chronic fatigue syndrome (recurrent sore throat, rash, cough, adenopathy, and low-grade fevers) among FMS patients (Buchwald, Sullivan & Komaroff, 1987).

2.1.2 *Psychopathology*

Dysphoric mood is common among FMS patients (Clark et al., 1985; Goldenberg, 1986; Wolfe, 1986). While one study reported a high frequency of major depression among FMS patients (Hudson et al., 1985), others have not confirmed this finding (Ahles et al., 1987; 1991; Kirmayer, Robbins & Kapusta, 1988). FMS patients in our earlier study were, however, much more likely to report multiple somatic symptoms across all bodily systems that could not be explained by medical investigation. Of the 40 symptoms in the DIS used to diagnose DSM-III somatization disorder, FMS patients reported an average of 5.7 (s.d.=3.7) symptoms compared to only 1.9 (s.d.=1.7) for RA patients. The co-occurrence of FMS with major depression, somatization disorder and other FSS in the community is not known.

2.2 Irritable Bowel Syndrome (IBS)

Irritable bowel is a syndrome of abdominal pain, distension and alteration of bowel habits (Drossman, Powell & Sessions, 1977). Until recently, clinicians have viewed IBS entirely as a diagnosis of exclusion, ruling out organic bowel disease with extensive investigations that included blood tests, sigmoidoscopy, air contrast barium enema, upper GI tract radiography and/or endoscopy, stool cultures, parasite studies, and lactose tolerance tests. Kruis et al. (1989) found that a combination of symptom questions, physical examination and minimal basic blood tests (ESR, white cell count and hemoglobin) could distinguish IBS from organic disease with a sensitivity of 83% and a specificity of 97% compared to the usual extensive work-up. Manning and colleagues (1978) provided evidence that IBS could be distinguished from organic gastrointestinal disorders solely on the basis of detailed information on symptomatology. These authors noted that clinicians did not routinely collect this symptom information. In a study of GI patients and healthy controls, Talley et al. (1990) found that Manning's criteria were moderately specific but not sensitive to IBS. The

inclusion of one additional criterion, “stools that were loose and watery”, improved the accuracy of the Manning criteria. A factor analytic study has also confirmed the existence of a pattern of symptoms consistent with IBS and uncorrelated with lactose intolerance. Taken together, these studies suggest that it is possible to achieve a diagnostic accuracy for IBS of greater than 80% purely with questions about symptoms. Recently, an international commission of established researchers and experts has proposed consensus criteria for the diagnosis of IBS (Thompson et al., 1989): (1) abdominal pain that is relieved with defecation or associated with a change in frequency or consistency of stools; and/or (2) disturbed defecation (defined as altered stool frequency, altered stool form, straining or urgency, feeling of incomplete evacuation, or passage of mucus), usually associated with (3) bloating or a feeling of abdominal distension. These criteria can be implemented by modifying existing GI symptom questionnaires (Talley et al., 1989).

2.2.1 *Prevalence and Comorbidity*

IBS is the single most common diagnosis in gastroenterological practice (Harvey, Salih & Read, 1983). IBS-related symptoms are reported by 8-22% of the general population although in the United States only a small proportion of people seek medical help (Drossman, et al., 1982; Sandler et al., 1984). In Britain and Canada, up to 20% of sufferers may seek help, perhaps owing to the greater accessibility of medical care. Surveys using self-reported diagnoses of “spastic colon” or IBS yield a community prevalence of 2.9% (Sandler, 1990)]. There are no published studies of the prevalence of IBS based on current consensus criteria.

IBS patients often have many other nonspecific somatic complaints including headache, fatigue, dysmenorrhea and dysuria (Drossman, Powell & Sessions, 1977). IBS is common in patients with FMS (Yunus et al., 1981). There are no studies of the prevalence of IBS among CFS patients.

2.2.2 *Psychopathology*

Several clinic-based studies using different methodologies have reported higher frequencies of symptoms of depression and unspecified psychiatric morbidity in IBS subjects compared to normal controls (Hislop, 1971; Lydiard et al., 1993; Sammons & Karoly, 1987). Whitehead et al. (1980) found elevated levels of anxiety, depression and hostility in IBS patients but these appeared to be unrelated to changes in colonic motility or severity of symptoms. More recently, two studies found no evidence of increased psychopathology among individuals with IBS in the community on the MMPI (Drossman et al., 1988) and the Hopkins Symptom Checklist (Whitehead et al., 1988). In both studies, IBS sufferers who sought medical help did show elevated levels of psychological distress, leading these authors to suggest that psychopathology may influence help-seeking behaviour rather than symptom development. There are no studies using DSM-III-R diagnostic criteria that examine the psychiatric comorbidity of IBS in the community.

2.3 Chronic Fatigue Syndrome (CFS)

There has been much attention to the possibility that certain acute viral infections may result in a prolonged post-viral syndrome characterized by easy fatigability, muscular weakness, myalgias, and mild cognitive impairment. Attention originally focused on Epstein-Barr virus as a causal agent although virological studies were equivocal, with many patients giving no evidence of infection (Holmes et al., 1987; Tobi & Straus, 1985). Other specific infectious agents continue to be proposed but viral infection may contribute to CFS as a nonspecific precipitant of immune dysfunction. CFS is usually described as a chronic disorder with a poor prognosis. Although patients do not seem to suffer from excess medical morbidity they do tend to report persistent work and social disability (Kroenk et al., 1988; Wessely & Powell, 1989).

At present CFS is a poorly defined condition and the role of physical signs and laboratory findings in its diagnosis remain controversial. Syndromes of generalized malaise closely related to CFS include: neurasthenia, neurocirculatory asthenia, chronic brucellosis, hypoglycemia, benign or myalgic encephalomyelitis, “twentieth century disease”, total allergy syndrome or multiple chemical sensitivity, and chronic candidiasis (Stewart, 1990). In an effort to promote further research, a restrictive case definition of CFS was proposed by the U.S. Centers for Disease Control (Holmes et al., 1988). This required two major criteria—(1) new onset of debilitating fatigue, persisting or relapsing for at least six months; (2) no evidence of any other clinical condition that can produce such symptoms—and at least 6 of 11 minor criteria including: mild fever; sore throat; painful cervical or axillary lymph nodes; generalized muscle weakness; myalgia; prolonged fatigue after exercise; headache; arthralgias; neuropsychological symptoms (e.g. photophobia, irritability, difficulty thinking, depression); sleep disturbance. Physical criteria—which must be documented by a physician on at least two separate occasions at least one month apart— include: low-grade fever, nonexudative pharyngitis and palpable or tender cervical or axillary lymph nodes. The inclusion of physical signs was intended to aid in the distinction between CFS and other nonspecific causes of fatigue. To date, however, most studies have employed more liberal criteria, relying primarily on the presence of medically unexplained chronic fatigue to make the diagnosis.

Manu et al. (1988) applied the CDC 1988 diagnostic criteria to 135 patients with chief complaints of persistent fatigue attending an internal medicine Fatigue Clinic. Only 6 patients met the restrictive criteria. One-fourth of patients had insufficient symptoms or signs to meet criteria while 67% of patients had current psychiatric disorders (an exclusion criterion in the restrictive case definition). This study makes it clear that, with the restrictive case definition, CFS is a rare condition in primary care and cannot account for the high frequency of fatigue as a presenting complaint (Cathébras et al., 1991).

In an attempt to provide criteria that rely less on the exhaustive exclusion of organic disease, Lloyd et al. (1988) proposed revised CFS criteria: (1) generalized chronic persisting or relapsing fatigue of over 6 months duration, exacerbated by very minor exercise and causing significant disruption of usual daily activities; and (2) neuropsychiatric dysfunction including impaired concentration and / or new onset of short-term memory impairment; and / or (3) abnormal cell-mediated immunity indicated by reduction in absolute count of T8 and / or T4 lymphocyte subsets, and / or cutaneous anergy. The authors followed 100 patients meeting these criteria for 12 months and found only 2 patients merited alternative diagnoses (1 with major depression and 1 with chronic active hepatitis).

The neuropsychiatric symptoms of CFS may not be associated with objective abnormalities on neuropsychological testing. Consequently, it is important to assess patients' subjective symptoms of cognitive impairment in detail. Given the controversy over the value of laboratory tests in the diagnosis of CFS, some authorities have argued for the utility of defining a syndrome of chronic fatigue and cognitive impairment independent of laboratory findings (Manu, Lane & Matthew, 1988; Vassend, 1989; Wessely, 1989).

In 1994 an international working group proposed new research diagnostic criteria for CFS based on the 1988 CDC (Cope et al., 1994; See Appendix E). These criteria eliminated the physical signs of the 1988 criteria as well as the symptom of muscle weakness.

2.3.1 *Prevalence and Comorbidity*

Community surveys in Britain and North America find that more than 20% of adults report feeling "tired all the time" (cf. Wessely, 1989). Fatigue is the seventh most common presenting complaint in primary care medicine in the U.S.A. (National Center for Health Statistics, 1978). A survey of 500 unselected patients attending a teaching hospital primary care clinic found that 21% were suffering from symptoms consistent with CFS (Buchwald, Sullivan, Komaroff, 1987). The mean duration of fatigue was 16 months (ranging from 6 to 458 months) and 28% of patients had been completely bedridden at some time due to the severity of their fatigue. Sixty percent reported that their symptoms had caused considerable stress at work or at home. Common associated symptoms included: depression or mood changes, difficulty sleeping, difficulty concentrating, anxiety, nausea, stomach ache, diarrhea, odd sensations in skin, and joint pain. These studies have estimated the prevalence of some CFS related symptoms; the actual prevalence of CFS in the community is unknown.

Symptoms of CFS are common in other FSS. Buchwald et al. (1988) studied fifty patients with primary FMS and found a high prevalence of recurrent sore throat, rashes, adenopathy and low-grade fevers as well as chronic cough. In a group of 27 patients with debilitating fatigue of 6 months duration, Goldenberg et al. (1990) found that 19 also met criteria for FMS.

2.3.2 *Psychopathology*

The use of psychiatric disorder as an exclusion criterion prejudges an issue that requires empirical investigation (Matthew, Lane & Manu, 1988). Several studies have now confirmed a high prevalence of psychiatric disorders (> 75%)—primarily major depression (50%), anxiety and somatization disorder—among patients with CFS seen in tertiary care clinics (Hickie et al., 1990; Kruesi, Dale & Straus, 1989; Manu, Lane & Matthew, 1989). In many cases, however, the depressive episode occurs after the onset of CFS symptoms and so could be interpreted as a response to chronic illness. The co-occurrence of CFS and major psychiatric disorders in the community is unknown.

2.4 Co-occurrence of Functional Somatic Syndromes

As described above, patients with FSS often report somatic symptoms in many different bodily systems. The overlap in symptomatology between FSS raises the possibility that a single polysymptomatic disorder or propensity to experience and report distressing symptoms underlies all these syndromes. Medical specialists who focus on a limited range of somatic distress may identify these disorders as discrete by discounting co-occurring symptoms in other bodily systems. Current psychiatric nosology recognizes a discrete somatization disorder characterized by high levels of medically unexplained symptoms. The criteria of DSM-III-R require a lifetime history of 13 medically unexplained symptoms resulting in help-seeking or significant impairment (American Psychiatric Association, 1987). The DIS was designed to implement these criteria by assessing 37 somatic symptoms and counting those for which the patient could report no plausible medical explanation. Using the DIS, the ECA studies found a prevalence of somatization disorder of 0.1% in the community (Escobar et al., 1989; Swartz et al., 1986). Escobar et al. (1989) proposed abridged criteria of 4 symptoms for men and 6 for women to define a "subsyndromal" somatization disorder or somatization trait . The prevalence of this subsyndromal somatization disorder in community surveys ranges from 9-20%. With these criteria many patients with FSS confined to a single bodily system would be classified as having subsyndromal somatization disorder or trait.

Some indication of the relationship between FSS and generalized somatization has been given by latent variable analyses. Swartz et al. (1986) used the latent structure technique of grade of membership analysis to study whether somatization symptoms naturally cluster into syndromes when no prior assumptions are made about the interrelationships among symptoms. Using data from the Piedmont ECA study, seven symptom clusters were derived. Of those, one loaded highly on many symptoms of somatization disorder, offering validation for the existence of DSM-III somatization disorder as a naturally occurring diagnostic entity. Other clusters loaded highly on: gastrointestinal symptoms, including core symptoms of irritable bowel syndrome; cardiovascular symptoms, including many associated with panic; and somatic and affective symptoms of depression. A further cluster loaded highly on symptoms of musculoskeletal pain, weakness and conversion symptoms. These results suggest that functional somatic syndromes similar to IBS, FMS and somatic anxiety and depression exist as discrete entities along with a more general construct of somatization disorder.

We have also obtained some preliminary results using latent variable modeling to address these questions in a sample of 700 family medicine patients (Robbins, Kirmayer, Hemami, and Tepper, 1994). While the results of our modeling must be considered tentative owing to methodological limitations, we found that the pattern of symptom reporting among patients was better characterized by several distinct functional syndromes than by a single somatization disorder.

2.5 Symptom Attribution and Social Stigma

Since patients with FSS often receive ambiguous or contradictory diagnoses, they may rely more than other patients on their own explanatory models in adapting to their condition. Attributions of functional symptoms to a disease may be much less threatening or stigmatizing than attributions to a psychiatric disorder. For example, Wessely and Powell (1989) compared patients with CFS to a group of depressed psychiatric pa-

tients. Symptomatology was similar in the two groups, suggesting that many CFS patients in fact suffered from depression. However, the CFS patients viewed their symptoms as entirely viral in origin and hence did not seek psychiatric help. The depressed patients were found to have lower self-esteem than the CFS patients but sought effective treatment and recovered. Attributing symptoms of concomitant depression to physical illness may protect some FSS patients from psychological distress while inhibiting help-seeking and thus, increasing disability. We studied the role of symptom attributions in help-seeking and disability among FSS patients with a symptom attribution questionnaire we designed and validated in previous studies (Robbins & Kirmayer, 1991b).

Conditions like FSS that receive conflicting or inadequate medical explanations may also lead patients to feel frustrated, misunderstood, and stigmatized by their illness. Ironically, efforts to obtain medical treatment and validation for distress may lead to disqualification and rejection. As Lennon et al. (1989) suggest, medical consultations are usually seen by others as a sign that the patient wishes to be well. When diagnosis is ambiguous and treatment fails repeatedly, however, as it often the case with FSS, others may begin to question the patient's motivation, the medical validity of their complaints and even the reality of their suffering. These doubts, whether expressed by the doctor or significant others, may cause FSS patients to feel that they are being held personally responsible for their condition and to feel estranged from others. Lennon et al. have shown how the stigma and estrangement felt by chronic pain patients is influenced by their treatment experiences and can carry over into wider difficulties with social relationships. We studied FSS patients' experience of social stigma by comparing FSS patients to controls on measures designed by Lennon et al. (1989) for this purpose.

3. METHOD

3.1 Development of the Diagnostic Instrument

The development of the Diagnostic Interview for Functional Somatic Syndromes involved adapting the format of the DIS and using similar validation procedures. The DIS is a structured psychiatric diagnostic interview designed to be used by trained lay interviewers for the diagnosis of psychiatric disorders according to established criteria. It employs highly specific diagnostic criteria pertaining to symptom inclusion, exclusion, severity, frequency and duration. The structured format of the DIS ensures consistent and comprehensive coverage of diagnostic criteria by preventing examiners from inadvertently overlooking symptom items, failing to consider alternative diagnoses or allowing early judgments to overly influence later questioning (Helzer & Robins, 1988).

We selected the DIS as a model for the following reasons: (1) it can be used by trained lay interviewers, thus limiting the expense of studying disorders that are rare in the population; (2) it already incorporated some of the questions needed to generate diagnoses of FSS (Robbins et al., 1990); (3) it evolved in stages similar to those we planned in this project—thus providing a model for instrument construction (Robins et al., 1985); (4) it included probes to rule out organic explanations and to determine the clinical significance of symptoms (Helzer & Robins, 1988).

In the DIS somatization disorder section, each question about a somatic symptom is followed by probes to determine whether the symptom was sufficiently severe to cause a visit to the doctor, use of medication or significant interference with life. Further questions ascertain whether the symptom occurred only while taking alcohol, drugs or medication, or only as the result of a physical illness or injury. Finally, the doctor's diagnosis (if relevant and known by the subject) is recorded. Only if this diagnosis is absent or not plausible *and* if the symptom is not a result of injury or drug use, is it scored positive. In this way the DIS identifies symptoms that are likely to be functional.

However, the DIS has several limitations as an instrument to diagnose FSS: (a) the DIS does not ascertain the complete set of symptoms and signs that characterize the common syndromes of fibromyalgia, irritable bowel or chronic fatigue; (b) the DIS does not ask for pertinent negatives—that is, symptoms and signs whose presence would suggest that the somatic syndrome is not functional but rather associated with probable organic pathology; (c) the DIS does not determine the duration of symptoms or whether they were acute or chronic; (d) the DIS does not determine the co-occurrence of somatization symptoms as syndromes; (e) the DIS has no direct measure of somatized presentations of depression or anxiety; (f) the DIS has no measure of hypochondriasis. The research instrument we developed addresses each of these issues.

The content of the new questionnaire ascertains the full range of symptoms central to the FSS. The format and structure of the new instrument includes the following features:

1. All questions are pre-coded and close-ended. Those in the main body of the interview ascertain the presence, frequency, duration and clustering of symptoms.

2. Hierarchically structured modules are used with screening questions followed by more detailed syndrome specific symptom lists (i.e. global questions about change in bowel habits followed by detailed bowel habit questionnaire when appropriate).

3. A flow chart with standard probe questions is used to decide whether symptoms meet criteria for severity: i.e. were presented to a doctor or other health care professional, took medication for it more than once, interfered with life.

4. The probe flow chart is also used to determine whether symptoms can be explained by organic factors (e.g. physical illness, injury, alcohol, drugs).

5. Verbatim reports of diagnoses or symptom explanations were recorded. As with the DIS somatization section, a physician audit was performed to rule out plausible organic explanations for somatic symptoms.

6. While incorporating the logical or diagnostic grammar of existing criteria for FSS, the instrument retained measures of a range of discrete symptoms to allow for the subsequent revision of diagnostic criteria, the application of new syndrome definitions (if within the range of symptoms identified) and latent variable modeling of symptom co-occurrence.

3.1.1 *Tender points*

Tender points required to make the diagnosis of FMS were measured by the procedure developed and validated by the American College of Rheumatology (ACR) collaborative study (Wolfe et al., 1990). This group found that a dolorimeter (a spring-loaded mechanical device that delivers a set amount of pressure) was no more reliable than finger pressure, provided the examiner used at least 4 kg of pressure. We used a dolorimeter (Chatillon, N.Y., Model #716) to train interviewers to apply adequate finger pressure. The diagnosis of FMS requires that the patient report pain on pressure at 11 out of 18 specified anatomical sites in both the upper and lower body. Additional sites on the upper body may be substituted for those on the lower back, iliac crest or knees if the latter are felt to be intrusive by subjects. Interviewers were trained to recognize anatomical sites and conduct the physical examination with the videotape used to train examiners in the ACR study under the supervision of a rheumatologist. During the course of the study, interviewers were periodically re-tested against the dolorimeter to ensure they were using adequate pressure in their examination.

3.2 Measures of Patient Characteristics, Illness Impact & Service Utilization

In addition to the structured interview based on the DIS, the study employed self-report measures of personality, hypochondriacal worry, symptom and illness attributions, life

events, disability, self-perceived family burden and social stigmatization, and interview-based measures of health care utilization.

3.2.1 *Personality*

The personality trait of negative affectivity (NA) has been linked to individuals' general propensity to report high levels of symptoms and distress (Costa & McCrae, 1987; Vassend, 1989; Watson & Clark, 1984). It is important to control for the level of NA in studies of symptom reporting to identify other effects (Pennebaker & Watson, 1991). Accordingly, we measured NA with the Neuroticism scale of the NEO-FFI. This scale has good internal consistency and its construct validity is supported by high correlations with other measures of negative mood and neuroticism. The NEO-FFI also allowed measure of the four other major dimensions of personality—Extraversion, Openness, Agreeableness and Conscientiousness—which have been hypothesized to be related to chronic somatization and which may contribute to coping with chronic illness (Kirmayer, Robbins & Paris, 1994).

3.2.2 *Hypochondriacal Worry*

Hypochondriacal worry was measured by the Whitely Index of Hypochondriasis (Pilowsky, 1967); this 12 item scale measures the tendency to worry about being ill, to be convinced that one is ill, and to feel more sensitive to pain and vulnerable to illness than others. High scorers on this scale may have hypochondriacal fears or may have legitimate health concerns in proportion to the severity of their symptoms.

3.2.3 *Symptom & Illness Attributions*

The symptom attribution measure (SIQ), developed in our previous study of family medicine patients, consists of 13 common somatic symptoms for which the respondent must choose the most likely causal explanation he/she would make if he/she had the symptom (Robbins & Kirmayer, 1991b). The SIQ generates measures of psychological, somatic and normalizing attributions which have moderate internal and test-retest reliability. The SIQ has been shown to be a predictor of the somatization and psychologization of distress among family medicine patients. A shortened version of the SIQ was found to be the best predictor of chronicity of fatigue in a sample of general practice patients with acute viral illness (Cope, David, Pelosi & Mann, 1994).

3.2.4 *Life Events*

Serious life events experienced in the three months prior to the onset of the respondent's current health problems were measured with a 16 item scale drawn from the Explanatory Model Interview Catalogue (EMIC; Weiss et al., 1992), a semi-structured interview and coding method for eliciting the subject's concepts of the symptoms, cause, course, appropriate treatment and outcome of illness.

3.2.5 *Disability*

Functional limitations were measured by the MOS SF-36 (McHorney, Ware & Raczek, 1993; Ware & Sherbourne, 1992). This scale consists of 36 items divided into 9 subscales : (1) Physical Functioning ; (2) Role Functioning-Physical; (3) Bodily Pain; (4) General Health; (5) Vitality; (6) Social Functioning; (7) Role Functioning-Emotional; (8) Mental Health; and (9) Reported Health transition (a single 4 point item asking the respondent to evaluate how his / her health has changed compared to one year ago). With the exception of health transition (for which a higher score indicates more deterioration in health since last year), each of the scales indicates disability due to illness with a low score, while better functioning due to relatively good health is given a high score. Although most scales are appropriately labeled, this results in the counter-intuitive result that a high score on the bodily pain scale indicates *less* bodily pain. A summary of the composition and reliability of the scales is presented in Appendix F. The scales were scored according to procedures developed for the MOS. A scale score was calculated if a respondent answered at least half of the items in the multi-item scale. Missing values were replaced with the average score across completed items in the same scale.

3.2.6 *Family Burden and Social Stigma*

Burden of illness on the family was measured with 12 items, 9 of which were adapted from a scale used to measure the impact of chronic psychiatric illness on the family (Fenton, Tessier & Streuning, 1979). Three new items were devised for this study. The new scale showed good reliability with Cronbach's $\alpha = 79$.

Scales designed to measure perception of stigma among chronic pain patients were adapted for the FSS case. The pain-stigma questionnaire (Lennon et al., 1989; Link et al. unpublished ms, 1985) consists of 4 scales derived from a factor analysis of 25 Likert-type items. Two scales assess perceived stigma (attribution to personality problem and estrangement) and 2 scales assess strategies of stigma management (secrecy and disclosure). In chronic pain patients, reliabilities of the 4 scales range from $\alpha = .72$ to .82. Additional items were adapted from the EMIC (Weiss et al., 1992).

3.2.7 *Health Care Utilization*

Health care utilization was measured with interview items adapted from the ECA survey (Eaton & Kessler, 1985) and the Quebec Health Care survey. Further questions on type of help sought, perception of helpfulness and degree to which the patient felt understood by the practitioner were modeled on the EMIC (Weiss et al., 1992). Helpfulness was scored as a binary variable ('helpful' or 'not helpful') while understanding was rated on a 4 point scale (not at all, somewhat, well, very well).

3.3 Sample

Pre-testing of the questionnaire required 24 subjects (12 French interviews and 12 English). The subsequent reliability and validity study enrolled a total of 240 patients. Specialty clinics in university teaching hospitals and affiliated private practice specialist internists in rheumatology, gastroenterology and chronic fatigue participated for each of the three FSS and comparison groups. Each clinic or practice enrolled consecutive eligible patients with the specific FSS diagnosed according to standard practices, and con-

secutive control patients with non-FSS diagnoses matched for age and sex. For the purposes of diagnostic and clinical comparison, fibromyalgia was matched with rheumatoid arthritis, irritable bowel with inflammatory bowel (Crohn's disease and ulcerative colitis) and chronic fatigue with multiple sclerosis. These comparison groups have been used in much previous research on the respective FSS.

3.4 Procedure

3.4.1 *Questionnaire Development*

This phase of the project involved consultation with specialists to insure that diagnostic criteria were covered and testing of the pilot questionnaire for intelligibility, flow and comprehensiveness. Diagnostic criteria for syndromes were abstracted from the literature, taped interviews were studied for question wording, and DIS-based probes for clinical significance and pertinent negatives were adapted to the FSS condition. Preliminary drafts of sections were distributed to expert medical specialists in rheumatology (n=11), gastroenterology (8) and chronic fatigue (9) with the request that each item be evaluated for clarity and precision. This was facilitated by the organization of a scientific meeting at the Jewish General Hospital for which leading experts on FSS were brought to Montreal. Consultants included members of the standing committees on diagnostic criteria of the relevant professional organizations (American College of Rheumatology, International College of Gastroenterology, Centers for Disease Control).

Of particular value to our efforts were the International Working Team on Functional Gastrointestinal disorders chaired by Douglas Drossman, and the Multicenter Criteria Committee of the American College of Rheumatology chaired by Frederick Wolfe. These groups composed consensual diagnostic criteria for irritable bowel (Thompson et al., 1992) and fibromyalgia (Wolfe et al., 1990), and the GI group designed and validated a diagnostic interview for irritable bowel (Drossman et al., 1992). We adapted sections of their instrument for our purposes.

We were aided greatly in the design of our instrument by parallel work on diagnoses of "affective spectrum disorders." In a paper appearing soon after our grant award, Pope and Hudson (1991) reported on the development of new structured interview modules to be used by clinicians to diagnose seven medical conditions thought to have a common origin in affective illness. These conditions included irritable bowel, fibromyalgia and chronic fatigue. Modules to diagnose these syndromes use the format of the Structured Clinical Interview for DSM-III-R (SCID) (Spitzer et al., 1988). Similar to our project, questions were drafted based on published diagnostic criteria, then sent to medical experts for suggestions and revisions. Revised modules are being tested on 130 patients. No validity data have been reported to date.

The SCID must be administered by a trained clinician and, thus, is more appropriate for small scale studies of clinical samples. Our instrument, while drawing from the work of Pope and Hudson, used the format of the Diagnostic Interview Schedule (DIS) which is designed to be used by trained lay interviewers and is appropriate for use in large-scale community surveys (Robins et al., 1981) . Nevertheless, we benefited from the careful attention of Pope and Hudson to question wording. Sources of items in our diagnostic interview are indicated in the annotated versions of the questions (Appendix B.)

An iterative pre-test was conducted to identify and correct difficulties with language, sequence, recall, and diagnostic grammar (Robins, 1989). The instrument was translated into French and checked for semantic equivalence by back-translation. Discrepancies were resolved by discussion among the investigators and the translators.

3.4.2 *Clinical Study of Validity and Reliability of Instrument*

In this phase, patients with FSS and control patients with non-FSS diagnoses were assessed by clinicians using standard diagnostic practices and again by lay interviewers blind to clinicians' evaluations. Diagnostic agreement between interviewers and clinicians was assessed, as was the temporal stability of FSS diagnoses. At this time data were also collected to examine the relationship between FSS, health care utilization, disability and social stigma.

Lay interviewers with a background in health research (i.e. M.A. and Ph.D. students or mature women with previous experience in health care interviewing) were recruited and trained on the diagnostic instrument, the probe sheet and the tender points examination. A detailed interviewer's manual was prepared to accompany the questionnaire (Appendix E).

Physicians were recruited by invitation from the investigators. The project coordinator visited the clinic to establish procedures and lines of communication with an aide in the physician's office and to arrange locations for interviewing. Consecutive patients meeting eligibility criteria for the study were invited to participate in the study by their physician and a list of potential respondents was forwarded to the project coordinator. Patients were then telephoned and invited to participate. Interviews were arranged at a time and place convenient for the subject: at the clinic, at a room set aside in the Jewish General Hospital or in his/her home. At the time of the interview, patients received an explanation of the project and gave informed consent. The interviews took from 1 to 2 hours to complete. In some instances, the interview required two meetings to complete; if necessary these were scheduled within 1-2 weeks of each other.

A separate set of self-report measures were administered and returned through the mail. When required, the interviewer read through portions of the self-report measures with subjects unable to complete them unassisted.

A subsample of 84 patients with FMS, IBS and CFS were re-tested after 2 months to ascertain the test/re-test reliability of the diagnostic instrument (or temporal stability of the diagnoses). A second questionnaire was prepared for the re-test. The retest instrument included questions to make the diagnosis of FMS and IBS and a limited subset of the questions for CFS.

After the patient's interview for the study was completed, the referring clinician completed a diagnostic assessment form which asked for the criteria used to diagnose the FSS and co-existing conditions (See Appendix D).

3.5 Data Analysis

We examined the reliability of the diagnostic interview by calculating its agreement with clinician diagnosis. For categorical data like diagnoses, agreement between raters (in this case clinician diagnosis and the structured diagnostic interview) is usually indicated by a coefficient of concordance. While raw agreement may be measured by a correlation coefficient, a more meaningful measure corrects for chance agreement. For binary data, Cohen's kappa is generally held to be the best indirect measure of diagnostic concordance (Cohen, 1960; Feinstein, 1987; Streiner, 1995). No definite standards have been established for the level of kappa that indicates good concordance. Suggested guidelines view a kappa of 0 - .20 as indicating slight concordance, .21-.40 as fair, .41 - 60 as moderate, .61 - .80 as substantial and .81 - 1.00 as almost perfect (Feinstein, 1987; p. 185). Inter-rater reliabilities for the DIS have ranged widely across diagnoses but have typically been in the region of .4-.5 (Streiner, 1995). We calculated kappa for both interview-clinician concordance and for the test-retest reliability of the interview.

Groups were compared on interval variables using a one-way analysis of variance with an F-test followed, when significant, with pairwise t-tests. Tests were calculated using separate or pooled variance estimates depending on whether the Levene test indicated a significant difference in population variances (Norusis, 1990; p. 215). Comparison of groups on categorical variables used the chi-square test for contingency tables and pairwise analysis.

4. RESULTS

In this section we present the major findings of the study. After discussing the development of the instruments and the characteristics of the study sample, we summarize findings on the reliability and validity of the diagnostic interview. We then present findings on the co-occurrence of FSS. Subsequent sections consider psychological characteristics of patients with FSS compared to non-FSS disorders and illness impact, including: disability, family burden, stigma and patterns of health care utilization.

4.1 Development of Instruments

Consultation with experts revealed unequal diagnostic specificity across the three syndromes. Disagreement among experts reflects the differing degree of consensus within the medical community about the nature and existence of these syndromes as discrete entities. This is particularly evident in the case of CFS where multiple criteria have been proposed. We constructed an instrument capable of making diagnoses according to several different criteria with adjustment of the diagnostic algorithm.

The completed Diagnostic Interview for Functional Somatic Syndromes is presented in Appendix B along with the probe sheet derived from the DIS. The interview is annotated to indicate the source or basis for each item. The interview includes sections on: (A) basic demographic information; (B) identity and explanation of health problems; (C) diagnosis of fibromyalgia; (D) diagnosis of irritable bowel syndrome; (E) diagnosis of chronic fatigue syndrome; (F) a list of current (within the last month) associated symptoms used to determine the diagnosis of CFS and IBS; (G) lifetime and current help-seeking for any personal or health problems along with perceptions of health care professionals' attitudes, experiences with the first and with the most important source of help sought; (H) use of specific treatments.

Within the diagnostic section for each FSS, we obtained information for a current and lifetime diagnosis and a test of the temporal co-occurrence of the cardinal symptoms of the syndrome with other FSS, as well as associated disability, pain, stigma, embarrassment and health care utilization.

The interviewer's manual is reproduced in Appendix C. The diagnostic criteria and algorithms for the FSS are presented in Appendix E.

The self-report measures (Appendix B) consisted of sections on: (J) serious life events occurring in the three months prior to the onset of the current health problems; (K) household impact of illness; (L) hypochondriacal worry; (M) self-perceived stigmatization of illness (attitudes of others); (N) symptom attribution; (O) personality (the NEO-FFI); (P) causal attributions of health problems; (Q) disability (MOS 36-item short-form health survey, SF-36).

4.2 Characteristics of Sample

A total of 265 subjects were enrolled in the study: 41 FMS, 41 IBS, 45 CFS and 138 controls. Table 1 presents the distribution of subjects by group and their sociodemographic

characteristics. Patients in the FSS groups were representative of their respective clinics and practices from which they were drawn. Samples of patients with the corresponding 'organic' disorders may be less representative of their respective clinic populations because they were chosen to match the FSS patients on age and gender. The matching procedure was successful in that there were no significant differences between FSS patients and corresponding 'organic' disease patients on sociodemographic variables except for employment status, which differed significantly between the FMS and RA groups (χ^2=15.04 , df=5 , p<.01). This difference was due to a greater proportion of homemakers in the FMS group and a greater proportion of retirees in the RA group.

Comparing the three FSS groups, FMS patients tended to be older than CFS patients, who in turn tended to be older than IBS patients. (IBS may have been the youngest group because one of the referring gastroenterologists had an express interest in younger patients who were accordingly over-represented in his practice.)

Again, while women comprised 75% of the overall sample, a greater proportion of FMS patients were female (93%) than IBS (73%) and CFS (62%). Perhaps as a reflection of the age and gender differences, slightly more FMS patients than IBS were married. Across the three FSS groups, mean household income was lowest for FMS and highest for IBS.

Table 1. Description of Sample by Entry Diagnosis

	FMS	RA	IBS	IBD	CFS	MS	Total
	n=41	n=43	n=41	n=55	n=45	n=40	N=265
Age X (SD)	48.7 (11.6)	52.7 (13.6)	34.8 (11.0)	34.8 (12.8)	39.4 (9.3)	43.0 (11.3)	41.8 (13.4)
Gender							
Male	3 (7%)	6 (14%)	11 (27%)	19 (35%)	17 (38%)	10 (25%)	66 (25%)
Female	38 (93%)	37 (86%)	30 (73%)	36 (65%)	28 (62%)	30 (75%)	199 (75%)
Education X (SD)	11.7 (4.3)	11.9 (3.4)	14.3 (2.9)	14.5 (3.2)	14.8 (2.9)	13.8 (3.2)	13.6 (3.5)
Marital Status							
Married	27 (66%)	23 (54%)	24 (59%)	25 (47%)	21 (49%)	25 (62%)	145 (56%)
Widowed	3 (7%)	6 (14%)	1 (2%)	2 (4%)	1 (2%)	1 (3%)	14 (5%)
Separated	0	3 (7%)	2 (5%)	1 (2%)	0	0	6 (2%)
Divorced	7 (17%)	4 (9%)	0	4 (8%)	6 (14%)	5 (13%)	26 (10%)
Never Married	4 (10%)	7 (16%)	14 (34%)	21 (39%)	15 (35%)	9 (22%)	70 (27%)
Employment Status*							
Employed	20 (49%)	17 (40%)	28 (69%)	34 (61%)	16 (36%)	16 (40%)	131 (50%)
Unemployed	12 (29%)	9 (21%)	3 (7%)	8 (14%)	24 (54%)	16 (40%)	72 (27%)
Retired	1 (2%)	10 (23%)	2 (5%)	2 (4%)	1 (2%)	3 (8%)	19 (7%)
Student	0	0	3 (7%)	7 (13%)	0	0	10 (4%)
Homemaker	8 (20%)	3 (7%)	2 (5%)	2 (4%)	2 (4%)	5 (12%)	22 (8%)
Other	0	4 (9%)	3 (7%)	2 (4%)	2 (4%)	0	10 (4%)
Household Income X	$46,550	$43,964	$57855	$62,029	$49,784	$48,227	$51,865
Religion							
Jewish	9 (22%)	9 (21%)	4 (10%)	9 (16%)	9 (21%)	7 (18%)	47 (18%)
Roman Catholic	21 (51%)	16 (37%)	21 (53%)	33 (60%)	15 (34%)	26 (65%)	132 (50%)
Protestant	6 (15%)	9 (21%)	9 (23%)	7 (13%)	10 (23%)	0	41 (16%)
Other	5 (12%)	9 (21%)	5 (14%)	6 (11%)	11 (22%)	7 (17%)	43 (16%)
Language Of Interview							
English	32 (78%)	37 (86%)	30 (73%)	36 (66%)	38 (84%)	24 (60%)	197 (74%)
French	9 (22%)	6 (14%)	11 (27%)	19 (44%)	7 (16%)	16 (40%)	68 (26%)

* FMS significantly different from RA. See text.

Patients were accrued from a total of 18 physicians at 16 different sites—these are grouped according to type of practice setting in Table 2. In general, the FSS group and the non-FSS comparison group came from similar settings. The exceptions were CFS and MS: all of the MS patients were referred from hospital based neurology practices while the CFS were referred by both hospital and private office-based clinicians with specific interest in this problem, including general internists, infectious disease specialists, immunologists, and psychiatrists. In the cases of CFS referred to the study by a psychiatrist, the diagnosis had been previously ascertained by a medical specialist.

Table 2. Source of Sample by Entry Diagnosis (N=265)

Source (type of settings)	FMS	RA	IBS	IBD	CFS	MS
	n=41	n=43	n=41	n=55	n=45	n=40
Rheumatologist						
Private (n=2)	13 (32%)	7 (16%)				
Hospital (n=2)	28 (68%)	36 (84%)				
Gastroenterologist						
Hospital (n=2)			41(100%)	55 (100%)		
Immunologist or Infectious Disease Specialist						
Private (n=2)					6 (13%)	
Hospital (n=3)					12 (26%)	
Psychiatrist						
Hospital (n=2)					5 (11%)	
Neurologist						
Hospital (n=2)						40(100%)
General Practitioner or General Internist						
Private (n=1)					1 (2%)	
Hospital (n=2)					16 (36%)	

4.3 Validity and Reliability of Diagnostic Instrument

In this section we present results on the reliability and validity of the diagnostic instrument. We examined the concordance between clinician and interview using Cohen's kappa. To calculate diagnostic specificity and sensitivity, we used the clinicians diagnosis as the 'gold-standard'. However, despite efforts to obtain reliable diagnoses from clinicians known for their expertise in the respective FSS, there was some inconsistency in labeling of patients between entry diagnosis (basis of referral to the study) and the final diagnosis confirmed on the Clinician's Diagnostic Evaluation Form (Appendix D). In some cases, this evaluation form was received soon after the patient was referred but in other cases, owing to clinicians' busy practices, the return of the form was delayed or it was never received. Table 3 depicts the changes from entry diagnosis and subsequent diagnosis confirmed on the clinician's evaluation form. Only cases for which the entry diagnosis was confirmed by standard diagnostic criteria were used as 'gold standard' cases in reliability analysis. However, entry diagnoses, which reflected usual diagnostic practices, were used for analyses of patient characteristics and illness impact present in Sections 4.5 and 4.6.

Table 3. Changes in Diagnosis from Entry to Doctor's Final Report

	Doctor's Entry Diagnosis						
Doctor's Final Diagnosis	**FMS** (n=41)	**RA** (n=43)	**IBS** (n=41)	**IBD** (n=55)	**CFS** (n=45)	**MS** (n=40)	**Total** (N=265)
FMS	38 (93%)						**38**
FMS (not ACR criteria)[1]	1 (2%)						**1**
RA		40 (93%)					**40**
RA+Ostomy[2]		2 (5%)					**2**
IBS			35 (86%)	6 (11%)			**41**
IBD			3 (7%)	40 (73%)			**43**
IBD+RA				2 (4%)			**2**
IBD+Ostomy				4 (7%)			**4**
CFS					30 (67%)		**30**
CFS (not CDC criteria)[1]					4 (9%)		**4**
CFS+FMS+IBS[3]					1 (2%)		**1**
MS						40 (100%)	**40**
Missing Doctor's form	2 (5%)	1 (2%)	3 (7%)	3 (5%)	10 (22%)	0	**19**
Total Confirmed Cases by	**38**	**42**	**38**	**52**	**31**	**40**	**241**

1 Case not included as confirmed because of use of alternative diagnostic criteria by clinician (n=5).

2 Ostomy= ileostomy or colostomy. 3 Case counted as CFS in reliability analysis below.

As shown in Tables 4a through 4d, the coefficients of chance-corrected concordance (Cohen's kappa) were fair to moderate throughout, indicating substantial discrepancy between clinician and interview based diagnoses. Kappa is sensitive to the prevalence of the disorder in the sample and so we calculated it for both the FSS versus its control non-FSS discrimination (with a prevalence of the FSS of about 44-48%) and for the FSS versus the total sample (with a FSS prevalence of about 13-17%). Kappas ranged from .37 for CFS to .48 for IBS.

In general, accuracy (uncorrected or raw concordance) was high, ranging from 85 to 89% for the FSS versus non-FSS controls. Compared to controls, specificity for all three syndromes was very high (93 to 97%) but sensitivity was low (35% for CFS, using 1988 CDC criteria, to 63% for IBS).

Table 4. Reliability Analysis: Diagnostic Interview *vs* Doctor's Final Diagnosis

Table 4a. Fibromyalgia

	FMS *vs* NON FMS (N=241)		**FMS *vs* RA** (N=80)	
Prevalence	16%	38/241	48%	38/80
Sensitivity	45%	17/38	45%	17/38
Specificity	93%	188/203	100%	42/42
Accuracy	85%	205/241	74%	59/80
Kappa	.39		.50	

Table 4b. Irritable Bowel Syndrome

	IBS *vs* NON IBS (N=241)		**IBS *vs* IBD** (N=90)	
Prevalence	17%	41/241	46%	41/90
Sensitivity	63%	24/41	63%	24/41
Specificity	93%	181/203	98%	48/49
Accuracy	85%	205/241	80%	72/90
Kappa	.48		.58	

Table 4c. Chronic Fatigue Syndrome (CDC 1988)

	CFS *vs* NON CFS (N=241)		CFS *vs* MS (N=71)	
Prevalence	13%	31/241	44%	31/71
Sensitivity	35%	11/31	35%	11/31
Specificity	97%	201/203	100%	40/40
Accuracy	89%	214/241	72%	51/71
Kappa	.39		.38	

Table 4d. Chronic Fatigue Syndrome (CDC 1994)

	CFS *vs* NON CFS (N=241)		CFS *vs* MS (N=71)	
Prevalence	13%	31/241	44%	31/71
Sensitivity	42%	13/31	42%	13/31
Specificity	93%	196/210	100%	40/40
Accuracy	87%	209/241	75%	53/71
Kappa	.37		.45	

We used both CDC 1988 and 1994 criteria for CFS (see Appendix E for a comparison of criteria and the corresponding diagnostic interview items and algorithm). With the latter criteria, which eliminate physical signs, using a smaller range of symptoms and a lower diagnostic threshold, sensitivity was somewhat better (42%). The 1994 criteria omit muscle weakness as a symptom of CFS which improves the discrimination from MS.

Table 5 displays the test / re-test results for the FMS and IBS sections of the diagnostic interview. Re-test interviews were completed an average of 2 months following the initial interview. All the follow-up interviews were included in the analysis. Levels of re-test reliability were generally low. The raw concordance (accuracy) of the initial and follow-up interviews was 75% for FMS, 77% for IBS and 94% for CFS. The chance-corrected coefficient of concordance between the initial and follow-up interviews was kappa = .28 for FMS, .48 for IBS and .35 for CFS (using truncated criteria).

Table 5. Test-Retest Reliability of Diagnostic Interview (N=84)

Table 5a. Fibromyalgia

	Time 2	
	FMS	**NON FMS**
Time 1		
FMS	7	18
NON FMS	3	56
Total	10	74

Table 5b. Irritable Bowel Syndrome

	Time 2	
	IBS	**NON IBS**
Time 1		
IBS	16	15
NON IBS	4	49
Total	20	64

4.4 Co-occurence of Syndromes

Referring physicians were asked to note all co-existing diagnoses and were specifically prompted for the three FSS under study on the Diagnostic Evaluation Form (Appendix D). Rates of co-occurrence of syndromes, as observed by the physicians, were very low. These data were presented in Table 3.

The co-occurrence of FSS according to the interview-based diagnoses is presented in Table 6. Pure types and combinations of syndromes are listed separately. Diagnosis is based on symptoms in the past month. There was substantial co-occurence among the three syndromes. While a majority of patients with IBS had only IBS, 53% of patients with FMS (17/32) met criteria for IBS, CFS or both and 90% (16/18) of patients with CFS met criteria for FMS, IBS or both.

Table 6. Co-occurence of Syndromes by Diagnostic Interview(N=93)

	FMS	IBS	CFS
FMS	15(47%)*	5	7
IBS	5	29(67%)*	4
CFS	7	4	2(11%)*
IBS+CFS	5	-	-
FMS+CFS	-	5	-
FMS+IBS	-	-	5
Total # times diagnosis given	32	43	18

* No co-occurence of syndromes detected

Graphic views of physician and interview rates of co-occurrence of syndromes is provided in the Venn diagrams of Figures 1 and 2.

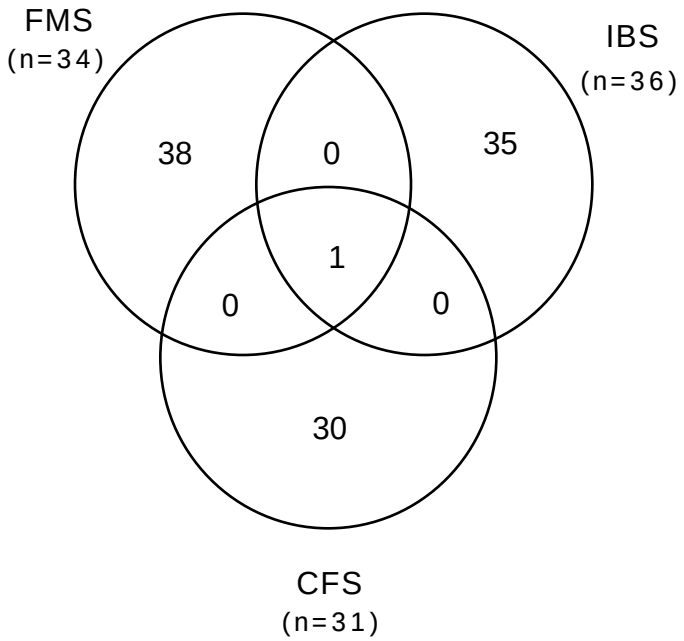

Figure 1. Co-occurrence of FSS by Doctors' Final Diagnoses

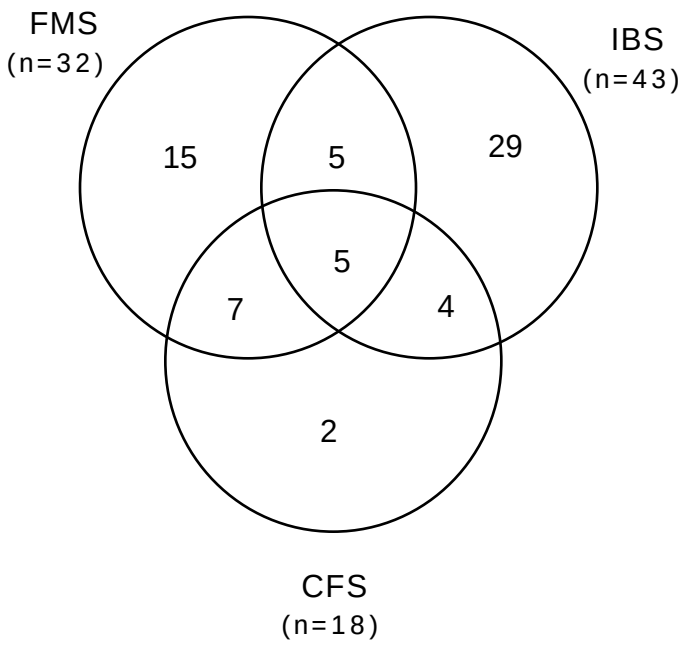

Figure 2. Co-occurrence of FSS by Interview-based Diagnosis

The basis of this co-occurrence may be overlap in symptoms held to be important for each syndrome. Tender points which are viewed as distinctive to FMS may in fact have little pathognomonic value. As shown in Table 7, a high frequency of tender points—with the mean exceeding the diagnostic threshold for FMS— was found in all diagnostic groups. Bivariate t-tests indicated the following pairwise differences: FMS>RA, IBS, IBD, MS ($p<.01$); CFS > RA, IBS, IBD, MS ($p<.05$). Tender points were examined only among subjects with a history of diffuse musculoskeletal aches and pains (i.e., who answered "yes" to the question: "Have you ever had a period of one month or longer during which you were bothered by persistent aches and pains in several different parts of the body?"). As a result these rates of tender points cannot be taken as representative of the frequency in the FSS.

Table 7. Number of Tender Points by Entry Diagnostic Group

	FMS n=41	**RA** n=41	**IBS** n=22	**IBD** n=26	**CFS** n=39	**MS** n=17	**Total** N=186	Significance Test
Total Number of Tender points								
Mean	19.8	13.0	11.8	12.6	17.7	12.3	15.2	F=4.79
Min.-Max.	3-34	0-34	0-22	0-33	1-36	0-3	10-36	df=5, 180
SD	7.8	9.3	6.4	9.3	9.6	10.2	9.3	p<.001

4.5. Patient Characteristics

This section presents results on social and psychological characteristics of patients categorized according to entry diagnosis.

4.5.1 *Personality*

We examined personality traits in patients using the NEO-FFI. This inventory yields scores for the five major dimensions of personality. As shown in Table 8, groups differed significantly only in Openness, with the CFS group scoring higher than all the groups ($p<.01$) except IBD. There was a trend toward a overall difference on the Neuroticism scale, with FMS scoring higher than RA ($p<.05$).

Interestingly, many CFS patients reported it was difficult to answer the personality question because they were uncertain whether to answer vis-a-vis their experience before or since the onset of their illness. In some cases, they felt that their personality had changed since the onset of their illness.

Table 8. Comparison of Diagnostic Groups on Personality Scales*

	FMS (n=36)	**RA** (n=39)	**IBS** (n=40)	**IBD** (n=53)	**CFS** (n=43)	**MS** (n=38)	**TOTAL** (n=249)	Significance Test (df=5, 242)
NEO-FFI Dimensions								
Neuroticism								
Mean	35.9	31.8	34.2	32.8	32.5	34.1	33.5	F=1.05
SD	9.1	8.6	9.3	8.1	9.6	10.0	9.1	p<.39
Extraversion								
Mean	39.6	39.3	40.3	39.8	39.2	37.8	39.4	
SD	5.8	5.9	7.4	6.1	6.7	6.9	6.5	
Openness								
Mean	38.3	38.7	38.7	40.2	42.4	37.7	39.4	F=3.10
SD	5.5	5.6	6.1	7.7	5.5	6.1	6.4	p<.01
Agreeableness								
Mean	43.9	44.7	43.9	43.7	45.1	43.6	44.1	
SD	5.9	5.3	6.3	6.3	5.1	5.0	5.7	
Conscientiousness								
Mean	46.5	47.5	48.0	47.0	46.7	47.8	47.2	
SD	6.7	6.5	6.3	6.2	6.6	4.9	6.2	

* Doctor's Entry Diagnosis

Taken as a group, FSS patients did not differ significantly from non-FSS patients on any persona dimension (Table 9).

Table 9. Comparison of FSS and non-FSS Groups* on Personality Scales

	Syndromes (FSS) (n=119)	**Diseases (non-FSS)** (n=129)	Significance Test
Neuroticism			
Mean	34.1	32.9	NS
SD	9.4	8.8	
Extraversion			
Mean	39.7	39.1	NS
SD	6.6	6.3	
Openness			
Mean	39.9	39.0	NS
SD	6.0	6.7	
Agreeableness			
Mean	44.3	44.0	NS
SD	5.7	5.6	
Conscientiousness			
Mean	47.1	47.4	NS
SD	6.5	5.9	

*Doctor's Entry Diagnosis

4.5.2 *Hypochondriasis, Symptom Attribution and Life Events*

Further characteristics of the study patients are presented in Table 10. The 12 item Whiteley index of hypochondriasis had modest internal reliability in this sample with Cronbach's a = .66 (n= 244). Although levels of illness worry varied more within than between groups, CFS patients reported significantly more illness worry than all other groups ($p < .01$), while MS patients reported significantly more illness worry than RA patients ($p < .05$). When diagnostic groups were aggregated, FSS patients scored higher than non-FSS patients on the hypochondriasis scale ($X = 16.64 \pm 2.55$ vs 15.77 ± 2.41, $t = 2.70$, $df = 242$, $p < .007$).

The Symptom Interpretation Questionnaire had good internal reliability in this sample with Cronbach's a = .85 (Psychological Attribution Scale, N=242), .73 (Somatic Attribution Scale, N=235) and .77 (Normalizing Attribution Scale, N=242). There were no significant differences between groups on the Somatic and Psychological scales. On the Normalizing scale, MS patients had significantly lower scores than IBS and IBD patients while FMS patients had significantly lower scores than IBD patients (all $p < .01$).

FMS patients reported a significantly greater number of life events in the 3 months preceding the onset of their illness than did RA, IBS, CFS and MS groups ($p < .05$). Table 11 compares each FSS to its control group on specific causal events. FMS patients were significantly more likely than RA patients to report serious financial troubles, family conflict or other serious trauma or stress. IBS patients were more likely than IBD to report having been the victim of a non-physical crime or having been injured at home or

at work. IBD patients were significantly more likely to report a serious car accident than their controls.

Table 10. Comparison of Diagnostic Groups on Illness Worry, Symptom Attributions and Life Events Preceding Illness Onset

	FMS	RA	IBS	IBD	CFS	MS	Total	Significance Test
Illness Worry								
N	37	38	38	53	41	37	244	F=6.26
Mean	16.19	15.37	15.68	15.58	17.90	16.46	16.18	df=5, 238
SD	2.3	2.3	2.3	2.4	2.5	2.5	2.5	p<.001
Somatic Symptom Attribution (SIQ)								
Psychological Attribution								
N	37	33	40	52	43	37	242	
Mean	24.1	23.6	26.7	25.1	24.0	23.7	24.6	NS
SD	7.7	7.1	7.1	6.6	7.2	8.0	7.3	
Somatic Attribution								
N	36	33	39	49	42	36	235	
Mean	22.6	22.4	23.4	23.5	25.5	24.1	23.6	NS
SD	6.6	5.6	6.0	5.2	6.0	7.1	6.1	
Normalizing Attribution								
N	37	33	40	53	42	37	242	F=2.21
Mean	27.2	29.3	29.9	30.8	29.3	26.9	29.0	df=5, 236
SD	5.8	7.8	5.8	6.1	7.2	7.3	6.8	p<.05
Number of Serious Life Events Prior to Illness Onset								
N	37	39	38	54	42	38	248	F=2.38
Mean	1.9	.9	1.1	1.4	1.0	1.2	1.2	df=5, 242
Min.-Max.	0-6	0-7	0-4	0-5	0-5	0-5	0-7	p<.05
SD	1.7	1.5	1.1	1.4	1.3	1.2	1.2	

Table 11. Life Events Prior to Onset of Illness by Diagnostic Group

Life Events	FMS n=39 Mean (SD)	RA n=38 Mean (SD)	IBS n=40 Mean (SD)	IBD n=55 Mean (SD)	CFS n=44 Mean (SD)	MS n=3 Mean (
Serious illness	.13 (.34)	.08 (.27)	.05 (.22)	.09 (.29)	.16 (.37)	.13 (.
Death	.23 (.43)	.28 (.46)	.15 (.36)	.16 (.37)	.09 (.39)	.10 (.
Lost job	.03 (.16)	.03 (.16)	.03 (.16)	.04 (.19)	.02 (.15)	.05 (.
Serious financial problems	.23** (.43)	.05(.22)	.08 (.27)	.05 (.23)	.05 (.21)	.10 (.

Serious problems at work	.18 (.37)	.05 (.22)	.07 (.27)	.13 (.34)	.07 (.26)	.18 (.3
Serious problems with marriage	.23 (.43)	.10 (.30)	.23 (.43)	.25 (.44)	.09 (.29)	.13 (.3
Victim of physical abuse	0	0	.02 (.13)	0	.03 (.16)	.01 (.(
Victim of sexual abuse	0	0	0	0	0	0
Victim of a non-physical crime	0	.03 (.16)	.08** (.27)	0	0	0
Involved with a legal problem	.08 (.27)	.05 (.22)	.10 (.30)	.04 (.19)	.05 (.21)	.03 (.1
Serious family conflict	.33** (.48)	.08 (.27)	.10 (.30)	.25 (.44)	.19 (.39)	.21 (.4
Political persecution	.03 (.16)	0 0	.02 (.13)	0	0	.01 (.(
Serious car accident	.05 (.22)	.03 (.16)	.02 (.13)	.07* (.26)	0	.03 (.1
Injury at home or work	.08 (.27)	.03 (.16)	.08* (.27)	0	.02 (.15)	0
Seen someone badly injured	.05 (.22)	.05 (.22)	.05 (.22)	.04 (.19)	.02 (.15)	0
Other serious trauma or stress	.37* (.47)	.15 (.36)	.15 (.37)	.27 (.45)	.17 (.38)	.21 (.4

Pairwise comparisons for syndromes versus respective controls only
* p<.05; **p<.01, ***p<.001

Table 12. Causal Attributions of Health Problems by Diagnostic Group

Causes of Health Problems	FMS n=39	RA n=38	IBS n=40	IBD n=55	CFS n=44	MS n=38	Total N=254
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SI
Problems with immune system	2.1 (1.2)	2.6*(1.1)	2.0 (1.1)	2.4 (1.2)	3.5 (.80)	3.1 (1.3)	2.6 (1.3
Physical abuse as a child	1.6 (1.3)	1.4 (.92)	1.4 (.95)	1.5 (1.1)	1.9 (.59)	1.4 (.75)	1.4 (.93
Sexual abuse as a child	1.5 (1.1)	1.3 (.92)	1.4 (.92)	1.4 (1.0)	1.1 (.52)	1.3 (.87)	1.3 (.90
Repeated actions	2.5 (1.3)	2.2 (1.2)	1.3 (.65)	1.3 (.69)	1.6 (.90)	1.4 (.85)	1.7 (1.0
Infection	1.6 (1.0)	2.1 (1.2)	2.0 (1.1)	1.8 (.95)	3.4*** (.87)	2.4 (1.3)	2.2 (1.2
Not enough sleep	2.7* (1.1)	2.2 (1.1)	2.3 (1.1)	1.9 (.98)	2.9*** (1.1)	2.1 (1.2)	2.3 (1.1
Sensitivity to toxins	2.2 (1.3)	2.1 (1.2)	1.9 (1.1)	1.8 (.98)	2.5 (1.2)	2.2 (1.1)	2.1 (1.1
Recent physical abuse	1.6 (1.1)	1.4 (.87)	1.4 (1.0)	1.5 (.97)	1.1 (.54)	1.3 (.72)	1.4 (.90
Recent sexual abuse	1.5 (1.0)	1.3 (.86)	1.5 (1.1)	1.4 (.87)	1.1 (.46)	1.1 (.36)	1.3 (.84
Weaker physical constitution	2.0 (1.1)	1.9 (1.1)	2.1 (1.1)	1.8 (.88)	2.0 (1.0)	1.8 (.98)	1.9 (1.0
Accident or injury	1.9* (1.2)	1.5 (.94)	1.6 (1.1)	1.4 (.87)	1.7 (1.1)	1.3 (.74)	1.5 (.74
Crises	2.5 (1.3)	2.1 (1.2)	2.3 (1.2)	2.5 (1.2)	1.9 (1.1)	2.1 (1.2)	2.2 (1.2
Anxiety/worry	2.7* (1.1)	2.3 (.97)	2.7 (.94)	2.7 (1.1)	2.2 (1.1)	2.4 (1.1)	2.5 (1.1
Personal hangups	2.3* (1.2)	1.8 (1.0)	2.3 (1.0)	2.3 (1.1)	1.7 (.84)	1.9 (.98)	2.1 (1.1
Depression	2.2* (1.2)	1.7 (1.0)	2.1 (1.1)	2.2 (1.2)	1.7 (.94)	1.9 (1.0)	2.0 (1.1
Poor diet	2.1 (1.2)	1.9 (1.1)	2.5 (.96)	2.4 (.98)	1.5* (.79)	2.0(1.1)	2.1 (1.1

Pairwise comparisons for syndromes versus respective controls
* p<.05; **p<.01, ***p<.001

4.5.3 *Illness Attributions*

Table 12 compares causal attributions of health problems for each diagnostic group. Compared to RA patients, FMS patients were significantly less likely to attribute their illness to problems with the immune system but more likely to attribute it to insufficient sleep, accident or injury, anxiety / worry, and personal hang-ups and depression. There were no significant differences between IBS and IBD patients. CFS patients were more likely than MS patients to attribute their illness to infection and insufficient sleep and less likely to attribute it to poor diet.

To further examine differences in casual attributions we conducted a factor analysis (principal components followed by varimax rotation) of the 16 possible causes of health problems. This analysis identified 4 components accounting for 68.6% of the variance; however, the fourth factor included only one item (E6. *Not enough sleep*). A three-component solution was forced and this accounted for 62% of the variance. The three factors were labeled 'sexual or physical abuse' (38.6% of variance), 'anxiety / depression' (12.8%) and 'infection / immune / toxins' (10.7%) (see Table 13).

Table 13. Factor Loading for Causes of Health Problems

		FACTOR 1 Sexual or Physical Abuse	**FACTOR 2** Anxiety/Depression	**FACTOR 3** Infection/Immune/Toxins
El9.	Recent sexual abuse	.92		
El3.	Sexual abuse as a child	.89		
El8.	Recent physical abuse	.88		
E2.	Physical abuse as a child	.84		
E11.	Accident or injury	.65†		
E13.	Anxiety/worry		.86	
E14.	Personal hang-ups		.82	
E15.	Depression		.82	
E12.	Crises		.79	
E16.	Poor diet		.59†	
E6.	Not getting enough good sleep		.43†	
El5.	Infection			.83
El1.	Problems with immune system			.80
El7.	Sensitivity to toxins			.69

† Item deleted from scale as inconsistent in content with dominant items.

Three scales were formed by summing responses to the items loading on a given factor (deleting items with loadings <.65 which were inconsistent with the strongest factor loadings; indicated in Table 13).

Table 14 compares the diagnostic groups on the three causal factors. There was no difference between groups on sexual / physical abuse. FMS patients, as well as those with IBD, tended to report anxiety / depression as a more important cause than did RA patients. CFS patients reported anxiety / depression as a *less* important cause than did FMS, IBS and IBD patients. In contrast, CFS patients viewed infection / immune / toxin as a significantly more important causal factor than all other groups; MS patients viewed this same factor as more important than did FMS, IBS and IBD patients.

Table 14. Causal Factors by Diagnostic Group

		FMS (n=41)	RA (n=43)	IBS (n=41)	IBD (n=55)	CFS (n=45)	MS (n=40)	Total (N=265)	Significance Test
Sexual or Physical Abuse NS	Mean	6.2	5.4	5.6	5.9	4.5	4.9	5.4
	SD	4.1	3.5	3.7	3.6	1.9	2.1	3.3	
Anxiety/depression df=5, 247	Mean	9.8	7.9	9.4	9.6	7.5	8.4	8.8	F=2.95,
	SD	4.2	3.4	3.6	4.0	3.4	3.7	3.8	p<.01[1]
Infection/Immune/Toxins F=13.31, df=5, 244	Mean	5.9	7.0	5.9	5.9	9.5	7.8	7.0	
	SD	2.8	2.7	2.7	2.5	2.0	2.8	2.9	p<.001[2]

[1] FMS>RA (p<.05), FMS>CFS (p<.01), IBD>RA (p<.05), IBS>CFS (p<.05), IBD>CFS (p<.01)
[2] CFS>all (p<.01), MS>FMS (p<.01), MS>IBS (p<.001), MS>IBD (p<.001)

4.6 Illness Impact

This section presents findings on the impact of FSS on disability and health care utilization. Patients were categorized by entry diagnosis.

4.6.1. *Disability*

Table 15 summarizes findings with the MOS SF-36 disability scales (raw scores). There were significant group differences on all scales except *Role-Emotional* and *Mental Health*.

On *Physical Functioning*, FMS, RA, CFS and MS were all functioning significantly lower than IBS and IBD (p<.001).

On *Role Functioning-Physical*, mean score for FMS was lower than RA, IBS and IBD ($p<.001$), RA was lower than IBS ($p<.01$) and MS was lower than IBD ($p<.001$); both CFS and MS were lower than RA ($p<.001$ and $p<.05$, respectively).

On the SF-36 *Bodily Pain* scale, low scores denote more pain. FMS patients reported more pain than RA ($p<.01$), IBS, IBD and MS ($p<.001$); CFS patients reported more pain than IBS, IBD and MS patients ($p<.001$); and RA patients reported more pain than IBS, IBD and MS patients ($p<.01$)

On *General Health*, CFS had lower mean score than FMS and RA ($p<.01$) and MS was lower than IBD ($p<.01$).

On *Vitality*, mean level for CFS patients was significantly lower than all groups ($p<.001$); FMS was lower than RA ($p<.001$), IBS ($p<.01$) and IBD ($p<.001$); MS was lower than RA ($p<.01$) and IBD ($p<.001$).

On *Social Functioning*, CFS was lower than all groups ($p<.01$); FMS was lower than RA, IBS, IBD ($p<.001$) and MS ($p<.01$); MS was lower than IBS ($p<.05$) and IBD ($p<.001$).

Finally, on *Reported Health Transition*, FMS reported a greater decrease in health in the last year than did RA ($p<.05$) and IBS, IBD, CFS and MS ($p<.001$) patients; RA patients reported a greater diminution that did IBS ($p<.05$); MS reported more deterioration in health than IBS ($p<.001$), IBD ($p<.01$) and CFS ($p<.05$) patients.

Table 16 display scores on the MOS scales for patients aggregated into two groups: FSS ('syndrome') and non-FSS ('disease'). There were significant differences between groups on three scales, with FSS patients showing greater bodily pain, lower social functioning and less role-emotional functioning.

Table 15. SF-36 Disability Scales by Entry Diagnostic Group (N=265)

	FMS	RA	IBS	IBD	CFS	MS	Total	Significance Test (df=5, 259)
Physical functioning subscale								
N	41	43	41	55	45	40	265	F=21.63
Mean	20.1	20.2	26.3	26.8	20.0	18.7	22.2	p<.001
SD	5.8	5.0	4.8	4.0	4.9	6.6	6.1	
Role-Physical								
N	41	43	41	55	45	40	265	F=18.32
Mean	4.9	6.1	6.9	6.4	4.5	5.4	5.7	p<.001
SD	1.4	1.5	1.4	1.7	.9	1.7	1.7	
Bodily pain								
N	37	40	38	49	44	38	246	F=11.26
Mean	5.4	7.0	8.7	8.6	6.5	8.5	7.5	p<.001
SD	1.9	2.3	1.9	2.9	2.4	3.3	2.8	
General Health								
N	41	43	41	55	45	40	265	F=5.61
Mean	15.6	15.7	16.5	16.9	12.8	14.6	15.4	p<.001
SD	4.8	3.7	4.2	3.9	4.2	4.9	4.5	
Vitality								
N	41	43	41	55	45	40	265	F=13.37
Mean	10.8	14.1	13.1	14.6	8.6	11.8	12.3	p<.001
SD	4.5	4.1	4.3	4.3	3.7	4.3	4.7	
Social functioning								
N	41	43	41	55	45	40	265	F=19.66
Mean	6.2	8.0	8.4	8.3	5.2	7.4	7.3	p<.001
SD	2.3	2.0	1.6	1.6	2.1	2.1	2.3	
Role-Emotional								
N	41	43	41	55	45	40	265	
Mean	4.7	5.3	5.1	5.3	4.8	5.0	5.0	NS
SD	1.3	1.1	1.2	1.1	1.3	1.1	1.2	
Mental health								
N	41	43	41	55	45	40	265	
Mean	20.3	22.5	21.4	22.3	21.4	21.9	21.7	NS
SD	5.9	3.8	4.9	4.9	5.0	3.8	4.8	
Reported health transition								
N	39	40	40	55	44	39	257	F=6.13
Mean	3.5	2.9	2.4	2.6	2.6	3.2	2.8	p<.001
SD	1.0	1.3	1.1	1.2	1.2	1.12	1.2	

Table 16. SF-36 Scales by Type of Illness (N=265)

	SYNDROME (n=127)	DISEASE (n=138)	Significance Test
Physical functioning			
N	127	138	
Mean	22.1	22.4	NS
SD	5.9	6.3	
Role-Physical			
N	127	138	
Mean	5.4	6.0	NS
SD	1.6	1.7	
Bodily pain			
N	119	127	t=3.33
Mean	6.9	8.0	df=241.54
SD	2.5	2.9	p<.001
General Health			
N	127	138	
Mean	14.9	15.9	NS
SD	4.7	4.2	
Vitality			
N	127	138	
Mean	10.8	13.6	NS
SD	4.5	4.4	
Social functioning			
N	127	138	t=5.18
Mean	6.6	8.0	df=238.17
SD	2.4	1.9	p<.001
Role-Emotional			
N	127	138	t=2.28
Mean	4.9	5.2	df=247.51
SD	1.3	1.1	p<.05
Mental health			
N	127	138	
Mean	21.0	22.3	NS
SD	5.3	4.3	
Reported health transition			
N	123	134	
Mean	2.8	2.9	NS
SD	1.2	1.2	

4.6.2 *Impact on Family and Social Stigma*

Patients' own ratings of the impact or burden of their illness on their families and the social stigma associated with their illness are presented in Table 17. Two measures of household impact or family burden were constructed: one that deleted and one that included items that addressed impact on children and child care: a 9 item version with Cronbach's $\alpha = .70$ (n=196); and a 12 item version with Cronbach's $\alpha = .79$ (n=71). The longer scale was used only with patients living in households with children at home.

On the 9 item Household Impact scale, the mean score of family burden of CFS was higher than FMS, RA, IBS ($p<.001$) and IBD ($p<.002$); the mean level of MS was higher than FMS, IBS ($p<.002$) and IBD ($p<.05$).

A very similar pattern was found with the 12 item Household Impact scale, although the smaller number of subjects (i.e., only those with children in their households) resulted in lower levels of significance: again, CFS reported higher levels of family burden than FMS, RA, IBS ($p<.001$) and IBD ($p<.01$); MS reported higher levels than FMS, IBS, ($p<.01$) and IBD ($p<.05$).

The 23 item stigma scale showed excellent reliability, with Cronbach's $\alpha = .91$ (n=236). CFS patients reported significantly higher levels of stigma than all other groups ($p<.001$); FMS were higher than IBS ($p<.05$); and MS were higher than RA, IBS, ($p<.001$), and IBD ($p<.01$).

Table 17. Illness Impact by Diagnostic Group

	FMS	RA	IBS	IBD	CFS	MS	Total	Significance Test
Household impact (9 items)								
N	34	34	31	48	39	30	216	F=6.28
Mean	18.5	19.2	18.5	19.9	22.7	21.8	20.1	df=5, 210
SD	5.1	4.7	4.4	3.4	3.6	4.0	4.4	p<.001
Household impact (12 items, including children)								
N	14	14	9	11	13	10	71	F=3.49
Mean	23.3	24.8	22.7	22.5	31.0	27.7	25.4	df=5, 65
SD	8.0	6.5	8.5	3.5	4.4	5.3	6.8	p<.01
Stigma								
N	35	39	38	51	42	33	238	F=16.54
Mean	48.9	44.2	42.9	45.7	61.5	52.6	49.2	df=5, 232
SD	13.0	11.4	10.4	10.9	10.8	8.1	12.6	p<.001

4.6.3 *Help-seeking and Health Care Utilization*

Patterns of help-seeking and health care utilization are reported in Tables 18 through 25. As shown in Table 18, the total number of different sources of help consulted in their lifetime was significantly higher for CFS patients than for any other group, and lower for MS than all groups except CFS. CFS patients also reported current use of significantly higher numbers of helpers or sources than all other groups.

Table 18. Lifetime Health Care Utilization by Diagnostic Group

	FMS (n=41)	RA (n=43)	IBS (n=41)	IBD (n=55)	CFS (n=45)	MS (n=40)	Total (N=265)	Significance Test (df=5, 259)
Total number of people or sources ever used								
Mean	8.5	8.3	8.6	8.9	12.1	7.1	9.0	F=17.67
Min.-Max.	4-15	3-14	3-14	2-16	8-19	2-13	2-19	p<.001[1]
SD	2.8	2.6	2.6	2.7	2.4	2.5	3.0	
Total number of people or sources used currently								
Mean	6.1	6.2	6.1	7.1	11.5	6.8	7.4	F=18.13
Min.-Max.	2-15	1-15	2-16	2-17	4-22	3-13	1-22	p<.001[2]
SD	3.2	3.0	3.5	3.5	3.6	2.9	3.8	
Proportion of sources used currently found to be helpful								
Mean	.47	.62	.46	.64	.60	.78	.60	F=8.74
SD	.23	.26	.26	.27	.24	.29	.28	p<.001[3]
Degree to which sources currently used found to be understanding								
Mean	1.79	2.42	2.02	2.45	2.21	3.02	2.32	F=8.68
SD	.78	1.10	.93	.97	.64	1.00	.98	p<.001[4]

1 CFS>all groups (p<.001), FMS>MS (p<.05), RA>MS (p<.05), IBS>MS (p<.01), IBD>MS (p<.001)

2 CFS>all groups (p<.001)

3 RA>FMS (p<.01), IBD>FMS (p<.01), CFS>FMS (p<.05), MS>FMS (p<.001), RA>IBS (p<.01), MS>RA (p<.01),
IBD>IBS (p<.001), CFS>IBS (p<.01), MS>IBS (p<.001), MS>IBD (p<.01), MS>CFS (p<.001).

4 MS>All (p<.01), FMS<RA (p<.01), FMS<IBD (p<.001), FMS<CFS (p<.05), IBS<RA (p<.05), IBD>IBS (p<.05)

Compared to their corresponding control groups, FMS, IBS and CFS groups all found that a smaller proportion of the help they sought was actually helpful to them. Similarly, each of the three FSS groups also found their helpers were less understanding of their condition than did their control group of patients with a non-FSS disease. CFS patients found their clinicians more understanding than did FMS patients. MS patients found their clinicians significantly more understanding than did patients from any other group.

As shown in Table 19, taken as a group, FSS patients saw significantly more health providers than non-FSS patients, both over their lifetime and currently. FSS patients

found a significantly lower proportion of the health care providers they saw to be helpful and also found them significantly less understanding of their condition than did control patients.

Table 19. Lifetime Health Care Utilization of FSS and non-FSS Groups*

	SYNDROME (n=127)	DISEASE (n=138)	Significance Test
Total number of people or sources ever used			
Mean	9.8	8.2	t=4.49; df=263
SD	3.1	2.7	p<.001
Total number of people or sources used currently			
Mean	8.0	6.7	t=2.74; df=230.12
SD	4.3	3.2	p<.01
Helpfulness of Sources			
Mean	.51	.68	t=4.93; df=263
SD	.25	.28	p<.001
Understanding of Sources			
Mean	2.01	2.61	t=5.18, df=254.81
SD	.80	1.05	p<.001

* Based on Doctor's Entry Diagnosis

Table 20 examines health care utilization for the cardinal symptoms of the three FSS: widespread muscular aches and pains, abdominal discomfort and fatigue. This analysis was only done on patients who had experienced aches and pains, abdominal discomfort or fatigue *in the last month* or who did not have pains or discomfort in the past month but had *ever had* such pains or fatigue for at least one month.

As expected, most patients with each FSS had sought help for the cardinal symptom of that syndrome . However, there were also high rates of help seeking for symptoms most closely associated with another syndrome. Fully 61% of IBS and 80% of CFS patients reported a history of widespread musculoskeletal pain and of these, 92% and 97% respectively, had sought help. Similarly, 57% of FMS and 68% of CFS patients reported abdominal discomfort and 94% and 93%, respectively, had sought help for this symptom specifically. The most prevalent symptom, fatigue, had affected 88% of FMS and 80% of IBS and 87% and 84% respectively had sought help. It should be noted, however, that the high rates of symptom prevalence and help-seeking for pain and fatigue were also found among the non-FSS control group diseases. FMS patients were more likely than RA patients to report abdominal discomfort and fatigue (p<.05). CFS patients were more likely than MS patients to have widespread pain, abdominal discomfort and fatigue (p<.01).

Table 20. Lifetime Health Care Utilization for Specific Symptoms

	FMS	RA	IBS	IBD	CFS	MS	Total

	(n=41)	(n=43)	(n=41)	(n=55)	(n=45)	(n=40)	(n=265)
Widespread pains							
N with symptom	41	38	25	31	36	17	188
% with symptom	100%	88%	61%	57%	80%Ω	22%	71%
% Seeking Help$	100%	98%	92%	97%	97%	100%	96%
Abdominal discomfort							
N with symptom	23	15	35	40	30	11	154
% with symptom	57%◊	35%	85%	73%	68%Ω	27%	59%
% Seeking Help$	94%	86%	100%	100%	93%	82%	96%
Fatigue							
N with symptom	36	33	33	40	44	32	218
% with symptom	88%◊	77%	80%	73%	98%Ω	80%	82%
% Seeking Help$	87%	79%	84%	94%	100%	97%	91%

* Doctor's Entry Diagnosis

$ Of those with symptoms

◊ Significantly greater proportion than for corresponding controls ($p<.05$)

Ω Significantly greater proportion than for corresponding controls ($p<.01$)

Table 21 displays the mean number of health care providers seen over the lifetime by patients in each diagnostic group for the cardinal symptoms of each syndrome (widespread muscular aches and pains, abdominal discomfort, fatigue). Again, this analysis was only done for patients who had experienced aches and pains, abdominal discomfort or fatigue *in the last month* or who did not have pains or discomfort in past month but had *ever had* pains or fatigue for at least one month. Two CFS cases were deleted from the analysis because they were outliers: one case reported 150 professionals seen for pain and 150 seen for fatigue; another case reported 50 professionals seen for pain.

Of those patients who had widespread aches and pains, CFS patients had seen significantly more health care providers for this problem than all other groups. CFS patients also saw significantly more health care providers for fatigue than all other groups. Among patients with abdominal discomfort, CFS had seen significantly more care providers than those with MS, RA or FMS. FMS patients saw more care providers than RA patients for widespread pain and for fatigue.

Table 21. Lifetime Number of Health Care Providers Seen for Specific Symptoms

	FMS	**RA**	**IBS**	**IBD**	**CFS**	**MS**	**Total**	Significance Test		
Number of professionals seen for widespread pains							N	38	41	22
29 36	18	184	F=4.64							
Mean	5.2	3.9	3.8	4.7	7.6	4.1	5.0	df=5, 178		

Min.-Max.	2-18	0-9	0-15	0-15	0-25	1-9	0-25	p<.001[1]		
SD	3.4	1.9	3.9	4.0	5.6	2.6	4.0			
Number of professionals seen for abdominal discomfort N							18	7	40	53
27	11	156	F=2.92							
Mean	2.8	3.1	4.7	5.4	5.2	1.6	4.5	df=5, 150		
Min.-Max.	0-7	0-7	1-11	1-22	0-25	0-3	0-25	p<.05[2]		
SD	1.8	2.4	3.0	3.7	6.1	1.1	3.9			
Number of professionals seen for fatigue N					31	28	25	35	43	32
194	F=23.46									
Mean	2.4	1.3	2.9	2.8	8.8	2.8	3.9	df=5, 188		
Min.-Max.	0-9	0-4	0-11	0-13	3-25	0-12	0-25	.001[3]		
SD	2.2	1.1	2.7	3.2	5.7	2.4	4.3			

1 FMS<CFS (p<.01), RA<CFS (p<.001), IBS<CFS (p<.001), IBD<CFS (p<.01), MS<CFS (p<.01)

2 FMS<IBD, CFS (p<.05); MS<IBS, IBD, CFS (p<.05).

3 CFS>all groups (p<.001)

The number of different types of treatments tried for current symptoms and the number of treatments found to be helpful are presented for each diagnostic group in Table 22. CFS patients had tried significantly more different types of treatment than all other groups. However, CFS patients found treatments less helpful than did RA, IBS, IBD and MS patients. FMS and IBS patients tended to find treatments less helpful than did their corresponding non-FSS comparison groups, RA and IBD.

Table 22. Number of Treatments Tried and Found Helpful for Current symptoms by Diagnostic Group

	FMS (n=41)	RA (n=43)	IBS (n=41)	IBD (n=55)	CFS (n=45)	MS (n=40)	Total (N=265)	Significance Test (df=5, 259)
Total number of treatments tried	Mean		6.0	5.6	4.9	5.7	7.9	5.3
5.9	F=5.73							
Min.-Max.	0-13	2-15	0-12	1-13	1-14	0-12	0-15	p<.001[1]
SD	2.9	2.3	3.0	2.4	3.7	2.8	3.0	
Helpfulness of Treatments	Mean		.66	.83	.70	.84	.59	.75
.73	F=8.05							
SD	.25	.22	.30	.17	.23	.25	.25	p<.001[2]

1 CFS>all groups (p<.01)

2 RA>FMS (p<.001), IBD>FMS (p<.001), RA>IBS (p<.01), RA>CFS (p<.001), IBD>IBS (p<.01), IBS>CFS (p<.05), IBD>CFS (p<.001), MS>CFS (p<.01)

Table 23 compares the number of different types of treatment tried and found helpful by FSS and non-FSS patients. FSS patients tried significantly more types of treatments than non-FSS patients but tended to find them less helpful. In fact, FSS patients pursued treatments to accumulate a similar level of successful experiences to that achieved by non-FSS patients with fewer treatments.

Table 23. Comparison of FSS and non-FSS Groups on Number of Treatments Tried and Found Helpful for Current Symptoms

	SYNDROME (n=127)	DISEASE (n=138)	Significance Test
Total number of treatments tried			Mean
6.3	5.6	t=2.08; df=226.81	
SD	3.5	2.5	p<.05
Helpfulness of Treatments			
Mean	.65	.81	t=5.49; df=237.1
SD	.27	.21	p<.001

In Table 24, sources of care are subdivided into conventional care and alternative care. Conventional care included practitioners of allopathic medicine and allied professionals (GPs, internists and specialists, emergency room and hospital care, physiotherapy) ; alternative care includes acupuncturists, chiropractors, homeopaths, faith healers and meditation or prayer. CFS patients made use of more types of conventional medicine than all other groups ($p<.001$); CFS patients were more likely to have sought alternative care than MS patients ($\chi^2=12.10$, df=1, $p<.05$) and made more frequent use of alternative care than all other groups ($p<.01$). CFS patients were much more likely than MS patients ($\chi^2 = 17.49$, $p<.001$) and all other groups to have made use of a clinical ecologist / allergist.

Table 24. Use of Alternative and Conventional Care by Diagnostic Group

	FMS (n=41)	**RA** (n=43)	**IBS** (n=41)	**IBD** (n=55)	**CFS** (n=45)	**MS** (n=40)	**Total** (N=265)	Overall Significance Test
Conventional care								
Mean number of health care uses in lifetime	5.80	6.00	5.69	5.78	7.24	4.70	5.88	F=12.6; df=5, 259
SD	1.72	1.31	1.46	1.58	1.52	1.36	1.66	p<.001
Alternative care								
Percentage who have ever sought care (%)	56.1	44.2	51.2	58.2	82.2	52.5	58.1	χ^2=41.13, df=5 p<.05
Mean number of health care uses in lifetime	.93	.67	.88	1.07	1.80	1.03	1.07	F=4.66, df=5, 259
SD	1.08	.92	.98	1.27	1.41	1.38	1.23	p<.001
Clinical Ecologist/Allergist								
Percent ever used	37	26	33	20	62	18	32.1	χ^2=27.17, df=5, 259 p<.001

As shown in Table 25, CFS patients were more likely than MS patients to have received and to be making current use of psychological or psychiatric care ($\chi^2=13.08$, df=1, $p<.001$). Those receiving such care tended to find it useful (mean = 71%) but CFS patients rated the mental health practitioner they were seeing as significantly less understanding of their problem than did MS and RA patients.

Table 25. Use of Psychological or Psychiatric Care by Diagnostic Group

	FMS (n=41)	RA (n=43)	IBS (n=41)	IBD (n=55)	CFS (n=45)	MS (n=40)	Total (n=265)	Overall Significance Test
Use of Psychological and/or Psychiatric Care								
Lifetime	22 (54%)	18 (43%)	16 (39%)	20 (37%)	38 (84%)	19 (48%)	133 (51%)	χ^2=28.11; df=5 p<.001[1]
Current	10 (44%)	9 (50%)	7 (41%)	11 (55%)	31 (84%)	15 (79%)	83 (62%)	χ^2=17.75; df=5 p<.01
Of Patients Receiving Psychological and/or Psychiatric Care								
N (%) Who Found it Helpful	6 (60)	7 (78)	5 (71)	10 (91)	20 (63)	12 (75)	60 (71)	NS
Degree to which psychologist or psychiatrist understands problem[2]								
Mean	2.70	3.44	2.57	3.00	2.23	3.53	2.78	F=3.23; df=5, 77
SD	1.41	.73	1.13	1.00	1.43	.74	1.27	p=.01[3]

[1] Pairwise comparisons

[2] Range of score: minimum 1 to maximum 4 ('not understanding' to 'very understanding')

[3] RA>CFS (p<.01), MS>CFS (p<.001)

5. DISCUSSION

5.1 Utility of the Diagnostic Instrument

The Diagnostic Interview for Functional Syndromes (DIFS) showed good levels of diagnostic accuracy measured against known groups with clinicians' standard diagnosis. However, the fair to moderate kappas (chance corrected coefficients of concordance) of .37 to .58 indicated substantial discrepancy between clinical and interview diagnoses. As well, while specificity was good (>90%), the level of diagnostic sensitivity was disappointingly low and limits the usefulness of the instrument for screening in epidemiological surveys. In fact, the relatively good specificity resulted in part from the use of DIS-type probes which asked for doctor's diagnoses. Since all of the patients had received doctor's diagnoses, the diagnostic algorithm was able to eliminate a number of potential false positives who had symptoms similar to the FSS which could be attributed to a non-FSS disease. However, it should be noted that there are probably high rates of clinically unrecognized comorbidity between FSS and non-FSS disorders (e.g. RA and FMS) which complicates tests of diagnostic specificity based on discriminating patients with the two disorders.

There are at least four possible explanations for the moderate levels of diagnostic reliability found in this study: (1) clinicians use additional information unavailable in the interview format, i.e. more extensive history, pertinent negatives, physical examination and laboratory tests; this would imply that clinicians' diagnoses are more accurate and that there is an inevitable limit on the accuracy of any purely interview based instrument; (2) clinicians use different diagnostic criteria than those used for the interview based algorithm; although physicians indicated on a diagnostic form that they were following the same ('official') criteria employed in constructing the instrument, it may be that in actual practice they were using looser criteria or differentially weighting symptoms and other factors in unknown ways; (3) FSS may have a varying course, relapsing and remitting, and patients' symptom reporting, attributions and recall may all be strongly influenced by these temporal variations; in the case of FMS, the requisite number of tender points may be present on one occasion and absent later; (4) patients respond differently to different interviewers or to the clinical versus the research context.

There is some evidence for all four explanations in our data. Clinicians were able to use the physical signs of the 1988 CDC criteria for CFS and so diagnose patients who did not meet criteria on purely symptoms; with the 1994 criteria which eliminate physical signs, the sensitivity of the interview improved. However, even with the 1994 criteria many patients diagnosed as CFS by clinicians did not report sufficient symptoms on interview, suggesting that clinicians were lax in their requirement for multiple symptoms. This is consistent with earlier observations in the literature that the diagnosis of CFS is often inconsistent. Use of the 1994 CDC criteria did improve discrimination between CFS and MS.

Both FMS and IBS appeared to have a relapsing/remitting course according to patients. This might have contributed to the low test/re-test reliabilities and to the discrepancy between the clinicians initial diagnosis and our interview-based diagnosis which was made weeks, months or, in some cases, years after the onset of symptoms. Once a

clinical diagnosis is made, it tends to stick so that clinicians may label patients with milder or a limited range of syndromes, ordinarily insufficient to merit the diagnosis, with the same FSS they were noted to have on a previous occasion.

Finally, previous studies with the DIS and other instruments make it clear that symptom reports vary widely from one occasion to the next, limiting the reliability of all interview-based diagnoses. This may reflect the normal functioning of memory and the response to the demand characteristics of the interview situation.

Given these problems inherent in interview-based diagnoses of disorders defined as symptom clusters, the diagnostic interview may be limited in the reliability it can achieve. While discrepant with clinician ratings, in some cases the interview may be more valid since it stringently adheres to symptom lists and thresholds that may be ignored by clinicians responding to patient style of clinical presentation and other extrinsic factors.

5.2 Co-occurrence of Functional Somatic Syndromes

Although clinicians reported low to non-existent levels of co-occurrence of syndromes, the diagnostic interview indicated substantial overlap of syndromes, ranging from 33% of IBS patients to 89% of CFS patients meeting criteria for at least one other syndrome. The fact that the overlap was greatest for CFS may be an artifact of requiring many different somatic symptoms for the diagnosis of CFS. If clinicians tend to view patients with few other symptoms besides idiopathic fatigue as CFS patients, the lower degree of overlap they report would be expected. Nevertheless, the finding of high degrees of overlap with the interview suggests that some of these patients are not well served by the segmentation of care common in specialty medical practice.

We found high levels of tender points in patients in all diagnostic groups. Tender point examinations were completed on almost all FMS, RA and CFS patients. The levels among CFS patients were almost as high as those among FMS patients. Although tender point examinations were done only for those IBS (22/41), IBD (26/55) and MS (17/40) patients who reported widespread musculoskeletal pain, significant levels were found in these groups as well. This raises questions about the specificity of tender points as a diagnostic sign for FMS or else suggests that the pathophysiological process that gives rise to tender points may be provoked by a wide range of illnesses. One explanation for this would be the possibility that tender points (and indeed, FMS) result from selective deprivation of stage 4 non-REM sleep which would therefore constitute a final common pathway by which a great range of symptoms and conditions could give rise to some level of musculoskeletal pain and tender points (Moldofsky, 1986). This intriguing possibility requires further research.

5.3 Characteristics of Patients with FSS

Overall, patients with FSS were remarkably similar to non-FSS diseased patients in their psychological characteristics. There was no identifiable 'FSS personality' shared by syndromes. FMS patients did score slightly higher on the neuroticism scale than RA but no higher than the other groups including MS patients. Neuroticism has been linked to the tendency to report bodily symptoms (Costa & McCrae, 1985; 1987; Kirmayer et

al., 1994; Pennebaker & Watson, 1991) and could account for observations of elevated levels of dysphoria and multiple somatic symptoms in some FMS patients (Kirmayer et al., 1988; 1994). CFS patients scored higher than all the other patients except IBD on the Openness Scale. Previous observations of alexithymia in inflammatory bowel disease (particularly externally oriented or operatory thinking) reported by Taylor et al. (1981) were not supported by our findings.

FSS patients were more hypochondriacal than non-FSS patients. Indeed, CFS patients expressed the highest levels of hypochondriacal concerns, even exceeding the levels of illness worry of MS patients. The high levels of the MS patients may reflect the affective instability and anxiety that can accompany that condition or realistic illness worry commensurate with concern about the eventual course of the illness. Similarly, the higher levels for patients with CFS could be attributed to legitimate worry about the course of the illness in the face of the lack of definitive diagnosis and effective treatment. Alternatively, CFS may arise in part from hypochondriacal fears which lead an individual to respond to the fatigue that follows a viral illness with prolonged bed rest and excessive efforts at self-protection (Sharpe et al., 1992; Wessely et al., 1989).

There were no significant differences among groups in symptom attributional style, except for a tendency for FMS patients to make fewer normalizing attributions than IBD patients, and a tendency for MS patients to do the same compared to both IBS and IBD patients. Thus, our results did not confirm the recent finding that elevated scores on the somatic scale of the SIQ were a good predictor of chronicity in patients attending general practice with new onset of fatigue secondary to an acute viral illness (Cope et al., 1994). The use of specialty clinic samples in the present study may have muted potential diagnostic differences related to help-seeking behavior and chronicity since all of our sample had sought medical help repeatedly and all had chronic illnesses.

FMS patients recollected having experienced a greater number of serious life events in the three months preceding the onset of their illness than most other groups. Compared to RA patients, FMS patients reported more family conflict, financial troubles and other serious trauma or stress before the onset of their illness. There were no overall differences between FSS and non-FSS groups on life events.

On illness attributions, while FMS patients were more likely than RA and CFS patients to acknowledge psychological factors as causes of their illness (including anxiety or worry, personal hang-ups and depression), CFS had the lowest levels of endorsement of these items. When these causes were grouped together into an anxiety / depression factor, CFS patients had a significant lower level of attribution of their illness to this cause than did FMS, IBS and IBD. The relative reluctance of CFS patients to consider psychosocial factors as causal contributors to their distress raises the possibility that CFS patients are denying any psychological problems or actively countering any suggestion they may have emotional, psychological or interpersonal problems.

5.4 Impact of FSS

On illness impact, FSS were found to be highly disabling conditions. Differences among diagnostic groups in physical disability were consistent with the known effects of RA and MS on mobility and physical functioning. Patients with FSS were more severely

disabled than the non-FSS comparison group on dimensions of bodily pain, social functioning and the extent to which emotional troubles interfered with life roles. FMS patients reported the highest levels of pain of any group. CFS patients reported significantly lower levels of vitality and social functioning than all other groups. The picture that emerges is of illnesses in which pain or fatigue gives rise to impairments in social and emotional functioning without marked physical impairment. This profile is quite different from that of the non-FSS diseases in which social functioning tends to be relatively preserved. Just why social functioning should be so affected in FMS and CFS remains for further study but raises, once again, the notion that social-psychological factors contribute directly to the level of distress and disability.

Consistent with the findings of impaired social functioning, CFS patients reported higher levels of household impact of their illness than any other group except MS. CFS patients also reported the highest levels of self-perceived social stigmatization of their condition. This may reflect the highly politicized nature of the condition. The combination of marked social disability and enervation disproportionate to the level of physical disability presents dilemmas for families, employers and insurers. The lack of definitive diagnostic markers and the generally poorly understood nature of the problem put patients in an ambiguous situation in which the severity of their illness and, indeed, their sincerity, is sometimes contested. In a vicious circle, this predicament may contribute substantially to the distress and disability of CFS patients.

The predicament of CFS patients was also reflected in higher levels of health care utilization of both conventional and alternative medicine than all other diagnostic groups. Whether measured by number of sources of help, number of different types of practitioner or number of different types of treatment, CFS patients consistently had the highest rates of health care use, both lifetime and current. This was marked, however, by lower levels of satisfaction with health care received. On average, CFS patients perceived their treatments as less helpful and their helpers as less understanding of their condition than did other groups. In our sample, CFS patients also made higher rates of use of psychological or psychiatric care. This may be an artifact of our referral sources which included a psychiatrist specialized in the treatment of CFS. However, in their continued search for effective treatment many of these patients end up seeing mental health practitioners. In general, the CFS patients found psychological treatment helpful but rated the mental health practitioner as less understanding of their condition than did patients from other groups.

The pattern of results with CFS is representative of the FSS overall (though of IBS to a lesser extent). When groups were aggregated and compared to non-FSS patients, FSS patients saw greater numbers of health care practitioners and sources (both lifetime and current), and found these sources less helpful and less understanding of their condition. Interestingly, the absolute levels of satisfaction with health care, and degree of understanding, when summed across all providers, were no different across groups; it is only when this value is corrected for the number of providers seen that the FSS groups show lower levels of satisfaction. This suggests that individuals keep seeking help until they find someone who understands them and something that works. If so, then the high rates of utilization by FSS patients should not be interpreted as 'abnormal illness behaviour', excessive help-seeking or over-utilization of services but as a pragmatic search for an effective response to poorly understood and managed conditions.

5.5 Conclusion

This study represents several steps in the development and validation of the Diagnostic Interview for Functional Syndromes (DIFS). Further refinements may improve sensitivity for population screening and concordance with clinician diagnoses. However, the relatively high levels of specificity may still make the instrument useful for community studies of medically unexplained somatic distress in both medical clinics and the community. Given that clinicians may apply diagnostic criteria for FSS quite inconsistently, the development of a structured interview may also lead to refinements in the clinical diagnosis of FSS, particularly in research studies. Determination of the degree of overlap of different FSS will sensitize clinicians to the need for broader diagnostic evaluation, and may lead to screening instruments that can be used in clinical settings to circumvent the narrow perspective of specialized medical care. Clarification of the role of psychiatric disorders in FSS may enable clinicians to apply specific psychiatric treatments to patients with somatized depression, anxiety or hypochondriasis. Positive diagnosis of functional somatic syndromes and early recognition of somatization may reduce needless laboratory tests and investigations with their excess cost and risk of iatrogenic morbidity.

More precise epidemiological study of these conditions would be valuable to health researchers, planners and providers. Reliable estimates of the prevalence and co-occurrence of cases of FSS in the clinic and in the general population would aid in the study of the etiology of discrete conditions. Previous studies of somatization in the community have examined only a single FSS or have studied the generalized somatic distress of somatization disorder. By studying cases of discrete FSS we may identify etiological factors obscured when disorders that affect many bodily systems are studied independently or are lumped together indiscriminately under the rubric of somatization disorder.

Estimation of the prevalence of FSS in the community would provide health care planners with a basis for determining the likely demand for care. It is known that FSS patients make substantial use of primary care and make up a large portion of the practice of the medical specialties that treat them. Prevalence estimates could be valuable in determining the number of cases of untreated FSS in the community, the likely regional

differences in requests for care, and information needed to devise an optimal distribution of increasingly limited health care resources.

Identification of cases of FSS will provide a baseline from which to judge the change in prevalence of these conditions over time. Although there is no clear evidence that FSS are increasing or decreasing in the community, media attention suggests the former. Attention given to chronic fatigue syndrome and the very recent recognition of the FMS-like condition of repetitive-strain-injury syndrome (RSI) in the media give the impression of an epidemic of functional somatic distress (Reid & Reynolds, 1990). The changing prevalence of these conditions is worthy of further study (Stewart, 1990).

Finally, we have provided data that the FSS are disabling conditions with great impact on household, social functioning and well-being. They are associated with very high levels of help-seeking and health care utilization but these are proportionate to the difficulty patients have in finding practitioners who offer them effective treatment and understanding. In future studies, we hope to disentangle some of the social and psychological factors that contribute to coping with FSS or to frustration, disablement and chronicity. Clearly, these reside not only in patients and their families but also in the health care system itself.

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APPENDIX

A. Consent forms (English and French)

B. Questionnaires (English and French)

Diagnostic Interview Questionnaire and Self-report Measures

Probe Sheet

Follow-up Questionnaire and Errata (Jan. 1996)

Annotated Diagnostic Interview Questionnaire and Self-report Measures with Sources of Items

Annotated Follow-up Questionnaire with Sources of Items

C. Interviewer's Manual

D. Clinician's Diagnostic Evaluation Form

E. Diagnostic Criteria and Algorithms

F. MOS Disability Scales, SF-36

Development and Validation of a Structured Diagnostic Interview for Functional Somatic Syndromes

Final Report

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