

# Functional impairment in chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivity

M. Ruth Lavergne MSc Donald C. Cole MD MSc FRCPC Kathleen Kerr MD Dip Env Health Lynn M. Marshall MD FAAEM FRSM

## ABSTRACT

**OBJECTIVE** To characterize patients diagnosed with multiple chemical sensitivity (MCS), chronic fatigue syndrome (CFS), or fibromyalgia (FM), to compare their level of function with Canadian population average values, and to assess factors associated with function.

**DESIGN** Chart review and abstraction of clinical information.

**SETTING** The Environmental Health Clinic (EHC) at Women's College Hospital in Toronto, Ont, which is a provincial referral centre for patients with illnesses with suspected environmental links, especially MCS, CFS, and FM.

**PARTICIPANTS** A total of 128 consecutive patients diagnosed with 1 or more of MCS, CFS, or FM, seen between January 2005 and March 2006 at the EHC.

**MAIN OUTCOME MEASURES** Demographic and socioeconomic characteristics, comorbid diagnoses, duration of illness, health services usage, life stresses, helpful therapeutic strategies, and functional impairment measured by the Short Form-36, compared with Canadian population average values. Factors significantly associated with function in bivariate analyses were included in multiple linear and logistic regression models.

**RESULTS** The patient population was predominantly female (86.7%), with a mean age of 44.6 years. Seventy-eight patients had discrete diagnoses of 1 of MCS, CFS, or FM, while the remainder had 2 or 3 overlapping diagnoses. Most (68.8%) had stopped work, and on average this had occurred 3 years after symptom onset. On every Short Form-36 subscale, patients had markedly lower functional scores than population average values, more so when they had 2 or 3 of these diagnoses. Having FM, younger age at onset, and lower socioeconomic status were most consistently associated with poor function.

**CONCLUSION** Patients seen at the EHC demonstrated marked functional impairment, consistent with their reported difficulties working and caring for their homes and families during what should be their peak productive years. Early comprehensive assessment, medical management, and social and financial support might avoid the deterioration of function associated with prolonged illness. Education and information resources are required for health care professionals and the public, along with further etiologic and prognostic research.

## EDITOR'S KEY POINTS

- Multiple chemical sensitivity, chronic fatigue syndrome, and fibromyalgia are relatively common chronic conditions—about 5% of Canadians have been diagnosed with at least 1 of these illnesses—but little Canadian research has explored them.
- In this study, diagnosis of fibromyalgia was associated with decreases in physical functioning, emotional well-being, vitality (energy and fatigue), and social functioning and with increased bodily pain; chronic fatigue syndrome was associated with decreases in physical functioning and emotional well-being; and multiple chemical sensitivity was associated with less bodily pain than reported by the rest of the study population. Although the study population was predominantly female, men generally reported lower functional status than women did.
- This study was conducted among patients of the Environmental Health Clinic in Toronto, Ont, which might have biased patient selection toward those with longer duration and greater severity of symptoms.

This article has been peer reviewed.  
*Can Fam Physician* 2010;56:e57-65

# Baisse de l'état fonctionnel dans le syndrome de fatigue chronique, la fibromyalgie et l'hypersensibilité chimique multiple

M. Ruth Lavergne MSc Donald C. Cole MD MSc FRCPC Kathleen Kerr MD Dip Env Health Lynn M. Marshall MD FAAEM FRSM

## RÉSUMÉ

**OBJECTIF** Établir les caractéristiques des patients présentant un diagnostic d'hypersensibilité chimique multiple (HCM), de syndrome de fatigue chronique (SFC) ou de fibromyalgie (FM), comparer leur niveau de fonctionnement aux valeurs moyennes de la population canadienne et évaluer les facteurs associés à l'état fonctionnel.

**TYPE D'ÉTUDE** Revue de dossiers avec extraction des données cliniques.

**CONTEXTE** L'Environmental Health Clinic (EHC) du Women's College Hospital de Toronto, Ont., un centre de référence provincial pour patients souffrant de maladies pouvant être liées à l'environnement, dont la HCM, le SFC et la FM.

**PARTICIPANTS** Un total de 128 patients consécutifs vus au EHC entre janvier 2005 et mars 2006 et pour lesquels on a posé au moins un diagnostic de HCM, de SFC ou de FM.

**PRINCIPAUX PARAMÈTRES À L'ÉTUDE** Caractéristiques démographiques et socioéconomiques, présence de comorbidité, durée de la maladie, utilisation des services de santé, stress de la vie, stratégies thérapeutiques efficaces et baisse du statut fonctionnel mesurée par le questionnaire SF-36, en comparaison des valeurs moyennes pour la population canadienne. Les facteurs présentant une association significative avec l'état fonctionnel dans des analyses bivariées ont été inclus dans des modèles de régression multilinéaire et logistique.

**RÉSULTATS** L'échantillon était composé surtout de femmes (86,7%), l'âge moyen était de 44,6 ans; 78 patients n'avaient qu'un diagnostic (HCM, SFC ou FM), les autres en avaient chacun 2 ou 3. La plupart avaient cessé de travailler, en moyenne 3 ans après le début des symptômes. Pour chaque sous-échelle du questionnaire SF-36, les scores des patients pour l'état fonctionnel étaient très inférieurs à ceux de la population générale; ceux des patients avec 2 ou 3 diagnostics étant encore plus bas. Facteurs les plus régulièrement associés à une baisse fonctionnelle: diagnostic de FM, début plus jeune et statut socioéconomique bas.

**CONCLUSION** Les patients vus à l'EHC présentaient une importante baisse du statut fonctionnel, et une difficulté à s'acquitter des tâches quotidiennes habituelles à cet âge. Une évaluation précoce minutieuse, un traitement médical, et un support social et financier pourraient éviter la détérioration fonctionnelle associée à une maladie prolongée. Il faudra offrir des outils de formation et d'information au personnel soignant et au public, et faire d'autres recherches sur les aspects étiologique et pronostique.

## POINTS DE REPÈRE DU RÉDACTEUR

- Le HCM, le SFC et la FM sont des Canadiens fréquents – environ 5% des Canadiens ont au moins un de ces diagnostics – mais peu d'études canadiennes y ont été consacrées.
- Dans cette étude, le diagnostic de FM s'accompagnait d'une baisse de l'état fonctionnel physique, de la sensation de bien-être, de la vitalité et du fonctionnement social, et d'une augmentation des douleurs; le SFC, d'une baisse de l'activité physique et du bien-être émotionnel; et l'HCM, de moins de douleurs corporelles que ce qui est rapporté pour le reste de la population. Bien que les sujets de l'étude étaient surtout des femmes, les hommes rapportaient généralement un état fonctionnel inférieur à celui des femmes.
- Cette étude portait sur des patients de l'Environmental Health Clinic de Toronto, Ont, ce qui pourrait avoir biaisé la sélection des patients en faveur de symptômes plus sévères et plus durables.

Cet article a fait l'objet d'une révision par des pairs.  
*Can Fam Physician* 2010;56:e57-65

Chronic fatigue syndrome (CFS), fibromyalgia (FM), and multiple chemical sensitivity (MCS) are relatively common chronic conditions with the potential to substantially limit functioning and health-related quality of life.<sup>1-7</sup> The Statistics Canada 2005 Canadian Community Health Survey found that 1.2 million Canadians, or 5% of those aged 12 or older, reported having been diagnosed with at least 1 of these 3 illnesses: 1.3% with CFS, 1.5% with FM, and 2.4% with MCS.<sup>8</sup> The overall prevalence rose with age to 6.9% for women aged 45 to 64—a period in women's lives when they would usually be employed and active contributors to society. All 3 of these conditions have symptoms referable to multiple body systems, and studies in the United States show high rates of overlap among them.<sup>5,7,9,10</sup> However, they each have some distinct features, as outlined in the case criteria and descriptions provided in **Boxes 1 to 3**<sup>11-16</sup>; the most notable are the profound physical and cognitive fatigue of CFS, the widespread musculoskeletal pain of FM, and the common triggering of neurologic symptoms in MCS on exposure to diverse chemicals at previously tolerable levels or at levels tolerated by most people. There is a paucity of Canadian literature describing these commonly encountered illnesses, particularly in the clinical setting.

This study aimed to describe a clinical patient population in a Canadian context, to document functional status with the Medical Outcomes Study's 36-item short form (SF-36)<sup>17</sup> compared with Canadian population average values, and to determine whether level of function was associated with demographic or diagnostic characteristics.

## METHODS

### Setting and population

The Environmental Health Clinic (EHC) is the only

#### Box 1. Chronic fatigue syndrome case criteria and description\*

- New onset, unexplained, persistent fatigue that substantially reduces activity
- Postexertional malaise or fatigue with pathologic slow recovery
- Sleep dysfunction
- Pain in muscles and joints
- Neurologic or cognitive manifestations—at least 1 symptom in 2 categories:
  - autonomic
  - neuroendocrine
  - immune manifestations
- Illness persisting at least 6 mo (3 mo in children); onset is usually distinct, but can be gradual

\*Diagnostic checklists can be downloaded from [www.ocfp.ca](http://www.ocfp.ca). Click on the Environmental Health Committee link. Data from Fukuda et al<sup>11</sup> and Carruthers et al.<sup>12</sup>

#### Box 2. Fibromyalgia case criteria and description\*

- More than 3 mo of widespread musculoskeletal pain (bilateral, upper and lower body, axial)
- Report of pain by patient in 11 or more of 18 tender points when palpated at 4 kg of pressure (nail blanches) in addition to the following symptoms<sup>13</sup>:
  - fatigue, particularly after exertion
  - neurologic or cognitive complaints
  - headaches
  - loss of sleep rhythm
  - heat or cold intolerance
  - emotional numbness or anxiety
  - cardiovascular complaints (eg, dizziness, hypotension, heart rhythm abnormalities)
  - marked weight change

\*Diagnostic checklists can be downloaded from [www.ocfp.ca](http://www.ocfp.ca). Click on the Environmental Health Committee link. Data from the American College of Rheumatology.<sup>14</sup>

#### Box 3. Multiple chemical sensitivity case criteria and description\*

- Symptoms reproducible with exposure
- Condition is chronic
- Low levels of exposure provoke symptoms (lower than previously or commonly tolerated)
- Symptoms improve or resolve when incitants removed
- Responses occur to multiple chemically unrelated substances
- Symptoms involve multiple organ systems
- University of Toronto discriminating symptoms<sup>15</sup>
  - Having a stronger sense of smell than most people and 2 of the following:
    - feeling spacey
    - feeling dull or groggy
    - having difficulty concentrating

\*Diagnostic checklists can be downloaded from [www.ocfp.ca](http://www.ocfp.ca). Click on the Environmental Health Committee link. Data from the 1999 consensus definition.<sup>16</sup>

government-funded, academically affiliated clinic in Ontario that is provincially mandated to provide assessment of patients with complex, chronic environmentally linked conditions. Patients are referred by physicians with either previous diagnoses or possible diagnoses of CFS, FM, or MCS, or suspicion of another environmentally related condition. With approval from the Research Ethics Board of Women's College Hospital, data were extracted from charts of all consecutive patients seen between January 2005 and March 2006 who had been diagnosed by EHC physicians with at least 1 of CFS, FM, and MCS (N=128).

### Measures

Before being assessed, referred patients completed a 20-page intake questionnaire. The demographic

questions, exposure history, and symptoms, including those necessary to meet diagnostic criteria for MCS, CFS, and FM, were derived from the University of Toronto Health Survey, an instrument reproducible and validated for MCS.<sup>18</sup> Patient postal codes were linked to 2001 census dissemination areas to obtain median income and average value of dwellings.

Data extracted included the date of onset of the main symptoms, the date the patient last felt consistently well, and the date he or she stopped work, if applicable (permitting calculation of patient age for each); health care usage; helpful therapies; and sources of support. Stressful life events, including loss or illness of loved ones, loss of job, separation, divorce, addiction in self or someone close, and physical, emotional, or sexual abuse were summed before and after symptom onset.

The EHC physicians used consensus case definitions in diagnosing patients: for CFS and FM, the Canadian clinical working case definitions,<sup>12,13</sup> which built on earlier consensus definitions<sup>11,14</sup>; and for MCS, a combination of the 1999 consensus criteria<sup>16</sup> and 4 symptoms found to best discriminate among patients expected to have a high prevalence of the condition.<sup>15</sup> Additional clinical diagnoses were also recorded by EHC physicians as indicated by history, physical examination, laboratory investigations, or consultant reports. Given the small sample size, diagnostic subcategories were combined, with more specific diagnoses subsumed under a limited set of labels.

All patients completed the SF-36, which assesses functional status on 8 descriptively named subscales: physical functioning, role limitations due to physical health problems, bodily pain, general health perceptions, energy and fatigue, social functioning, role limitations due to personal or emotional health problems, and emotional well-being.<sup>17</sup> The derivation of these subscales has been well described by Ware and Sherbourne.<sup>17</sup> Each has been shown to have high reliability and validity. They have been used in general population surveys of Canadians,<sup>19,20</sup> in a range of patient populations, including those with CFS,<sup>1,2,7,21</sup> FM,<sup>22-24</sup> or MCS,<sup>6</sup> as well as in a comparative study of all 3 groups.<sup>7</sup> Scoring followed published guidelines,<sup>17</sup> resulting in scale ranges from 0 to 100, with higher values representing better function.

### Statistical analyses

Raw SF-36 score values were transformed into z scores based on the same Canadian age- and sex-specific population means and standard deviations.<sup>25,26</sup> Two subscales, physical and emotional role limitation, exhibited nonnormal distributions, with a high proportion of values clustered at zero. The z scores for these 2 subscales were dichotomized into 2 groups (greater than or equal to the median and less than the median) for subsequent analysis.

Descriptive statistics were calculated for independent variables by CFS, FM, or MCS diagnosis or combination of diagnoses. Associations between SF-36 subscale z scores and patient characteristics were first examined in a series of bivariate analyses, including 1-way ANOVA (analysis of variance) tests,  $\chi^2$  tests for dichotomous and categorical variables, and Spearman correlation and Satterthwaite *t* tests for continuous variables. Starting with all relevant variables significant at  $P < .10$  in bivariate analyses, multivariate regression analyses were conducted, with reduction to variables significant at  $P < .05$  in final regression models.

Linear regression was performed for normally distributed scores, with regression coefficients and 95% confidence intervals (CIs) reported; logistic regression was performed for physical and emotional role limitation scores, with odds ratios (ORs) and associated 95% CIs reported, corresponding to scores greater than or equal to the median.

## RESULTS

### Characterization of the patient population

Considerable overlap was evident in the distribution of MCS, CFS, and FM diagnoses (**Table 1**). All clinic patients had markedly low scores relative to Canadian population average values matched for age and sex categories. The lowest scores were among those with all 3 conditions (**Figure 1**).

Common additional diagnoses included depression (34.4%), irritable bowel syndrome (27.3%), food sensitivities (27.3%), sleep disorders (25.8%), and nutritional deficiencies (24.2%) (**Table 1**).

The mean age of the study sample was 44.6 years (SD 11.2), and patients were predominantly female (86.7%). On average, people stopped feeling well at age 36.9 (SD 12.6), usually before they identified the specific symptoms that brought them to the clinic. Among those who had stopped work (68.0%), a mean of 3 years had elapsed between symptom onset and their becoming unable to work. Of the 53 individuals who did not work for pay and did not receive disability benefits, 30 were married or cohabitating, likely supported by their partners' incomes. The remaining 23 might have been living on savings or local social assistance.

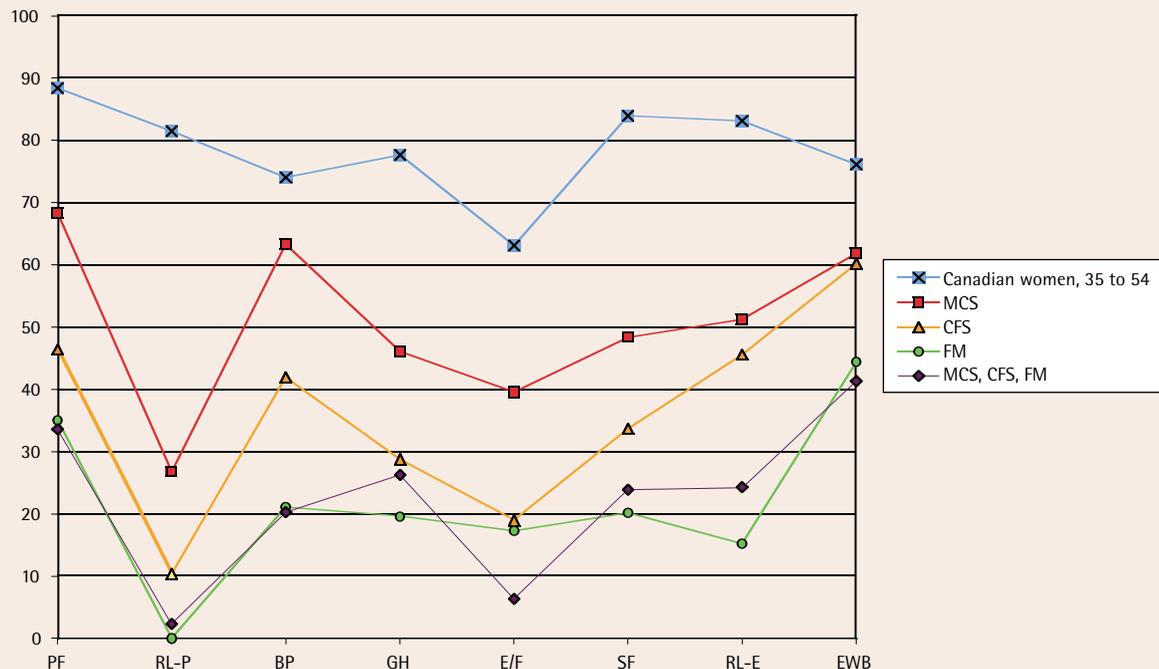
The mean number of visits to a family physician in the 12 months before completion of the intake questionnaire was 10.7 (SD 8.7;  $n=103$ ); the mean number of visits to other physicians was 13.7 (SD 18.2;  $n=123$ ). These numbers are far higher than comparable 2005 Canadian Community Health Survey values of 2.9 (SD 4.3) and 0.79 (SD 2.0), respectively, for Canadian adults aged 30 to 60 or 3.4 (SD 4.6) and 0.98 (SD 2.2), respectively, for Canadian women aged 30 to 60.<sup>26</sup>

**Table 1. Characteristics of the EHC patient population: A) Sex, relationship status, income, health coverage, additional diagnoses, and strategies for dealing with health problems; B) age, life stresses, health services usage, paid work hours, and average value of dwellings.**

A) CHARACTERISTICS	DIAGNOSES, N (% WITHIN DIAGNOSIS)								
	MCS ONLY N = 41	CFS ONLY N = 26	FM ONLY N = 11	CFS, FM N = 27	MCS, CFS N = 8	MCS, FM N = 4	MCS, CFS, FM N = 11	≥2 DIAGNOSES N = 50	TOTAL N = 128
Sex									
• Female	35 (85.4)	18 (69.2)	9 (81.8)	27 (100.0)	8 (100.0)	4 (100.0)	10 (90.9)	49 (98.0)	111 (86.7)
• Male	6 (14.6)	8 (30.8)	2 (18.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)	1 (2.0)	17 (13.3)
Relationship status									
• Single	15 (36.6)	10 (38.5)	1 (9.1)	7 (25.9)	2 (25.0)	1 (25.0)	5 (45.5)	15 (30.0)	41 (32.0)
• Divorced, separated, or widowed	8 (19.5)	2 (7.7)	4 (36.4)	6 (22.2)	1 (12.5)	1 (25.0)	2 (18.2)	10 (20.0)	24 (18.8)
• Married or cohabitating	18 (43.9)	14 (53.8)	6 (54.5)	14 (51.9)	5 (62.5)	2 (50.0)	4 (36.4)	25 (50.0)	63 (49.2)
Source of income									
• None stated	15 (36.6)	9 (34.6)	4 (36.4)	10 (37.0)	4 (50.0)	3 (75.0)	8 (72.7)	25 (50.0)	53 (41.4)
• Disability benefits	7 (17.1)	8 (30.8)	4 (36.4)	11 (40.7)	3 (37.5)	1 (25.0)	3 (27.3)	18 (36.0)	37 (28.9)
• Paid employment	19 (46.3)	9 (34.6)	3 (27.3)	6 (22.2)	1 (12.5)	0 (0.0)	0 (0.0)	7 (14.0)	38 (29.7)
Health coverage									
• No coverage	13 (31.7)	8 (30.8)	4 (36.4)	5 (18.5)	5 (62.5)	4 (100.0)	1 (9.1)	15 (30.0)	40 (31.3)
• Drug and some extended benefits	14 (34.1)	8 (30.8)	0 (0.0)	9 (33.3)	0 (0.0)	0 (0.0)	3 (27.3)	12 (24.0)	34 (26.6)
• Comprehensive coverage	14 (34.1)	10 (38.5)	7 (63.6)	13 (48.1)	3 (37.5)	0 (0.0)	7 (63.6)	23 (46.0)	54 (42.2)
Common additional diagnoses									
• Depression	11 (26.8)	7 (26.9)	4 (36.4)	13 (48.1)	5 (62.5)	0 (0.0)	4 (36.4)	22 (44.0)	44 (34.4)
• Irritable bowel syndrome	9 (22.0)	4 (15.4)	2 (18.2)	11 (40.7)	2 (25.0)	1 (25.0)	6 (54.5)	20 (40.0)	35 (27.3)
• Food sensitivities	13 (31.7)	4 (15.4)	4 (36.4)	4 (14.8)	4 (50.0)	2 (50.0)	4 (36.4)	14 (28.0)	35 (27.3)
• Sleep disorder	6 (14.6)	8 (30.8)	8 (72.7)	7 (25.9)	2 (25.0)	1 (25.0)	1 (9.1)	11 (22.0)	33 (25.8)
• Nutritional deficiencies	7 (17.1)	5 (19.2)	4 (36.4)	7 (25.9)	3 (37.5)	3 (75.0)	2 (18.2)	15 (30.0)	31 (24.2)
• Anxiety disorder	2 (4.9)	4 (15.4)	1 (9.1)	5 (18.5)	0 (0.0)	0 (0.0)	2 (18.2)	7 (14.0)	14 (10.9)
Strategies for dealing with health problems									
• None identified	1 (2.4)	4 (15.4)	2 (18.2)	1 (3.7)	0 (0.0)	0 (0.0)	1 (9.1)	2 (4.0)	9 (7.0)
• Avoiding triggers	21 (51.2)	0 (0.0)	1 (9.1)	5 (18.5)	4 (50.0)	2 (50.0)	4 (36.4)	15 (30.0)	37 (28.9)
• Rest	2 (4.9)	14 (53.9)	2 (18.2)	13 (48.2)	2 (25.0)	1 (25.0)	4 (36.4)	20 (40.0)	38 (29.7)
B) CHARACTERISTICS	DIAGNOSES, MEAN (SD)								
	MCS ONLY N = 41	CFS ONLY N = 26	FM ONLY N = 11	CFS, FM N = 27	MCS, CFS N = 8	MCS, FM N = 4	MCS, CFS, FM N = 11	≥2 DIAGNOSES N = 50	TOTAL N = 128
Age, y									
• Current	46.5 (11.0)	45 (21)	56 (14)	45.5 (13)	38.5 (12)	45.0 (11.0)	41.0 (22)	44 (11.0)	44.6 (11.2)
• Stopped work (n = 87)	45.4 (10.5)	39.7 (17.1)	53.9 (18.2)	43.6 (14.2)	33.9 (15.6)	40.44 (9.3)	38.9 (25.2)	38.9 (10.2)	41.6 (11.3)
• Symptom onset	44.5 (11.4)	39.6 (25.4)	52.7 (17.0)	41.3 (17.5)	30.3 (12.9)	45.3 (13.9)	39.2 (22.3)	36.8 (12.5)	38.6 (12.8)
• Last felt well	40.7 (13.1)	39.5 (25.4)	46.8 (17.0)	41.1 (19.4)	29.2 (14.7)	37.7 (4.7)	34.6 (21.6)	34.9 (11.6)	36.9 (12.6)
Count of life stresses									
• Before symptom onset	4.5 (6.0)	7 (10.0)	7 (14.0)	3.5 (5.0)	11.0 (3)	4.0 (3.0)	4.0 (8.0)	5.0 (4.0)	6.0 (4.0)
• After symptom onset	3.0 (3.0)	5.0 (5.5)	8.0 (9.0)	2.5 (6.0)	9.0 (12.0)	9.0 (6.0)	2.0 (5.0)	5.0 (4.0)	4.0 (7.0)
Health services usage									
• No. of visits to FP or GP in past 12 mo	6.7 (4.2)	9.0 (6.4)	11.8 (2.5)	13.7 (7.7)	8.0 (7.9)	16.5 (5.0)	16.3 (15.5)	12.0 (10.0)	10.7 (8.7)
• No. of visits to any other physician in past 12 mo	16.1 (20.5)	4.4 (5.1)	10.4 (8.7)	18.7 (9.9)	5.3 (5.8)	6.5 (6.4)	25.9 (36.7)	14.0 (18.0)	13.7 (18.2)
Hours of paid work/wk (n = 125)	16.7 (19.3)	9.5 (16.3)	3.8 (10.9)	5.6 (12.7)	4.4 (12.4)	0 (0.0)	3.2 (10.6)	4.4 (11.5)	9.4 (16.2)
Census average value of dwellings, \$ (n = 125)	241 146 (146 409)	216 705 (167 875)	173 353 (81 628)	225 820 (129 068)	266 649 (70 609)	135 170 (103 937)	242 078 (170 125)	227 645 (130 741)	225 020 (140 765)

CFS—chronic fatigue syndrome, EHC—Environmental Health Clinic, FM—fibromyalgia, MCS—multiple chemical sensitivity.

**Figure 1. Comparison of EHC patients and Canadian population averages (women, aged 35 to 54) on the 8 scales of the SF-36**



BP—bodily pain, CFS—chronic fatigue syndrome, E/F—energy and fatigue, EHC—Environmental Health Clinic, EWB—emotional well-being, FM—fibromyalgia, GH—general health perceptions, MCS—multiple chemical sensitivity, PF—physical functioning, RL-E—emotional role limitation, RL-P—physical role limitation, SF—social functioning, SF-36—Short Form-36.

### Factors associated with functional status

In bivariate analyses, any diagnosis of FM, either alone or with another condition, was associated with significantly lower scores on all subscales ( $P < .05$ ) except physical role limitations. A diagnosis of CFS was associated with lower scores on physical function, emotional well-being, bodily pain, and general health ( $P < .05$ ). In multivariate linear regression analysis, having FM remained strongly associated with lower function on all subscale models except general health. In logistic regression it was associated with better function on the emotional role limitations subscale and was not associated with physical role limitations (Table 2). A diagnosis of CFS remained significantly associated with lower physical function ( $R = -0.67$ , 95% CI -1.17 to -0.17) and emotional well-being ( $R = -1.04$ , 95% CI -1.56 to -0.52), while a diagnosis of MCS was significantly associated with improved function on the bodily pain subscale ( $R = 0.19$ , 95% CI 0.07 to 0.83), relative to the rest of the patient population (Table 2).

Men generally reported lower functional status than women, significant for energy and fatigue ( $R = -0.72$ , 95% CI -1.23 to -0.13) and social functioning ( $R = -1.00$ , 95% CI -1.60 to -0.39) despite the small number of patients ( $n = 17$ ). However, their functioning with respect to

physical role limitations was significantly higher (OR 0.20, 95% CI 0.06 to 0.59) (Table 2). Neither reported lifetime stress nor abuse was associated with current function. While 42 of the 128 patients (32.8%) indicated that they had no support for dealing with their health problems or in their day-to-day lives, no significant difference on any SF-36 subscale was associated with lack of support. Unmarried people scored significantly better than married people on the emotional well-being subscale ( $R = 0.53$ , 95% CI 0.03 to 1.03) (Table 2).

The younger patients were when their symptoms began, the greater the reported reduction in their physical functioning. Longer duration of symptoms, as reflected by months passed since patients last felt well, was associated with greater emotional role limitation (Table 2). As SF-36 scores included in this analysis have been standardized to age- and sex-specific population average values, it appears that younger patients with CFS, FM, or MCS experience greater functional impairment.

Higher numbers of visits to family physicians reported in the previous 12 months were associated with lower scores on general health, and visits to other physicians were associated with lower physical function scores (Table 2). Patients who had not identified

**Table 2. Factors associated with EHC patients' functional status in linear and logistic regression: Negative coefficients and ORs signify that factors are associated with reduced function; blank cells represent results that were not statistically significant ( $P < .05$ ).**

FACTORS	MULTIPLE LINEAR REGRESSION, COEFFICIENT ESTIMATES (95% CI)						LOGISTIC REGRESSION, OR (95% CI)*	
	PHYSICAL FUNCTIONING (N = 122)	EMOTIONAL WELL-BEING (N = 128)	ENERGY AND FATIGUE (N = 128)	SOCIAL FUNCTIONING (N = 128)	BODILY PAIN (N = 128)	GENERAL HEALTH (N = 128)	PHYSICAL ROLE LIMITATIONS (N = 128)	EMOTIONAL ROLE LIMITATIONS (N = 128)
Male sex	-	-	-0.72 (-1.23 to -0.13)	-1.00 (-1.60 to -0.39)	-	-	0.20 (0.06 to 0.59)	-
Unmarried	-	0.53 (0.03 to 1.03)	-	-	-	-	-	-
Supplementary health coverage	-	-	-	0.29 (0.05 to 0.52)	-	-	-	-
Sleep disorder diagnosed	-	-0.66 (-1.24 to -0.08)	-	-	-	-	-	-
Age at symptom onset, y	0.029 (0.008 to 0.047)	-	-	-	-	0.04 (0.02 to 0.05)	-	-
Last felt well, mo	-	-	-	-	-	-	-	0.994 (0.989 to 0.999)
No. of visits to any physician (past 12 mo)	-0.014 (-0.026 to -0.001)	-	-	-	-	-	-	-
No. of visits to family physician (past 12 mo)	-	-	-	-	-	-0.032 (-0.058 to -0.006)	-	-
Nothing helpful in dealing with health condition	-	-	-	-0.99 (-1.78 to -0.20)	-	-	-	-
Avoiding triggers found helpful	-	-	-	-	-	-	-	2.61 (1.11 to 6.14)
Hours paid work/wk	0.020 (0.005 to 0.035)	-	-	-	-	-	-	-
Census average of dwelling values/\$1000	0.0024 (0.0006 to 0.0043)	-	-	0.0006 (0.0002 to 0.0027)	0.0019 (0.0004 to 0.0037)	-	-	-
MCS diagnosed	-	-	-	-	0.19 (0.07 to 0.83)	-	-	-
CFS diagnosed	-0.67 (-1.17 to -0.17)	-1.04 (-1.56 to -0.52)	-	-	-	-	-	-
FM diagnosed	-0.92 (-1.44 to -0.40)	-0.71 (-1.24 to -0.18)	-0.91 (-1.32 to -0.51)	-0.92 (-1.33 to -0.51)	-0.20 (-1.42 to -0.65)	-	-	0.35 (0.16 to 0.76)
Adjusted $R^2$	0.377	0.233	0.142	0.222	0.306	0.215	NA	NA

CFS—chronic fatigue syndrome, CI—confidence interval, EHC—Environmental Health Clinic, FM—fibromyalgia, MCS—multiple chemical sensitivity, NA—not applicable, OR—odds ratio.

\*Role limitations due to physical health and emotional problems have nonnormal distributions owing to a clustering of values at zero. Linear regression was therefore inappropriate; z scores for these scales have been dichotomized at the median, and ORs corresponding to a score greater than or equal to the median and associated 95% CIs are reported.

anything on the previsit questionnaire as being helpful for their health conditions (7.0%) had lower scores on all SF-36 subscales, with significant differences for social functioning ( $P = .003$ ). Those who reported that avoiding observed environmental symptom triggers was helpful (28.9%) had higher odds for better emotional role function (Table 2). No other therapies, including use of naturopathic or homeopathic remedies,

supplements, or dietary changes, were associated with significant differences in SF-36 scores. It must be stressed that patients seen at the EHC represent those with greater duration and severity of illness, and that some individuals who identified helpful management strategies might have been less likely to be included in our population because they did not present to the clinic for care.

Higher reported weekly hours of paid work were associated with better scores on physical function in multivariate analysis (Table 2). Patients in census areas with higher socioeconomic status, measured using the proxy of average value of dwellings, had better scores for physical function, bodily pain, and general health (Table 2).

### DISCUSSION

The substantial functional impairment we observed among CFS, FM, and MCS patients is consistent with findings in other countries.<sup>1-4,6,7</sup> The SF-36 profile for CFS differs from that for depression, in that the last subscale (emotional well-being) is relatively high.<sup>1,2</sup> Although not necessarily comparable because of difference in methods, EHC patients appear to be more impaired than other persons of the same sex and age range with these disorders in the recent Canadian Community Health Survey, of whom a quarter reported "dependency."<sup>8</sup> Because the EHC is the only Ontario government clinic of its kind accepting referrals from family physicians and specialists, there are long wait times for assessment. This biases patient selection toward those with greater duration and severity of illness and lack of sufficient response to earlier management attempts, including symptom trigger avoidance and rest. The high number of visits to physicians that we observed is likely related to the complex nature of these conditions, the associated comorbidities, and the low reported functional status. Given the limited perceived effectiveness for these patients of current management approaches, clinical consultation might also represent a search for clearer answers and the need for ongoing medical support. Physician visits might also be influenced by reported limitations in social support and illness-related family relationship difficulties.

As EHC patients completed the SF-36 at their first visits, they might have been unaware that frequent exposure to triggering substances could mask associations with chronic symptoms.<sup>27</sup> Information provided by the EHC about how to do elimination and reexposure challenges, a strategy consistently reported to be helpful,<sup>28-30</sup> might have subsequently assisted EHC patients in identifying and avoiding more triggering substances. Similarly, before EHC consultation, patients can be unaware of the tendency for people with chronic low energy to be more active on days they feel somewhat better, then to be bedridden for several days.<sup>12</sup> Instead, pacing of rest and gentle exercise have been found to be helpful.<sup>12,31</sup> Nevertheless, reliance on recall for measurement of many of the historical variables might limit their validity. The small sample sizes in some of the diagnostic categories likely reduce their explanatory power.

To be diagnosed with FM, patients must experience widespread musculoskeletal pain. For that

reason, poorer function related to bodily pain would be expected in this subgroup; but why our patients experienced poorer function on 4 other subscales and somewhat better function on the emotional role limitation subscale is less clear. Further, half our sample had MCS; this could be because MCS is more widely recognized than CFS and FM as being environmentally linked and, because referring physicians perceive EHC's expertise to be in environmentally linked conditions, they are more likely to refer patients with MCS to the clinic.

The unclear origin and course of each disorder, the subjective nature of diagnostic criteria, and the absence of consistently abnormal physical (except with FM) and laboratory findings have generated difficulties for patients with CFS, FM, or MCS in securing disability support awards in Canada. This has recently led to commission of a literature review and report on environmental sensitivities (including MCS) by the Canadian Human Rights Commission,<sup>32</sup> which recognizes CFS and FM as conditions overlapping with MCS. Low rates of employment and lack of access to disability support payments can lead to strains on household resources and greater declines in function, as suggested by the better function among those in wealthier residential census tracts.

A Canadian national research agenda with sustained funding is needed for comprehensive study of these 3 common conditions. Etiologic studies should build upon the recent identification of genetic polymorphisms associated with diagnoses of CFS,<sup>33-36</sup> FM,<sup>37</sup> and MCS,<sup>38,39</sup> which might render patients with these conditions more susceptible to adverse effects from exposure to ubiquitous toxins or infectious agents. International collaboration would be worthwhile, given the promising research advances being made in the United Kingdom on differential gene expression linked to viral or pesticide exposures, which can perturb mitochondrial, immune, and neurologic functions.<sup>40,41</sup> Prospective cohort studies, initiated earlier in the clinical course, could aid further understanding of prognosis and guide clinical management approaches.

### Conclusion

Substantial functional impairments relative to Canadian same age and sex population averages were observed in EHC patients diagnosed with CFS, FM, or MCS, consistent with findings in other countries and with patients' reported difficulties working and caring for their homes and families. The association of poorer function with younger age at symptom onset, lower socioeconomic status, having more than 1 of these diagnoses or FM alone suggests that early comprehensive assessment and medical management, as well as nondiscriminatory recognition by social service agencies with attendant financial support<sup>32</sup> might avoid the deterioration of function associated with prolonged illness. Provincial referral centres like the EHC can serve as foci for identification of

best practices, collaborative educational, and research efforts, as well as support to front-line health professionals. Expanded health professional training and continuing education in Canada, along with expanded public and professional information resources, such as those recently launched by the US Centers for Disease Control and Prevention,<sup>42</sup> are imperative to reduce the large gaps in response to the burdens observed in these patients and their families. 

At the time of writing, **Ms Lavergne** was a master's candidate in Community Health and Epidemiology at Dalhousie University in Halifax, NS, and a research intern for the Population Council of Vietnam. **Dr Cole** is an Associate Professor in the Dalla Lana School of Public Health at the University of Toronto in Ontario, Head of the Agriculture and Health Division of the International Potato Center, and a Senior Scientist in Workplace Studies at the Institute for Work and Health. **Dr Kerr** is a staff physician and Medical Research Liaison in the Environmental Health Clinic at Women's College Hospital in Toronto and a Lecturer in the Department of Family and Community Medicine at the University of Toronto. **Dr Marshall** is an Assistant Professor in the Clinical Sciences Division at the Northern Ontario School of Medicine at Lakehead and Laurentian universities, a Lecturer in the Department of Family and Community Medicine at the University of Toronto, and a staff physician and Medical Education Liaison in the Environmental Health Clinic at Women's College Hospital.

#### Acknowledgment

We thank **Nancy Bradshaw** for her assistance with the logistics of chart access and **Drs Riina Bray** and **Alison Bested** for helpful reviews of the manuscript.

#### Contributors

All authors contributed to study conception and design. **Ms Lavergne** undertook the extraction of data from clinic charts, analysis of data, and drafting of the article. **Dr Cole** oversaw data analysis. **Drs Kerr** and **Marshall** acquired the data, assisted in the interpretation of results, and contributed to drafting the article. All authors provided critical review of the draft and approved the final version to be published.

#### Competing interests

None declared

#### Correspondence

**Dr Kathleen Kerr**, Women's College Hospital, Family and Community Medicine, 76 Grenville St, Toronto, ON M5S 1B2; telephone 416 351-3764; fax 416 323-6130; e-mail [k.kerr@utoronto.ca](mailto:k.kerr@utoronto.ca)

#### References

- Komaroff AL, Fagioli LR, Doolittle TH, Gandek B, Gleit MA, Guerriero RT, et al. Health status in patients with chronic fatigue syndrome and in general population and disease comparison groups. *Am J Med* 1996;101(3):281-90.
- Hardt J, Buchwald D, Wilks D, Sharpe M, Nix WA, Egle UT. Health-related quality of life in patients with chronic fatigue syndrome: an international study. *J Psychosom Res* 2001;51(2):431-4.
- Reeves WC, Wagner D, Nisenbaum R, Jones JF, Gurbaxani B, Solomon L, et al. Chronic fatigue syndrome—a clinically empirical approach to its definition and study. *BMC Med* 2005;3:19.
- Bennett RM, Schein J, Kosinski MR, Hewitt DJ, Jordan DM, Rosenthal NR. Impact of fibromyalgia pain on health-related quality of life before and after treatment with tramadol/acetaminophen. *Arthritis Rheum* 2005;53(4):519-27.
- Caress SM, Steinemann AC, Waddick C. Symptomatology and etiology of multiple chemical sensitivities in the southeastern United States. *Arch Environ Health* 2002;57(5):429-36.
- Black DW, Doebbeling BN, Voelker MD, Clarke WR, Woolson RF, Barrett DH, et al. Quality of life and health-services utilization in a population-based sample of military personnel reporting multiple chemical sensitivities. *J Occup Environ Med* 1999;41(10):928-33.
- Jason LA, Taylor RR, Kennedy CL. Chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities in a community-based sample of persons with chronic fatigue syndrome-like symptoms. *Psychosom Med* 2000;62(5):655-63.
- Park J, Kudson S. Medically unexplained physical symptoms. *Health Rep* 2007;18(1):43-7.
- Bell IR, Baldwin CM, Schwartz GE. Illness from low levels of environmental chemicals: relevance to chronic fatigue syndrome and fibromyalgia. *Am J Med* 1998;105(3A):74S-82S.
- Buchwald D, Garrity D. Comparison of patients with chronic fatigue syndrome, fibromyalgia, and multiple chemical sensitivities. *Arch Intern Med* 1994;154(18):2049-53.
- Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome: a comprehensive approach to its definition and study. International Chronic Fatigue Syndrome Study Group. *Ann Intern Med* 1994;121(12):953-9.
- Carruthers BM, Jain AK, De Meirleir KL, Peterson DL, Klimas NG, Lerner AM, et al. Myalgic encephalomyelitis/chronic fatigue syndrome: clinical working case definition, diagnostic and treatment protocols. *J Chronic Fatigue Syndr* 2003;11(1):7-115.
- Jain AK, Carruthers BM, van de Sande MI, Barron SR, Donaldson CCS, Dunne JV, et al. Fibromyalgia syndrome: Canadian clinical working case definition, diagnostic and treatment protocols—a consensus document. *J Musculoskeletal Pain* 2003;11(4):3-107.
- Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, Goldenberg DL, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990;33(2):160-72.
- McKeown-Eyssen GE, Baines CJ, Marshall LM, Jazmaji V, Sokoloff ER. Multiple chemical sensitivity: discriminant validity of case definitions. *Arch Environ Health* 2001;56(5):406-12.
- Multiple chemical sensitivity: a 1999 consensus. *Arch Environ Health* 1999;54(3):147-9.
- Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). 1. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.
- McKeown-Eyssen GE, Sokoloff ER, Jazmaji V, Marshall LM, Baines CJ. Reproducibility of the University of Toronto self-administered questionnaire used to assess environmental sensitivity. *Am J Epidemiol* 2000;151(12):1216-22.
- Hopman WM, Towheed T, Anastassiades T, Tenenhouse A, Poliquin S, Berger C, et al. Canadian normative data for the SF-36 health survey. Canadian Multicentre Osteoporosis Study Research Group. *CMAJ* 2000;163(3):265-71.
- Hopman WM, Berger C, Joseph L, Towheed T, vandenKerkhof E, Anastassiades T, et al. Stability of normative data for the SF-36: results of a three-year prospective study in middle-aged Canadians. *Can J Public Health* 2004;95(5):387-91.
- Herrell R, Goldberg J, Hartman S, Belcourt M, Schmalzing K, Buchwald D. Chronic fatigue and chronic fatigue syndrome: a co-twin control study of functional status. *Qual Life Res* 2002;11(5):463-71.
- Alanoglu E, Ulas UH, Ozdag F, Odabasi Z, Çakçi A, Vural O. Auditory event-related brain potentials in fibromyalgia syndrome. *Rheumatol Int* 2005;25(5):345-9. Epub 2004 Feb 21.
- Neumann L, Berzak A, Buskila D. Measuring health status in Israeli patients with fibromyalgia syndrome and widespread pain and healthy individuals: utility of the short form 36-item health survey (SF-36). *Semin Arthritis Rheum* 2000;29(6):400-8.
- Bergman S. Psychosocial aspects of chronic widespread pain and fibromyalgia. *Disabil Rehabil* 2005;27(12):675-83.
- Hopman WM, Berger C, Joseph L, Towheed T, Anastassiades T, Tenenhouse A, et al. Is there regional variation in the SF-36 scores of Canadian adults? *Can J Public Health* 2002;93(3):233-7.
- Statistics Canada. *Canadian Community Health Survey, cycle 3.1*. Ottawa, ON: Statistics Canada; 2005.
- Miller CS. Toxicant-induced loss of tolerance—an emerging theory of disease? *Environ Health Perspect* 1997;105(Suppl 2):445-53.
- Lax MB, Henneberger PK. Patients with multiple chemical sensitivities in an occupational health clinic: presentation and follow-up. *Arch Environ Health* 1995;50(6):425-31.
- Ziem GE. Profile of patients with chemical injury and sensitivity, part II. *Int J Toxicol* 1999;18(6):401-9.
- Gibson PR, Elms AN, Ruding LA. Perceived treatment efficacy for conventional and alternative therapies reported by persons with multiple chemical sensitivity. *Environ Health Perspect* 2003;111(12):1498-504.
- Mannerkorpi K, Iverson MD. Physical exercise in fibromyalgia and related syndromes. *Best Pract Res Clin Rheumatol* 2003;17(4):629-47.
- Sears ME. *The medical perspective on environmental sensitivities*. Ottawa, ON: Canadian Human Rights Commission; 2007. Available from: [www.chrc-ccdp.ca/pdf/envsensitivity\\_en.pdf](http://www.chrc-ccdp.ca/pdf/envsensitivity_en.pdf). Accessed 2007 May 17.
- Kaushik N, Fear D, Richards SC, McDermott CR, Nuwaysir EF, Kellam P, et al. Gene expression in peripheral blood mononuclear cells from patients with chronic fatigue syndrome. *J Clin Pathol* 2005;58(8):826-32.
- Kerr JR, Christian P, Hodgetts A, Langford PR, Devanur LD, Petty R, et al. Current research priorities in chronic fatigue syndrome/myalgic encephalomyelitis: disease mechanisms, a diagnostic test and specific treatments. *J Clin Pathol* 2007;60(2):113-6. Epub 2006 Aug 25.
- Carlo-Stella N, Badulli C, De Silvestri A, Bazzichi L, Martinetti M, Lorusso L, et al. A first study of cytokine genomic polymorphisms in CFS: positive association of TNF-857 and IFN $\gamma$  874 rare alleles. *Clin Exp Rheumatol* 2006;24(2):179-82.
- Vernon SD, Whistler T, Cameron B, Hickie IB, Reeves WC, Lloyd A, et al. Preliminary evidence of mitochondrial dysfunction associated with post-infective fatigue after acute infection with Epstein Barr virus. *BMC Infect Dis* 2006;6:15.
- Gürsoy S, Erdal E, Herken H, Madenci E, Alasehirli B, Erdal N. Significance of catechol-O-methyltransferase gene polymorphism in fibromyalgia syndrome. *Rheumatol Int* 2003;23(3):104-7.
- McKeown-Eyssen G, Baines C, Cole DE, Riley N, Tyndale RF, Marshall L, et al. Case-control study of genotypes in multiple chemical sensitivity: CYP2D6, NAT1, NAT2, PON1, PON2 and MTHFR. *Int J Epidemiol* 2004;33(5):971-8. Epub 2004 Jul 15.
- Schnakenberg E, Fabig KR, Stanulla M, Strobl N, Lustig M, Fabig N, et al. A cross-sectional study of self-reported chemical-related sensitivity is associated with gene variants of drug-metabolizing enzymes. *Environ Health* 2007;6:6.
- Kerr JR, Petty R, Burke B, Gough J, Fear D, Sinclair LI, et al. Gene expression subtypes in patients with chronic fatigue syndrome/myalgic encephalomyelitis. *J Infect Dis* 2008;197(8):1171-84.
- Kerr JR, Matthey DL. Preexisting psychological stress predicts acute and chronic fatigue and arthritis following symptomatic parvovirus B19 infection. *Clin Infect Dis* 2008;46(9):e83-7.
- Centers for Disease Control and Prevention [website]. *Chronic fatigue syndrome*. Health professionals. Atlanta, GA: Department of Health and Human Services; 2006. Available from: [www.cdc.gov/cfs/healthcareprofessionals.htm](http://www.cdc.gov/cfs/healthcareprofessionals.htm). Accessed 2008 Aug 23.