

# Recent insights into 3 underrecognized conditions

## Myalgic encephalomyelitis–chronic fatigue syndrome, fibromyalgia, and environmental sensitivities–multiple chemical sensitivity

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The Ontario Ministry of Health and Long-Term Care recently released the interim report<sup>1</sup> of a task force charged with providing recommendations on 3 symptom-based conditions that have both shared and distinctive features (**Box 1**): myalgic encephalomyelitis–chronic fatigue syndrome (ME-CFS), fibromyalgia (FM), and environmental sensitivities–multiple chemical sensitivity (ES-MCS).<sup>2</sup>

None of these conditions has consistent physical or laboratory findings, and the conditions vary in severity. Their underlying biological mechanisms remain unclear. As with many chronic conditions, patients are at risk of anxiety, depression, and other psychological symptoms. The foregoing attributes and the lack of proven treatments and clinical practice guidelines have led to decades of uncertainty regarding diagnosis, unnecessary investigations, ineffective treatment, and unmitigated suffering.

Nevertheless, as noted in the report, recent insights reveal both the need and opportunities for finding solutions. First is evidence underscoring the prevalence of these conditions in Canada and their effect on health care use and employment. Second is mounting evidence of biological mechanisms that might lead to effective treatments. These insights, including those summarized within this article, deserve wide dissemination in the primary care community.

### Box 1. Typical symptoms of ME-CFS, FM, and ES-MCS

Symptoms common to all 3 conditions include the following:

- Fatigue and, to varying degrees, pain, sleep disturbances, and neurologic and cognitive symptoms

Distinct symptoms among each condition include the following:

- The fatigue in ME-CFS is chronic, profound, and not improved by rest, and there is postexertional malaise
- The chronic musculoskeletal pain in FM is widespread
- The symptoms of ES-MCS are provoked by exposure to low levels of multiple (and often unrelated) chemical, biological, or physical agents. Symptoms are usually neurocognitive, and might involve respiratory and other systems, with relief or improvement when inciting agents are removed

ES-MCS—environmental sensitivities–multiple chemical sensitivity, FM—fibromyalgia, ME-CFS—myalgic encephalomyelitis–chronic fatigue syndrome.

### Prevalence and costs

Data from the 2014 Canadian Community Health Survey by Statistics Canada indicate that of Canadians aged 25 years or older, 5.5% (1.3 million) reported having 1 or more of the 3 conditions: 1.6% reported ME-CFS, 2.0% reported FM, and 2.7% reported ES-MCS. Women were more than twice as likely as men were to report each disorder. Comparing respondents who reported 1 or more of the conditions with those reporting none, 16% versus 10% reported at least 10 consultations in the past year with a primary care practitioner, 53% versus 32% reported at least 1 consultation with a specialist, 15% versus 8% reported at least 1 hospitalization, and 40% versus 26% reported joblessness.<sup>3</sup> The economic and human costs of these conditions appear considerable.

### Biological mechanisms: ME-CFS and FM

Some advances have clearly been made in recognition of and research into ME-CFS and FM. Recent reviews,<sup>4-7</sup> including those by the US Institute of Medicine and advice for patients by the American College of Physicians, support the existence of these conditions as distinct disabling disorders affecting millions with a likely organic or physiologic basis. Infections are the suspected initial trigger of ME-CFS, with contribution from environmental and polygenetic susceptibility factors. Evidence is mounting for involvement of immunologic and inflammatory pathologies, neurotransmitter signaling disruption, microbiome perturbations, and metabolic or mitochondrial abnormalities. Regarding FM, the central nervous system is likely involved, triggered by physical trauma or infections. Twin studies indicate inheritance might contribute to half the risk of developing FM.<sup>7</sup> Some studies suggest the involvement of genetic polymorphisms related to the metabolism of neurotransmitters involved in pain modulation.

### Stigma and meagre funding: ES-MCS

In contrast, recognition of and research into ES-MCS in North America has remained bleak. (The exception is some early work by the University of Toronto's Environmental Hypersensitivity Research Unit that found discriminant validity of 2 published case definitions<sup>8</sup> and identified associations with genetic polymorphisms that are known to alter metabolism of some chemicals.<sup>9</sup>) A detailed PubMed search uncovered only 320 references

specific to ES-MCS, compared with 7453 references specific to ME-CFS and 9846 references specific to FM, with relatively few describing original research. No high-level reviews of the evidence surrounding ES-MCS have occurred since a 1999 statement made by the American College of Occupational and Environmental Medicine<sup>10</sup> and a 2001 international workshop,<sup>11</sup> both concluding that substantial research investments were needed. No such investments followed.

Research funding for all 3 conditions has been meagre or nonexistent. From 2012 to 2015, for example, the Canadian Institutes of Health Research funded 2, 11, and 0 grants for ME-CFS, FM, and ES-MCS research, respectively, with a combined total of \$1.8 million—less than 10% of the funding for research on emphysema or on multiple sclerosis and epilepsy, which have lower prevalences.

Slow progress likely reflects, in part, the social stigmatization surrounding these conditions.<sup>12,13</sup> This is particularly severe for ES-MCS, given the common need for affected patients to avoid everyday exposures to items that trigger their symptoms, such as fragrances, cleaning products, and marking pens.<sup>14</sup> Stigmatization also increases the risk of anxiety, depression, and other psychological symptoms that can be mistaken for causes rather than effects of the diseases themselves. Moreover, the uncertainty surrounding management strategies and, in the case of ES-MCS, the legal struggles that often occur regarding causation and avoidance issues, also arguably cast a “chill” on clinicians and scientists, deterring involvement in clinical care and research.

### Future steps

But things might be turning around. For example, the Canadian Institutes of Health Research announced the results of a ME-CFS planning and dissemination grant competition,<sup>15</sup> a harbinger for important potential future funding of basic research. The US National Institutes of Health announced 3 ME-CFS Collaborative Research Centers with more than \$6 million in funding in 2017.<sup>16</sup> With respect to ES-MCS, there is a growing body of research being published by investigators in Europe and Japan, which has provided evidence supporting the involvement of neurobiological,<sup>17,18</sup> metabolic,<sup>19</sup> and genetic susceptibility factors.<sup>20</sup>


Finally, in its interim report, the Ministry of Health and Long-Term Care task force proposed that concrete steps be taken to establish a foundation for an effective, patient-centred system of care in Ontario (**Box 2**).<sup>1</sup> It is also now working on convening experts on all 3 conditions to establish case definitions and subsequently to create clinical practice guidelines that will be valuable both for everyday recognition and management and for formulating a basis for research.

Given the widespread nature of these conditions and the associated burden of suffering nation-wide, it is important for all clinicians and, in particular, front-line

### Box 2. Recommendations made by the Task Force on Environmental Health of the MOHLTC

1. Change the conversation and increase understanding and recognition of these conditions
  - Recommendation 1.1: Make a formal public statement recognizing ME-CFS, FM, and ES-MCS
    - The task force recommends the MOHLTC make a statement recognizing ME-CFS, FM, and ES-MCS, reinforcing the serious debilitating nature of these conditions, dispelling the misperception that they are psychological, and making a commitment to improving care, education, and support for caregivers
  - Recommendation 1.2: Establish academic chairs focused on ME-CFS, FM, and ES-MCS
    - The task force recommends that the MOHLTC fund academic chair positions in clinical environmental health focused specifically on ME-CFS, FM, and ES-MCS
  - Recommendation 1.3: Modernize the Ontario Health Insurance Program K037 fee code to include all 3 conditions
    - The task force recommends that the MOHLTC re-initiate the process to modernize the fee code K037—in collaboration with physician and patient experts—to ensure it recognizes all 3 conditions
2. Develop a common understanding of ME-CFS, FM, and ES-MCS
  - Recommendation 2.1: Develop clinical case definitions and clinical practice guidelines to support standardized, high-quality, patient-centred care
    - The task force recommends that the MOHLTC establish an expert panel to reach consensus on clinical case definitions and clinical practice guidelines for each of the 3 conditions
3. Lay the groundwork for a patient-centred system of care
  - Recommendation 3.1: Establish detailed clinical care pathways to support the development of an evidence-based system of care
    - The task force recommends that the MOHLTC provide funds to support the development of clinical care pathways for people with ME-CFS, FM, and ES-MCS and map out an appropriate patient-centred system of care for Ontario
  - Recommendation 3.2: Make hospitals safe for people with ME-CFS, FM, and ES-MCS
    - The task force recommends that the MOHLTC work with its partners, such as the Ontario Hospital Association, and with expert patients, caregivers, and physicians to ensure hospitals comply, as quickly as possible, with relevant accessibility and accommodation legislation
  - Recommendation 3.3: Make long-term care homes safe for people with ME-CFS, FM, and ES-MCS
    - The task force recommends that the MOHLTC work with its partners, such as long-term care provider organizations, and with expert patients, caregivers, and physicians to ensure long-term care homes comply, as quickly as possible, with relevant accessibility and accommodation legislation
4. Increase the number of knowledgeable providers
  - Recommendation 4.1: Continue to fund the enhanced skills program for third-year residents in clinical environmental health
    - The task force recommends that the ministry continue to fund this program until the task force makes further recommendations for advanced education specializing in ME-CFS, FM, and ES-MCS

ES-MCS—environmental sensitivities—multiple chemical sensitivity, FM—fibromyalgia, ME-CFS—myalgic encephalomyelitis—chronic fatigue syndrome, MOHLTC—Ontario Ministry of Health and Long-Term Care. Adapted from the Task Force on Environmental Health of the MOHLTC.<sup>1</sup>

primary care practitioners, to take note. We also call for a national effort to increase research directed at all 3 of these conditions as distinct entities, but with efficiencies associated with studying them together. 

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#### Competing interests

None declared

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Cet article se trouve aussi en français à la page 419.