



Quest

Newsletter



www.mefmaction.com

Quest 147, Fall 2025

mefminfo@mefmaction.com

Contents

Research News	1
Why Isn't Canada Investing in a New System of ME Care?	2
Some Releases since May 2025	3
The Network's Redesigned Website	15

Research News

From Dr. Moreau's lab

Dr. Alain Moreau's team at CHU Sainte-Justine in Montreal has published four recent studies that bring hope for people living with **myalgic encephalomyelitis (ME)** and **fibromyalgia (FM)**.

One major breakthrough was identifying an enzyme called **SMPDL3B** as a potential biomarker and treatment target for ME, detectable in both blood and urine - making future testing easier and less invasive.

Another study focused on **haptoglobin**, a protein that protects the body from oxidative stress. Researchers found that ME patients often have lower haptoglobin levels after exertion, which is linked to **post-exertional malaise (PEM)** and "brain fog." Importantly, genetics matter: haptoglobin comes in three phenotypes - **Hp1-1**, **Hp2-1**, and **Hp2-2** - based on two gene variants (Hp1 and Hp2). People with **Hp2-1** showed the most severe PEM and cognitive problems, while **Hp1-1** was associated with milder symptoms and better resilience. These findings suggest that haptoglobin could help identify high-risk patients and guide personalized therapies, such as restoring Hp function.

The team also discovered that a hormone called **FGF-21** may help classify subtypes of ME and FM, paving the way for precision medicine. In addition, they previously developed a blood test using **microRNAs** to distinguish ME from FM - even when both occur together - an important step since these conditions require different care strategies.

While more research is needed before these discoveries lead to clinical tools, they represent a major shift toward objective diagnosis and tailored treatments. Of course, more studies are needed to fit these pieces of information together, but it is exciting to see the work move forward.

Part of this progress was funded by community efforts via the National ME/FM Action Network, including donations raised during Armand Lupien's bike ride across Canada in 2024 for FM research, showing how patient advocacy can accelerate science.

- <https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-025-06829-0>
- <https://www.mdpi.com/1422-0067/26/18/8882>
- <https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-025-07006-z>
- <https://www.mdpi.com/1422-0067/26/16/7670>

From Edinburgh

The "DecodeME" study out of the University of Edinburgh shows that people with ME have differences in eight genetic areas when compared to the general public. These genetic areas are related to immunology and neurology, but not to anxiety or depression. This gives future researchers guidance on what to study and it supports a medical rather than a patient-at-fault model of ME. The project's website is at the link below. A good place to start is with the "Read our initial DNA results". <https://institute-genetics-cancer.ed.ac.uk/decodeme>

Why Isn't Canada Investing in a New System of ME Care?

Canada's front-line system of care for ME is not working for patients, for their families, for their employers, for the economy or for society. It is not working for the care system itself either.

The international ME community has been pushing for a new system of care for years. Despite convincing the top medical advisory committees in the US (2015) and the UK (2021) that existing ME systems are fundamentally flawed and need change, little has happened on the front lines. What is holding up this change?

It is possible that the people who could implement change (politicians, health policy makers, health system administrators...) still do not see the value of doing so. They could be thinking that:

- The old system is used in many jurisdictions, so it must be okay.
- The old system has been used for many years, so it must be okay.
- ME couldn't affect very many people and it couldn't be very serious.

Likewise, they seem reluctant to go through the work of changing the system. They could be thinking that:

- Staff in the health system won't want to change.
- It is not exactly clear what a new system would look like so we shouldn't get involved yet.
- The overall health system is under strain so this is not the time to take on something new.

Changing the care system will take work. Some issues will need to be sorted out including what the care system can do right now to help people with ME; what other health conditions should be addressed at the same time, since ME overlaps with conditions like Fibromyalgia, Long COVID, and dysautonomia; and how ME and related conditions can be incorporated into the broader health care system. There will be a need for education and awareness activities. Federal/provincial responsibilities will also have to be considered.



These are not insurmountable barriers. Introducing a new system is a change management exercise that can be worked through.

It is time that health system leaders across Canada stop thinking of the system change as an effort and expense, and start thinking of it as an investment in creating a new and better system. Considering how flawed the old system is, a new system for ME can be expected to result in better outcomes such as increased quality of life for individuals, less strain on families and greater participation in the economy and in society, along with better relations between patients and health care workers and more efficient and effective use of health care resources.

Some Releases since May 2025

In this section of the newsletter, we look at a selection of reports and podcasts from Canada, the US and the UK, all of which have been released since May of this year. They touch on issues such as what is wrong with the present system, the number of people with ME, the economic impact of ME, what patients think of the present system, and how clinical care could be delivered.

These releases show that pressure for system change is growing and that challenges are being discussed. Hopefully, it won't be long before governments across Canada realize that the situation is urgent, that change is viable, and that implementing a new approach to ME and related conditions would be a worthwhile investment.

Please note that, in this section, direct quotes are shown in italics.

- #1 Growing recognition of post-acute infection syndromes by Anthony L. Komaroff
- #2 Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and COVID by Leonard Jason and Arthur A. Mirin
- #3 Podcast: The Future of MedTech: A Strategic Investment in Canada's Economic Health
- #4 ME/CFS: the final delivery plan, UK Department of Health & Social Care
- #5 Regulation 28 Report to Prevent Future Deaths, Assistant Coroner, Area of Avon
- #6 Where is the Medical Home for Postinfectious Illness by Miriam E. Tucker
- #7 ME/FM/Lyme/Long COVID Patient Healthcare Experiences and Priorities in BC
- #8 Clinical Care Guide Managing ME/CFS, Long COVID, & IACCs, Bateman Horne Center
- #9 Mount Sinai Manual for Treating Infection-Associated Chronic Illness
- #10 Health outcomes of patients in the Complex Chronic Diseases Program
- #11 Podcast - UK and US Updates on ME/CFS and Long COVID

#1 Growing recognition of post-acute infection syndromes by Anthony L. Komaroff

<https://www.pnas.org/doi/10.1073/pnas.2513877122>

Long-time ME specialist, Dr Anthony Komaroff of Harvard, starts his commentary with some history. Four decades ago, the US health system decided that ME was not a medical condition.

"This illness first attracted attention in the 1980s...(S)ome scientists suspected that a novel human pathogen was causing the illness. Such speculation seemed reasonable, since a novel virus recently had been discovered to cause the AIDS. However, no single, novel pathogen has emerged as the cause of ME/CFS.

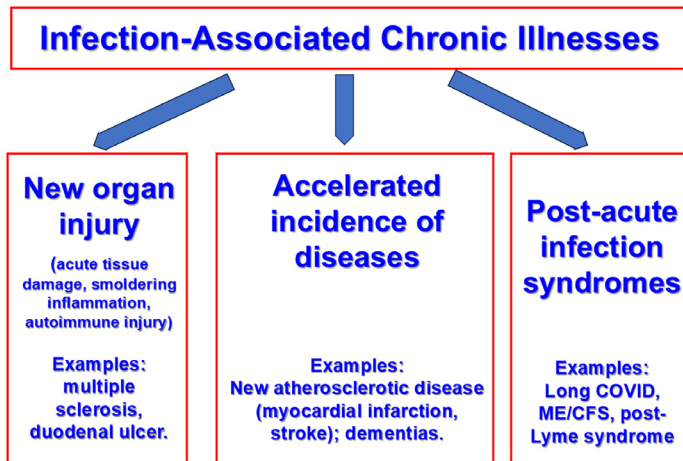
Moreover, the standard laboratory tests that were performed in the 1980s generally came back "normal," leading some to believe there were no underlying biological abnormalities to explain the symptoms. However, over the past 40 y(ears), thousands of studies have identified many underlying abnormalities involving the brain, immune system, energy metabolism, redox imbalance, vascular injury, and gut microbiota. The symptoms of the illness are, indeed, accompanied by objective abnormalities.

...(T)he initial skepticism about whether the illness had a biological basis may have created a lingering stigma."

Skepticism and stigma can be traced even further back. In 1955, there was an outbreak of ME at the Royal Free Hospital in the UK. In 1970, *"two psychiatrists concluded that epidemic hysteria was the likely cause"* (see <https://pmc.ncbi.nlm.nih.gov/articles/PMC7824095/#B7-medicina-57-00012>).

So both the UK and the US looked at ME and got it wrong and the ME community has been living with the consequences ever since.

Dr Komaroff then notes commonalities between ME and Long COVID, notably their pattern of symptoms, underlying biological abnormalities, comorbid diseases and response to therapies. He also notes that infections can trigger other problems, like speeding up the onset of Alzheimers or triggering the onset of ulcers. He puts forward this model, and proposes that the health system organize itself around it.



This model is a very good starting point, but there will of course be need for some flexibility. It is possible that ME symptoms could have non-infection triggers. Even if ME were started by infection, not everyone can trace back to the infection and we certainly do not want people to be denied care because the triggering event is unknown. And different pathogens might trigger different patterns of ME so there may be need to dig deeper into the PAIS category.

#2 Myalgic Encephalomyelitis/Chronic Fatigue Syndrome and COVID by Leonard Jason and Arthur A. Mirin

<https://www.counterpunch.org/2025/08/19/myalgic-encephalomyelitis-chronic-fatigue-syndrome-and-covid/>

This is a report updating the estimate of the number of people in the US with ME (including ME-qualifying Long COVID cases) and updating the estimate of the economic costs of ME. Their figures show that ME is indeed an issue with significant human and economic ramifications.

“An estimated 5.7 million individuals in the United States now are potentially affected by ME/CFS. The condition demands urgent attention not only for its debilitating impact on individual lives but also for its substantial economic ramifications. The estimated annual cost of ME/CFS, ranging from \$225 billion to \$305 billion, reflects both the direct strain on healthcare systems and the indirect costs of lost productivity and diminished quality of life.

These figures challenge longstanding underestimation of ME/CFS prevalence and impact, and they call for a recalibration of national health priorities.

Increased federal investment in biomedical research, development of evidence-based treatments, and the establishment of comprehensive care infrastructure for those affected by ME/CFS are imperative. Moreover, the syndemic relationship between COVID-19 and ME/CFS highlights the urgent need for post-viral surveillance, early diagnostic strategies, and preventive public health planning. Whether this moment catalyzes meaningful scientific and policy advances will depend on the willingness of stakeholders across health systems, government, and society to respond proportionately to the scale of this emerging crisis.”

Let us assume that Canada has the same prevalence rate of ME as the US. Adjusting for population (Canada’s population is roughly 12% of that of the US), for the size of the economy (Canada’s GDP is roughly 8% of that of the US), and for the value of the Canadian dollar, this would mean that there are about 700,000 Canadians with ME and that ME’s economic costs to Canada are in the range of \$25-33 Billion Cdn per year. That should be enough to invite questions into whether the care system could be working more efficiently and effectively.

#3 Podcast: The Future of MedTech: A Strategic Investment in Canada’s Economic Health

<https://santishealth.ca/podcasts/episode-44-the-future-of-medtech-a-strategic-investment-in-canadas-economic-health/>

This is a 30-minute Canadian podcast. It does not mention ME but its topic provides food for thought about how policymakers and others can think about ME. It is aimed at medical technology companies (eg labs and medical equipment suppliers) and discusses how they can talk to the Canadian federal government. Canada has recently moved from a prime minister interested in social issues to a prime minister interested in economic issues. The message of the podcast is that health care is often thought of as an expenditure. It can also be thought of as an investment in the health of the population. An example in the podcast was reducing health care in a small town would reduce health care expenditures, but it could discourage people from living there, potentially forcing the local industry out of business, thereby hurting the town’s, the province’s and the country’s economy.

#4 ME/CFS: the final delivery plan, UK Department of Health & Social Care

<https://www.gov.uk/government/publications/mecfs-the-final-delivery-plan/myalgic-encephalomyelitischronic-fatigue-syndrome-mecfs-the-final-delivery-plan>

The UK department of Health and Social Care released a “final delivery plan” which outlines principles for a new system of ME care for England. This came about after several years of public consultation. The plan identifies three themes requiring particular focus;

- research,
- attitudes and education (referring to healthcare system training and attitudes and to public awareness) and
- living with ME (referring to the availability and quality of health and social supports for patients).

The “Ministerial Forward” to the plan notes that there are conditions that overlap with ME such as Long COVID, POTS (Postural orthostatic tachycardia syndrome) and EDS (Ehlers-Danlos Syndrome), but reminds readers that the government had committed to focusing on ME in this report.

The Ministerial Forward also notes that the government has not been able to include and fund everything asked for by participants because the plan “*must of course reflect what is practically feasible and financially viable and affordable, especially within the challenging current fiscal climate*”.

Not surprisingly, reaction to the plan has been mixed. On one hand, it is great that people have been looking at the issues and it is great to have the document on record. On the other hand, the report itself does not add much that has not already been raised elsewhere. (See, for instance, the report of the Ontario Task Force on Environmental Health, 2018). Very importantly, the statement about funding constraints suggests that authorities have not grasped the scope and seriousness of the situation or the potential to make a difference. They are thinking about expenditures rather than investments.

#5 Regulation 28 Report to Prevent Future Deaths, Assistant Coroner, Area of Avon

<https://www.judiciary.uk/prevention-of-future-death-reports/sarah-lewis-prevention-of-future-deaths-report/>

A coroner in the UK looked at the 2024 death by suicide at home of Sarah Lewis, a woman with severe ME. The coroner sent a “report to prevent future deaths” to the UK Secretary of State for Health & Social Care. The message she sent was clear – problems in ME service have consequences and they should be fixed.

Government is under an obligation to respond to these reports. Two replies were indeed received, one from the Department of Health and Social Services and the other from NICE (National Institute for Health and Care Excellence). The responses largely repeated the recommendations of the UK’s final delivery plan which may or may not lead to action.

The three documents are available at the link above. Here is an excerpt from the coroner’s report identifying key issues. That report gives a stark example of the human cost of gaps in care. It also shows that these gaps are being noticed outside the ME community.

“During the course of the inquest the evidence revealed matters giving rise to concern. In my opinion there is a risk that future deaths will occur unless action is taken. In the circumstances it is my statutory duty to report to you.

The MATTERS OF CONCERN are as follows.

- *Despite ME having received some more recent attention, the provision of ME services around the country remains inconsistent. I understand that there are still areas where there is no provision. The evidence revealed that a very important first stage for ME sufferers is that they receive a diagnosis and validation for their severe symptoms. Without provision of a service, there remains a risk that this will not occur. I was told that there is still a belief by some that ME is not real and this has a profoundly negative effect on sufferers and their ability to seek support.*
- *Historically, there has been little research into ME. As a result of this, nobody knows what causes it, and there is therefore no cure. Whilst I note there has been a small investment recently in research, I was told that this is not enough, and that a perception remains*

about ME not being real. The resultant effect is that some ME sufferers have no hope that their symptoms will ever improve.

- *Other professionals do not understand ME, what it is or the symptoms it causes. This can be a barrier to those with ME receiving support, or accessing care/treatment they need. A hospital passport is now being utilised at North Bristol, which assists sufferers. However, it is not clear that this is being used in all areas, and there remains a lack of understanding about ME. Education and training about this has not been prioritised.*
- *NICE issued update guidance relatively recently but it is not clear whether this has been fully considered or implemented by commissioning bodies around the country.*

In my opinion action should be taken to prevent future deaths and I believe you, the Secretary of State for Health and Social Care has the power to take such action."

#6 Where is the Medical Home for Postinfectious Illness by Miriam E. Tucker

<https://www.medscape.com/viewarticle/where-medical-home-postinfectious-illness-2025a1000m05?form=fpf>

One issue that needs to be sorted out is who within the health system will be responsible for providing care for ME and related illnesses. Ms Tucker, a medical journalist, asks four US physicians for their comments.

The first interviewee was Dr Brittany L. Adler, a rheumatologist currently working at a POTS clinic at Johns Hopkins University. She wrote an essay entitled *Expanding the rheumatology lens: should we embrace POTS and post-infectious syndromes?* This essay was published in The Lancet Rheumatology in July. You can find the link in Ms Tucker's article. Dr Adler urges rheumatology to take on these patients, arguing that rheumatologists are uniquely trained to manage complex, multisystem illnesses. She notes that there will be a need for coordination between rheumatologists, other specialists and family doctors, then adds that there is currently no model for this type of coordinated care.

The second interviewee was Dr Komaroff. He suggests that choosing a discipline to provide specialist ME services is not the key. The key is rather having enough doctors throughout the system who are knowledgeable about these illnesses. He suggests that, with a stronger science foundation, more doctors will become involved.

Dr Brayden Yellman is the medical director of the Bateman Horne Center in Salt Lake City Utah. He agrees with Dr Adler that rheumatologists could manage these conditions. But then he identified barriers that might hold them back, including a lack of a biomarker, lack of familiarity with treatment options, and a shortage of rheumatologists. He also notes that care for complex conditions is complex and the healthcare system is not designed to deal with complex cases.

Dr Lisa Sanders is the medical director of the Yale Long COVID clinic. She would like to see more physicians taking an interest in post infectious conditions. She identifies the lack of research as a major barrier.

The interviewees are raising issues that will be encountered when bringing physicians on board. Hopefully those issues will be seen as challenges moving forward and not as reasons to delay change.

7 ME/FM/Lyme/Long COVID Patient Healthcare Experiences and Priorities in BC

https://www.mefmaction.com/images/stories/News/NetworkNews/2025_Community_Survey_Report.pdf

This report, conceived and commissioned by four BC organizations, presents the results of an on-line survey of ME, FM, Lyme and Long COVID patients in BC conducted during the winter of 2024-25. The survey asked people to give their perspectives on strengths and weaknesses of the existing health care system and to identify opportunities for improvement. Just over 1,000 people in BC participated in the survey.

The survey shows that respondents have had some good and many bad experiences in the health system. Bad experiences included being dismissed, disrespected or disbelieved, getting wrong diagnoses or harmful treatments, and receiving little help with financial applications. It is notable how appreciative the respondents were of good experiences, even when the experience was as basic as being believed.

Here are three specific take-aways from the survey:

- Despite all their bad experiences, the respondents said that they want one-on-one care from doctors. People understand that they need individualized, on-going, informed medical care.
- The health system has a role to play in helping patients access financial and social programs. For some patients, this is very important.
- Emergency rooms can be very difficult for these patients.

#8 Clinical Care Guide Managing ME/CFS, Long COVID, & IACCs, Bateman Horne Center

<https://batemanhornecenter.org/wp-content/uploads/2025/05/Clinical-Care-Guide-First-Edition-2025-1.pdf>

#9 Mount Sinai Manual for Treating Infection-Associated Chronic Illness

<https://www.mountsinai.org/about/newsroom/2025/mount-sinai-creates-first-manual-for-treating-infection-associated-chronic-illness-for-clinicians>

A number of diagnostic and treatment guides have been written over the years. Two more were added since May.

One of the guides was released by the Bateman Horne Center, a long-time and highly respected ME/FM clinic based in Salt Lake City. This new guide is 96 pages long and targets “ME/CFS, Long COVID, and Infection-Associated Chronic Conditions (IACCs)”.

The other guide was released by the Cohen Center for Recovery from Complex Chronic Illness (CoRE) at Mount Sinai Hospital in New York City which opened in 2024. This guide is 168 pages long and targets “IACIs” (Infection Associated Chronic Illnesses) such as “Long COVID, Long Lyme disease/Lyme+, myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) and Ehlers-Danlos syndrome”. A link to the Mount Sinai guide can be found in the press release above. You have to register to receive the guide itself.

The press release for the Mount Sinai guide says:

“Our clinic can only take on around 700 new patients a year, so clearly there’s a huge discrepancy there. Releasing this manual is a way for us not only to continue setting the standard of care, but also to help ensure that any clinician can have the tools and knowledge they need in order to adopt our practices and provide high-quality, evidence-informed practice for people with IACIs all over the world.”

“Infection-associated chronic illnesses remain disabling, costly, and widely misunderstood across much of medicine. Recent research from our team shows that even a single well-designed educational intervention can dramatically increase clinicians’ confidence, preparedness, and empathy in managing these conditions,” says Raven

Baxter, PhD, Director of Science Communication at the Cohen Center. “We hope to positively shift how the field understands and responds to infection-associated complex chronic illness and this manual is a proactive answer to calls for better training, less stigma, and more practical support for both new and experienced clinicians.”

Both guides confront the fact that some patients do not get better. The Bateman Horne guide says that “Clinicians must contend with...the frustration of seeing patients who do not improve despite best efforts” (see pages 9-10 of this newsletter). The Mount Sinai guide says that “While cure may not always be possible, recovery focuses on achieving the best possible quality of life by addressing not only physical symptoms but also emotional resilience and social well-being” (see pages 11-12 of this newsletter).

When it comes to care, the Mount Sinai guide says “Rather than thinking of IACIs as ‘mysterious’ we would urge providers to think of them as ‘complex’.” The guide then lists 9 “drivers of disease” such as mitochondrial dysfunction, coagulation and vascular dysfunction, and autonomic dysfunction. The guide states “While we are starting to better understand these drivers in detail, the complexity of treating IACIs comes from the fact that a person diagnosed with an IACI may be experiencing many of these drivers all at once, or just once...The purpose of this chapter is to dive into the details of some of the most well-established drivers of symptoms and pathobiology in IACIs, so that we can pave the way to better strategize actionable treatments.” (see pages 13-14 of this newsletter).

The Bateman Horne guide also talks about strategizing care. It says that, given the challenges, “a shift in clinical approach is necessary – one that moves beyond rigid protocols and toward patient-centered, adaptable, and collaborative care.” It then identifies the patient-clinician relationship as one of the most valuable tools available.

#10 Health outcomes of patients in the Complex Chronic Diseases Program

<https://bcmj.org/articles/health-outcomes-patients-complex-chronic-diseases-program>

“ABSTRACT

Background: Complex chronic diseases affect almost 3% of Canadians and lead to persistent, debilitating symptoms. The BC Ministry of Health funded the Complex Chronic Diseases Program to address service gaps for affected individuals. We evaluated health outcomes of the program's patients.

Methods: Analysis of data from the Complex Chronic Diseases Program Data Registry (June 2017–September 2022) focused on patient-reported outcomes and clinical measures at baseline, 6-month follow-up, and discharge, and on changes in symptoms across these time points.

Results: Among the 668 participants included in the study, slight improvements in overall physical and mental health were observed between baseline and discharge. However, symptoms such as sleep dysfunction, fatigue, and pain showed no significant changes.

Conclusions: While participation in the Complex Chronic Diseases Program yielded some health benefits, further research and interventions are required to address symptoms and optimize patient outcomes. The further development and use of objective outcome markers are needed for improved program evaluation.”

It is hard to know what to make of this study. It covers 668 participants, about a third of the people who went through the one-year program between 2017 and 2022, a period that was affected by COVID and by program design changes. About half of the study participants had ME and FM, about a third had ME only and the rest had FM only. Around 90% were women. Half of the participants had been sick more than 11 years. They had been referred to the program which means they had some prior medical recognition and support. There was no control group.

The two clinical care guides discussed above note that some patients do not get better, so the measurable improvement seen in this study might qualify as a success. It is also interesting that the study measured the change in symptoms, while the two guides focus on overall well-being, a broader concept.

#11 Podcast - UK and US Updates on ME/CFS and Long COVID

<https://paradigms.life/2025/dr-charles-shepherd-and-dr-ken-friedman-uk-and-us-updates-on-me-cfs-and-long-covid/>

The guests on this hour-long podcast were Dr Charles Shepherd of the UK and Dr Ken Friedman of the US. Both have been heavily involved in ME advocacy for decades.

The podcast begins with introductions and a description of ME. That is followed at minute 19 by a description of the state of ME research. The situation in the US is somewhat discouraging. Dr Friedman talks about Dr Komaroff's commentary (#1) which he summarizes as saying that the US has been on the wrong research path for 40 years. He then talks about the current upheavals at the US National Institutes of Health (NIH) and the US Centers for Disease Control and Prevention (CDC). Dr Shepherd is more upbeat, talking about the surge in interest in ME that comes from Long COVID, research findings like the DecodeME study (see above), and the release of the UK final delivery plan (#4).

At minute 36, the discussion turns to what people can do, considering the state of understanding of ME. Dr Friedman emphasizes the need to become aware of the illness and to find a health care provider who can make a diagnosis and work with you to try to abate the symptoms. He talks about the need to adjust expectations and find a new way forward. Dr Shepherd, who worked on the NICE guidelines (see Quest 145), emphasizes the need for early and correct diagnosis in conjunction with appropriate activity and symptom management on an ongoing basis. He notes that bad management at the start of the illness can lead to long term problems.



The following two pages come from the Bateman Horne Clinical Care Guide (#8). The four pages after that come from the Mount Sinai Manual (#9).

CHAPTER 1: NAVIGATING CLINICAL UNCERTAINTY

Zeest Khan, MD, March 2025



The practice of medicine is built on pattern recognition and evidence-based interventions, but post-infectious conditions like Long COVID and ME/CFS disrupt this framework. Their heterogeneous presentation, evolving research, and lack of established biomarkers leave clinicians facing diagnostic and treatment uncertainty—a discomforting challenge in a field that values precision. Yet, uncertainty does not mean inaction. As clinicians, our role is not just to provide definitive answers but to guide patients through structured, personalized, and evolving care, even when we do not have all the answers.

Challenges in Treating Long COVID & ME/CFS

Both patients and clinicians face significant obstacles in managing these conditions:

- Patients experience long wait times, limited treatment options, and medical skepticism/gaslighting. Many arrive at appointments exhausted, cognitively impaired, and wary of being dismissed.
- Clinicians must contend with evolving recommendations, limited patient visit times, the absence of definitive biomarkers, and the frustration of seeing patients who do not improve despite best efforts. Traditional diagnostic models often fail when dealing with multisystem dysfunction and fluctuating symptoms.

Given these challenges, a shift in clinical approach is necessary—one that moves beyond rigid protocols and toward patient-centered, adaptable, and collaborative care.

Embracing a Collaborative Care Model

In uncertain clinical landscapes, the patient-clinician relationship is one of the most valuable tools available. Instead of positioning clinicians as sole authorities, an integrated approach—where providers and patients share knowledge and decision-making—can enhance care quality.

- Recognize the patient's lived experience. Many patients have spent significant time tracking symptoms, researching treatments, and testing their own limits. Clinicians should validate and leverage this knowledge while providing a framework for safe, structured treatment trials.
- Trial-and-pivot over trial-and-error. Without clear guidelines, treatment often relies on carefully monitored interventions rather than definitive cures. Adjusting strategies based on patient response is not failure—it is informed decision-making.
- Set clear expectations. Patients and providers must establish realistic treatment goals, acknowledge that progress may be slow, and agree on boundaries—clinicians should not feel pressured to prescribe unproven treatments, and patients should not be criticized for declining interventions due to cost or side effects.

CHAPTER 1: NAVIGATING CLINICAL UNCERTAINTY

Zeest Khan, MD, March 2025



Building a Practical Clinical Framework

To navigate uncertainty effectively, providers can implement structured approaches to care:

1. Prioritize regular check-ins. Long COVID and ME/CFS symptoms fluctuate, making frequent assessments critical. Given time constraints, appointments should focus on one or two key issues per visit to ensure meaningful progress.
2. Support goes beyond prescriptions. Helping patients secure workplace/school/home accommodations, disability resources, and access to interdisciplinary care is just as crucial as medication-based management.
3. Referrals should be strategic. Given the multisystem impact of these conditions, interdisciplinary care is often needed. However, referrals should be intentional, with clear questions for specialists rather than a simple transfer of care.
4. Guide patients toward reputable resources. Patients inevitably turn to online sources, where accurate information coexists with misinformation. Clinicians should recommend trusted organizations to empower informed decision-making.

Redefining How We Approach Complex Illnesses

Long COVID and ME/CFS challenge conventional clinical practice, but they also present an opportunity to reshape how we approach medicine in the face of uncertainty. By embracing adaptability, patient collaboration, and evidence-informed clinical reasoning, providers can deliver meaningful care despite incomplete research.

Navigating uncertainty is not about waiting for perfect data—it is about using the best available knowledge, engaging in structured clinical reasoning, and remaining open to new insights. This mindset shift not only benefits patients with post-infectious conditions but strengthens our ability to manage other complex, poorly understood illnesses across medicine.



What Is Recovery?

At the Cohen Center for **Recovery** from Complex Chronic Illness, our focus is to help our patients live a fulfilling life despite the limitations of chronic conditions.

While a cure may not always be possible, recovery focuses on achieving the best possible quality of life by addressing not

only physical symptoms but also emotional resilience and social well-being.

For patients, this often means learning to navigate their new reality with the support of healthcare professionals, social networks, and tailored care strategies. For providers, this means a multidisciplinary approach to care.

Recovery is not One-Size-Fits-All



Recovery is about helping individuals reclaim control over their lives and find ways to thrive, even in the presence of ongoing health challenges. Recovery is a multifaceted, deeply personal process that varies between individuals. It does not necessarily mean a complete cure or the elimination of symptoms. It encompasses the restoration or improvement of various aspects of life—including physical health, emotional well-being, social connections, and overall functionality.

Recovery Does Not Equate to a Cure



The goal is to help patients move from a state of overwhelming symptoms to one where their condition is stabilized and more manageable. Recovery is still attainable in the sense of improving functionality, managing symptoms effectively, and adapting to a new normal.

Recovery of Function



For some patients, recovery involves regaining the ability to participate in meaningful activities like work and hobbies. This requires medical interventions, physical therapy (PT), and [energy management strategies \(pacing\)](#). The goal is to help patients rebuild practical aspects of their lives and engage in what matters most. Recovery includes regaining strength, mobility, and endurance, approached carefully to prevent setbacks. For IACIs, pacing rest are essential to manage energy and avoid flares. Tailored exercise and medical therapy support improved function over time, with each small step contributing to a better quality of life.

Infection-Associated Chronic Illnesses Provider Manual

First Edition



Mental and Social Health as Part of Recovery



Social support is vital for recovery as social isolation and loneliness can have profound effects on many aspects of physical and mental health, including immune and hormonal health. Social health interventions need to be tailored to an individual's personal energy and comfort level, with some preferring in-person gatherings and others benefiting from online communities. Chronic illness can significantly impact mental health, leading to anxiety and depression, making mental health support essential. Therapy, mindfulness practices, and connecting with professionals can help patients build resilience and manage emotional challenges.

The Importance of the Right Environment



Recovery is influenced not only by medical interventions but also by the environment in which patients live, work, and heal. Creating a supportive environment—both physically and socially—is vital. This includes ensuring spaces are comfortable, accessible, and stress-free, as well as fostering social environments that emphasize understanding, compassion, and encouragement.



Chapter 3 | Current Research on the Drivers of IACIs

IACIs are often incorrectly referred to as “mysterious” due to a perception that we do not understand why people who are diagnosed with IACIs are actually sick and what may be driving their symptoms. Rather than thinking of IACIs as “mysterious” we would urge providers to think of them as “*complex*.” This is because many of the drivers of IACI symptoms and pathobiology have been established through literally thousands of high-quality, peer-reviewed research studies.

While we are starting to better understand these drivers in detail, the *complexity* of treating IACIs comes from the fact that a person diagnosed with an IACI may be experiencing many of these drivers all at

once, or just once. They may be experiencing just these drivers with no other relevant past medical history, or they may be managing multiple comorbidities and chronic illnesses alongside their IACI, and frankly, we do not have a detailed understanding of how these chronic illnesses intersect with one another. The purpose of this chapter is to dive into the details of some of the most well-established drivers of symptoms and pathobiology in IACIs, so that we can pave the way to better strategize actionable treatments.

Please see drivers of disease on the following page.

Infection-Associated Chronic Illnesses Provider Manual

First Edition



Drivers of Disease

Understanding drivers of IACIs is imperative for HCPs. These factors clarify the complex biological mechanisms

underlying persistent symptoms associated with IACIs and enable HCPs to strive for the best diagnostic and therapeutic approaches.

Driver	Description
Persistence of pathogens in tissue	Chronic symptoms may result from the inability to fully clear infections, leaving pathogens in tissue or host cells as reservoirs that drive ongoing inflammation and other downstream effects. These reservoirs are often difficult to detect with standard blood tests.
Pathogen reactivation	Dormant pathogens, such as herpesviruses or <i>Bartonella</i> , can reactivate under stress or immune suppression, contributing to chronic illness symptoms like fatigue, inflammation, and vascular dysfunction.
Mitochondrial dysfunction	Pathogens and the inflammation that they cause can severely disrupt mitochondrial function, reduce energy production, and increase oxidative stress, which can lead to fatigue, inflammation, and other chronic symptoms.
Coagulation and vascular dysfunction	Pathogen-induced hypercoagulation, microclots, and endothelial dysfunction impair blood flow, oxygen delivery and tissue perfusion, exacerbating symptoms like fatigue, pain, and organ dysfunction.
Autonomic dysfunction	Disruptions in the autonomic nervous system, including conditions like postural orthostatic tachycardia syndrome (POTS), cause issues with heart rate, blood pressure, and other involuntary processes, leading to symptoms such as dizziness, fatigue, and nausea.
Neuroinflammation and cognitive dysfunction	Chronic inflammation in the brain, often linked to vascular abnormalities and/or persistent pathogen reservoirs, contributes to cognitive impairment, fatigue, and neuropsychiatric symptoms.
Immune activation, dysfunction, and autoimmunity	Persistent immune activation, often driven by pathogen presence, can lead to T-cell exhaustion, autoantibody production, and systemic inflammation, worsening chronic illness symptoms.
Microbiome imbalance and small intestinal bacterial overgrowth (SIBO)	Disruptions in gut microbiota and increased intestinal permeability ("leaky gut") lead to systemic inflammation, hormonal imbalances, and immune dysregulation, contributing to chronic symptoms.
Hormonal imbalance	Pathogen-driven changes in hormone production, such as cortisol, testosterone, estrogen and serotonin, contribute to systemic symptoms like fatigue, mood changes, and metabolic dysfunction, with sex-specific immune response differences noted in some conditions.
Mast cell activation and immune cell priming	Overactive mast cells and glial cells, often responding to persistent pathogen reservoirs or microbiome imbalances, can become perpetually over-active, amplifying inflammation and immune responses and contributing to chronic symptoms like pain, fatigue, and sensory sensitivities.



The Network's Redesigned Website

Key Benefits and Importance of the New Website Design for Members

- Clearer, More User-Friendly Interface
- Easier Access to Information
- Responsive Across All Devices
- Better Engagement and Staying Informed
- Smart Search with PDF Indexing

Updating our website is all about putting our members first. By making the site clearer, more responsive, and up to date with the latest technology, we're improving the overall experience—making it easier for you to find information, stay informed, and engage with us. Whether you're browsing on a phone, tablet, or desktop, the new design will adapt seamlessly to your screen, ensuring content is easy to read and navigate. This upgrade focuses on clarity, ease of use, and a cleaner, more user-friendly interface to give our members the best possible online experience.

MANAGEMENT COMMITTEE

Lydia E. Neilson, M.S.M.

- Founder, Chief Executive Officer

Margaret Parlor

- President

BOARD OF DIRECTORS

Philipa Corning, PhD, BSc, CD

Judith Day

Sherri Todd

Anne Marie MacIsaac

Margaret Parlor

ADVISORS

Alison Bested, M.D.

Gordon D. Ko, M.D.

Leonard Jason, Ph.D.

Ellie Stein, M.D.

Ellen N. Thompson, M.D.

Abdolamir Landi, M.D., Ph.D.

Margaret Oldfield, Ph.D.

Gordon Broderick, Ph.D.

Michelle Skop, Ph.D.

LEGAL COUNSEL: Hugh R. Scher, Scher Law Group

CPP-DISABILITY ADVISOR: Dr John Wodak

STATISTICS ADVISOR: Erika Halapy

QUEST EDITOR: Margaret Parlor

Quest Layout: Anne Marie MacIsaac



<http://mefmaction.com>



<http://www.facebook.com/MEFMAActionNetwork>

Copyright Notice:

The National ME/FM Action Network newsletter QUEST is published quarterly. Its contents are © 2022 by the National ME/FM Action Network, a not-for-profit, all-volunteer Canadian charitable organization. Articles may be reproduced in their entirety, without alteration, by other not-for-profit publications as long as copyright notices are included and items are clearly attributed to the National ME/FM Action Network.



NEW MEMBERSHIP or RENEWAL fees

ANNUAL MEMBERSHIP FEE :
\$30.00 per year including quarterly newsletter Quest

IN ADDITION, I would like to donate *\$_____ to help with the many projects of the National ME/FM Action Network.

**Tax Receipt issued for all donations*

TOTAL PAYMENT:

\$_____

PAYMENT OPTIONS

☐ Cheque

Please make Cheque Payable to the:

NATIONAL ME/FM ACTION NETWORK

☐ VISA

☐ Master Card

☐ Other _____

Card Number:

Expiry Date:

month _____ year _____

CVV _____ (3 digit code on back of card)

Name on Card:

Signature:

☐ I would like to be a member.
Please waive the annual fee.

MEMBERSHIP APPLICATION or RENEWAL FORM

*For online application and renewals go to
MEFMaction.com*

Date: _____

Name / Organization

Contact Name _____

Address _____

City _____

Province/State _____ Postal Code/Zip _____

Country _____

Email _____

Phone _____

Website _____

☐ Please send news updates to my email address

☐ Do not send news updates to my email address

☐ Please send an electronic version of the Quest newsletter

☐ Please send the Quest newsletter to my mailing address

MAIL FORM & PAYMENT TO:

**NATIONAL ME/FM ACTION NETWORK
512-33 Banner Road
Nepean, ON K2H 8V7**

THANK YOU FOR YOUR SUPPORT!

CREDIT CARD TRANSACTIONS CAN BE FAXED TO 613-829-8518

Our phone number is 613-829-6667