

Email header:

Consensus criteria for ME/CFS research – seeking your support (action requested)

Dear Soh

We are writing to you today regarding an international consensus statement for which we are seeking your support. We are at a time of unprecedented opportunity for new research into Long COVID and ME/CFS. Yet we note, with concern, that many of the basic lessons learned in ME/CFS, as well as many of the recognised standards for good research, are not reliably and consistently being applied in the field. New research has been published and is being planned in ME/CFS, but there continues to be confusion over ME/CFS diagnostic criteria. For this reason, we believe it is critical to build international consensus for critical research criteria in ME/CFS, which can be used by scientists, patients, charities, and funders which will result in higher standards of research both in ME/CFS and in Long COVID. Please read the attached document and sign below if you endorse this document.

With warm regards,

Leonard A Jason PhD

Caroline Kingdon RN, MSc, NICE Committee Member

Adam Lowe Poet, Patient Advocate, NICE Lay Committee Member

Research Case Definition Consensus Statement

Internationally, clinical definitions for ME/CFS have been adopted in many countries, but there is still no consensus around research criteria. In 2015, the Institute of Medicine in the US developed a clinical case definition for ME/CFS, but this was never meant to be used for research. For decades, research into Myalgic Encephalomyelitis (ME), sometimes called ME/CFS, has been hampered by heterogeneous diagnostic criteria and the inclusion of participants who may not actually have ME. This has impacted the validity of many studies and created a risk of harm for patients. There is still not an international consensus on a research case definition or case definitions.

The core problem is that many case definitions do not require key symptoms such as post-exertional malaise and do not take the severity of the symptoms into account. Further, methods for evaluating cases have been inconsistent. The time has come to improve cross-study comparability and ensure study participants have ME. We the undersigned believe the time has come to sponsor an international effort to create a consensus on the criteria and methods for selecting cases in research. Such a consensus will need to address multiple issues, including those below.

- A consistent set of required inclusion criteria. One example is the requirement for **substantial impairment in functioning** and **post-exertional malaise**¹ lasting six months or more in all research criteria for people with ME, with **cognitive impairment** and **unrefreshing sleep** considered key features.^{2,3,4*}

- A consistent approach to **exclusionary conditions**. This includes any previously diagnosed medical condition whose resolution has not been documented beyond reasonable clinical doubt and whose continued activity may explain the symptoms of ME.^{5**} Research publications should indicate which illnesses were considered exclusionary and which were not.
- A consistent **approach for evaluation of key criteria**. This is done with structured questionnaires that evaluate both symptom severity and frequency as well as level of functional impairment. An example of a widely used method is the DePaul Symptom Questionnaire.^{6,7,8} Research publications should outline how criteria have been operationalized.
- A consistent approach to characterizing and labeling overall disease severity of cases ^{9,10,11,12,13***}

* There are many secondary symptoms that may be experienced by people with ME including orthostatic intolerance, pain, immune, and gastro-intestinal complaints.

** While clinically a patient can have both ME and other diagnoses, in research, it's important to have a consistent approach to exclusions to improve cross-study comparability.

The Canadian Consensus Criteria, ME-International Consensus Criteria, and NICE 2021 criteria meet many of these standards. The IOM criteria meet these standards when using the proposed exclusionary criteria and when cognitive impairment is required. The Fukuda criteria do not meet these standards.

The following individuals and organizations support the statements above to convene an international effort to develop a consensus on using a research case definition:

Please add your name and affiliation here:

Name: Emily Taylor Organisation/Institution: Solve M.E.

Footnotes

¹Recently, the World ME Alliance, with 24 member organizations across 17 countries, supported the inclusion of PEM as a core symptom. Standing Strong: Global ME Community unified in support of NICE 2021 ME/CFS Guideline. 2023. Available at: <https://worldmealliance.org/2023/08/standing-strong-global-me-community-unified-in-support-of-nice-2021-me-cfs-guideline/>

²Kingdon, C, Abken, E, Lacerda, E & Nacul, L. A proposal for consensus diagnostic criteria for ME/CFS research. Poster presented at the meeting of the International Association of ME/CFS, Stonybrook University, N.Y. 2023

³Jason, L. A. & Ravichandran, S. An effort to develop a consensus on critical ME/CFS definitional issues. Poster presented at the meeting of the International Association of ME/CFS, Stonybrook University, N.Y. 2023

⁴Nacul L, Authier FJ, Scheibenbogen C, Lorusso L, Helland IB, Martin JA, Sirbu CA, Mengshoel AM, Polo O, Behrends U, Nielsen H, Grabowski P, Sekulic S, Sepulveda N, Estévez-López F, Zalewski P, Pheby DFH, Castro-Marrero J, Sakkas GK, Capelli E, Brundsdlund I, Cullinan J, Krumina A, Bergquist J, Murovska M, Vermuelen RCW, Lacerda EM. European Network on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (EUROMENE): Expert Consensus on the Diagnosis,

Service Provision, and Care of People with ME/CFS in Europe. *Medicina* (Kaunas). 2021 May 19;57(5):510. doi: 10.3390/medicina57050510.

⁵See Table 2 in Jason, L.A., Ravichandran, S., Katz, B.Z., Natelson, B.H., & Bonilla, H.F. Establishing a consensus on ME/CFS exclusionary illnesses. *Fatigue: Biomedicine, Health & Behavior*, 2023; 11(1), 1-13. <https://doi.org/10.1080/21641846.2022.2150487>

⁶Nacul L, Kingdon CC, Bowman EW, Curran H, Lacerda EM. Differing case definitions point to the need for an accurate diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome. *Fatigue: Biomedicine, Health & Behavior*, 2017;5(1):1-4. doi: 10.1080/21641846.2017.1273863. PMID: 29250461; PMCID: PMC5730342.

⁷Sunnquist, M., Lazarus, S., & Jason, L.A. The development of a short form of the DePaul Symptom Questionnaire. *Rehabilitation Psychology*, 2019, 64(4), 453–462. [PMCID: PMC6697554
https://doi.org/10.1037/rep0000285](https://doi.org/10.1037/rep0000285)

⁸Cotler, J., Holtzman, C., Dudun, C., & Jason, L.A. A brief questionnaire to assess post-exertional malaise. *Diagnostics*, 2018, 8, 66. doi:10.3390/diagnostics8030066

⁹Carruthers BM, van de Sande MI, De Meirleir KL, et al. Myalgic encephalomyelitis: International Consensus Criteria. *J Intern Med*. 2011; 270: 327-338.

¹⁰Bateman L, Bested AC, Bonilla HF, et al. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: essentials of diagnosis and management. *Mayo Clinic Proc*. 2021;96(11):2861–2878. Available from: <https://www.mayoclinicproceedings.org/action/showPdf?pii=S0025-6196%2821%2900513-9#page=10>.

¹¹Cox, D. L., & Findley, L.J. The Management of Chronic Fatigue Syndrome in an Inpatient Setting: Presentation of an Approach and Perceived Outcome. *British Journal of Occupational Therapy*, 1998, 61(9), 405–09. <https://journals.sagepub.com/doi/10.1177/030802269806100907>

¹²Conroy, K., Bhatia, S., Islam, M., & Jason, L.A. Homebound versus bedridden status among patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Healthcare*, 2021, 9(2), 106. <https://doi.org/10.3390/healthcare9020106>

¹³Wiedbusch, E., & Jason, L.A. Comparing operationalized approaches for substantial reduction of functioning in Chronic Fatigue Syndrome and Myalgic Encephalomyelitis. *Archives of Community Medicine*, 2022, 4(1), 59-63. PMCID: PMC9168545 <https://doi.org/10.36959/547/653>





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