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Dear Dr. Unger,

The Myalgic Encephalomyelitis Action Network (#MEAction) is deeply concerned about the lack of transparency and stakeholder engagement in CDC's ME/CFS program, especially since CFSAC was disbanded. CDC's ME/CFS SEC calls do not fill this gap and have never been used to provide program-level engagement and transparency. As a result, stakeholders have limited information on ME/CFS programs and lack the opportunity to provide formal input. Given the urgency of need, the debility that patients experience and the critical lack of doctors willing and able to care for these patients, this is not acceptable.

Accordingly, as a first step to achieve the needed transparency, we request that you provide a full and prompt update in writing regarding CDC's ME/CFS program, building on what was stated in the update provided in NIH's Stakeholder call on August 19, 2019 and with specific attention to the following questions:

1. **Multi-Site Clinical Assessment of ME/CFS (MCAM) Adult:** This study began in 2011. However, only one paper, on the study methods, has been published. In the face of such urgent need for foundational knowledge about this disease, this pace is unacceptably slow. We expect CDC to significantly accelerate its efforts to complete and publish this study.
    a. You stated that you had completed the enrollment and data delivery from the original MCAM sites. Does that mean that no additional studies or data collection are expected from these sites?
    b. You stated that CDC intended to collect additional information on other diseases such as rheumatoid arthritis, multiple sclerosis, and post-cancer fatigue for comparison to ME/CFS. You also acknowledged that the current MCAM sites do not have many of these patients in their practices. Is CDC contracting with other sites to provide these patients and if so, which ones? Are any other disease comparison groups included? Will those sites collect the full complement of MCAM related questionnaires, studies, and lab tests?

c. What specific additional MCAM study publications have been planned, including the articles on exercise/cognition, NKC function testing, and validation of fatigue questionnaires mentioned on the NIH call? What is the expected schedule of submission for publication?
d. NIH and CDC have stated that additional research is needed to clarify the ME/CFS case definition. CDC has been conducting the MCAM study using expert clinicians since 2011, an opportunity that is unlikely to present itself in the future as these clinicians are nearing retirement. What has CDC learned from these ME/CFS experts about the case definition? Have the experts provided consensus about the key features required for diagnosis? Has the MCAM study sufficiently clarified the case definition or required features? What additional research is needed?

2. **MCAM Pediatric study:** Very little public information is available and the community has not been involved in this recent study. We expect transparency and prompt answers to some basic questions about this study, including but not limited to the following:
    a. Which pediatricians are involved in this study and how were they selected?
    b. What methods are being used to select patients, including inclusion and exclusion criteria and the specific methods to ascertain that patients meet those criteria?
    c. Which disease experts are advising these pediatricians? Are Dr. Peter Rowe and those clinicians involved in the MCAM adult study and NIH's CRCs providing advice, particularly on validation of the diagnosis?
    d. What specific types of studies, evaluations, and tests are being conducted as part of this study?
    e. What is the anticipated timeline for completion of this study?
    f. When do you expect that the publication(s) to be completed and submitted for publication?

3. **Epidemiological research study:** As a result of prior poorly-conducted epidemiologic research, no reliable and comprehensive information exists about prevalence, risk factors, natural history, or prognosis for ME/CFS. CDC must undertake a large-scale, comprehensive, and carefully-designed epidemiologic survey to capture this sorely-needed information.

    We understand that CDC's current strategy for ME/CFS epidemiological research is to leverage existing but separate initiatives - particularly the Behavioral Risk Factor Surveillance Survey (BRFSS), as discussed on the NIH call, supplemented with other information such as that from the MCAM studies, the contract with nurses for school surveillance of causes of chronic absenteeism, and a Vaccines Safety monitoring program.

    We are deeply concerned that these plans, as we understand them, are disparate initiatives that have not been designed as part of a cohesive whole, do not adequately assess the full range of epidemiological factors, and do not all employ the same standards for diagnosing patients. Thus, these are not a sufficient replacement for the kind of rigorous, large-scale, and comprehensive epidemiological research that is needed. Worse, this approach could result in

erroneous conclusions about prevalence, risk, natural history, comorbidities, prognosis, access to health case, and presence of comorbidities.

Given the critical need for accurate, updated epidemiological research, we have the following questions:

a. Are there any other components to CDC's strategy for epidemiological research not listed above?
b. Given that ME/CFS is underdiagnosed and "CFS" over- and mis-diagnosed, what is CDC doing to address the fact that the BRFSS and use of medical records rely on a diagnosis of "CFS" which has been demonstrated to be unreliable? You stated that the pilot BRFSS results were comparable to the Canadian study, but we understand that this study also used broad patient selection methods that could have inflated results.
c. How will CDC integrate findings across these disparate initiatives that all have different standards for identifying CFS and/or ME/CFS patients?
d. Which stakeholders, including disease experts and patients/caregivers, have provided input on and reviewed CDC's overall epidemiological strategy?
e. What is the anticipated timeline to complete and publicize this work?
f. What is CDC doing to mitigate the limitations of its strategy?
g. Does CDC have a document that fully describes its epidemiological strategy, including that for both adult and pediatric patients? If so, can you please provide? If not, why not?
h. Why is CDC not conducting the kind of large-scale, comprehensive, thorough, carefully-designed epidemiologic study that includes validation of diagnosis by ME/CFS experts and adequately captures natural history, risk factors, prognosis, prevalence, and comorbidities?

4. **CDC ME/CFS website:** CDC's website serves as a critical platform for propagating disease-specific knowledge and medical guidelines to providers. Historically, insufficient and even harmful information has been published and, while CDC has taken some steps to improve this content in recent years, many deficiencies remain. We expect comprehensive, appropriate and up-to-date guidance to be regularly published through this venue.
    a. Multiple callers to the NIH call stated that doctors are still recommending CBT and GET, which can cause harm to patients. To its credit, CDC removed these recommendations from its website. But CDC never issued a statement on why *PACE-style* CBT and GET - treatments - based on the theory that the debility of the disease is the result of false cognitions and deconditioning - should not be recommended for people with ME/CFS. These are specific treatments that are not the same as pacing and stretching but are often conflated. To protect patients, CDC must issue a warning to care providers about these treatments. Why has this not been done?
    b. What plans does the CDC have to address concerns previously raised by #MEAction with the current site's content?
    c. We are pleased to hear that the information collected from stakeholders at the August 2018 Medical Education Roundtable is being reviewed for release. How will that new content be provided (e.g. website or through some other mechanism) and when will it be published?

5. **Development of CMEs:** Consensus about appropriate clinical management practices is evolving rapidly. Given the demand and urgency for medical education, we expect more frequent development and release of CME materials. We appreciate that CDC has released a Medscape CME, a tool for the clinical practical assessment of ME/CFS to assess clinician knowledge, and a test and teach module that includes two patient case scenarios and interactive test questions.
    a. Which ME/CFS disease experts provided the patient case scenarios and test questions and/or validated this content?
    b. Does the CDC have any additional CMEs planned? If so, what are they, which ME/CFS disease experts are involved, who will be the target audience(s), and when will they be released?

6. **Partnership with school nurses:** A year ago, the CDC awarded a contract to the National Association of School Nurses to conduct active surveillance of students with chronic absenteeism, including that caused by ME/CFS as well as other conditions, in schools. We appreciate that a clinical presentation was given at NASN's annual conference and this will be converted into an enduring educational resource.
    a. What clinical diagnostic criteria will the nurses in the surveillance program use to identify students as having ME/CFS?
    b. Will the surveillance program ensure that a physician has done a full diagnostic workup before the student has been designated as an ME/CFS case?
    c. If a clinician is confirming the diagnosis, what criteria have they been instructed to use?
    d. Have ME/CFS disease experts been involved in validating the approach for confirming an ME/CFS diagnosis and if so, which ones?
    e. What other attributes are being investigated as part of this surveillance? E.g. socioeconomic demographics, family life, behavioral factors, ethnicity, etc.

7. **Partnership with Georgia pediatricians:** There is a desperate need for more expert pediatricians nationwide as there is currently only one expert ME/CFS pediatrician who is nearing retirement.
    a. Beyond the banner on the Georgia chapter of the American Academy of Pediatrics site, the presentation by Dr. Pendergras at the Georgia Pediatric Nurses Association, and the presentation by Dr. Rowe, is anything else being developed as part of this initiative? If so, what is the nature of the project, and when will it be delivered?
    b. What clinical management content (e.g. the ME/CFS Pediatric Primer) did Dr. Pendergras use in his presentation and which specific ME/CFS disease experts validated the program?
    c. What plans does either CDC or the Georgia chapter of American Academy of Pediatricians have to leverage this with the national organization or chapters in other states?

8. **CDC Treatment Guidelines Evidence Review:** This evidence review is critical because it will have a profound impact on the recommendations in evidence-based medical education. As has

been the case in previous evidence reviews, we are concerned that inappropriate conclusions about treatments will be drawn from studies that include patients with other diseases.

a. When will the Prospero description of this initiative be released by the Oregon Health Center?
b. Will stakeholders be given a chance to review and provide input on the Prospero description, and what will be the process of incorporating this input?
c. When is the draft review expected?
d. Will stakeholders be given a chance to review and provide input on the draft review?

9. **Proactive outreach to medical community:** We understand that CDC has conducted efforts to educate the medical community including its website, its biannual medical education roundtable, its recently released CME, contracts with the school nurses and Georgia pediatricians, and presentations at several conferences. These are commendable preliminary efforts. However, we have a crisis in clinical care that has left patients mistreated and neglected. CDC's efforts are not sufficient to address the current crisis that has resulted from stigma, lack of knowledgeable clinical providers, and inappropriate guidelines on the sites of some medical societies and medical education providers. One example is Mayo Clinic's continued recommendations for CBT and GET, as discussed on the NIH call. Another example is the very common rejection that patient advocates encounter when they try to get state health departments to follow the New York state example as suggested by Dr. Whittemore. Patients are not able to overcome the stigma, misinformation, and neglect without proactive support from HHS.
   CDC must leverage its leadership position and political capital to challenge widespread medical misinformation. Patients continue to be harmed by inaccurate recommendations and popular myths around the nature of ME.
   a. Beyond the above initiatives, what is CDC doing to proactively engage leaders of the major medical societies to convince their members to take responsibility for the care of these patients?
   b. What efforts are underway to further engage primary care providers, especially those who work in underserved communities and regions?
   c. What efforts are underway to engage key specialists such as neurology, immunology, pediatrics and infectious disease?
   d. What has CDC done to discuss this issue with Mayo Clinic?
   e. CDC provides funding to state health departments to support medical education. When advocates have gone to state health departments, they have told us they do not have money to promote ME/CFS medical education and that CDC does not provide funding for ME/CFS in its state grants. Why not? What is required to change this?

We have an urgent crisis. Tackling these problems is going to require strong stakeholder engagement and transparency, as part of an aggressive and comprehensive strategy. We look forward to future opportunities to engage more deeply with CDC's ME/CFS efforts. We appreciate your time and attention to these specific questions, and expect your timely response within 45 days.

Sincerely,

#MEAction CDC Working Group

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