National Institutes of Health

Final Report

NATIONAL INSTITUTES OF HEALTH
Pathways to Prevention Workshop:
Advancing the Research on Myalgic Encephalomyelitis/
Chronic Fatigue Syndrome

December 9–10, 2014

EXECUTIVE SUMMARY

Carmen R. Green, M.D.; Penney Cowan; Ronit Elk, Ph.D.; Kathleen M. O'Neil, M.D.;
Angela L. Rasmussen, Ph.D.

This National Institutes of Health (NIH) workshop was co-sponsored by the NIH Office of Disease Prevention (ODP) and the Trans-NIH Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) Research Working Group. A multidisciplinary working group developed the workshop agenda, and an Evidence-based Practice Center prepared an evidence report through a contract with the Agency for Healthcare Research and Quality (AHRQ) to facilitate the workshop discussion. During the 1½-day workshop, invited experts discussed the body of evidence, and attendees had opportunities to provide comments during open discussion periods. After weighing evidence from the evidence report, expert presentations, and public comments, an unbiased, independent panel prepared a draft report that identified research gaps and future research priorities. The report was posted on the ODP website for 4 weeks for public comment. This article is an abridged version of the panel's report, the full version of which is available at https://prevention.nih.gov/programs-events/pathways-to-prevention/workshops/me-cfs/workshop-resources.

Introduction

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a chronic, complex, multi-faceted condition characterized by extreme fatigue and other symptoms including pain, impaired memory, sleep disturbance, and insomnia that are not improved by rest. People with ME/CFS may experience significant disability and some may become homebound and bedbound. The etiology and pathogenesis remain unknown; there are no laboratory diagnostic tests; and there are no known cures. One million people, mostly women, are affected. ME/CFS is an unmet public health need with an economic burden estimated to be between $2 billion and $7 billion in

the United States. ME/CFS results in major disability for a large proportion of the people affected. Limited knowledge and research funding creates an additional burden for patients and health care providers. Unfortunately, ME/CFS is an area where the research and health care community has frustrated its constituents, by failing to appropriately assess and treat the disease and by allowing patients to be stigmatized.

On December 9 and 10, 2014, the National Institutes of Health (NIH) convened a Pathways to Prevention Workshop: Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. Purposes were to identify research gaps, determine methodological and scientific weaknesses, and provide future research recommendations. An independent panel considered a systematic review of the scientific evidence report conducted by the Pacific Northwest Evidence-based Practice Center and opinions presented by a group of experts and the ME/CFS community during the public meeting. They weighed the evidence and developed a set of conclusions. This report presents their main findings and recommendations.

Incidence, prevalence and manifestations

ME/CFS clearly exists though there is an absence of a universally accepted definition. A workshop speaker stated that the Centers for Disease Control and Prevention estimates that one million adults in the United States have ME/CFS. The lack of a universally accepted case definition makes determining incidence and prevalence difficult and leads to variability in such estimates. The lack of a specific and sensitive diagnostic test and clearly defined diagnostic criteria has hampered research on pathogenesis, treatment, and conceptualization of ME/CFS as a distinct entity.

ME/CFS has a tremendous impact at the individual, family, and societal level. Clinicians have a poor understanding of the condition, and patients are typically underserved. Studies of ME/CFS are fraught with methodological problems, preventing a clear understanding of who is affected by ME/CFS: there are no agreed-upon parameters for defining ME/CFS, no accurate ways of identifying and diagnosing ME/CFS, and, as one speaker pointed out, 163 possible combinations of symptoms associated with ME/CFS. Small sample sizes, the inclusion of participants with differing symptoms across studies, and the failure to include men, minorities, homebound individuals, and rural residents limits the applicability of current studies. Some instruments used to evaluate ME/CFS are not validated, are inappropriate, and may be misleading. All of these issues contribute to inconclusive research results and a lack of definitive knowledge about incidence and prevalence and potential causes and treatments.

Fatigue has been the defining symptom and focus of recent research on ME/CFS. According to a workshop speaker, ME/CFS patients have neurocognitive dysfunction with abnormalities in functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) studies. Strong evidence indicates immunologic and inflammatory pathologies, neurotransmitter signaling disruption, micorobiome perturbation, and metabolic or mitochondrial abnormalities in ME/CFS that are potentially important for defining and treating ME/CFS. It remains unclear whether the available evidence in adults is applicable to children with similar symptoms. Thus, other symptoms, primarily neurocognitive deficit ("brain fog"), post-exertion malaise, and pain must be explored across the lifespan. There are few disease-specific clinical trials; a disconnect on ways patients, clinicians, and researchers define meaningful outcomes; a lack of well-

controlled, multifaceted studies using large, diverse samples; and limited public and private research dollars directed at ME/CFS.

Both society and the medical profession have contributed to ME/CFS patients feeling disrespected and rejected. They are often treated with skepticism, uncertainty, and apprehension and labeled as deconditioned or having a primary psychological disorder. ME/CFS patients often make extraordinary efforts at extreme personal and physical costs to find a physician who will correctly diagnose and treat their symptoms while others are treated inappropriately causing additional harm. Overall, the debilitating effects of ME/CFS can result in financial instability due to the consequences of the illness (e.g., the loss of employment, home).

Ways to foster research and enhance development of treatments

The public, provider, and research communities are is frustrated with the minimal progress to improve the state of science for ME/CFS over the last 20 years. Patients want their concerns to be heard, a meaningful recovery (not just incremental improvement), and a cure. Educational efforts are needed to assist patients and clinicians to better understand ME/CFS. The scientific community also has a responsibility to address issues that are meaningful to ME/CFS patients.

Limited patient and professional education has impaired progress in managing ME/CFS, and treatments remain unproven. Clinical studies have focused on predominately Caucasian, middle-aged women. Representative, ethnically diverse samples across the lifespan are lacking.

Investigations of natural history and familial linkages may identify genetic predispositions and lead to early identification and primary strategies.

Although psychological repercussions (e.g., depression) may accompany ME/CFS, it is not a primary psychological disease in etiology. Several symptoms associated with ME/CFS have substantial overlap with other pathologic diseases (e.g., fibromyalgia, major depressive disorder, and several chronic pain or inflammatory conditions). Although focusing on fatigue alone may identify many ME/CFS cases, it does not capture the essence of this complex condition. Prior studies may have inadequately excluded individuals with these distinct diseases, leading to delayed or conflicting diagnoses, contradictory treatments, suboptimal care, and inappropriate health care utilization. Future studies that aim to better define cellular and molecular mechanisms for targeted treatments should distinguish between ME/CFS alone, ME/CFS with comorbidities, and other diseases.

Carefully designed and adequately powered studies defining the spectrum of ME/CFS in urban and rural communities are lacking; the current available evidence base has limited applicability to an increasingly diverse society. It is critical that research studies include patients with limited access to clinical services (e.g., non-ambulatory patients). Although research has shown that ME/CFS patients often have a consistent constellation of symptoms, including fatigue, post-exertional malaise, neurocognitive deficit, and pain; work is urgently needed to develop a clear case definition as well as validated diagnostic tools for the case definition. Agreeing on a case definition and clarifying comorbidities could launch bench-to-bedside science.

People with ME/CFS remain hopeful that research will lead to a cure. However, existing cross-sectional studies and small clinical trials with limited applicability have provided few insights into ME/CFS treatment. Adequately powered clinical trials require large investments of time and energy, while interventions tested in trials may be associated with harms such as precipitating increased symptoms or medication toxicity. Existing treatment studies examining counseling and behavior therapies or graded exercise therapy demonstrate measureable improvements, but may not yield improvements in quality of life (QOL). Thus, these interventions are not a primary treatment strategy and should be used only as a component of multimodal therapy.

Small clinical trials, most with methodological limitations and all constrained by the lack of a gold standard for diagnosis of ME/CFS, have led to confusion. Most studies have significant methodological limitations and primarily take place in specialty clinics in relatively homogeneous populations. These trials often use subjective, unclear, and poorly defined end points (that may not be meaningful to patients) and fail to provide information on why there were high dropout rates. Thus, variability in inclusion and exclusion criteria such as the case definition, co-morbidities, patient population, and disease severity has significantly hampered progress in the clinical and research domains focused on assessing and treating ME/CFS.

Little attention was given to how self-management may empower and improve health and QOL for people with ME/CFS. Physicians are inadequately trained to instruct patients in self-management skills (e.g., pacing, realistic goals, physical self-awareness, basic rights, understanding emotions, exercise, and relaxation) and there is limited data demonstrating the efficacy of self-management on health outcomes. The focus on exercise programs has

discouraged patient participation in any type of physical activity (e.g., mild stretching) due to concerns of precipitating increased symptoms.

There is little understanding of the inciting event or the cellular and molecular mechanisms that underlie ME/CFS, preventing quantitative assessments of disease severity or prognosis. The failure to give adequate attention to the severity of the physical, social, and emotional impact of ME/CFS has caused harm and diminished hope. A variety of symptoms are often "lumped" into ME/CFS. Carefully defining comorbid conditions is necessary to determine ME/CFS subgroups and to move the field forward. Interdisciplinary collaborations to develop tools or disease measures that encompass the full spectrum of possible ME/CFS signs and symptoms are needed.

Defining ME/CFS requires standard, validated tools and measures. Individual ME/CFS studies are too small to have power for subgroup analyses; rarely meet the criteria for good quality evidence; frequently do not address early disease or ME/CFS in children; fail to adequately address harms or who dropped out and why; and include only a short follow-up. Additionally, participant variability at different study centers may, in part, be responsible for conflicting results.

End points need to be clarified: what is statistically significant, what is clinically significant, and what is significant to the patient. To move ME/CFS research forward, there is an urgent need to get all of the information from the control population, responders, and non-responders. Simple patient-centered tools need to be developed to ensure patient comprehension. Overall, there is a need to simplify measures while prioritizing face-to-face interactions.

To advance the field, practical retrospective, prospective, and longitudinal studies that are reproducible are needed. Longer follow-up and a life span perspective are needed to understand ME/CFS effects on the whole individual (e.g., patient expectations and decision-making and sexual health and childbearing). The symptoms patients consider clinically meaningful are not in the scientific literature; this discordance must be rectified.

Current research has neglected many of the biological factors underlying ME/CFS onset and progression. Research priorities should be shifted to include basic science and mechanistic work that will contribute to the development of tools and measures such as biomarker or therapeutics discovery. The following questions need to be answered:

- What is the pathogenesis of ME/CFS? What is the role of virologic mechanisms, especially herpes viruses? Does mononucleosis lead to ME/CFS in adolescents?
- What is the role of other pathogenic agents?
- Is this a genetic disease? Is there a gene-environment interaction?
- Is ME/CFS a spectrum disease?
- Are different pathways responsible for different symptoms?

Future Directions and Recommendations

Overall, there has been a failure to implement what we already know for ME/CFS patients while the disease steals their health and well-being. Scientifically rigorous research is needed to improve this situation. The subjective nature of ME/CFS, associated stigma, and lack of a

standard case definition has stifled progress. Patients must be at the center of the research efforts, and their engagement is critical, as is outreach to underserved and vulnerable populations.

Innovative biomedical research is urgently needed to identify risk and therapeutic targets. The scientific community and funding agencies responsible for conducting trials in an ethical way that is meaningful for patients. The influence of health literacy and cognitive impairment on informed consent must be considered. Investigators have a responsibility to hear the patient's perspective, engage the community, and be accountable for translating and reporting research results to the ME/CFS community while responding to their feedback. The dissemination of diagnostic and therapeutic recommendations should begin by focusing on primary care providers and expand to other areas such as neurology, rheumatology, and infectious disease. Potential conflicts of interest among investigators need to be properly vetted, discussed, and addressed by all stakeholders.

To accelerate the progress of ME/CFS treatment, we recommend the following overarching research strategies:

1. *Define disease parameters.* Assemble a team of stakeholders (e.g., patients, clinicians, researchers, federal agencies) to reach consensus on the definition and parameters of ME/CFS. A national and international research network should be developed to clarify the case definition and to advance the field. NIH Institutes and Centers not presently represented in the Trans-NIH ME/CFS Working Group should be incorporated to capitalize on the tremendous opportunities to learn from other

disciplines and diseases (e.g., Gulf War Syndrome, Lyme disease, fibromyalgia, multiple sclerosis, and Parkinson's disease).

2. *Create new knowledge.* Investing in bench-to-bedside research for ME/CFS is recommended. A priority should be placed on developing biomarkers and diagnostic tests. The field could be energized and diversified by creating opportunities for junior and new investigators to be involved. The NIH Institutes and Centers (e.g., the National Center for Advancing Translational Sciences [NCATS] and the National Center for Complementary and Alternative Medicine [NCCAM]) and other U.S. Department of Health and Human Services (HHS) agencies should coordinate research efforts to promote efficiency and effectiveness, while using public/private partnerships to leverage existing NIH infrastructure and dollars. Specific activities should focus on:

    - Developing valid prognostic tests that can guide treatment strategies using genomic, epigenomic, proteomic, and metabolomic strategies to identify critical biomarkers that will be clinically applicable. Gene expression, protein, or metabolite signatures that can correctly diagnose ME/CFS and distinguish it from other chronic conditions, while predicting disease severity and clinical outcomes, are needed. Determining the most important physiologic measures and pathophysiology, as well as genome-wide association studies (GWAS) and phenotyping, is essential for stratifying patients. fMRI and imaging technologies should be further studied as diagnostic tools and as methods to better understand the neurologic dysfunction of ME/CFS.

- Biologic samples (e.g., serum and saliva, RNA, DNA, whole blood or peripheral blood mononuclear cells, and tissues) and de-identified survey data should be linked in a registry/repository to understand pathogenesis and prognosis, and facilitate biomarker discovery. Further exploration is needed of the intestinal microbiome, and the effect, if any, of the environment and microbiome on ME/CFS development using cutting-edge technologies (e.g., high-throughput sequencing), neurocognitive tests, and neuroimaging.
- Epidemiological studies of ME/CFS, including incidence and prevalence, who is at high risk, risk factors, geographical distribution, and the identification of potential health care disparities are critical. A repository for qualitative and quantitative research is needed.
- Previously collected research data should be analyzed to advance knowledge and inform trial development and design and facilitate necessary clinical trials. Specifically, drug therapies used for fibromyalgia or other pain-related syndromes and disorders should be examined for their effectiveness for ME/CFS. Existing registries should be leveraged.
- Studies that stratify by clinical characteristics should be used to develop diagnostic and prognostic algorithms to identify who will develop ME/CFS following infection or other triggers.
- There is a need for "omics"-based drug repurposing and neurobiology studies. Using bioinformatics techniques, large datasets should be developed and stored in a central, publicly accessible database for future investigations. New knowledge might include an understanding of molecular mechanisms

underlying ME/CFS, new ways to perform pathway analyses, and/or new pharmacogenomic drug discovery or repurposing.

- An integrated, systems-level approach should be followed to understand how immunologic, neurologic, and metagenomic factors may contribute to ME/CFS. Immunologic mechanisms of ME/CFS and pathways associated with disease progression must be defined and characterized (e.g., defining cytokine profiles involved in pathogenesis; studying inflammation; and comprehending the basis for natural killer cell dysfunction observed in many ME/CFS patients). Longitudinal studies to explore the possibility of a progressive immune exhaustion or dysfunction in ME/CFS remain important.
- Studies of gene expression among identical twins to identify gene expression biomarkers are needed. Both male and female models must be used to explore the role of gender, X-chromosome genes, and hormones in developing ME/CFS.
- How patients' background medications (including psychiatric drugs) affect function and outcome should be explored. Patients often choose clinical trials or complementary and alternative medicine because effective treatment is not available and because traditional health care is not meeting their needs. Studies investigating homeopathy, non-pharmacologic, complementary and alternative medicine treatments, and biopsychosocial parameters (including the mind-body connection), function, and QOL should be encouraged.

3. *Improve methods and measures.* There is a critical need for improved measures to identify ME/CFS while including the patient's voice through patient-reported

outcomes. Without a diagnostic test, stratification must occur to reduce and comprehend variability (e.g., onset, time course, comorbid conditions), and to identify clearly defined end points for treatment trials and interventions. The NIH should develop an ME/CFS methodological workgroup.

- A community-based participatory research approach is needed to increase patient involvement in determining priorities for research and care.
- Use of already well-validated measures developed by the NIH such as the Patient-Reported Outcomes Measurement Information System (PROMIS) and the Center for Epidemiological Studies Depression scale (CESD) should be encouraged. Although ME/CFS is not a psychiatric disease, exploring psychiatric comorbidities such as depression, anxiety, and fear is critical to improve QOL. Response burden must be considered; a battery of simplified measures is strongly encouraged, as well as the triangulation of qualitative and quantitative data. The NIH should leverage the power of other longitudinal studies (e.g., the Health and Retirement Study, the Nurses' Health Study) to better understand ME/CFS.
- Telemedicine or home visits for those unable to participate in clinical trials/treatment in person and outreach to underserved communities are needed. New technologies to address underserved populations and unmet needs (e.g., mobile technology, online tracking tools) should be developed and employed to measure progress and to enable communication, especially for those who are not served in the clinic setting.

4. *Provide training and education.* Many clinicians do not fully understand ME/CFS. We believe ME/CFS is a distinct disease that requires a multidisciplinary care team (e.g., physicians, nurses, case managers, social workers, psychologists). Primary care clinicians will be instrumental in ensuring that patients are treated appropriated and care is optimized. Thus, a properly trained workforce is critical, and we strongly encourage engaging with:
    - Health professional licensing and accreditation agencies to ensure a curriculum that facilitates ME/CFS knowledge acquisition
    - Health Resources and Services Administration (HRSA) to facilitate training
    - Professional societies and patient organizations to facilitate a public-private partnership, as well as training and funding of health care professionals
    - Clinicians and researchers, who have a responsibility to encourage and track progress
    - Patients must become active participants in their overall treatment.

5. *Finding new funding resources.* With a relatively small number of researchers in the field and finite resources, there is a need for partnerships across institutions to advance the research and develop new scientists. New collaborative models, investigator-initiated studies, career development, and small grant mechanisms with specific attention to developing a cadre of junior investigators, including women and minorities who may offer innovative new approaches, are needed. Opportunities exist within HHS to engage new ME/CFS working group members, to create efficiency, and to co-fund research to promote diversity in the pipeline, eliminate disparities, and enhance the quality of the science (e.g., the National Institute on Minority Health

and Health Disparities [NIMHD], the National Cancer Institute [NCI], the Department of Education's National Center for Medical Rehabilitation Research, [NCMRR], the Department of Defense [DoD]).

- Create a network of collaborative centers working across institutions and disciplines, including clinical, biological, and social sciences. These centers will be charged with determining the biomarkers associated with diagnosis and prognosis, epidemiology (e.g., health care utilization), functional status and disability, patient-centered QOL outcomes, cost-effectiveness of treatment studies, the role of comorbidities in clinical and real-life settings, and providing a complete characterization of control populations, as well as those who recover from ME/CFS. Ideally, these collaborative studies will recruit from the broad spectrum of individuals and will use reproducible measures.
- Establish a central archive of de-identified data and tissue samples from prior and ongoing studies to enable data and sample sharing.

6. *Conduct clinical trials.* An ongoing need for participants in clinical trials was noted. The NIH should work with ME/CFS partners and stakeholders to create a website for patient and clinician educational materials as well as information regarding clinical trials. Opportunities to utilize the NIH Clinical Center for clinical trials and to fast-track testing of new therapies should also be explored.
7. *Improve treatment.* Patients should be active participants in care and decision-making. Lessons can be learned from palliative care, such as communication and symptom management to improve the quality of care. Studies examining the role of

self-management techniques as part of a comprehensive treatment plan for people with ME/CFS during and after clinical interventions should be explored. The modest benefit from cognitive behavioral therapy should be studied as adjunct to other modalities. Future treatment studies should evaluate multifaceted therapies focusing on biomedical and supportive care. Comparative effectiveness research is also needed. We recommend that the NIH and the FDA convene a meeting on the state of ME/CFS treatment.

Conclusions

Quality care begins with assessment and depends upon optimizing patient and clinician decision-making. Interpersonal (e.g., age, race, ethnicity, gender, class, and personality) and patient- and clinician-related factors (e.g., perceptions, knowledge, communication styles, and stigma) influence quality care. People with ME/CFS want their stories to be heard, and the ME/CFS community may benefit from education on how to effectively communicate their concerns to clinicians. Clinicians could benefit from enhanced active listening skills and increased education. We note that education alone cannot fix this problem, but will facilitate a partnership in medical decision-making, thereby optimizing care. Furthermore, the multiple case definitions for ME/CFS have hindered progress. Specifically, continuing to use the Oxford definition may impair progress and cause harm. Thus, for needed progress to occur we recommend (1) that the Oxford definition be retired, (2) that the ME/CFS community agree on a single case definition (even if it is not perfect), and (3) that patients, clinicians, and researchers agree on a definition for meaningful recovery.

Attention should be focused on providing access to high-quality, multidisciplinary care; refining assessment; and clarifying end points that suggest improvement and quality care. We believe there is a specific role for multimodal therapies. Although no data on primary prevention were presented, this does not prohibit secondary and tertiary prevention efforts. Once a cause is determined, primary prevention efforts should begin. The NIH should incorporate concepts from public health prevention and HHS efforts to decrease disability and promote health and well-being for the ME/CFS population across the lifespan.

There is a role for new and ongoing policies to spark innovation and fund new research. For instance, new avenues are needed to fund research, such as the Prescription Drug User Fee Act. The NIH should work with the Centers for Medicare & Medicaid Services (CMS) and the Patient-Centered Outcomes Research Institute (PCORI) to develop demonstration projects of patient-centered medical homes for people with ME/CFS. This should be done using a comparative effectiveness research framework with clear end points and continuous evaluations to improve health care and to determine best practices that are evidence-based. Best practices should then be translated to primary care clinicians. Federal agencies (e.g., AHRQ, the U.S. Department of Veterans Affairs [VA]) and professional societies should work together to create quality metrics and a standard of care. We also recommend that federal departments, advocacy groups, and industry work together in public-private partnerships to help advance research for ME/CFS. Lastly, we recommend that the ODP convene another ME/CFS Expert Panel in five years to monitor progress. We hope our work has dignified ME/CFS and those affected, while providing expert guidance to the NIH and the broader research community.

Acknowledgements

The panel was charged with providing guidance to the NIH on research gaps and research priorities for ME/CFS. While this report was being developed, the Institute of Medicine developed a report entitled, "Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness" and released their findings in February 2015. Although many would like for this panel to consider and incorporate the IOM's recommendations within this report, this is beyond our scope and charge. Nonetheless, the panel believes it is important for federal agencies, clinicians, and people with ME/CFS patients and ME/CFS advocates to consider both reports to move the science forward. Furthermore, we believe the panel's recommendations provide many opportunities to incorporate both reports and new knowledge during the deliberations of other proposed meetings and more specifically when the panel is reconvened in five years.

In general, a two-week public comment period is provided for P2P workshops. The panel's initial report was completed in December 2014. The public comment period was extended to four weeks to allow for maximum participation of people living with ME/CFS who may experience significant physical, social, and emotional disabilities, and to accommodate the holidays. Unfortunately and inadvertently, some of the comments from the final day were not included and considered by the panel during the initial review period. Once this oversight was identified, publication was paused to consider these comments as individual panel members and then as a panel via conference call. An opportunity was provided to consider all public comments. The panel believes this process allowed for a rigorous and inclusive review and a final product that moves the science forward. Lastly, the panel specifically wishes to thank the many ME/CFS patients who shared their stories.

Panel

Chairperson: **Carmen R. Green, M.D.**
Associate Vice President and Associate Dean for Health Equity and Inclusion
Professor of Health Management and Policy, Anesthesiology, and Obstetrics and Gynecology
Office for Health Equity and Inclusion
University of Michigan Health System
Ann Arbor, Michigan

Penney Cowan
Founder and Executive Director
American Chronic Pain Association
Rocklin, California

Ronit Elk, Ph.D.
Research Associate Professor
University of South Carolina College of Nursing
Columbia, South Carolina

Kathleen M. O'Neil, M.D.
Professor of Pediatrics
Indiana University (IU) School of Medicine
Chief
Division of Pediatric Rheumatology
Riley Hospital for Children at IU Health
Indianapolis, Indiana

Angela L. Rasmussen, Ph.D.
Research Assistant Professor
Katze Laboratory
Department of Microbiology
University of Washington
Seattle, Washington

Speakers

Niloofar Afari, Ph.D.
Associate Professor
University of California, San Diego
Healthcare System
Director of Clinical Research
Veterans Affairs (VA) Center of Excellence
for Stress and Mental Health
Division Co-Director
Mental Health Integrative and
Consultative Services
VA San Diego Healthcare System
La Jolla, California

James M. Anderson, M.D., Ph.D.
Director
Division of Program Coordination,
Planning, and Strategic Initiatives
Office of the Director
National Institutes of Health
Bethesda, Maryland

Abigail A. Brown, M.A.
Doctoral Candidate
Clinical-Community Psychology
DePaul University
Chicago, Illinois

Dedra Buchwald, M.D.
Professor of Epidemiology and General
Internal Medicine
Center for Clinical and Epidemiological
Research
University of Washington School of
Public Health
Seattle, Washington

Daniel J. Clauw, M.D.
Professor of Anesthesiology, Medicine,
and Psychiatry
University of Michigan Medical School
Director
Chronic Pain and Fatigue Research Center
University of Michigan Medical Center
Ann Arbor, Michigan

Fred Friedberg, Ph.D.
Research Associate Professor of Psychiatry
and Behavioral Science
Stony Brook University
Stony Brook, New York

Carmen R. Green, M.D.
Associate Vice President and Associate Dean
for Health Equity and Inclusion
Professor of Health Management and Policy,
Anesthesiology, and Obstetrics and
Gynecology
Office for Health Equity and Inclusion
University of Michigan Health System
Ann Arbor, Michigan

Mady Hornig, M.D., M.A.
Director of Translational Research
Center for Infection and Immunity
Associate Professor of Epidemiology
Columbia University Mailman School of
Public Health
New York, New York

Leonard A. Jason, Ph.D.
Professor of Psychology
Director
Center for Community Research
DePaul University
Chicago, Illinois

Nancy G. Klimas, M.D.
Director
Miami Veterans Affairs Gulf War Illness and
ME/CFS Research Program
Professor and Chairperson
Department of Clinical Immunology
Scientific Director
Institute for Neuro-Immune Medicine
Nova Southeastern University
Fort Lauderdale, Florida

Andreas M. Kogelnik, M.D., Ph.D.
Founder and Director
Open Medicine Institute
Mountain View, California

Susan E. Maier, Ph.D.
Deputy Director
Office of Research on Women's Health
Office of the Director
National Institutes of Health
Bethesda, Maryland

Robert Miller
Patient and Advocate
Reno, Nevada

David M. Murray, Ph.D.
Associate Director for Prevention
Director
Office of Disease Prevention
Division of Program Coordination, Planning, and Strategic Initiatives
Office of the Director
National Institutes of Health
Bethesda, Maryland

Luis Nacul, M.D., Ph.D., M.F.P.H.
Chief Investigator
CURE-ME
London School of Hygiene & Tropical Medicine
London
United Kingdom

Benjamin H. Natelson, M.D.
Director
Pain and Fatigue Study Center
Mount Sinai Beth Israel
Professor of Neurology
Icahn School of Medicine at Mount Sinai
New York, New York

Heidi D. Nelson, M.D., M.P.H.
Medical Director of Cancer Prevention and Screening
Providence Cancer Center
Providence Health & Services
Vice-Chair and Research Professor
Departments of Medical Informatics and Clinical Epidemiology
Pacific Northwest Evidence-based Practice Center
Oregon Health & Science University
Portland, Oregon

Leorey N. Saligan, Ph.D., R.N., CRNP, FAAN
Investigator
Symptom Management Branch
National Institute of Nursing Research
National Institutes of Health
Bethesda, Maryland

M.E. Beth Smith, D.O.
Associate Professor
Department of Medical Informatics and Clinical Epidemiology
Pacific Northwest Evidence-based Practice Center
Oregon Health & Science University
Portland, Oregon

Christopher R. Snell, Ph.D.
Scientific Advisory Committee Chair
The Workwell Foundation
Ripon, California

Lea Steele, Ph.D.
Director
Veterans Health Research Program
Institute of Biomedical Studies
Baylor University
Waco, Texas

Renée R. Taylor, Ph.D.
Vice Provost for Faculty Affairs
Licensed Clinical Psychologist
Professor
Department of Occupational Therapy
University of Illinois at Chicago College of Allied Health Sciences
Chicago, Illinois

Elizabeth R. Unger M.D., Ph.D.
Chief
Chronic Viral Diseases Branch
Division of High-Consequence Pathogens and Pathology
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention
Atlanta, Georgia

Suzanne D. Vernon, Ph.D.
Scientific Director
Solve ME/CFS Initiative
Los Angeles, California

Working Group

Working group members provided their input at a meeting held January 6–7, 2014. The information provided here was accurate at the time of that meeting.

Chairperson: **Susan E. Maier, Ph.D.**
Deputy Director
Office of Research on Women's Health
Office of the Director
National Institutes of Health
Bethesda, Maryland

Jody S. Engel, M.A., R.D.
Director of Communications
Office of Disease Prevention
Division of Program Coordination, Planning, and Strategic Initiatives
Office of the Director
National Institutes of Health
Bethesda, Maryland

Carmen R. Green, M.D.
Associate Vice President and Associate Dean for Health Equity and Inclusion
Professor
Health Management and Policy, Anesthesiology, Obstetrics and Gynecology
Office for Health Equity and Inclusion
University of Michigan Health System
Ann Arbor, Michigan

Mady Hornig, M.D.
Director of Translational Research
Center for Infection and Immunity
Associate Professor of Epidemiology
Columbia University Mailman School of Public Health
New York, New York

Suchitra Iyer, Ph.D.
Health Scientist Administrator
Center for Outcomes and Evidence
Agency for Healthcare Research and Quality
Rockville, Maryland

Leonard A. Jason, Ph.D.
Director
Center for Community Research
DePaul University
Chicago, Illinois

M. Katherine Jung, Ph.D.
Program Director
Division of Metabolism and Health Effects
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health
Rockville, Maryland

Nancy Klimas, M.D.
Professor of Medicine
Professor and Chairperson
Department of Clinical Immunology
Scientific Director
Institute for Neuro-Immune Medicine
Nova Southeastern University
University Park Plaza
Fort Lauderdale, Florida

Deborah Langer, M.P.H.
Senior Communications Advisor
Office of Disease Prevention
Division of Program Coordination, Planning, and Strategic Initiatives
Office of the Director
National Institutes of Health
Bethesda, Maryland

Janet W. Maynard, M.D., M.H.S.
Acting Clinical Team Leader
Division of Pulmonary, Allergy, and Rheumatology Products
Food and Drug Administration
Silver Spring, Maryland

WORKING GROUP

Marian McDonagh, Pharm.D.
Associate Professor
Department of Medical Informatics and Clinical Epidemiology
Associate Director
Pacific Northwest Evidence-based Practice Center
Oregon Health & Science University
Portland, Oregon

Robert Miller
Patient and Advocate
Reno, Nevada

Elizabeth Neilson, Ph.D., M.P.H., M.S.N.
Senior Communications Advisor
Office of Disease Prevention
Division of Program Coordination, Planning, and Strategic Initiatives
Office of the Director
National Institutes of Health
Bethesda, Maryland

Eun-Chung Park, Ph.D., M.P.A.
Program Officer
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, Maryland

Wilma Peterman Cross, M.S.
Deputy Director
Office of Disease Prevention
Division of Program Coordination, Planning, and Strategic Initiatives
Office of the Director
National Institutes of Health
Bethesda, Maryland

Peter C. Rowe, M.D.
Professor of Pediatrics
Director
Children's Center Chronic Fatigue Clinic
Sunshine Natural Wellbeing Foundation Professor
The Johns Hopkins University School of Medicine
Baltimore, Maryland

Leorey N. Saligan, Ph.D., R.N., CRNP
Chief
Symptoms Biology Unit
National Institute on Nursing Research
National Institutes of Health
Bethesda, Maryland

Mariela C. Shirley, Ph.D.
Associate Director for Special Projects and Centers
Chairperson
Trans-NIH Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome Research Working Group
Office of Research on Women's Health
Division of Program Coordination, Planning, and Strategic Initiatives
Office of the Director
National Institutes of Health
Bethesda, Maryland

M.E. Beth Smith, D.O.
Assistant Professor
Department of Medical Informatics and Clinical Epidemiology
Pacific Northwest Evidence-based Practice Center
Oregon Health & Science University
Portland, Oregon

Paris A. Watson
Senior Advisor
Office of Disease Prevention
Division of Program Coordination, Planning, and Strategic Initiatives
Office of the Director
National Institutes of Health
Bethesda, Maryland

Jessica Wu, Ph.D.
Health Scientist
Office of Disease Prevention
Division of Program Coordination, Planning, and Strategic Initiatives
Office of the Director
National Institutes of Health
Bethesda, Maryland