

CFS/ME International Conference: Research Innovation and Discovery





Overview of CDC's ME/CFS Initiatives

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CFS/ME International Conference: Research Innovation and Discovery

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November 26, 2018

Disclaimers

- No conflict of interest to declare
- The findings and conclusions in this talk are mine and do not necessarily represent the official position of the US Centers for Disease Control and Prevention (CDC)

CDC's Role Among Federal Agencies

- Focus on public health questions
 - Burden of disease (epidemiology)
 - Risk factors/causes (epidemiology)
 - Health promotion and education (education)

CDC Recognizes Public Health Problem of ME/CFS

- At least 1 million Americans have ME/CFS
 - Estimated prevalence from population-based surveys 0.2% – 0.7%
- Estimated \$9 - \$14 billion annually in direct medical costs in US
 - Nearly one-quarter of these expenses paid out of pocket
- Estimated \$9-\$37 billion annually in lost productivity in US
 - Patients less likely to be employed due to illness related disability
 - Caregivers employment may be affected
 - Illness onset before age 25 frequently blocks full educational potential, thereby limiting lifetime earnings

Questions of Public Health Importance (partial list)

- How could ME/CFS surveillance be simplified and made cost-effective?
 - Regular monitoring of ME/CFS in population is needed
- How can patients receive appropriate health care?
 - Few ME/CFS experts
 - Primary care physicians remain largely unaware of how to make diagnosis and provide support
- What are best practices for treatment and care of ME/CFS?
 - Need practical diagnostic methods and treatment guidelines

Adding ME/CFS to an Ongoing CDC Surveillance System

- Behavioral Risk Factor Surveillance System (BRFSS)



- Established in 1984 with 15 states

- Now collects data in all 50 states, District of Columbia and 3 US territories

- Partnership with shared decision-making

- Phone survey interviewing more than 400,000 adults annually

- Data on health-related behaviors, chronic health conditions, and use of preventive services

- Data at state and local level is powerful tool for public health action

Rationale for Adding ME/CFS Questions to BRFSS

- Estimates on the prevalence and burden of ME/CFS are based on a few population-based studies covering limited areas of the US
- No national or state-level information on the prevalence and burden of ME/CFS among adults in the US
- Sustainable surveillance needed to identify prevalence trends
- ME/CFS can be related to other topics covered by BRFSS such as nutrition, health care access, quality of life, physical activity, and health status
 - Identify co-morbidities and factors that influence ME/CFS

How could ME/CFS be added?

- Develop questions, conduct cognitive testing to establish validity and reliability
 - Questions are understood and easily answered
- Introduce topic and need for questions at Annual BRFSS Conference
 - Submit proposal to meeting organizers
 - Accepted proposals are presented at the meeting
 - Round table sessions to address questions
 - Proposals voted on by state coordinators
 - New questions or modules that are approved require cognitive and field testing

Status of ME/CFS Module

- First presented at 2013 BRFSS Conference
 - Did not receive required number of votes
 - Presentation and individual outreach raised state health department awareness of ME/CFS
 - Five states included as state-added questions in 2014 BRFSS survey
 - Alabama, Connecticut, Kansas, Nebraska, North Carolina
 - Three states continue to include in 2016 BRFSS survey
 - Alabama, Kansas and North Carolina
- Presented again at 2018 BRFSS Conference
 - **Approved** as new optional module for 2019 BRFSS survey

What made the difference in 2018?

- Increased familiarity with ME/CFS from prior BRFSS Conference presentations and booth
- Preliminary data on ME/CFS from state-added questions in 2014 and 2016 BRFSS surveys
- Advocacy support
 - Lily Chu and #MEAction
 - Call-to-Action: Urge your State Health Department to Track ME!

<https://www.meaction.net/2018/03/19/call-to-action-urge-your-state-health-department-to-track-me/>

ME/CFS Prevalence Questions: Lifetime and Current

- 1. Have you ever been told by a doctor or other health professional that you had Chronic Fatigue Syndrome (CFS) or ME (Myalgic Encephalomyelitis)?
 - (1) YES
 - (2) NO (go to next section)
 - (7) Don't Know/Not Sure (go to next section)
 - (9) Refused (go to next section)

- 2. Do you still have Chronic Fatigue Syndrome (CFS) or ME (Myalgic Encephalomyelitis)?
 - (1) YES
 - (2) NO (go to next section)
 - (7) Don't Know/Not Sure
 - (9) Refused

ME/CFS Disability: Work Limitation

- 3. Thinking about your CFS or ME, during the past 6 months, how many hours a week on average have you been able to work at a job or business for pay?
 - (1) 0 or no hours -- cannot work at all because of my CFS or ME
 - (2) 1 - 10 hours a week
 - (3) 11- 20 hours a week
 - (4) 21- 30 hours a week
 - (5) 31 - 40 hours a week
 - (7) Don't know / Not sure or (9) Refused (go to next section)

For these three questions:

- Cognitive test was conducted by Westat in 2013 through BRFSS program;
- The lifetime and current prevalence questions were included in state-added questions for 2014 and 2016 BRFSS surveys by 5 states.

Results of State-Added ME/CFS Questions¹

- Total respondents = 54,695
 - 2014 (5 states) and 2016 (3 states)
 - Mean age 54.8 (± 18.2) years, 42.3% female, 82.8% white/non-Hispanic
- ~1.6% ever diagnosed with ME/CFS
 - More likely to be female (81.6%)
 - Of those diagnosed, 71.4% still have ME/CFS
- Prevalence estimates of ME/CFS in these states (lifetime 1.6%; current 1.2%) similar to results from Canadian Community Health Survey 2005, 2010 and 2014

¹From abstract presentation to 2018 CSTE Annual Conference June 10-14, 2018

Characteristics of Current Self-Reported ME/CFS¹

- 78.8% reported function limitations in at least one area:
 - Concentrating, remembering or making decision
 - Walking or climbing stairs
 - Dressing or bathing
 - Doing errands alone
- 83.4% had two or more of 11 chronic health conditions included in BRFSS core questions as co-morbidity
 - Heart attack, stroke, angina, current asthma, skin cancer, other cancer, COPD, arthritis, depression, kidney disease, diabetes

¹From abstract presentation to 2018 CSTE Annual Conference June 10-14, 2018

Access to Healthcare Among Current ME/CFS¹

- 89% had insurance
- 91% had at least one healthcare provider

Despite this:

- 36% did not receive needed healthcare because of cost
- 16% had not received routine check-up within two years

¹From abstract presentation to 2018 CSTE Annual Conference June 10-14, 2018

Additional Plans for ME/CFS Surveillance

- Active National Surveillance in Schools – Contract with National Association of School Nurses
 - Collect data on conditions causing chronic school absenteeism and educate school nurses about ME/CFS
- ME/CFS Diagnoses within Vaccine Safety Datalink (VSD) project
 - Awarded to Kaiser Permanente Northwest
 - Advantageous indirect benefit - increased awareness of ME/CFS in large managed care organization
 - Identify ME/CFS in 9-39 year olds using ICD codes
 - Electronic medical record abstraction for verification

Healthcare Provider Education

- CDC's webpages updated to reflect recommendations of the IOM Report
 - <https://www.cdc.gov/me-cfs>
 - Section for general public launched June 2017, updated May 2018
 - Healthcare provider section June 2018
- Medscape Spotlight CME expected release by January 2019
 - Video of 4 physicians addressing how to diagnose ME/CFS
 - **Dr. Lucinda Bateman** (Bateman Horne Center, UT); **Dr. Natalie Azar** (NYU Langone Medical Center, NY); **Dr. Nancy Klimas** (Nova Southeastern University, FL); **Dr. Jose Montoya** (Stanford University, CA)

Additional Plans for Education and Outreach

- Roundtable 2018 – Stakeholder engagement about educational needs for healthcare providers and information patients what their providers to know
 - In-person meeting in Atlanta, August 30, 2018
- Educational services for healthcare providers serving pediatric population
 - Contract with Georgia chapter of the American Academy of Pediatrics
 - CME event, webinars, articles in chapter newsletter about ME/CFS
- Stakeholder Engagement and Communication Calls
- Additional Medscape CMEs and evaluation of impact

Pathway Towards Treatment Guidelines

- Standards for guideline development require rigorous process
- Best practices follow Institute of Medicine's Report (now NAM) "Clinical Practices Guidelines We Can Trust" – Standards for Developing Trustworthy Clinical Practice Guidelines
- Principles include
 - Transparency
 - Systematic review of literature
 - Rating strength of recommendations
 - External review and regular updating

Unique Challenges for ME/CFS

- Clinical trial data is sparse, majority of evidence comes from expert experience
- Lack of standardized methods for case ascertainment makes comparisons difficult

Starting the Process

- Contract with Oregon Health Sciences to assist
- Develop questions framing literature review (key to process)
- Assist in developing a plan leading to federal guidelines
 - Transparency requires Federal Advisory Committee
 - Workgroup of committee needs to be identified to represent all required expertise and avoid conflict of interest

Multi-site Clinical Assessment of ME/CFS

MCAM: Introduction and Update

Rationale for Multi-site Clinical Assessment of ME/CFS

- Work with clinical experts in ME/CFS
 - Rely on expert clinical diagnosis
 - Avoid restriction of case definition
- Enroll from multiple clinical practices in US
 - Do patients differ between clinics?
 - How do experts diagnose and manage ME/CFS?
- Collect standardized information on illness domains
 - Data to inform dialogue on case definition and to identify biologically meaningful subgroups

Participating Clinics

- **Institute for Neuro Immune Medicine, Ft. Lauderdale FL**
 - Nancy Klimas, MD
- **Mount Sinai Beth Israel, New York City NY**
 - Benjamin Natelson, MD

Open Medicine Institute Consortium

- **Bateman Horne Center, Salt Lake City UT**
 - Lucinda Bateman, MD
- **Hunter-Hopkins Center, Charlotte NC**
 - Charles Lapp, MD
- **Open Medicine Clinic, Mountain View CA**
 - Andreas Kogelnik, MD
- **Richard Podell Medical, Summit NJ**
 - Richard Podell, MD
- **Sierra Internal Medicine, Incline Village NV**
 - Daniel Peterson, MD



Protocol

- Developed by participating clinics and CDC
 - Fit into clinic routine as much as possible; minimize patient burden
- Enrollment criteria (Stage 1)
 - Any patient (18-70 years old) diagnosed with ME/CFS
 - Relies on clinical judgment rather than case definition
 - Exclusions: HIV +, age at diagnosis older than 62 years
- Rolling cohort design
 - Cohort followed longitudinally (annually) with new participants added
 - Added healthy and ill comparison groups; pediatric/adolescent patients, recent onset and homebound
 - Collection of biologic samples

Additional studies underway

- Combined exercise and cognition protocol
 - Cardiopulmonary exercise testing – cycle ergometry
 - Cognitive testing before, after CPET (at clinic) and online at 6-12, 24 and 48 hrs after clinic visit
 - Cogstate battery – processing speed, vigilance, memory
- Natural killer cell function
 - Pilot study verified validity of next-day testing
- Wakening profile of salivary cortisol and amylase

Strengths and Limitations of MCAM Study

- Strengths
 - Reliance on clinical expertise rather than case definition provides data for evaluation of case definitions
 - Large number of patients from multiple clinics
- Limitations
 - Patients in specialty clinics may not represent ME/CFS patients in primary health care settings
 - Difficult to identify patients with new onset of disease
 - Recruitment of pediatric patients has been slow

Update - Supplementing MCAM

- Goal – increase enrollment of children and adolescents with ME/CFS and adults with other illnesses as comparison groups
- Contract awarded to Eagle Global Scientific
 - Contractor identifies clinicians with required expertise, appropriate patient population and interest

Update – Use of MCAM data

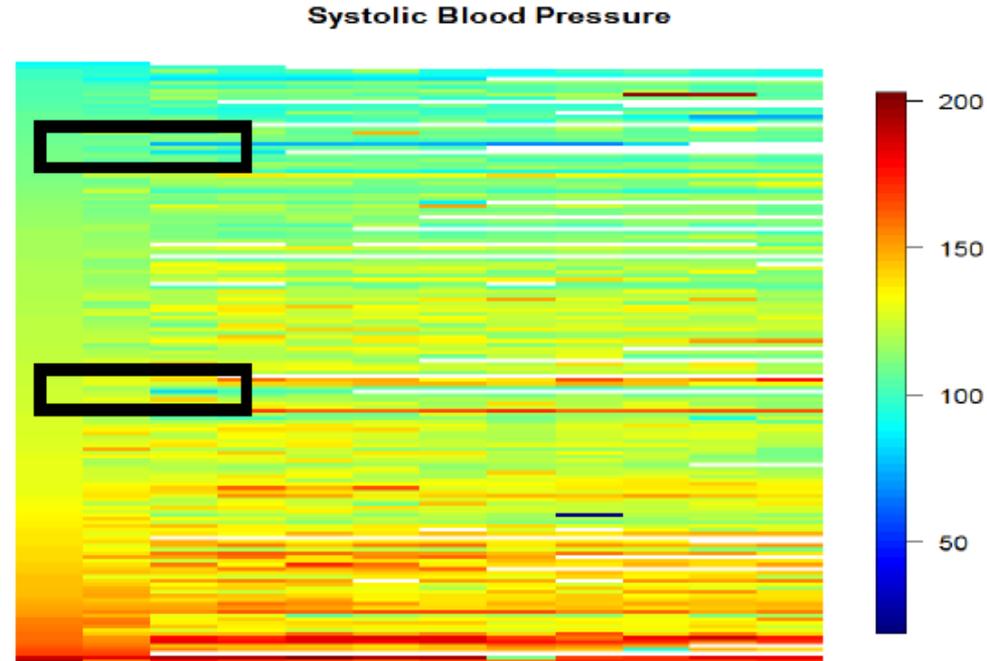
- Research Collaboration Agreement with American Institutes for Research to analyze MCAM data to evaluate endpoints for ME/CFS clinical trials (FDA's Drug Development Tool Qualification Program)

Update – Standardized Physical Examination

- Romberg Test
 - Results varied between clinics and discussion identified variation in how test was performed
- Introduction of NASA Lean Test
 - Developed by NASA to assess orthostatic symptoms experienced by astronauts returning from flight
 - Suggested by Dr. Natelson
 - Pulse and blood pressure (after resting 5-10 min), every minute while standing, leaning on wall to avoid use of accessory muscles
- Simple phone-video developed by Dr. Natelson used to standardize both tests

Importance of NASA Lean Test

- Tool for clinic use, providing objective signs of abnormality
- Analysis in progress
 - Data visualization in image
 - Each row = one person
 - Columns = time points
 - Boxes – two examples of significant drop in blood pressure (decrease of ≥ 20 mm Hg)



Enhance Measurement Methods to Improve Understanding

- Study ME/CFS by focusing on multiple facets of illness
 - Refine phenotypic measures of all illness domains
 - Basic agreement on illness domains in most case definitions
 - Same measures can be applied regardless of case definition
 - Stratify on dynamic range of measures
 - Optimize instruments and standardize scoring
 - Correlate with biologic measures
 - Identify subgroups reflecting etiology and response to therapy
- Develop Common Data Elements (CDEs) for ME/CFS
 - Joint project of NIH (National Institute of Neurologic Diseases and Stroke) and Centers for Disease Control and Prevention



NINDS/CDC ME/CFS Common Data Element Project

- NINDS initiated development of Common Data Elements (CDEs) to develop data standards for funded clinical research in neuroscience
- CDEs are content standards that can be applied to various data collection models
 - Dynamic and evolve over time
 - Not a database
 - Uniform format to systematically collect, analyze and share data
- CDE Projects develop common definitions and standardize case report forms and other instruments
- ME/CFS has been added to disease areas covered by NINDS CDEs

Thank You

Acknowledgements to: ME/CFS Program and Study Participants



Chronic Viral Diseases Branch

Sally Lin
Dana Brimmer
Robert Chen
Yang Chen
Monica Cornelius
Robin Curtis
Miranda Daniel
Irina Dimulescu
Liz Fall
Britany Helton
Joyce Ho
Niyai Johnson
Maung Khin
Troy Querec
Mangalathu Rajeevan

Division of High-Consequence Pathogens and Pathology

Inger Damon, Director
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