WG 4 on clinical research enablers and diagnostic criteria

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WG4 members

- Elin Strand (leader, Norway)
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TASKS FOR THE WG4

1. Survey clinical criterions used in EU countries to set-up diagnosis of ME/CFS ;
2. Analyse existing clinical criterions guidelines in order to find- out optimal criteria set allowing excluding over-diagnostic and un-diagnostic;
3. Analyse the used ME/CFS treatment and its efficacy/safety in order to find-out optimal treatment approaches lowering severity of clinical course.
4. Survey in EU countries existing data on neurological picture of ME/CFS (including association with similar diseases and symptoms, like fibromyalgia)
5. Synchronize diagnostic criteria and develop common strategy protocol to identify and understand the biological disease pathways

What have we done

- Survey among Euromene countries (N=17)
- Decision on diagnostic criteria
- Decision on symptom registrations/classification tools for research
- Assessment among 6 countries:
  - other health (topic) information
  - Standardized Questionnaires/tools used for other health information
  - Priorization
- Preliminary report

1. Survey clinical criterions used in EU countries to set-up diagnosis of ME/CFS

- Questionnaire sent to all members (23 Q)

- Asks questions about guidelines for criteria applied /other diagnosis used, guidelines for treatments/coping/rehabilitation, other health information assessments used, and asked for existing national patients registre/biobank/research funding

2. Analyse existing clinical criterions guidelines in order to find-out optimal criteria set

- **Results: N= 17 (20) countries**
- **National guidelines for diagnosis**:
  - N= 5; UK, Italy, Spain, Netherlands and Norway
- **Diagnostic criteria suggested in guidelines**:
  - Canada and Fukuda (N=2), Fukuda (2), Oxford, (N=1)
- **Assessment methods**:
  - use different test, sometimes depends on specialitst available
  - Psychsocial assessment: N=7
  - Neurophysiological/psychological testing: N=3
  - Cardiopulmonary exersice test

- **National guidelines for counselling/treatment /coping:**
  - N=8; CBT,GET (7), activity regulation/pacing/mind-body strategies
- **4 National registries, 5 National funding of research, 6 Biobank**

WG4: suggestions for diagnostic criteria and assessment in European countries

For clinical and Research purpose:

- **Canadian Consensus Criteria 2003** or **Fukuda/SEID** (for clinical and research purpose)

and also

- **Extended exclusion examination** (Canada criteria, Reeves et al 2003)
  - Somatic examination (blod tests, comorbidities/other illnesses)
  - Psychiatric/psychological examination

for research pupose:

- **Symptom registrations (mandatory)**
  - DePaul Symptom Questionnaire (Jason et al. 2012)
  - SF-36 (free version)
  - HADS (Hospital/depression scale)

- **Assessments/questionnaires for other health information**

Theme being registered, common in several countries

- Demografics
- Symptoms
- Physical functioning level (50% reduced)
- Anxiety/depression/mental health
- Fatigue
- Sleep problems
- Cognitive functioning
- Pain
- Neurpsychological functioning
- Neurevegetative symptoms
- Cognitve dysfunction
- UK: self/familiy health, health history, work, mood, activity etc
- Oxidative stress
- Cardiac functionality
- An array of different standardized questionnaires and instruments were used

3. Analyse the used ME/CFS treatment and its efficacy/safety in order to find-out optimal treatment approaches lowering severity of clinical course: Review paper from JC`s group (2017)

BJP British Journal of Pharmacology
British Journal of Pharmacology (2017) •• ••–•• 1

REVIEW ARTICLE

Treatment and management of chronic fatigue syndrome/myalgic encephalomyelitis: all roads lead to Rome

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This review explores the current evidence on benefits and harms of therapeutic interventions in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME) and makes recommendations. CFS/ME is a complex, multi-system, chronic medical condition whose pathophysiology remains unknown. No established diagnostic tests exist nor are any FDA-approved drugs available for treatment. Because of the range of symptoms of CFS/ME, treatment approaches vary widely. Studies undertaken have heterogeneous designs and are limited by sample size, length of follow-up, applicability and methodological quality. The use of rintatolimod and rituximab as well as counselling, behavioural and rehabilitation therapy programs may be of benefit for CFS/ME, but the evidence of their effectiveness is still limited. Similarly, adaptive pacing appears to offer some benefits, but the results are debatable: so is the use of nutritional supplements, which may be of value to CFS/ME patients with biochemically proven deficiencies. To summarize, the recommended treatment strategies should include proper administration of nutritional supplements in CFS/ME patients with demonstrated deficiencies and personalized pacing programs to relieve symptoms and improve performance of daily activities, but a larger randomized controlled trial (RCT) evaluation is required to confirm these preliminary observations. At present, no firm conclusions can be drawn because the few RCTs undertaken to date have been small-scale, with a high risk of bias, and have used different case definitions. Further, RCTs are now urgently needed with rigorous experimental designs and appropriate data analysis, focusing particularly on the comparison of outcomes measures according to clinical presentation, patient characteristics, case criteria and degree of disability (i.e. severely ill ME cases or bedridden).

Abbreviations

APT, adaptive pacing therapy; CBT, cognitive behavioural therapy; CDC, Centres for Disease Control and Prevention; CFS/ME, Chronic fatigue syndrome/myalgic encephalomyelitis; CoQ_{10}, Coenzyme Q_{10}; DHA, docosa; EPA, eicosapentenoic acid; FINE, Fatigue intervention by nurses evaluation trial; GET, graded exercise therapy; GLA, γ-linolenic acid; HADS, Hospital anxiety and depression scale; Max HR, maximum heart rate; ICC-ME, 2011 International Consensus criteria for ME; IOM, Institute of Medicine; NSAIDs, Non-steroidal anti-inflammatory drugs; PACE, Pacing, graded activity, and cognitive behaviour therapy; a randomized evaluation for CFS patients; PVFS, Post-viral fatigue syndrome; RCT, randomized controlled trial; SEID, systemic exertion intolerance disease; SMC, standard medical care; SSRI, selective serotonin-reuptake inhibitor; SSNRI, selective serotonin-noradrenaline reuptake inhibitor

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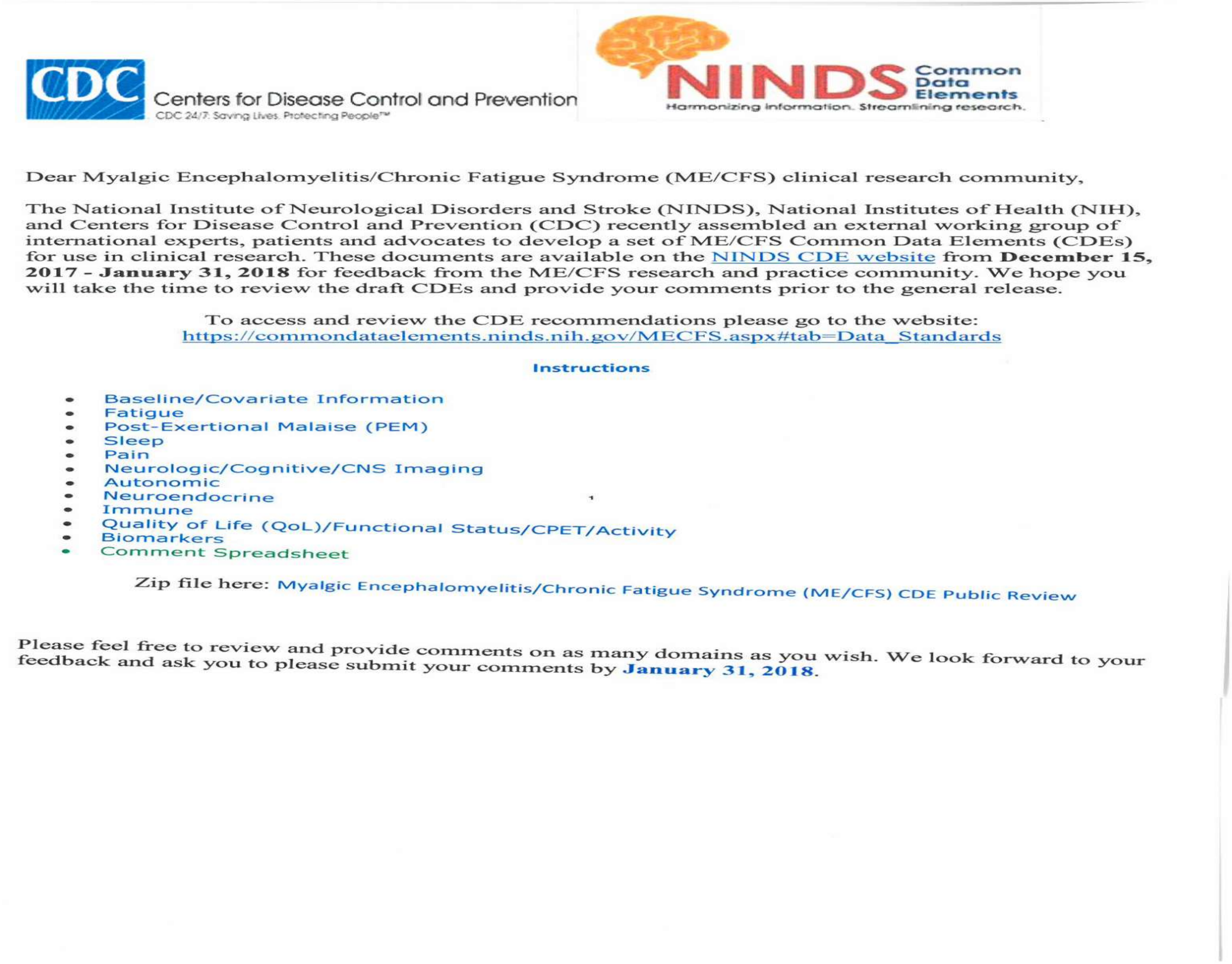
Status WG 4:

- Finished survey
- Preliminary report based on survey and – WG meeting discussions - finished
- Guidelines
    - Translate into English or in other ways review the three national guidelines or part of them (Norway*, Italy and Spain)
    - Suggests to use the short version of the Norwegian guideline as a starting point for an Euromene guideline
    - Revise according to new information/research on clinical case and treatment
- Assessments and questionnaires for sampling non biological health information (to be further discussed)
- Look closer into CCC exclusion criteria, might be changed or further specified (Reeves et al. 2003).
- Review studies on symptom relief – use recent publications on this topic
- Survey in EU countries existing data on neurological picture neuroimmunological studies/cognitive tests of ME/CFS (including association with similar diseases and symptoms, like fibromyalgia) /by Jeroma Authier
- Write a brief report for publication based on the survey results/suggestions and discussion



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People™

NINDS Common Data Elements
Harmonizing information. Streamlining research.

Dear Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) clinical research community,

The National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health (NIH), and Centers for Disease Control and Prevention (CDC) recently assembled an external working group of international experts, patients and advocates to develop a set of ME/CFS Common Data Elements (CDEs) for use in clinical research. These documents are available on the NINDS CDE website from **December 15, 2017 - January 31, 2018** for feedback from the ME/CFS research and practice community. We hope you will take the time to review the draft CDEs and provide your comments prior to the general release.

To access and review the CDE recommendations please go to the website:
https://commondataelements.ninds.nih.gov/MECFS.aspx#tab=Data_Standards

Instructions

- Baseline/Covariate Information
- Fatigue
- Post-Exertional Malaise (PEM)
- Sleep
- Pain
- Neurologic/Cognitive/CNS Imaging
- Autonomic
- Neuroendocrine
- Immune
- Quality of Life (QoL)/Functional Status/CPET/Activity
- Biomarkers
- Comment Spreadsheet

Zip file here: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) CDE Public Review

Please feel free to review and provide comments on as many domains as you wish. We look forward to your feedback and ask you to please submit your comments by **January 31, 2018**.

Presentation in Norway 21th nov 2017«Euromene» (10 minutes)

- First Norwegian research network conference, Oslo:
  - Collaboration between NIPH, ME-patient organisation and National Advisory Unit on CFS/ME
  - 66 participants from Norwegian research environment
  - 26 project presentations
  - BEHOV-ME (4), NRC, 30 mill NKR
- **Focus:** inform and tell about Euromene and in particular about the possibilities of STSM and training schools

Presentation 2 in Helsinki, 19th Jan. 2018 (20 minutes)

- Arranged by the national CFS/ME organisation in Finland/CFS-peer support group
- 70-80 persons (patientes/relatives)
- The unrest, three presentations
  - Blomberg, Olli Polo, Elin Strand
- **My Focus:**
  - Introduction about ME/CFS
  - Euromene and the landscape
    - Aims, deliverables, status of the Euromene work
  - Example from Norway: development and organization of Health care services for CFS/ME patients and research the last ten years

Greetings from Norway