

Report for the GPI from Work group 4 “Clinical research enablers and diagnostic criteria” Elin B Strand (leader)

1 Objectives

At the very first Euromene meeting in Brussel 22th of April 2016 various working groups including Work group 4 (WG4) on clinical research enablers and diagnostic criteria were established. Elin B Strand (Norway) was elected as leader and Jerome Authier (France) as vice leader. The following tasks for the first year were decided:

- to survey clinical criteria used in EU countries to set-up diagnosis of ME/CFS
- to analyse existing clinical criteria guidelines in order to find-out optimal criteria set allowing excluding over-diagnosis and under-diagnosis
- to survey in EU countries, existing data on neurological picture of ME/CFS (including association with similar diseases and symptoms, like fibromyalgia)
- to analyse the used ME/CFS treatments and their efficacy/safety in order to find-out optimal treatment approaches lowering severity of clinical course.

2 Activities.

During the first year three meetings have been arranged in Latvia, Berlin and Barcelona. A survey has been carried out among participating European countries and at this point 14 (of 15) countries have responded. A report on this is under preparation.

2.1 Meeting, members and topic of discussions.

In the Latvia meeting 28th and 29th September members from France, UK, Romania, Bulgaria, Latvia and Norway participated. Preliminary results from the ongoing survey were presented and discussed in the work group. The following gaps were identified and discussed: National guidelines do not exist in most of the countries while four countries have comprehensive national guidelines for case definitions and diagnosis as well as recommendations for use of tests, questionnaires and for the exclusion part of diagnosis. Further the prevalence rate for severely ill patients varies from zero to 25% in different countries. Education of health providers for diagnosis varies greatly between the countries. It was decided that a summary report from the survey should be written, and it was discussed to meet between the Euromene meetings as well as to invite experts for future WG4 meetings.

At the Berlin meeting 28th February the following persons participated in the WG4 discussion: Angelika Krumina (Latvia), Patricia Grabowski (Germany), Jose Allege (Spain), Jerome Authier (France), Ingrid Helland (Norway) and Elin Strand (Norway).

A brief summary of the first results from the survey were presented. The following topics representing differences between countries were discussed: application of diagnostic criteria, exclusion process, assessments and standardized tests and questionnaires as well as symptom treatment and management. It was decided to use the four national guidelines on diagnosis and treatment/management that already exist as basis to find common European standards and guidelines. For the exclusion process guidelines are needed. An overview of and a list of tests and questionnaires already applied in the countries was suggested to be developed. Questionnaires applied in symptom assessments should be harmonized between countries and this is particularly important for research.

Symptom and illness management varies between countries and research on symptom relief/management should be reviewed. Before the next WG4 meeting material on guidelines and questionnaires applied should be shared between group members. In addition the group members will also have brief presentations in the WG and relevant topics and tasks were distributed among participants. A reminder will be sent to the Euromene countries who have not responded to the survey.

In the meeting in Barcelona 16th and 17th march 2017 there was a two hours meeting in the WG4 where the following persons participated: Angelika Krumina (Latvia), Jerome Authier (France), Magdalena Efraim (Rumenia), Luis Nacul (Uk), Ingrid B. Helland (Norway) and Elin Strand (Norway). Members not able to take part in the WG4 meeting: Jose Allegre (Spain) and Patricia Grabowski (Germany).

Materials from each country had been shared. There was no time to discuss this further in the current meeting, neither to present materials from all the countries as planned. Luis Nacul (UK) had a short presentation from their group's last paper on "Differing case definitions point to the need for an accurate diagnosis of myalgic encephalomyelitis/chronic fatigue syndrome". Jose Allegre (Spain) gave a speech in plenary on characteristics of the patient cohort in the Spanish unit at the Vall d'Hebron of Barcelona. In addition a plenary skype talk was arranged with Professor Leonard Jason from DePaul University. He presented research on case definitions, assessments etc. and also had some suggestions for our work on these topics.

3 Discussions and suggestions

3.1 Case definition.

The Canadian Consensus Criteria (CCC, 2003) was decided as standard case definition for research for the Euromene countries. The Fukuda criteria from 1994 may still be applied for those who already use them in addition to CCC. The IOM criteria can also be used as a complement.

3.2. Assessment tools/questionnaires

It was decided to also use an extended, standardized and validated symptom registration tool able to classify within different case definitions. Those who already are applying good symptom registrations and diagnostic tools can continue to use them. For those who do not have such tools, it is recommended to use DePaul Symptom Questionnaire, SF-36 and HADS, the latter for the mental health assessment. Additionally it may be necessary to assess other health information, such as family health, extended assessments on cardinal symptoms such as neurocognitive aspects or sleep. Further, additional tests and questionnaires will be discussed in more detail during the next year in WG4. Also it is necessary to apply an exclusionary examination (somatic and psychiatric/psychological).

A detailed overview of symptom assessments/ clinical signs and tests already used in the different countries in particular those suggested in the national guidelines, will be developed by the WG4 before further suggestions for European guidelines are given.

A review of literature on neurocognitive factors and relevant screening instruments also will be carried out by professor Authier.

3.3 Symptom relief/management

Regarding suggestions for symptom relief and management, research has not revealed any medical cure. There might be some symptom relieving medications, but this need to be further clarified. One study in the German group and one review on this from the Spanish group should be looked further into before any concrete suggestions are given. It was planned to present this in the Barcelona WG4 meeting, but there was no time for that. As no medical cure for CFS/ME exists, the patients need advice for coping and they need to learn self-management strategies for preventing worsening, maintaining or increasing their coping as well as their quality of life. Five of the countries have national guidelines for the management of ME/CFS and they all suggest Cognitive Behavioral Therapy, Graded Exercise Therapy, Pacing and mind-body strategies that may be useful as adjunct measures for patients, although the evidence for their effects have been questioned.

4 Summary

4.1 What have we done?

There have been three group meetings with discussions. According to the first years tasks we have conducted a survey among the Euromene countries on guidelines in terms of diagnostic criteria, the neurological picture, bio banks and guidelines and practice for treatment and management for CFS/ME patients. A summary from this work has been carried out, and a report is in progress. At our last meeting WG4 had a skype meeting with one of our experts on case definitions and for discussion of important questions. What case definitions to be used in the European guidelines as well as a few assessment tools to be applied in research, are suggested by the WG4.

4.2 Where have we failed?

The work and discussions in WG4 has generated some more work to be done and thus the report from the survey is not finished. We need more detailed information from the four national guidelines. Because of different languages are used the guidelines these should be translated into English. Thus it may take some more time to reveal the specific information we need about questionnaires, tests, symptom relieving medications and management. This is an ongoing process.

4.3 Project for the next year

The aim is to develop a lowest common denominator of the existing guidelines. It was decided to translate into English or in other ways make available to the WG4, part of the existing national guidelines from Italy, Norway and Spain.

A more detailed overview of the query forms used in the different countries should be made before further decisions are taken and suggestions on this topic are given.

More clear and reasoned suggestions for symptom relief and coping need to be made. More specific, a review of neuroimmunological studies/cognitive tests and of publications/studies of symptom relief in ME/CFS should be carried out. Also exclusion criteria for the suggested case definitions should be reviewed to see whether it might be changed or further specified. The report of the survey should be completed. In addition WG4 should prepare for a training school on diagnosis of ME/CFS as well as for publishing a paper on the WG4/Euromene work.