Forward ME

Minutes of the Meeting held in the Television Interview Room

House of Lords

Wednesday 7 December 2016, 2.00 pm

Present:

Countess of Mar (Chairman)

Janice Kent (reMEmber)

Bill Kent (reMEmber)

Hannah Clifton (ME Trust)

Jane Colby (TYMES Trust)

Christine Harrison (BRAME)

Clare Ogden (AFME)

Dr Charles Shepherd (ME Association)

Sue Waddle (ME Research UK)

1. **Apologies** had been received from Sonya Chowdhury (AFME), Dr Paul Worthley (ME Trust) and Cath Ross (25% Group)

2. **Professor Stephen Holgate, Chairman of UK CFS/ME Research Collaborative (CMRC)**

2.1 The Chairman welcomed Professor Holgate. She said that there was concern by many people about the Collaborative's MEGA study and that we would like to hear all about the study from him.

2.2 The Professor explained that he did not represent any ME organisation. He chaired the Collaborative – that was all. Some people who had posted comments on the internet seemed to think that he was a funder or represented a charity, or was a ME researcher. Some seemed to think that he was influential in the Medical Research Council (MRC). However, none of those things applied. Some people seemed to be confused about the role of the CMRC although he was sure that did not apply to those present. The reason he wanted to set up the CMRC was because he was appalled at the difficult situation many ME patients found themselves in and ashamed that so little was being done to research the illness and help those patients.

2.3 The collaborative exists, he explained, to bring together people with an interest in researching CFS/ME. It is made up mainly of scientists and the ME charities, and its purpose is to generate collaboration across the field. At last year's Newcastle conference he had set out what he called "the grand challenge" – to scrub out what had been done before and to start again. This is called the "hypothesis-free" approach; to look at the way the condition presents itself and try to determine what is "driving" it. This is a method that has been very successful in researching illnesses such as epilepsy and arthritis.

4. The method involves collecting together large numbers of patients who show different "expressions" of the disease in question (such as different degrees of severity, different times of onset). You then examine them and perform various measurements within those groups, use standard clinical tests and then enter all the data into a computer programme to identify sub-types. This is called "cluster analysis". The method makes no assumption about existing criteria such as Fukuda or Canada – although a number of participants in the study will conform to those criteria, but others will not. This lack of restraint had been very successful with migraine recently. It was very important, he said, that we respect heterogeneity.

5. Once the data had been analysed, Prof Holgate said, we should end up with about 12 to 15 clusters within which there will be certain characteristics – age groups, degrees of severity etc. All this data will be anonymised. They would then move on to the second part of the study which was to collect biological samples such as blood, urine and saliva which were fairly easy to collect. These samples must be kept carefully to ensure that protein didn't break down or that DNA was not damaged. They would then be sent to a biobank (which is similar to the UK

Biobank) where each sample would be annotated with a code to indicate the cluster from which it came. Otherwise each sample would be anonymised, so that the name or address of the donor is not known.

6. The next stage, Prof Holgate said, was the really exciting part. This was the "omics" – looking at hundreds of thousands of molecules to sequence the genome of each participant (they hope to have about 10,000 participants). They will look at mutations in the DNA and see how these relate to the patient's symptoms. What they hope to find is multiple patients having similar associations.

7. Epigenetics. The professor said we can tell whether the genome is switched "on" or "off" by looking at the methylation. We can look at the protein wrapped around the DNA which can also affect genes being switched on or off. This enables us to identify what environmental factors are influencing the expression of the genetic part of the disease (viruses, air pollution, chemicals etc). The third level of epigenetics is to look at the proteome, where you take the serum or plasma and look at the many proteins in it which may help to identify the sub-groups. The final bit is the metabalome, where you take the plasma and from that identify what pathways are activated in the metabolism. Those are the different levels of epigenetics. There might be another if funding can be obtained. It's called the Microbiome. In the human body there is much more bacterial and fungal DNA than human DNA and that could affect the condition.

8. Finally, Professor Holgate said, there is the need to bring all of this together; an enormous job, which is why he had contacted the Farr Informatics Centre and the Alan Turing Centre about analysing these complex datasets with their sophisticated computers. He had tried to put all this in a nutshell but inevitably it was complicated and took time to explain. They had tried to encapsulate it all on their new website www.megaresearch.me.uk. There will be a page on it enabling you to put questions to the MEGA team. (see: www.megaresearch.me.uk) They are also convening a Patient Advisory Group (PAG), and members of Forward-ME might wish to join it. The requirements and an application form are on the website. The closing date for applications is December 13th.

3. Discussion and questions

3.1 The Chairman said she had received a number of enquiries about MEGA and asked Prof Holgate if he could answer such questions at this meeting. He said he would try, but some might be best put to the MEGA team.

3.2 Christine Harrison asked for clarification of the PAG. Prof Holgate said the Advisory Group was a hugely important one. They needed to take account of the very strong feelings held by some patients and groups. The Chairman said it would be necessary for patients and their carers/families to have complete trust in this project. Their trust had been undermined by the PACE trial and other exercises. Prof Holgate assured the meeting that MEGA had nothing to do with the PACE trial etc.

3.3 Janice Kent asked whether representatives of the ME charities who were sceptical about NICE could join the PAG. Prof Holgate assured her they could. Janice said she would certainly apply, then, because she thought it was a brilliant project.

3.4 The Chairman expressed concern about the very short time scale. The Professor agreed the time was short but it would all be done via the website. The team would be working on it over Christmas after which there would be more time for deep discussion and refining the application. Dr Charles Shepherd said he understood the application scheduled to go in on 17th January was very much an outline, and didn't get down to the "nitty gritty" of how patients will be selected including the severely affected. Prof Holgate explained that the selection of patients would not be looked into until the PAG had been convened which would be after the New Year.

3.5 For the benefit of the Group, Charles Shepherd asked what would be required of the PAG selection panel. Prof Holgate said the qualifications for PAG members were on the website. Sue Waddle said MERUK did not know what was expected of PAG members. Prof Holgate said there was information on the website. Clare added that AFME could help and asked Sue to send her an e-mail.

3.6 Jane Colby referred to the requirement for 10,000 patients. Were they to be recruited from the ME/CFS clinics? If so, what about those who were too unwell to attend them? Prof Holgate said recruitment would not be restricted to those clinics. Patients with ME attended many clinics – such as neurology, rheumatology and pain clinics, so it would not just

draw from ME/CFS clinics. MEGA would need to approach all organisations who deal with ME sufferers. Some of the severely affected might need to be visited at home, and MEGA might have to apply for special funding to employ nurses for that purpose. Dr Charles Shepherd said the information on the MEGA website ought to be amended to make these points clear.

3.7 In response to Christine Harrison and the Chairman, Prof Holgate gave an assurance that recruitment would not be confined to clinics that were "signed up to" NICE. He added that the PAG would need to get together with the MEGA team to resolve the many queries that surrounded the condition of ME/CFS patients. He could not answer these himself as he was not a ME/CFS clinician. Jane Colby suggested it might be helpful to put the words "Chronic Fatigue" into the title to indicate the breadth of the study. Prof Holgate said they could consider that, but MEGA should not be constrained by historic descriptors which had not been established scientifically.

3.8 The professor confirmed that MEGA would not be looking at fatigue per se because that could attend all sorts of conditions. They would be guided by broad definitions of symptoms. He confirmed that it would not be mandatory for patients to take part in this study, and indeed no conditions for participation had been set yet. In response to Jane and the Chairman he said they could suggest to MEGA that consideration be given to the name of the study to more accurately reflect the condition of the participants.

3.9 Sue Waddle said ME Research UK was already getting many queries about the study which she was struggling to answer. For example, what definitions of the illness were to be used for the purposes of this study? Prof Holgate said there were none; to establish them was an important purpose of the study. The research was likely to show a number of "clusters" each of which could then be investigated separately. This had happened in other conditions that had been researched in this way. In lung cancer, for example, it was now known that there were seventeen different clusters each with its own characteristics and for which different treatments were appropriate. In the same way it was necessary to "drill

down" into ME/CFS to discover the causative mechanisms. At the moment none of us know what those are.

3.10 Christine Harrison asked what would be the PAG's method of working. She referred to the experience of the patient reference group of the CMO'S Working Group on CFS/ME. The professor said that would be a matter for the PAG to decide. Each patient representative would be an equal of every other member of the MEGA team. Clare Ogden confirmed that this would be the case. Prof Holgate added that MEGA would be quite different from the CMO's group which had basically looked at the lack of provision for ME/CFS patients. The work of MEGA was more akin to astro-physics. Think about discovering black holes in space. He said this was probably why some people had difficulty with the concept.

3.11 Sue Waddle said she was concerned that the study should include the full spectrum of patients. Prof Holgate said he was signed up to that, and it was a discussion the patient representatives would need to have with the scientists. Jane Colby asked what software the study would be using. Prof Holgate explained that the equipment in question was far beyond software; they would be using the resources of the Turing Centre, the Farr Informatics Centre and five other centres across the UK, all full of informaticists, physicists and computer engineers who can put together enormous databases that can analyse the sort of complex data this study is likely to generate. That is what they did with astro-physics. This is a field in which the UK is in the lead.

3.12 Patient selection. Dr Charles Shepherd said this was a matter of great concern to many patients. He said although he had many criticisms of the NICE Guidance he thought the diagnostic descriptor was a useful starting point for considering the diagnosis of ME/CFS. It was important to include post-exertional malaise. Prof Holgate said the wider the spectrum the better and noted the importance of including post-exertional malaise, but it would be for the PAG to decide. There should be a basic minimum diagnostic requirement.

3.13 The Chairman thanked Professor Holgate for being so helpful, and asked to whom we should send questions. The Professor said we should send them to the website. Clare Ogden added that she was collating questions, so they could be sent to her.

4. Minutes of meeting held on 16th October 2016

The minutes were agreed to be a true record.

5. Matters arising

Capita. Christine Harrison pointed out that we had not received the papers they had said they would send (item 3.4 of last meeting). The Chairman said she would chase this up. Charles Shepherd said he had received an e-mail from Rebecca Papanicoulas of Capita saying they would let us have papers. We would need to keep a careful eye on them to ensure the material we are seeking is provided soon. The Chairman added that Rebecca had written to her thanking us for information we had sent.

6. NICE

1. Proposed review of NICE Guideline. The Chairman referred to a communication from NICE received the day before seeking any comments we wished to make on this subject. It was agreed we would send any such information to the Chairman who would collate it and forward it to NICE.
2. Dr Charles Shepherd wondered whether there was any deadline for NICE receiving comments. He had the impression that NICE's checking process would probably go on for several months. He added that NICE seemed to be seeking published papers that throw new light on clinical assessment features or management features of the illness, NOT opinions.

7. DWP

Dr Shepherd said the expression “radical reform of ESA” had come up again. What did it mean? Was this referring to reform of the WRAG (work related activity group)? Clare Ogden said AFME were working through the Green Paper which was enormous. If other charity members were planning a response, it could be helpful if we could broadly agree key messages across our individual submissions. Clare offered to liaise with other members on this, and said she would send a link to details of the Green Paper consultation.

7.1. Christine Harrison said that she had just left a meeting with Atos who informed her they would be more than happy to come and speak to us again.

8. Research

8.1. Sue Waddle said MERUK had agreed to fund three or four interesting studies involving international co-operation. She could not give details at this stage but she requested that we make an effort to assure these researchers their work is valued.

8.2. Charles Shepherd said they had discovered an excellent researcher at Oxford, Karl Morton, who is interested in mitochondrial research. He had become interested in running a metabolomics study that would look for similar metabolomics abnormalities that had been reported in the Naviax study. MEA had put this out as their Christmas Appeal and had raised the £50,000 needed in three weeks. The study would start in January. The Chairman and members congratulated MEA.

9. Any other business

9.1 The Chairman announced she had had a meeting with people from the PHSO who deal with complaints about hospital treatment. They would like to come and speak to us next summer. James Bolton had moved on from DWP. She was now sending everything to Lord Freud that she would have sent to James Bolton.

9.2 The Chairman also announced she had received a letter from a lady with private health insurance. Her State Pension age had been put up to 67 but her private insurers would not extend her cover to age 65 to put her on a par with

men. Everyone including the Insurance Ombudsman saw this as discrimination. However, it was “legal discrimination” because it was written into the relevant Act that it was allowed. She would take up this cause.

9.3 Child Protection. Jane Colby reminded members that when the Chief Social Worker (CSW) had spoken to us she had said she would look into the subject and come back to speak to us again. Had we heard any more from her? The Chairman said she had heard from the CSW several times. She would invite her to come and speak again. She was also waiting to hear about speakers from the GMC and Public Health England.

9.4 Review of ME/CFS Services (item 7 of last meeting). Janice and Bill Kent explained they had received a favourable response from a leading academic organisation to a proposal for an “arm’s length” review of the services nationally, including the training of doctors and why it has been difficult to recruit doctors to this area. Their contact was a highly regarded consultant in rheumatology and in the field of medical research. Through his involvement with fibromyalgia he had also become knowledgeable about ME. He was very hopeful of finding researchers and funding, and would get back to us when he had investigated the matter fully. Christine Harrison asked whether the information she had sent about research on this subject in the Eastern Region had been helpful. Bill Kent thanked her and said it had been. reMEmber would be happy to receive information from other members on work done in this area; it could all inform the proposed study.

9.5 Drugs. The Chairman said she had great concerns about the many different drugs that some ME patients (and others) were taking. She was sure these would often react together badly. Other members agreed. She also wanted to mention the BBC. She had written to them complaining about the broadcast on 2 November about Fitnet-NHS and had received an unsatisfactory reply. She was considering what her response would now be. She had also complained to the Advertising Standards Authority about a misleading Fitnet leaflet.

10. The meeting concluded with some general discussion about MEGA and the PAG. The Chairman thanked all members Date of next meeting to be announced. The meeting ended at 3.20 pm