NICE CG53 Guidelines Stakeholder Comment for 2017 Review

The following document is in three parts , that will discuss the recognition of ME as a mutisystemic disease , diagnostic criteria and treatment and management .

- Recognition of ME as a serious , chronic mutisystemic disease

The CG53 guidelines does not take a position on the physiological or psychological debate that has clearly been outgrown by the abundance of biological research showing deregulations across multiple bodily systems, with multiple symptoms occurring in each category. [1]

This position does not increase the recognition of ME/CFS as a biological multi-systemic disease . [2] This does not create a culture among the medical community to achieve the rest of the guidelines objectives , and maintains the recognition of ME as medical unexplained symptoms. NHS Imparts states that CFS is medically unexplained symptoms and to be treated as such .[3] [4] [5]

Nor do the guidelines mention that the Royal College of General Practitioners (RCGP) removed their classification of CFS as a mental health disorder.[6] The DWP standpoint on the

[1] Categorised available research by abnormality. http://www.cfs-ireland.com/listing.htm

[2] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[3] http://www.kcl.ac.uk/ioppn/depts/pm/research/imparts/Quick-links/Seminar-Slides/Seminar-7/Trudie-Chalder-intro.pdf

[4] https://keats.kcl.ac.uk/course/view.php?id=28600

[5] https://keats.kcl.ac.uk/pluginfile.php/1208842/mod_folder/content/0/MUS%20presentation%202015.pptx?forcedownload=1

[6] http://www.meassociation.org.uk/2008/07/rcgp-agrees-to-stop-classifying-cfs-as-a-mental-health-disorder/

acceptance of neurological classification of ME and recognition as an organic disease is also omitted from NICE Guidelines . [7]

This continues to validate the heavy involvement of psychiatry in the development of the guidelines treatment recommendations and research , as well as being viewed as leading ME experts in the UK , when they do not have the skill set to study this mutisystemic disease , and have overstated their research in the PACE Trail , yet continue to chair and be involved in biological research[8] , author NICE Guidelines , utilise Oxford diagnostic criteria , and invalidate the biological research . [9]

The P2P Report stated, "Although psychological repercussions (e.g., depression) may accompany ME/CFS, it is not a primary psychological disease in etiology. Although focusing on fatigue alone may identify many ME/CFS cases, it does not capture the essence of this complex condition."[10] The IOM report clearly stated, that patients have long suffered from "the misconception that [ME/CFS] is a psychogenic illness or even a figment of the patient's imagination."[11]

This results in ME patients under the care of the NHS , not being informed of , or given access to investigations[12] and personalised biological treatments that is accessible privately[13],[14] where private testing does reveal biological abnormalities , in the gut micro

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[7] http://www.investinme.org/Article-704%20UK-Government%20Position%20on%20ME.htm

[8] http://www.megaresearch.me.uk/mega-team/

[9] http://download980.mediafire.com/om8ze08d5qug/yk1zt79v93tu9ek/20161105+Esther+Crawley+FITNET+-+BBC+Radio+Bristol.pdf

[10] https://prevention.nih.gov/docs/programs/mecfs/ODP-P2P-MECFS-FinalReport.pdf

[11] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[12] https://chriskresser.com/chronic-fatigue-treating-the-cause-not-the-symptoms/

[13] https://breakspearmedical.com/treatments/chronic-fatigue-syndrome/

[14] http://www.dramyyasko.com/resources/

biome[15] , and biochemistry[16] , and the affect of microbial , environmental and predisposing factors[17] , as evident in the biological research literature on the development multifactorial diseases [18]. Nor are patients informed of the success of personalised biochemical treatment .[19] or drug interventions[20] [21].

The results of private testing is also dismissed by practitioners who do not understand their relevance or how they correspond to the research literature , due to the lack of inclusion of biological research in the NICE Guidelines and the lack of clinical education on ME .

Nor are patients informed of the harms of recommended phycological interventions[22] [23] , which do not have evidence of being effective according to the recent AHRQ downgrade[24] of these treatment recommendations , which are harmful considering the various biological experts research , using objective , advanced technologies , that reinforce findings on

[15] https://microbiomejournal.biomedcentral.com/articles/10.1186/s40168-016-0171-4

[16] http://www.openmedicinefoundation.org/wp-content/uploads/2016/08/Naviaux-PNAS-CFS-Metabolomics-2016.pdf

[17] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4872418/

[18] http://www.dramyyasko.com/resources/

[19] http://www.cpnhelp.org/files/113616573-Application-of-Yasko-Protocol-to-the-Treatment-of-Chronic-Fatigue-Syndrome-by-Rich-Van-Konynenburg-Ph-D-and-Neil-Nathan-M-D.pdf

[20] https://cdn.fbsbx.com/v/t59.2708-21/13438444_1058999074194618_1499272198_n.pdf/Collatz-A-Systematic-Review-of-Drug-Therapies-for-Chronic-Fatigue-Syndrome-Myalgic-Encephalomyelitis.pdf?oh=1d97fdce8eca0b4e0f7780fd66c7e62e&oe=584454F0&dl=1

[21] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[22] https://niceguidelines.files.wordpress.com/2009/10/twisk-maes-cbt1.pdf

[23] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[24] https://effectivehealthcare.ahrq.gov/ehc/products/586/2004/chronic-fatigue-report-160728.pdf

energy impairment[25] [26], damaged aerobic system[27][28] and the harms of exertion above the anaerobic threshold[29] [30] [31] , as well as cardiac output abnormalities that are correlated with severity of post exertion malaise [32]. This supports the IOM reports conclusions that " a central characteristic of the disease is the fact that exertion of any sort (physical, cognitive, or emotional) can adversely affect patients in multiple organ systems." [33]

Furthermore, the World Health Organisation has classified CFS as a chronic (long-term) neurological condition and this classification has been accepted by the Department of Health. However, the WHO's decision remains controversial and is not accepted by everyone working in the field. Members of the team of health professionals who drew up the National Institute of Health and Care Excellence (NICE) guidelines for CFS could not agree that this classification is the right decision, and 84% of members of the Association of British Neurologists surveyed in 2011 said they did not view CFS as a neurological condition[34].

However , no mention to the rest of the text from the research survey is mentioned , or reference to the survey provided , which states "The majority of surveyed neurologists did

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[25] http://www.openmedicinefoundation.org/wp-content/uploads/2016/08/Naviaux-PNAS-CFS-Metabolomics-2016.pdf

[26] http://www.healthrising.org/blog/2016/11/10/metabolomics-chronic-fatigue-syndrome-starvation-australia/

[27] http://www.healthrising.org/blog/2016/11/10/metabolomics-chronic-fatigue-syndrome-starvation-australia/

[28] [28] http://www.workwellfoundation.org/research-and-latest-news/

[29] http://www.workwellfoundation.org/research-and-latest-news/

[30] http://www.jacobspublishers.com/images/Physiology/J_J_Physiology_1_2_007.pdf

[31] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[32] https://docs.google.com/document/d/1-72Kb14gKC3qU5Il8DEljeGliGgfpOHpUhW6eBuFw-U/mobilebasic

[33] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[34] http://www.nhs.uk/Conditions/Chronic-fatigue-syndrome/Pages/Causes.aspx

not view CFS as a neurological condition , but many doctors might hesitate in considering it a psychiatric one. In most classification systems, but even more in the informal hierarchy of what is diagnostically important, psychiatric diagnoses are trumped by medical ones. In part, this reflects a moral hierarchy instilled at medical school , and by society at large, that physical disease should be excluded before turning to psychiatric illness." [35]Moreover psychiatric illness is increasingly being found to have biological underpinnings in regard to gut micro biome imbalances , inflammation , methylation function, [36], and with continued application of metabolomics , and systems biology research [37].[38]

Misrepresenting ME/CFS as a psychosomatic illness has to end. Not only does it trivialise the disease, it makes it more difficult for society and clinicians to be able to be aware of and inform patients of harms [39]and benefits of recommended treatments of CBT and GET , and alternatives , in accordance with the law change to consent[40] , and the advice given to patients in the management of their energy limitations and validated symptoms including pain .[41]

This standpoint on NICE Guidelines and the Guidelines in its current state continues to be used as validation for unethical phycological research on children using these

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[35] https://www.researchgate.net/publication/51176665_Is_chronic_fatigue_syndrome_a_neurological_condition_A_survey_of_UK_neurologists

[36] http://www.dramyyasko.com/resources/

[37] https://www.functionalmedicine.org

[38] http://functionalforum.com/

[39] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[40] https://www.supremecourt.uk/cases/docs/uksc-2013-0136-judgment.pdf

[41] http://www.tandfonline.com/doi/abs/10.1080/21641846.2016.1207400?journalCode=rftg20&

downgraded[42], and harmful treatment recommendations[43] , and invalidated Pace trial research results[44] on adults to pass ethical review , which NICE has used to influence past reviews on the Guidelines[45] .

The GMC has stated that there is no evidence to prove differences or similarities between children and adults with ME[46] . Therefore there is no research , and importantly , biological research , to support the safety of recommendations of CBT and GET or different treatments for children, such as lightning process[47] and FITNET in NICE Guidelines , and continued unethical and harmful research on children using CBT and GET, [48] [49] considering the harms of exercise reported in numerous biological studies [50] [51], patient experience of harms of CBT and GET and benefits of Pacing[52] , and biological research that identifies and reinforces the necessity and importance to implement energy conservation and pacing with a heart rate

[42] https://effectivehealthcare.ahrq.gov/ehc/products/586/2004/chronic-fatigue-report-160728.pdf

[43] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[44] http://www.virology.ws/2016/09/21/no-recovery-in-pace-trial-new-analysis-finds/

[45] https://www.nice.org.uk/guidance/cg53/evidence/review-decision-2011-546258781

[46] https://frownatsmile.wordpress.com/2011/05/26/gmc-says-case-closed/

[47] http://www.bristol.ac.uk/ccah/research/childdevelopmentdisability/chronic-fatigue/smile.html

[48] http://www.bristol.ac.uk/ccah/research/childdevelopmentdisability/chronic-fatigue/magenta-trial/

[49] http://www.bristol.ac.uk/ccah/research/childdevelopmentdisability/chronic-fatigue/fitnet-nhs/

[50] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[51] https://niceguidelines.files.wordpress.com/2009/10/twisk-maes-cbt1.pdf

[52] http://www.meassociation.org.uk/2015/05/23959/

monitor, to utilise the intact anaerobic system and avoid and lessen duration of post exertion malaise and pain[53] caused by , using the damaged aerobic system[54] .[55] [56]

NICE Guidelines, as well as the law change to consent[57] states that a patient can refuse treatment , and yet children with ME that do refuse the recommended treatment of CBT and GET , experience institutionalisation and NICE Guidelines treatment recommendations enforced on them , and when they deteriorate from following these treatment recommendations , are diagnosed with phycological conditions , and the parents are blamed[58]. The patients and parents are treated as having phycological disorders[59], following no investigation or treatment for the organic mutisystemic disease which they have . This continues to be evident in the FITNET study[60] where treatment for the mother is recommended when a child does not improve, even though longterm follow up of the study showed no benefit to patients following the intervention. Leaflets for the UK study on FITNET[61] , refers patients to NICE Guidelines to validate the treatment recommendations being studied , and for participants to learn more about CFS , which the Guidelines in its current state fails to do . NICE Guidelines was also mentioned as obligatory , by the same researcher carrying out FITNET, and Guidelines author for ME , stating on a resent BBC television broadcast that, " NICE Guidelines tell us what to do . " [62]

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[53] [53] http://www.tandfonline.com/doi/abs/10.1080/21641846.2016.1207400?journalCode=rftg20&

[54] http://www.workwellfoundation.org/research-and-latest-news/

[55] http://www.openmedicinefoundation.org/

[56] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[57] https://www.supremecourt.uk/cases/docs/uksc-2013-0136-judgment.pdf

[58] http://www.tymestrust.org/pdfs/falseallegations.pdf

[59] http://bmcneurol.biomedcentral.com/articles/10.1186/1471-2377-11-23

[60] http://bmcneurol.biomedcentral.com/articles/10.1186/1471-2377-11-23

[61] http://www.bristol.ac.uk/ccah/research/childdevelopmentdisability/chronic-fatigue/fitnet-nhs/

[62] http://www.margaretwilliams.me/2016/bbc-complaint-mar-nov16.pdf

NICE Guidelines needs to communicate the law change to consent[63] to clinicians and patients and ensure that it is adhered to , as well as reinforce the Guidelines statement that a patient can refuse treatment, in order to protect ME patients from institutionalisation . A phycological diagnosis of a patient or parent should not be made unless all biological abnormalities have been investigated and treated[64] , in accordance to all research available. According to law change on consent[65] it is now up to the patient and not the doctor to decide which treatment option they consent to , following being informed of all harms no matter how small according to all research available . This is particularly of concern when the treatment recommendations being refused have proven biological harms[66] , and are forced on patients who are institutionalised , and as a result deteriorate , due to post exertion deterioration[67] following exertion , which is proven in the biological literature and patient experience .[68]

There is no feedback system to GPs or NICE of patient experienced harms or benefit following acceptance of a referral to CBT and GET,
and failure of reporting of harms in research trials studying these interventions . [69]. As is the continued case with a current study , FITNET , where only the sponsor will be notified of adverse events[70]

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[63] https://www.supremecourt.uk/cases/docs/uksc-2013-0136-judgment.pdf

[64] https://www.researchgate.net/publication/51176665_Is_chronic_fatigue_syndrome_a_neurological_condition_A_survey_of_UK_neurologists

[65] https://www.supremecourt.uk/cases/docs/uksc-2013-0136-judgment.pdf

[66] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[67] http://www.investinme.org/Documents/Guidelines/Myalgic%20Encephalomyelitis%20International%20Consensus%20Primer%20-2012-11-26.pdf

[68] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[69] http://iacfsme.org/PDFS/Reporting-of-Harms-Associated-with-GET-and-CBT-in.aspx

[70] http://www.bristol.ac.uk/ccah/research/childdevelopmentdisability/chronic-fatigue/fitnet-nhs/

This results in NICE , clinicians and patients being uniformed of patients and research participants experience of these treatments , and how this reflects the biological research findings of a damaged aerobic system[71] and energy impairment[72] . This results in patients being told there is nothing with them , and the condition is all in their heads, and that their behaviour is preventing them from doing more , and to continue with the recommendations of CBT and GET .

This is particularly of concern in the case of FITNET where GPS are referring patients to this study[73] , when NICE Guidelines in its current state does not inform GPs of the biological nature of this disease , IOM report[74] , harms [75]and alternatives , and downgraded effectiveness of CBT and GET by the AHRQ [76]. Particularly , where the researchers are not adhering to law change to consent and informing patients of harms of CBT and GET according to all research , and stated "there is no harm" , when asked on BBC radio Bristol if they were doing so . [77] [78]

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[71] http://www.workwellfoundation.org/research-and-latest-news/

[72] http://www.openmedicinefoundation.org/wp-content/uploads/2016/08/Naviaux-PNAS-CFS-Metabolomics-2016.pdf

[73] http://www.bristol.ac.uk/media-library/sites/ccah/cfsme/study-docs/Flyer%20for%20GPs_v2.0.pdf

[74] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[75] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[76] https://effectivehealthcare.ahrq.gov/ehc/products/586/2004/chronic-fatigue-report-160728.pdf

[77] http://www.virology.ws/2016/11/28/trial-by-error-continued-a-follow-up-post-on-fitnet-nhs/

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http://download980.mediafire.com/om8ze08d5qug/yk1zt79v93tu9ek/20161105+Esther+Crawley+FITNET+-+BBC+Radio+Bristol.pdf

This is a surprising claim, given that the 2015 IOM report [79]noted a systemic intolerance to exertion. The reality, as noted by the AHRQ Evidence Review[80], is that studies had underreported harms and compliance. The claims that CBT and GET do not harm ME/CFS patients have no factual basis, as the harms experienced by patients were not reported .

NICE Guidelines places undue credence and reliance on behavioural researchers and theorists , even though their theories have long since been debunked throughout the international medical community . PACE trial was found to have overstated its results , but is still defended[81] [82] , and paediatric researcher Esther Crawley has stated that advanced biological research technologies such as metabolomics does not contribute to the literature and is "confusing things" . [83]Is evident that there is an unwillingness to give up the phycological paradigm in the face of new information, and reach consensus [84].[85] [86]

The 2015 IOM report[87] highlighted the medical community's hostility toward this disease and noted that the biggest challenge to moving forward is not medical provider knowledge but rather medical provider attitudes. [88] [89]

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[79] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[80] https://effectivehealthcare.ahrq.gov/ehc/products/586/2004/chronic-fatigue-report-160728.pdf

[81] http://www.virology.ws/2016/09/21/no-recovery-in-pace-trial-new-analysis-finds/

[82] http://download980.mediafire.com/om8ze08d5qug/yk1zt79v93tu9ek/20161105+Esther+Crawley+FITNET+-+BBC+Radio+Bristol.pdf

[83] http://download980.mediafire.com/om8ze08d5qug/yk1zt79v93tu9ek/20161105+Esther+Crawley+FITNET+-+BBC+Radio+Bristol.pdf

[84] http://www.sophiaandme.org.uk/collusion.html

[85] http://www.meactionuk.org.uk/Quotable_Quotes_Updated.pdf

[86] http://www.meactionuk.org.uk/SELECT_CTTEE_FINAL_VERSION.htm

[87] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[88] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[89] http://www.tymestrust.org/pdfs/shiningalight.pdf

This results in the Guidelines being ineffective in providing ME patients and clinicians with treatment recommendations that prevent worsening of their condition such as energy conservation [90] , and biological interventions and treatments[91] , and recognition of comorbidities such as POTS and fibromyalgia as outlined in the IOM report[92] , as this would invalidate the view of patients having medically unexplained symptoms ,which should not be investigated or treated , should not be given access to benefits or family assistance , and have exercise avoidance behaviour that needs to be challenged . Please read the quotations on these areas taken from phycological researchers opinion on ME patients .[93]

Additionally there is a conflict of interest where the researchers on CBT and GET and designated UK ME experts , are included as authors of the guidelines, as well as being in positions of authority of multiple stakeholders for the guidelines , and having close relationships to disability insurers[94] . " PACE authors promised in their protocol to abide by the Declaration of Helsinki (obviously in effect in 2003) which requires investigators to disclose "any possible conflicts of interest" in obtaining informed consent. The PACE authors failed to tell prospective participants about their close relationships to disability insurers with a clear interest in the results of the study." [95]

This makes it difficult to reach consensus on the guidelines development , particularly where the evidence review board , Guidelines development group and stakeholders listed , lack biological ME experts, clinicians and researchers , and is heavily weighted with individuals and organisations from the phycological field . Moreover , the chair of the

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[90] http://www.workwellfoundation.org/research-and-latest-news/

[91] http://www.dramyyasko.com/resources/

[92] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[93] http://www.meactionuk.org.uk/Quotable_Quotes_Updated.pdf

[94] http://www.sophiaandme.org.uk/collusion.html

[95] http://www.thefacultylounge.org/2016/11/an-open-letter-to-dr-simon-wessely-defender-of-the-pace-study.html

evidence review board is a representative from the pharmaceutical company that now owns part of Kings Collage London .

NICE Guidelines should be removed from the static list pending publication of further metabolomics studies[96] [97] , utilising superior technologies for research , that have already identified the biochemistry signature for the disease , as well as the publication of research identifying possible biomarkers[98] [99] [100], that could be available within the next 5 years according to Griffith university [101] . None of which is currently included in the NICE Guideline.

Nice Guidelines currently excludes results from autopsy research on ME patents[102] , as well as the first official death from ME[103] , and research on cause of death in ME patients[104] , and deaths from ME [105]

NICE Guidelines has failed to in the past to for fill its remit[106] , and must now take the ethical and proactive leadership needed to decisively break away from the decades-long

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[96] http://www.openmedicinefoundation.org/current-studies/

[97] http://www.meassociation.org.uk/2016/11/newcastle-university-experts-in-hunt-for-smoking-gun-of-chronic-fatigue-syndrome-me-the-northern-echo-29-november-2016/

[98] https://docs.google.com/document/d/1-72Kb14gKC3qU5Il8DEljeGliGgfpOHpUhW6eBuFw-U/mobilebasic

[99] [99] https://app.secure.griffith.edu.au/news/2016/12/01/4m-grant-to-aid-chronic-fatigue-syndrome-diagnosis/

[100] http://www.mecfsnsw.org.au/research/three-new-biomarkers-for-mecfs/

[101] https://app.secure.griffith.edu.au/news/2016/12/01/4m-grant-to-aid-chronic-fatigue-syndrome-diagnosis/

[102] http://www.meassociation.org.uk/2011/01/pathology-of-mecfs-pilot-study-of-four-autopsy-reports/

[103] http://www.sophiaandme.org.uk/

[104] http://www.name-us.org/ResearchPages/ResearchArticlesAbstracts/JasonArticles/Jason2005Mortalityfull.pdf

[105] http://www.ncf-net.org/memorial.htm

[106] http://www.meactionuk.org.uk/FACTS_re_GET.htm

legacy of disbelief, mistreatment, and harm that Tuller's *Worse than the Disease* so comprehensively explains . [107] [108] And prevent harm to patients currently undertaking CBT and GET , and children participating in harmful , and unethical research trials, in accordance to the latest research findings , reports , patient testimonials and reviews , and prevent more patients from being made worse by exceeding their energy imitations , and dying[109] , following years of lack of biological treatment and recognition of the organic biological nature of this mutisystemic disease.

"The chemical signature that we discovered is evidence that CFS is an objective metabolic disorder that affects mitochondrial energy metabolism, immune function, GI function, the micro biome, the autonomic nervous system, neuroendocrine, and other brain functions. These 7 systems are all connected in a network that is in constant communication. While it is true that you cannot change one of these 7 systems without producing compensatory changes in the others, it is the language of chemistry and metabolism that interconnects them all."[110]

Action required :

Remove NICE Guidelines from the static list pending publication of biomarker research in the next five years by Griffith University , and metabolomics research being conducted .

Feedback system to GP and NICE be put in place from patients receiving CBT and GET .

Inclusion in the Guidelines the blood and organ donation policy for ME/CFS patients which was introduced from 1st November 2010

[107] http://undark.org/article/chronic-fatigue-graded-exercise-pace/

[108] http://bjgp.org/content/66/649/437/tab-article-info

[109] http://www.ncf-net.org/memorial.htm

[110] http://www.openmedicinefoundation.org/2016/09/09/updated-metabolic-features-of-chronic-fatigue-syndrome-q-a-with-robert-naviaux-md/

Change balance of stakeholders to include more biological researchers , clinicians and foundations treating and investigating ME

Change balance of evidence review board and chair

All clinical, government, research , patient and public resources need to be updated to support the muti-system, biological nature of this condition , in accordance with the Institute Of Medicine Report on ME , following a year long review of the scientific evidence.This supports a biological classification of this disease by the World Health Organisation.

Stop research on children using Oxford criteria , and CBT and GET that has passed ethical review utilising flawed PACE research , which has included previous NICE Guidelines review , and outdated and harmful , treatment recommendations in NICE Guidelines , in light of the IOM report , metabolomics and CPET testing , and researcher presented at the IACFS/ME conference 2015 and 2016 on the harms of exercises and exertion for ME patients .

- Retire the use of Oxford Criteria in medical Guideline development and research

The case definition known as the Oxford criteria, developed by PACE investigator Michael Sharpe in the 1990s. And seminal report from the U.S. National Institutes of Health [111]suggested, this case definition is so broad that it scoops up many people with fatiguing illnesses who do not have the disease known as ME/CFS. According to the NIH report, the Oxford criteria can "impair progress and cause harm," and should therefore be "retired" from use. The reason is that any results could not accurately be extrapolated to people with ME/CFS specifically. This is especially so for treatments, such as CBT and GET, that are likely to be effective for many people suffering from other fatiguing illnesses.

Many of the CBT and GET studies used the 1991 Oxford definition, which only requires 6

[111] https://prevention.nih.gov/programs-events/pathways-to-prevention/workshops/me-cfs

months of chronic fatigue and no other symptoms while allowing the inclusion of mental disorders. The 2014 AHRQ Evidence Review[112] stated that the use of the Oxford definition "results in a high risk of including patients [in studies] who may have an alternate fatiguing illness or whose illness resolves spontaneously with time."That review and NIH's 2015 Pathways to Prevention (P2P) Workshop report[113] called for Oxford criteria to be retired, stating Oxford criteria could "impair progress and cause harm."

Because of concerns with Oxford's lack of specificity, AHRQ reanalysed the evidence for CBT and GET and issued an Addendum to its evidence review in 2015[114]. That Addendum reported insufficient evidence for GET and barely any evidence for CBT *once Oxford studies were excluded*. The Addendum also noted that CBT and GET had not been studied using disease definitions requiring post-exertional malaise or other criteria considered mandatory by the 2015 IOM report[115], further demonstrating the lack of evidence for these therapies specifically in ME/CFS.

NICE Guidelines should therefor retire the use of the Oxford criteria in the development of the Guidelines and in research , and should omit inclusion of studies that utilise Oxford criteria in evidence review for treatment recommendations .

Beyond treatments, studies using Oxford have claimed that patients' behaviour, personality, and beliefs are responsible for or contribute to disease pathology, predisposition, and perpetuation. The Afari article claims that "patients' perceptions, attributions, and coping skills...may help perpetuate the illness" and that patients' "perceptions" of difficulty contribute to their negative reaction to exertion. Afari recommends CBT and GET based on

[112] http://effectivehealthcare.ahrq.gov/index.cfm/search-for-guides-reviews-and-reports/?productid=1906&pageaction=displayproduct

[113] https://prevention.nih.gov/docs/programs/mecfs/ODP-P2P-MECFS-FinalReport.pdf

[114] https://effectivehealthcare.ahrq.gov/ehc/products/586/2004/chronic-fatigue-report-160728.pdf

[115] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

"research suggesting that cognitive and behavioural factors play a role in perpetuating the symptoms of chronic fatigue syndrome."[116] The referenced research included Oxford studies and studies performed by those later involved in PACE. This theory and that of social depravity continues to be used in studied using CBT and GET on children .[117]

NICE Guidelines in its current state does not recognise that exertion causes harm or that post exertion malaise is hallmark feature of ME , and excludes other existing and superior alternative diagnosis criteria such as the IOM report[118] , ICC [119]and CCC[120] , which all recognise ME as a biological , systemic illness . Nor does NICE Guidelines mention if these can be used by clinicians in making a diagnosis and explaining the nature of ME and Post Exertion Malaise , and alternative treatment recommendations and harms[121] of exertion .

This is a requirement in order to obtain informed patient consent according to the change in UK law on consent on 11th March 2015 [122]. NICE Guidelines in its current form does not assist clinicians and patients in being informed of the harms and benefits of treatment recommendations such as CBT and GET and alternatives , such as energy conservation[123] theory and pacing , and biological treatments , according to all available research. This is particularly important when the law change states that clinicians can no longer rely solely on a reasonable body of evidence such as a guideline , and where in research this law

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[116] http://www.ncbi.nlm.nih.gov/pubmed/12562565

[117] http://adc.bmj.com/content/early/2013/10/21/archdischild-2012-302156.abstract

[118] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[119] http://www.investinme.org/Documents/Guidelines/Myalgic%20Encephalomyelitis%20International%20Consensus%20Primer%20-2012-11-26.pdf

[120] http://sacfs.asn.au/download/consensus_overview_me_cfs.pdf

[121] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[122] https://www.supremecourt.uk/cases/docs/uksc-2013-0136-judgment.pdf

[123] http://www.workwellfoundation.org/research-and-latest-news/

change particularly applies in the case of research trails .[124] NICE Guidelines also needs to make patients and clinicians aware that the Guidelines are not law abiding and only offers guidance .

Comorbidities are also not recognised by NICE Guidelines , such as orthostatic intolerance which is identified by the IOM report[125] as being included in the diagnostic criteria . NICE Guidelines excludes investigation for POTS and tilt table testing. Though confusingly the NHS website states that many people with ME actually have POTS . POTS is not an alternative diagnosis , as orthostatic intolerance is included in the IOM report diagnostic criteria due to the fact the research on ME patients identifies orthostatic intolerance being commonly found in ME patients . Nor does the Guidelines include the World Health Organisation's ICD10 classification Diagnosis of postural orthostatic tachycardia syndrome (POTS) in association with CFS/ME. Research has confirmed that Cardiac responses to exercise distinguish postural orthostatic tachycardia syndrome variants. [126]

Action :

NICE Guidelines should retire the use of the Oxford criteria in the development of the Guidelines and in research , and should omit inclusion of studies that utilise Oxford criteria in evidence review for treatment recommendations

That the IOM report 2015 , CCC and ICC and treatment primer to be included in the Guidelines

[124] https://m.youtube.com/watch?v=HHaM69l0whc

[125] http://www.nationalacademies.org/hmd/Reports/2015/ME-CFS.aspx

[126] http://onlinelibrary.wiley.com/doi/10.14814/phy2.13040/full

Removal of all recommendations for CBT and GET and the removal of information based on Oxford and the psychogenic disease theory , and replacement with content such as that provided in the 2014 and 2016 IACFS/ME primer and 2012 ME-ICC primer

Investigation and reanalysis of the flawed PACE trial

NICE and NHS to remove all recommendations and risk and prognosis statements based on PACE and other Oxford studies from its current and planned medical education material, including IMPARTS which classifies and provided diagnostic criteria for ME as medically unexplained symptoms .

The Agency for Healthcare Research and Quality (AHRQ) report to be included in NICE Guidelines , who just downgraded recommendations for CBT and GET in the AHRQ Addendum once Oxford studies were excluded.

- Management and treatment recommendations

Subjective research conducted has also come to the same conclusions me the harms of CBT And Get as the biological research findings . There is an abundance of patient reports of harm from ME/CFS patients and charities confirming that GET makes people with ME/CFS worse , including children . Patient surveys have repeatedly reported harm from CBT and GET. A 2011 review of eight GET surveys and five CBT surveys found that 51 percent of survey respondents reported that GET worsened their health while 20 percent said that CBT worsened their health. One survey in severely ill patients reported that 82 percent of respondents experienced harm due to GET. A 2014 survey of 1428 patients conducted by U.K.'s ME Association also reported adverse reactions to GET and CBT.[127]

[127] http://www.meassociation.org.uk/2015/05/23959/

Such harms are predictable given the systemic intolerance to exertion that the 2015 IOM report defined as the hallmark of the disease, yet harms[128] have been largely ignored in mainstream clinical guidance.

As well as pace trial participants testimonials of adverse effect of participating in the trial , which was found to overstated the research findings on the benefit of CBT and GET [129] The authors of the Guidelines and researchers on cost effectiveness of CBT and GET have been found to have overstated the results of their research which was conducted to validate the recommendations of these treatments in the Guidelines , and in fact invalidated it , and should be used accordingly to revise the recommendations of these treatments as being most effective for ME patients . This coincided with the AHRQ [130]review on CBT and GET which concluded that these treatments are not effective .

A large publicly funded study, known as the FINE trial, also failed to find any benefit in the use of CBT over and above routine doctors visits[131].

An additional similar study to the PACE trial, which was carried out in Spain, and published in January 2011, found no benefits from CBT and GET when compared to standard medical care. Abstract can be found here: [132]

Furthermore, conflicting results by similar larger scale research conducted by the ME Association at the same time as the Pace Trial is not considered in the formation of NICE

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[128] http://iacfsme.org/ME-CFS-Primer-Education/News/IACFSME-2016-Program.aspx

[129] https://b1ad200d-a-62cb3a1a-s-sites.googlegroups.com/site/pacefoir/pace-trial-participants-experiences.pdf?attachauth=ANoY7cpldfzGBFTUL3ZmuIV9piYPIX3gQDy0r0RqYEaGj4kLECm1hWH-nvbHYDCho9e2JQxCl_0BMQpz0Ubr8gyHv31kCNfvmYG6U8TMaTZzMuYeBjrtmMg4EDK6YIQ_LxCPGrZ4-JVp9oIlvetyaATImQxFX0L5HtZwQPOs6zbDtfYN1v12z2i0ySxzWJ2lTDAnR45z_iW35QARgcaSv20dYOSE_7Eda9QqJrcuq7O1m8t8EpzfY_0%3D&attredirects=0

[130] https://effectivehealthcare.ahrq.gov/ehc/products/586/2004/chronic-fatigue-report-160728.pdf

[131] . http://www.ncbi.nlm.nih.gov/pubmed/20418251

[132] http://www.ncbi.nlm.nih.gov/pubmed/21234629

guidelines. Pacing is rated very strongly as the most effective form of management and is consistent with several other surveys of patient opinion and a large amount of anecdotal ME association 2010 survey feedback. Full report available here[133]

The PACE trial , is therefore incapable of informing of the effectiveness of CBT and GET compared to other treatment recommendations , which was used to support the current assertions made in the NICE Guidelines , which it has in fact invalidated them following reanalysis. Pending a comprehensive review or audit of trial data, it seems prudent that the published trial results should be treated as potentially unsound, as well as the medical texts, review articles, and public policies based on those results.

Nor can PACE , or NICE Guidelines in its current state , continue to be used to inform trial participants of the benefits of these interventions , as is the case with current research trials , MAGENTA and FITNET[134] , which are studying CBT and GET on children .

MAGENTA is increasing activity and utilising 30min of aerobic activity a day and increasing the intensity . FITNET[135] is increasing activity with the goal of 8 hours of cognitive activity a day , despite the IOM report that any activity (physical , cognitive or emotional ,) , can adversely affect patients in multiple organ systems .

This is not stabilising activity as the authors publicise through the media , but increasing it . The sports scientist and neurologist Mark Van Ness has identified a need to stabilise activity through energy conservation and pacing using a heart rate monitor to stay within the anaerobic threshold , and is working with the CDC on their Guideline recommendations [136]. It is surprising that in the UK phycologists have become experts on the benefit and harm of exercise using subjective research , and ignore the harms identified by specialists in this field

[133] : http://www.meassociation.org.uk/?page_id=1345

[134] http://www.bristol.ac.uk/media-library/sites/ccah/cfsme/study-docs/Flyer%20for%20GPs_v2.0.pdf

[135] http://www.bristol.ac.uk/media-library/sites/ccah/cfsme/study-docs/Flyer%20for%20GPs_v2.0.pdf

[136] http://www.workwellfoundation.org/research-and-latest-news/

, who identified a damaged aerobic system , which has been further validated by metabolomics studies that have identified biochemistry involved in impaired energy metabolism in ME patients .

These findings has been substantiated and reinforced by research presented at the IACFS/ME conference 2016 . Where multiple researchers presented findings of , an immune system attack on the mitochondria could be causing the energy problems in ME/CFS .That putting healthy cells in ME/CFS patients blood causes their energy production to drop , and suggests that what's causing ME/CFS could be in the blood . Problems with the pyruvate dehydrogenase enzyme complex could explain much about the energy problems in ME/CFS .Thirty minutes of submaximal exercise caused reductions in ME/CFS patients brain activity and cognitive capability the next day. .High hypoxanthine levels suggest ME/CFS is in some ways similar to starvation. increased lactate levels during exercise indicate the more toxic, inefficient and far less powerful anaerobic energy production pathway is used more in ME/CFS .Reduced heart rates during exercise indicate an inability to appropriately engage the heart during exercise. Problems with hydrogen sulphide could explain many of the mitochondrial and other issues in ME/CFS.Exercise triggered sympathetic nervous system activity caused about half the ME/CFS patients in a small study to temporarily come down with POTS. Over exertion pushes ME patients into an adrenaline cycle[137] and is dangerous considering the cardiac , metabolite , impaired mitochondrial function and oxidative stress that is present .

What's more these MAGENTA's public documents, including the participant-information sheets given to prospective patients and their parents/carers in the feasibility trial do not convey the magnitude of the harm reported by patients or the research literature on exertion according to the IOM report , or the reanalysis of PACE trial data , or AHRQ

[137] http://www.hfme.org/adrenalinesurgetips.htm

downgrade of these treatments , or alternatives as recommended by the Work Well Foundation on energy conservation[138] , or drug and personalised medicine alternatives[139] .

A document addressed to parents reads “We have used both treatments [GET and activity management] in our service and we are not aware of side effects. Studies in adults have also not shown that there are any side effects.” [140]Therefore, the children in MAGENTA and those responsible for their well-being may not have given informed consent. The FITNET study will also be using the same consent forms as MAGENTA . Nor does the FITNET study inform patients how to manage an adverse effect experienced in the study , or mention biological adverse effects that can occur[141] , as mentioned above and identified in the biological research presented at the IACFS/ME conference 2016 , and stated in the IOM report on ME done in 2015 .

In sharp contrast, the 2015 AHRQ [142]Addendum stated that the CBT had a “disputable underlying rationale regarding the fear avoidance theory contributing to the perpetuation of symptoms in ME/CFS.” The 2015 IOM Report definitively stated that ME/CFS is not a psychological problem. Dr. Ellen Clayton, NAM panel chair, and Dr. Peter Rowe, panel member, also roundly dismissed the idea that the debility of ME/CFS could be the result of deconditioning ·Instead, the IOM report provided a broad cross-section of biomedical evidence and decisively noted that ME/CFS is characterised by a systemic exacerbation of all symptoms following even trivial activity that is accompanied by a range of abnormal physiological responses. As demonstrated at the 2015 and 2016 IACFS/ME conference, numerous studies have confirmed and extended these findings, demonstrating widespread pain , energy production impairment , neurological, autonomic, and immunological

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[138] http://www.workwellfoundation.org/research-and-latest-news/

[139] http://www.dramyyasko.com/resources/

[140] http://www.bristol.ac.uk/media-library/sites/ccah/cfsme/study-docs/FITNET-NHS%20PIL_11-15%20yrs_v2.0.pdf

[141] http://www.bristol.ac.uk/media-library/sites/ccah/cfsme/study-docs/FITNET-NHS%20PIL_11-15%20yrs_v2.0.pdf

[142] https://effectivehealthcare.ahrq.gov/ehc/products/586/2004/chronic-fatigue-report-160728.pdf

impairment.

Get and CBT causes harm to the patients, because it encourages patients to ignore their symptoms and exceeded their energy limitations , and exercise despite mounting evidence that exercise is dangerous for people with this illness , CBT can be helpful for all chronic illness but not when the primary underling reason for the CBT is to change wrong illness belief and encourage vulnerable patients especially children with ME/CFS to ignore their symptoms , as is the case with the Lightning process and FITNET and GET , when patients symptoms are validated by biological research[143] [144] , and warning signs that they are utilising an impaired aerobic system and result of the underlying biochemistry , and not deconditioning or a result of illness behaviour and thought processes , or parental behaviour .

Professor Mark Van Ness and the Workwell Foundation recommend utilising intact anaerobic pathway , knowing that aerobic exercise will worsen the pathologies of ME/CFS, Their recommendations are consistent with their understanding of ME/CFS pathology, identified with 2 day CPET testing . which has been further been reinforced with metabolomics studies on ME patients .

The biochemistry of ME patients needs to be treated , through access to personalised medicine[145] , and the investigations required . Not indirectly through sleep regulation and increasing activity , which makes ME patients worse , which phycologists now propose can improve a mutisystemic disease , without testing or treating the underlying biochemistry , which they don't specialise in . Patients and clinicians should be taught about pacing and energy conservation advised by the Workwell Foundarion[146] , in order to utilise the intact

[143] http://www.tandfonline.com/doi/abs/10.1080/21641846.2016.1207400?journalCode=rftg20&

[144] http://www.openmedicinefoundation.org/wp-content/uploads/2016/08/Naviaux-PNAS-CFS-Metabolomics-2016.pdf

[145] http://www.dramyyasko.com/resources/

[146] http://www.workwellfoundation.org/research-and-latest-news/

anaerobic system and not exceed their anaerobic threshold , to prevent worsening of their condition and manage the use of their limited energy capacity[147] .

NICE Guidelines does not offer patients any biological treatment or investigations alternative to this approach , nor inform patients and clinicians of other superior diagnosis and treatment primers such as the IOM report , ICC and CCC . NICE continues to promote harmful treatments that increase exertion , and CBT that inform patients and parents that they have illness beliefs and self limiting behaviour that has caused biological abnormalities through deconditioning , which has been disproved . Physical deconditioning does not seem to be a perpetuating factor in CFS .[148].

Even though this theory and has been disproven , the treatment recommendations are still promoted by NICE , and GPS continue to be taught and believe that ME is medically unexplained symptoms, as a result . And patients continue to receive no treatment , be misinformed and harmed with referrals to CBT an GET , as well as research trials using CBT and GET on children , and institutionalised .

ME patients are not offered personalised biological treatment and are only offered psychological interventions of CBT and GET . "About 75% of the metabolite abnormalities were unique to the individual and useful in guiding personalised treatment.The finding of an objective chemical signature in CFS helps to remove diagnostic uncertainty, will help clinicians monitor individualised responses to treatment, and will facilitate multi center clinical trials.Only about 25% of the metabolite disturbances found in each person were needed for the diagnosis of CFS," [149]

Nor are patients referred to biological experts in gut micro biome , methylation , mitochondria function and orthostatic intolerance nor offered testing in these areas , even

[147] http://www.workwellfoundation.org/research-and-latest-news/

[148] http://www.ncbi.nlm.nih.gov/pubmed/11200949

[149] http://www.openmedicinefoundation.org/wp-content/uploads/2016/08/Naviaux-PNAS-CFS-Metabolomics-2016.pdf

though research has identified abnormalities in these areas in ME patients , and are left with receiving no biological treatment or having to try afford what private treatment they can , if they are able to do so .

Even then once private test results are presented to GPs , there is no recognition or understanding by the GP on the significance of the results and how they apply to ME , as NICE Guidelines fails to inform clinicians of the biological research .

Following abnormalities found on private test results , there is no assistance with probiotics , supplementation for identified deficiencies , or referral to biological specialists for methylation and mitochondrial function , or how to stabilise activity with heart rate monitor to stay within anaerobic threshold in order to reduce oxidative stress and Post Exertion Malaise , as advised by the Workwell Foundation , and resulting reduced function which has proven to be the result of exertion, as stated in the 2015 IOM report on ME and metabolomics research on ME .

Clinical guidelines need to include the findings of system wide abnormalities .Clinicians need to be all informed that ME / CFS affects multiple systems of the body with biomedical abnormalities that need to be monitored throughout the illness, Clinicians need to be informed and aware of the latest medical research findings and ongoing projects conducted by research alliances, as well as the methods and success of personalised biological testing and treatments offered by biological multifactorial disease specialists[150] , which is recommended by biological ME experts and researchers[151] , systems biology researchers and clinicians. [152] [153]

NICE has the responsibility to ensure that it provides accurate information and protects the

[150] http://www.dramyyasko.com/resources/

[151] http://www.openmedicinefoundation.org/

[152] http://functionalforum.com/

[153] https://www.functionalmedicine.org/

lives of patients. The continued inclusion of these recommendations, statements and references are not medically ethical nor scientifically defensible. . To protect patients currently undertaking referrals for these treatments and being referred to research studies and recruited for research studies implementing these interventions , as well as GPs referring patients to these study's without fully informing them of the risks according to the law change on consent , it is essential that these concerns be addressed immediately.

Action :

Inform patients and clinicians of harms of CBT and GET alternative treatments and investigations available privately and reflected in the biological literature , and ICC treatment primer , including that offered by Breakspear medical group and Dr Amy Yasko , in accordance to the law change on consent .

Inform patients and clinicians of the Law change to consent .

Provide patients with specialist , personalised biological treatment and investigation of metabolites, gut micro biome , mitochondrial function and methylation function.

Provide tilt table testing to ME patients .

Stop IMPARTS from classifying ME as medically unexplained symptoms and training clinicians in this disproven, harmful and unfounded view .

Replace CBT and GET with energy conservation and pacing with heart rate monitor as described by Professor Mark Van Ness and the Workwell Foundation

Remove recommendations for CBT and GET and stop the application and referral for these treatment recommendations and referral of children to research trials applying these interventions .

Stop all CBT and GET research trails on ME patients .

Release patients that have been institutionalised with ME under a phycological diagnosis , when they have not received treatment for metabolic dysfunction , as identified in the research literature , and stop the forced administration of CBT and GET .