

Proposal for the ICD-10 G93.3 legacy terms for ICD-11

How the G93.3 terms are currently represented in ICD-10: (CFS is included in the Index, only)

ICD-10 Version:2016

Search [Advanced Search] ICD-10 Version

Syndrome - fatigue - chronic G93.3

- ▶ VI Diseases of the nervous system
- ▼ G90-G99 Other disorders of the nervous system
 - ▶ G90 Disorders of autonomic nervous system
 - ▶ G91 Hydrocephalus
 - G92 Toxic encephalopathy
 - ▼ G93 Other disorders of brain
 - G93.0 Cerebral cysts
 - G93.1 Anoxic brain damage, not elsewhere classified
 - G93.2 Benign intracranial hypertension
 - concept title** G93.3 Postviral fatigue syndrome
 - G93.4 Encephalopathy, unspecified

G93.3 Postviral fatigue syndrome
Benign myalgic encephalomyelitis

G93.4 Encephalopathy, unspecified
Excl.: encephalopathy:
• alcoholic (G31.2)
• toxic (G92)

Index Term (at G93.3)
Chronic fatigue syndrome

Proposal for ICD-11: (CFS and ME assigned to separate codes; PVFS under Synonyms to ME)

08 Diseases of the nervous system
(...)

- ▼ Other disorders of the nervous system
 - new concept title** ▶ **8D98** Chronic fatigue syndrome

Synonyms
CFS - chronic fatigue syndrome
 - new concept title** ▶ **8D99** Myalgic encephalomyelitis **"benign" deprecated**

Synonyms
ME - myalgic encephalomyelitis
myalgic encephalomyelitis (benign)
myalgic encephalomyelitis syndrome
myalgic encephalitis
myalgic encephalopathy
postviral fatigue syndrome **postviral fatigue syndrome**
PVFS - postviral fatigue syndrome **deprecated**

Index Terms
Akureyri disease
Iceland disease
epidemic neuromyasthenia

Codes for illustrative purposes only; Beta draft codes change daily as terms are added or reorganized.

The URL for viewing and for commenting on this Proposal on the ICD-11 Beta Proposal Mechanism is:

<http://bit.ly/2n8I9qc>

ICD Revision will only consider comments that are submitted via the Proposal Mechanism. You can register to access the Proposal Mechanism here: <http://bit.ly/2n7Kdj4>

Suzy Chapman: dxrevisionwatch@page1.myzen.co.uk

Mary Dimmock: medimmock@gmail.com

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Detailed Explanation of the Proposal

This Complex Hierarchical Changes Proposal is for the ICD-10 legacy entities coded and indexed to G93.3.

Declarations: This submission has been prepared by Mary Dimmock and Suzy Chapman. Mary Dimmock serves on the Board of Solve ME/CFS Initiative and also works with other ME organizations. Suzy Chapman has no affiliations. This proposal has been submitted in personal capacities and not on behalf of any organizations. The authors declare no conflicts of interest.

In ICD-10 Volume 1: Tabular List, the G93.3 ICD concept title is *Postviral fatigue syndrome*; the inclusion term is *Benign myalgic encephalomyelitis*. *Chronic fatigue syndrome* is included in Volume 3: Alphabetical Index, only, and is indexed to G93.3.

In the absence of any proposals or rationales published by Topic Advisory Group (TAG) for Neurology, or by any other TAG, or by the ICD-11 MMS Joint Task Force during the preparation of this submission, the authors propose the restructuring of these entities taking their classification within ICD-10 Version: 2016 as the reference point [1].

Recommendation: For ICD-11, the G93.3 legacy entities should be retained under *Chapter 08: Diseases of the nervous system*. (See Rationale 3.2)

In ICD-10 Volume 1: Tabular List, the concept title is a child entity under parent class: *Other disorders of brain*.

In May 2010, a change of hierarchy for the ICD-10 G93.3 legacy entities was recorded in the iCAT (Collaborative Authoring Tool). Parent: *Other disorders of brain* was removed and replaced with parent: *Other disorders of the nervous system* [2]. *Other disorders of brain*, which is the G93 parent to ten ICD-10 categories between G93.0 to G93.9, has been retired for ICD-11.

Recommendation: For ICD-11, the G93.3 legacy entities should be retained under parent: *Other disorders of the nervous system*. (See Rationale 3.3)

The following changes to the hierarchy between the three entities are proposed:

Add new Concept Title: Chronic fatigue syndrome (See Note 1)

Remove Concept Title: Postviral fatigue syndrome

Add new Concept Title: Benign myalgic encephalomyelitis (See Rationale 3.4)

Replace new Concept Title: Benign myalgic encephalomyelitis with Myalgic encephalomyelitis (See Note 2)

Add: Postviral fatigue syndrome under Synonyms to new Concept Title: Myalgic encephalomyelitis (See Note 3)

Assign unique sequential codes to each new Concept Title.

These new Concept Titles are proposed to be listed in the *Foundation*, *MMS Linearization*, and *Special tabulation neurological conditions* linearization.

References:

1 International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) Version: 2016. <http://apps.who.int/classifications/icd10/browse/2016/en#/G93.3> [Accessed March 12, 2017]

2 Change history, iCAT (Collaborative Authoring Tool) drafting platform, May 1, 2010. [Accessed May 24, 2010]

Proposed hierarchical restructure:

1. ICD Concept Title

1.1 Fully Specified Name: Chronic fatigue syndrome

2. Classification Properties

2.1 Parents:

Primary: Diseases of the nervous system > Other disorders of the nervous system

2.2 Type

Disease
Disorder / Syndrome

2.3 Use and Linearizations

Use: Primary Care / Clinical / Research
Linearization(s): Morbidity / Mortality / Neurology

3. Textual Definition(s)

[See Rationale 2 and 4]

4.1.1 Synonyms (See Note 3.1)

CFS - chronic fatigue syndrome

4.2 Inclusions

There are no inclusions for this entity

4.3 Exclusions (See Note 4)

1. ICD Concept Title

1.1 Fully Specified Name: Myalgic encephalomyelitis

2. Classification Properties

2.1 Parents:

Primary: Diseases of the nervous system > Other disorders of the nervous system

2.2 Type

Disease
Disorder / Syndrome

2.3 Use and Linearizations

Use: Primary Care / Clinical / Research

Linearization(s): Morbidity / Mortality / Neurology

3. Textual Definition(s)

[See Rationale 2 and 4]

4.1.1 Synonyms (See Note 3.1)

ME - myalgic encephalomyelitis

myalgic encephalomyelitis (benign)

myalgic encephalomyelitis syndrome

myalgic encephalitis

myalgic encephalopathy

postviral fatigue syndrome

PVFS - postviral fatigue syndrome

4.2 Inclusions

There are no inclusions for this entity

4.3 Exclusions (See Note 4)

The authors recommend the following historical terms for inclusion in the Index:

Index terms

Akureyri disease

Iceland disease

epidemic neuromyasthenia

Notes:

Note 1: Inclusion of chronic fatigue syndrome in Foundation and MMS Linearization: The authors support the principle set out in ICD-10 Volume 2: Instruction Manual (2010): *"The categories have to be chosen to facilitate the statistical study of disease phenomena. A specific disease entity that is of particular public health importance, or that occurs frequently, should have its own category."* [1].

The authors support the precedent set by the Canadian Institute for Health Information (CIHI) that is responsible for the development, update and maintenance of ICD-10-CA, and the German Institute of Medical Documentation and Information (DIMDI) that is responsible for the development, update and maintenance of ICD-10-GM in adding chronic fatigue syndrome to their Tabular Lists.

References:

1 International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Volume 2 Instruction Manual, 2010 Edition. http://www.who.int/classifications/icd/ICD10Volume2_en_2010.pdf

2 International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada, Volume One – Tabular List, Canadian Institute for Health Information 2015. <http://assets.ihc.ca/Documents/Auto%20Insurance/ICD-10-CA%202015.pdf>

3 Internationale statistische Klassifikation der Krankheiten und verwandter Gesundheitsprobleme 10. Revision German Modification Version 2017. <https://www.dimdi.de/static/de/klassi/icd-10-gm/kodesuche/onlinefassungen/htmlgm2017>

Note 2: Deprecation of "benign": The term "benign myalgic encephalomyelitis" was first introduced in 1956, in a Lancet editorial later attributed to the former Chief Medical Officer, Sir Donald Acheson [1]. The designation "benign" had originally been suggested because no fatalities had been recorded at the time from myalgic encephalomyelitis.

WHO included "benign myalgic encephalomyelitis" as an index entity within ICD-9 (published 1975). For ICD-10 (published 1992), WHO created a new category G93, *Other disorders of brain*, in *Chapter VI: Diseases of the nervous system*, and created a new code G93.3, Postviral fatigue syndrome, an entity previously in the symptom chapter of ICD-9. WHO moved benign myalgic encephalomyelitis under the new G93.3 code [2].

ICD-10 has continued to include the designation "benign" within its classification.

In 1978, an international symposium was held at the Royal Society of Medicine to discuss the disease and future research directions. A British Medical Journal editorial reported there had been clear agreement that myalgic encephalomyelitis was a distinct, organic, nosological entity and that dismissal of the disease as psychological was no longer tenable. Attendees discussed the variety of physical findings, in both epidemic and sporadic cases, and described the characteristic feature of post effort exhaustion and fatigability. There was agreement that future outbreaks should be studied by a collaborative team of neurologists, epidemiologists, virologists, and immunologists and that findings would also be important for other neurological disorders, including multiple sclerosis.

Attendees considered other terms used to describe the disease but rejected these as unsatisfactory. They agreed on "myalgic encephalomyelitis," omitting the prefix "benign" in response to the high burden of morbidity associated with the disease and because the term "benign" was misleading from the patient's perspective, "*since the illness may be devastating*" [3][4].

For at least the last 14 years, researchers have published studies reporting an increased risk of death due to cancer, cardiac disease, and suicide. While preliminary, these studies have reported similar findings which can be explained by what is known about the pathology of the disease and the stigma patients experience [5][6].

On July 11, 2009, autopsy evidence was presented at a Royal Society of Medicine meeting by Dr Abhijit Chaudhuri, Essex Centre for Neurosciences, where slides of inflammation of dorsal root ganglia in three patients with myalgic encephalomyelitis were discussed [7]. A disease specific post-mortem brain and tissue bank for the study of myalgic encephalomyelitis and chronic fatigue syndrome is proposed for the UK [8].

Given the high burden of morbidity and recorded mortalities (the earliest known recorded cause of death due to ME, CFS in the UK was 2003), the authors see no justification for retaining the designation "benign" for ICD-11.

Recommendation: Replace entity, "Benign myalgic encephalomyelitis" with "Myalgic encephalomyelitis."

For continuity and comparability with ICD-10 and with SNOMED CT International Edition and National Extensions, the authors propose listing "myalgic encephalomyelitis (benign)" under Synonyms to concept title: Myalgic encephalomyelitis.

References:

1 A new clinical entity? Editorial; Lancet 1956 (May 26);789-790.

<http://www.sciencedirect.com/science/journal/01406736/267/6926>

2 A Summary of Chronic Fatigue Syndrome and its Classification in the International Classification of Diseases, Centers for Disease Control and Prevention, National Center for Health Statistics, March 2001.

http://www.institutferran.org/documentos/icd_code.pdf

3 Epidemic myalgic encephalomyelitis. *British Medical Journal*. 1978 Jun 3; 1(6125): 1436-1437.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1604957/>

4 Postgraduate Medical Journal November 1978; 54(637): 709-774.

<http://pmj.bmj.com/content/54/637.toc#Articles>

5 ME/CFS: A Primer for Clinical Practitioners 2014. (p. 26).

http://iacfsme.org/portals/0/pdf/Primer_Post_2014_conference.pdf

6 Dimmock ME, Mirin AA, Jason LA (2016). Estimating the disease burden of ME/CFS in the United States and its relation to research funding. *J Med Therap 1*: doi:10.15761/JMT.1000102. <https://oatext.com/Estimating-the-disease-burden-of-MECFS-in-the-United-States-and-its-relation-to-research-funding.php>

7 O'Donovan D, Harrower T, Cader S, Findley L, Shepherd C, Chaudhuri A. Pathology of Chronic Fatigue Syndrome: Pilot Study of four autopsy cases. International Science Symposium 3-4 – Myalgic Encephalomyelitis/Chronic

Fatigue Syndrome (ME/CFS) Queensland, Australia: Population Health and Neuroimmunology Unit, Bond University; 2010.

8 Nacul L, O'Donovan DG, Lacerda EM, et al. Considerations in establishing a post-mortem brain and tissue bank for the study of myalgic encephalomyelitis/chronic fatigue syndrome: a proposed protocol. *BMC Research Notes*. 2014;7:370. <http://bmresnotes.biomedcentral.com/articles/10.1186/1756-0500-7-370>

Note 3: Deprecation of postviral fatigue syndrome: The term "postviral fatigue syndrome" appears to be an ill-defined term that is not found extensively in the literature.

A search via PubMed on March 12, 2017 returned 55 papers referencing "postviral fatigue syndrome" (1985 - 2005) and 39 papers referencing "post viral fatigue syndrome" (1985 - 2014). Whereas a search for "myalgic encephalomyelitis" returned 629 papers (1956 - 2017) and a search for "chronic fatigue syndrome" returned 6020 papers (1985 - 2017) [1].

The extent to which the term is used by practitioners in primary care and specialty clinical settings and the frequency of recording in electronic medical record systems has not been determined.

Other than the *Oxford Criteria for Post-infectious Fatigue Syndrome (PIFS)*, which is defined as "a subtype of CFS which either follows an infection or is associated with a current infection," the authors can find no working case definition for postviral fatigue syndrome [2]. The U.S. National Institutes of Health (NIH) has declared the *Oxford Criteria* severely flawed and recommended its retirement [3].

Postviral fatigue syndrome is an inappropriate concept title for myalgic encephalomyelitis, as not all cases of myalgic encephalomyelitis are preceded by a viral infection [4].

The authors consider there is insufficient justification for retaining postviral fatigue syndrome as a concept title for ICD-11.

Recommendation: For continuity and comparability with ICD-10, the recommendation is to include postviral fatigue syndrome as a synonym term under new concept title: Myalgic encephalomyelitis.

3.1 Synonyms: Synonym terms for Myalgic encephalomyelitis have been suggested with reference to those listed in SNOMED CT International Edition and SNOMED CT National Extensions [5].

References:

- 1 PubMed, US National Library of Medicine National Institutes of Health. <https://www.ncbi.nlm.nih.gov/pubmed>
- 2 Sharpe MC, Archard LC, Banatvala JE, et al. A report - chronic fatigue syndrome: guidelines for research. *Journal of the Royal Society of Medicine*. 1991;84(2):118-121. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1293107/>
- 3 National Institutes of Health Pathways to Prevention Workshop: Advancing the Research on Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome, Final Report. December 9–10, 2014 (p. 16). <https://prevention.nih.gov/docs/programs/mecfs/ODP-P2P-MECFS-FinalReport.pdf>
- 4 "The cause of ME/CFS remains unknown, although in many cases, symptoms may have been triggered by an infection or other prodromal event, such as "immunization, anesthetics, physical trauma, exposure to environmental pollutants, chemicals and heavy metals, and rarely blood transfusions" (Carruthers and van de Sande, 2005, p. 1)." National Academy of Medicine. Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness. The National Academies Press. May 2015. <https://www.nap.edu/catalog/19012/beyond-myalgic-encephalomyelitischronic-fatigue-syndrome-redefining-an-illness>
- 5 SNOMED International SNOMED CT Browser. <http://browser.ihtsdo.org/> [Accessed: March 16, 2017]

Note 4: Exclusions: One of the authors submitted proposals for adding exclusions for the G93.3 legacy entities under Fatigue and under Bodily distress disorder in December 2014 [1][2]. The ICD-11 principle is that exclusion terms must exist in the classification as entities to enable linking. It follows that until the G93.3 legacy entities are restored to the Beta draft, exclusions for these terms cannot be inserted.

It is the authors' understanding that the number, type and application of exclusions for ICD-11 have been under review since publication of the Content Model Reference Guide 2011, and that the principles for exclusions may be in the process of being updated [3][4].

On the basis that exclusion type: *"elsewhere classified, not to be coded here"* (with a link to where the entity should be coded) is being retained, the authors recommend that this type of exclusion should be inserted under Fatigue and also under Bodily distress disorder for concept title Chronic fatigue syndrome and concept title Myalgic encephalomyelitis to mitigate the risk of miscoding under Fatigue or misdiagnosis with, or misapplication of, an additional diagnosis of Bodily distress disorder.

4.1 Exclusions under Fatigue: In ICD-10: Tabular List, *Chapter XVIII: Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified*, there is an *Excl.* for "fatigue syndrome: • postviral (G93.3)" under R53 Malaise and fatigue.

For ICD-11, the legacy concept title, Malaise and fatigue, is replaced with new concept title, Fatigue, which is primary parented under General symptoms, and secondary parented to proposed grouping, *"Symptoms or signs involving motivation or energy."* It is noted that Bodily distress disorder is listed under exclusions to Fatigue.

Fatigue is a common complaint. Many disease processes cause symptoms of fatigue or prolonged fatigue which can be explained by the illness and which in some cases may be treatable. Fatigue, chronic fatigue, idiopathic fatigue and idiopathic chronic fatigue do not meet the specific criteria for chronic fatigue syndrome and myalgic encephalomyelitis [5].

The Canadian Institute for Health Information (CIHI) clinical modification, ICD-10-CA, and the German Institute of Medical Documentation and Information (DIMDI) clinical modification, ICD-10-GM, rightly retained an *Excl.* for "fatigue syndrome: • postviral (G93.3)" under R53 Malaise and fatigue.

Recommendation: Retain exclusions under Fatigue for concept title Chronic fatigue syndrome and concept title Myalgic encephalomyelitis to mitigate the risk of miscoding these defined diagnostic categories. Insert exclusions for Fatigue under concept title Chronic fatigue syndrome and concept title Myalgic encephalomyelitis.

4.2 Classificatory revisions to SNOMED CT and Clinical Terms version 3 (CTV3): Prior to July 2015, SNOMED CT International Edition and its National Extensions had Chronic fatigue syndrome (with Myalgic encephalomyelitis and several related and historical terms as Synonyms terms) classified under two parent disorder classes: *Mental disorder*; and *Multisystem disorder*.

In March 2015, Health and Social Care Information Centre (now NHS Digital) confirmed that the owners of SNOMED CT (IHSDO) had reviewed the relationship between the entry for SCTID: 52702003 Chronic fatigue syndrome and the *Mental disorder* parent and had retired the *Mental disorder* parent [6].

Since the July 2015 release of SNOMED CT International Edition, Chronic fatigue syndrome is classified under the single parent, SCTID: 281867008 *Multisystem disorder*. This revision was incorporated into all subsequent releases of the various SNOMED CT National Extensions.

The Clinical Terms version 3 (CTV3) primary care clinical terminology product (aka: the UK Read Codes v3) also had Chronic fatigue syndrome classified under two parent disorder classes: as a sub class of *Neurasthenia*, under *Mental health disorders*; and as a sub class of *Neurological disorders*. The April 2016 release for CTV3 also retired the *Mental health disorder* parent for Chronic fatigue syndrome to reflect the revised classification in the SNOMED CT International Edition and its Extensions [7].

4.3 Exclusions under Bodily distress disorder: For ICD-11, the *Somatic Distress and Dissociative Disorders Working Group (S3DWG)* proposes to replace F48.0 Neurasthenia and all the F45.0 – F45.9 somatoform disorder categories (with the exception of Hypochondriasis) with a new and much simplified, single diagnostic category, for which the current suggested name is "bodily distress disorder" [8][9].

As defined for ICD-11, the proposed bodily distress disorder diagnostic construct has strong conceptual, characterization and criteria alignment with DSM-5's somatic symptom disorder [10]. In the ICD-11 Beta draft, somatic symptom disorder is listed under Synonyms to bodily distress disorder.

For both bodily distress disorder (as defined for ICD-11) and DSM-5's somatic symptom disorder, the distinction between medically explained and medically unexplained somatic complaints is abolished. There is no longer the requirement for symptoms to be medically unexplained in order to meet the criteria, and the symptoms may or may not be associated with another medical condition: *"If a medical condition is causing or contributing to the symptoms, the degree of attention is clearly excessive in relation to its nature and progression."* [9].

Thresholds to meet the criteria for bodily distress disorder and for somatic symptom disorder are substantially lower than those of the somatoform disorders which they replace: the presence of bodily symptoms that are distressing to the individual and excessive attention directed toward the symptoms; or a single symptom, for example, pain or fatigue, in association with the psychobehavioural features that define the disorder, will be sufficient to meet the diagnosis.

Frances and Chapman (2013) argue that the somatic symptom disorder criteria – far looser than those of the ICD-10 and DSM-IV somatoform disorders, with low sensitivity and specificity and highly subjective, difficult to measure cognitions – present significant potential for misdiagnosis with, or misapplication of, an inappropriate psychiatric diagnosis [11].

Patients with chronic, troubling somatic complaints associated with *any* disease are potential candidates for an additional diagnosis of bodily distress disorder – if the clinician considers the criteria are otherwise met.

In a BMJ commentary, Frances (2013), highlights the particular vulnerabilities of some disease groups: patients with multisystem diseases like multiple sclerosis (MS), Behçet disease or systemic lupus erythematosus (SLE), where it may take several years before a diagnosis is arrived at; patients with one of the so-called, "functional somatic syndromes" (under which umbrella term chronic fatigue syndrome and myalgic encephalomyelitis have often been bundled); patients with rare diseases; patients presenting with single or multiple chronic somatic complaints of uncertain aetiology whose symptoms were, in hindsight, prodromal [12].

Patients diagnosed with chronic fatigue syndrome or myalgic encephalomyelitis, or awaiting a diagnosis, may be particularly vulnerable to misdiagnosis with, or misapplication of, an additional diagnosis of bodily distress disorder. The authors are not persuaded that the *S3DWG* sub working group has incorporated adequate safeguards for these patient groups within its proposed criteria [9][13].

Recommendation: Insert exclusions under Bodily distress disorder for concept title Chronic fatigue syndrome and concept title Myalgic encephalomyelitis to mitigate the risk of misdiagnosis with, or misapplication of, an *additional* diagnosis of bodily distress disorder. Insert exclusions for Bodily distress disorder under concept title Chronic fatigue syndrome and concept title Myalgic encephalomyelitis.

4.4 Potential for conflation of bodily distress disorder and bodily distress syndrome: One of the authors has demonstrated how the *S3DWG*'s suggested name for the proposed replacement for the ICD-10 somatoform disorders has a history of usage in the literature and in the field interchangeably with that of the already operationalized, divergent Fink et al. (2010) disorder construct, and has raised the alarm for the diagnostic and statistical implications for confusion and conflation between the two, and the difficulties for maintaining construct integrity, within and beyond ICD-11 [14].

The Fink et al. (2010) "bodily distress syndrome" disorder construct, already in use in Denmark and several other EU countries, in research and clinical settings, *is differently conceptualized, has a very different criteria set and is intended to capture a different patient population.*

Fink et al. (2010) consider their "bodily distress syndrome" disorder construct has the ability to capture the ICD-10 somatoform disorders, neurasthenia, "functional symptoms", noncardiac chest pain, chronic pain disorder, MCS and some others, but to also subsume chronic fatigue syndrome, myalgic encephalomyelitis, fibromyalgia and irritable bowel syndrome (well described categories that are discretely classified in other chapters within ICD-10, ICD-11, and SNOMED CT), under a single, unifying "BDS" diagnosis [15][16].

Since researchers, clinicians and commissioners of services already do not differentiate between these two terms (and in some cases, one observes the confluences, "bodily distress syndrome or disorder" and "bodily distress syndrome/disorder"), these patient groups will be especially vulnerable to being misclassified.

References:

1 Proposal: Bodily distress disorder, ICD-11 Beta drafting platform Proposal Mechanism, December 30, 2014. <http://bit.ly/2n86iNN>

2 Proposal: Fatigue, ICD-11 Beta drafting platform Proposal Mechanism, December 30, 2014. <http://bit.ly/2nrg1Sw>

3 Content Model Reference Guide ICD-11 Revision, World Health Organization Geneva, 2011 (p. 23, 4.3 Exclusion Terms). http://www.who.int/classifications/icd/revision/Content_Model_Reference_Guide_January_2011.pdf

4 Summary Report, Third Meeting of the JLMMS Task Force Cologne, Germany, 11-14 April 2016 (p. 12, 10.5 Exclusion Types). http://www.who.int/entity/classifications/icd/revision/2016.04.11-14_iSummaryMeetingReportCologne.pdf

- 5 ME/CFS: A Primer for Clinical Practitioners 2014. (p. 13).
http://iacfsmc.org/portals/0/pdf/Primer_Post_2014_conference.pdf
- 6 Correspondence: Health and Social Care Information Centre (now NHS Digital), FORWARD-ME March 20, 2015.
<http://www.forward-me.org.uk/Reports/SNOMED.pdf> [Accessed: March 16, 2017]
- 7 Correspondence: UK Terminology Centre (UKTC) (now NHS Digital), Suzy Chapman, November 20, 2015.
- 8 Creed F, Gureje O. Emerging themes in the revision of the classification of somatoform disorders. *Int Rev Psychiatry*. 2012 Dec;24(6):556-67. doi: 10.3109/09540261.2012.741063. [PMID: 23244611]
- 9 Gureje O, Reed GM. Bodily distress disorder in ICD-11: problems and prospects. *World Psychiatry*. 2016 Oct;15(3):291-292. doi: 10.1002/wps.20353. [PMID: 27717252]
- 10 American Psychiatric Association. (2013). Somatic Symptom and Related Disorders. In Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: Author.
- 11 Frances A, Chapman S. DSM-5 somatic symptom disorder mislabels medical illness as mental disorder. *Aust N Z J Psychiatry*. 2013 May;47(5):483-4. [PMID: 23653063]
- 12 Frances A. The new somatic symptom disorder in DSM-5 risks mislabeling many people as mentally ill. *BMJ*. 2013 Mar 18;346:f1580. [PMID: 23511949]
- 13 Frances A. DSM-5 Somatic Symptom Disorder. *J Nerv Ment Dis*. 2013 Jun;201(6):530-1. [PMID: 23719325]
- 14 Proposal: Bodily distress disorder, ICD-11 Beta drafting platform Proposal Mechanism, March 2, 2017.
<http://bit.ly/2nWnyKd>
- 15 Fink P, Toft T, Hansen MS, Ornbol E, Olesen F. Symptoms and syndromes of bodily distress: an exploratory study of 978 internal medical, neurological, and primary care patients. *Psychosom Med*. 2007 Jan;69(1):30-9. [PMID: 17244846]
- 16 Fink P, Schröder A. One single diagnosis, bodily distress syndrome, succeeded to capture 10 diagnostic categories of functional somatic syndromes and somatoform disorders. *J Psychosom Res*. 2010 May;68(5):415-26. [PMID: 20403500]

Rationale

In July 2015, the authors provided Dr Robert Jakob (*WHO, ICD-11 MMS Joint Task Force*) and Ms Anneke Schmitter (*ICD-11 Revision Project Manager*) with background materials and literature sources on myalgic encephalomyelitis and chronic fatigue syndrome for the consideration of the *Topic Advisory Group for Neurology* and to inform the revision process. This section includes selected of those materials plus new materials that have been published since then.

1. Scientific evidence that exists for neurological dysfunction: The document *Evidence Supporting a Classification of ME and CFS in the Neurological Chapter* [1] summarizes many of the neurological and neurocognitive studies in this disease going back to the early 1990s.

PDF: Evidence Supporting a Classification of ME and CFS in the Neurological Chapter 2017

<http://bit.ly/2nPj8Vv>

In addition to a list of relevant neurological studies, this document includes a 2011 review that summarized evidence of reduction in gray matter volume, reduction in blood flow in the brain, increases in brain lactate levels, changes on MRI and EEG, evidence of autonomic dysfunction, neuroendocrine dysfunction, the presence of abnormal proteins in the spinal fluid, and neurocognitive changes that include deficits in attention, memory and reaction time [2].

This document also includes a 2016 presentation by Professor Anthony Komaroff, Harvard Medical School, in which he discussed more recent studies that demonstrated brain inflammation that varies with disease severity and also studies showing impaired functional connectivity in the brain [3]. In that presentation, Komaroff concluded with the hypothesis that "low grade brain inflammation causes the symptoms of ME/CFS and this involves a connection between the brain, the immune system and possibly in some people the gut." He went on to state that according to this hypothesis, "there are different factors that can trigger ME/CFS but the hypothesis goes they all end up causing low grade inflammation in the brain and that low grade inflammation causes the symptoms of the illness."

References:

- 1 Evidence Supporting a Classification of ME and CFS in the Neurological Chapter 2017. <http://bit.ly/2mwLvYE>
- 2 Komaroff AL, Cho TA. Role of infection and neurologic dysfunction in chronic fatigue syndrome. *Semin Neurol* July 2011. <http://dx.doi.org/10.1055/s-0031-1287654>
- 3 Komaroff A. Presentation for U.S. disease organization *Solve ME/CFS Initiative*. November 2016. <https://youtu.be/ENrdrGj0p-c?t=555> Minute 14:23, 48:46.
Presentation slides: <http://solvecfs.org/wp-content/uploads/2016/11/SolveME-CFS-Webinar-Dr-Komaroff.pdf>

2. Recent federal agency reviews and scientific evidence: The Report of the U.S. Institute of Medicine (IOM), recently renamed, "The National Academy of Medicine," contains one of the most comprehensive literature reviews to date of the biomedical evidence for the disease [1]. The report concluded, as have numerous researchers, that the disease is a "*serious, chronic, complex, and multisystem disease*" that causes neurological, cognitive, immunological, autonomic, and energy metabolism impairment.

The Report further noted that the hallmark of the disease is post exertional malaise (PEM), where even very limited physical or mental exertion causes an exacerbation of all symptoms that can last for days, weeks or even months. As a result, the IOM concluded that "*some patients diagnosed by other criteria, such as the Fukuda [CFS] definition, will not fulfill*" the IOM's recommended diagnostic criteria. Noting the differences in inclusion and exclusion criteria between CFS and ME definitions, the IOM stated "*a diagnosis of CFS is not equivalent to a diagnosis of ME.*"

The IOM Report firmly dismissed the idea that this is a psychogenic disease. The Report also noted that the disease can result in prolonged and significant disability with impairment in ability to engage in educational, occupational, social and personal activities; that there is a considerable economic burden associated with these conditions, with many patients unable to continue in employment or in mainstream education; and that 25% of patients are bed- or house-bound during their illness and will require high levels of personal care and assistance from family or social caregivers.

2.1 2014 AHRQ Evidence Review: An evidence review was carried out by the U.S. Department of Health and Human Services' Agency for *Healthcare Research and Quality (AHRQ)* in parallel with the IOM evidence review [2]. The 2014 AHRQ review included studies using the Oxford CFS Criteria, studies often based on the biopsychosocial theory that patients' symptoms are caused by fear-avoidant decreased activity and resultant deconditioning.

The AHRQ evidence review on the *Diagnosis and Treatment of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome* was published in December 2014 and used as input by the 2015 National Institutes of Health *Pathways to Prevention (P2P) Workshop on Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome* [3].

The 2014 AHRQ review called for the Oxford CFS criteria to be retired because "*it is at high risk of including patients who may have an alternate fatiguing illness, or whose illness resolves spontaneously with time.*" The NIH P2P report concurred.

In 2016, AHRQ reanalyzed the evidence for Oxford CFS Criteria studies separately from the remaining studies and as a result, issued an addendum that downgraded previous findings once Oxford studies were excluded.

2.2 Highlights of Recent Research: In October 2016, the *International Association for CFS/ME* held its biannual conference which highlighted numerous scientific findings. As documented by Professor Anthony Komaroff of Harvard Medical School [4], presentations included studies on brain and nervous system, immunology, the microbiome, epigenetics, energy metabolism and metabolomics. Komaroff summarized that there was robust evidence of an underlying biological process involving a) the brain and autonomic nervous system, b) the immune system, c) energy metabolism, and oxidative and nitrosative stress. Given the scope of biological evidence, he concluded, "*The illness is not simply the expression of physical symptoms by people with a primary psychological disorder.*"

References:

- 1 National Academy of Medicine. *Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness*. The National Academies Press; May 2015. <https://www.nap.edu/catalog/19012/beyond-myalgic-encephalomyelitischronic-fatigue-syndrome-redefining-an-illness>

2 U.S. Agency for Healthcare Quality and Research. Research Review. Diagnosis and Treatment of Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome. Evidence Report/Technology Assessment Number 219. U.S. Agency for Healthcare Quality and Research. December 9, 2014. Addendum July, 2016. AHRQ Publication No. 15-E001-EF. <https://effectivehealthcare.ahrq.gov/ehc/products/586/2004/chronic-fatigue-report-160728.pdf>

3 Green CR, Cowan P, Elk R, O'Neil KM, Rasmussen AL. National Institutes of Health Pathways to Prevention Workshop: Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. *Ann Intern Med*. 2015. <http://annals.org/aim/article/2322804/national-institutes-health-pathways-prevention-workshop-advancing-research-myalgic-encephalomyelitis>

4 Komaroff A. 12th International IACFS/ME Conference Emerging Science & Clinical Care. October 2016. <http://iacfsme.org/Conferences/2016-Fort-Lauderdale/Agenda/Dr-Komaroff-s-2016-Summary-Slides/IACFSME-Komaroff-Slides.aspx>

3. Options and considerations: As noted above, the IOM expert panel concluded that a comprehensive review of the evidence demonstrates a serious, chronic, systemic disease with dysfunction in neurological, immunological, autonomic and energy metabolism systems.

In SNOMED CT, chronic fatigue syndrome, myalgic encephalomyelitis and other associated terms are already classified under the Parent: *Multisystem disorder*.

3.1 Classification of multisystem diseases within ICD-11: Previous editions of ICD have organized diseases into chapters based on aetiology or affected organ or body system. The architecture of ICD-10 does not facilitate scientific and taxonomical representation of diseases with varied manifestations that belong to or affect multiple body systems, for example, systemic lupus erythematosus (SLE) and Behçet disease, or where no single organ system predominates to guide chapter placement.

In 2010, the Revision Steering Group posted a discussion paper on the potential for incorporating within ICD-11 a new chapter for Multisystem diseases [1]. This proposal was subsequently rejected in preference to the consideration of generating a separate linearization from the Foundation, as a "virtual" multisystem chapter [2].

It is currently unclear whether ICD Revision intends to implement a multisystem linearization or whether diseases that would have been candidates for assigning to a "virtual" multisystem chapter will be represented solely through multiple parentage and the explicit listing in the content model of all body systems involved for that entity.

Regardless of how multisystem diseases will be handled in general in ICD-11, it is premature to suggest multiple chapter parentage at this time.

Noting the need for increased biological research, the director of the National Institutes of Health said in a recent article, "*ME/CFS is such a complex condition, affecting so many body systems, that we do not know where the answers will come from.*" [3].

However, given what we do now know as documented above, the authors see no justification for any proposal for secondary parenting under the *Symptoms, signs or clinical findings, not elsewhere classified* chapter or *Mental, behavioural or neurodevelopmental disorders* chapter.

References:

1 Aymé, Chalmers, Chute, Jakob (2010). ICD Revision: Discussion paper: Multisystem Disorders. <http://bit.ly/2nnilKW>

2 WHO ICD Revision Information Note 19: Multisystem Diseases Chapter in ICD, January 29, 2013.

3 Koroshetz W, Collins F. Moving Toward Answers in ME/CFS. NIH Director's Blog. March 2017. <https://directorsblog.nih.gov/2017/03/21/moving-toward-answers-in-mecfs/>

3.2 ICD-11 Joint Task Force position on precedence: General considerations for potential chapter relocations were discussed at a meeting of the Joint Task Force, in July 2016 [1]. According to the meeting Summary Report (5.2 Key discussion), a general principle was reiterated that:

"...in the absence of compelling evidence mandating a change, legacy should trump with regard to the question of moving certain conditions to new chapters...JTF members confirmed that continuity over time is desirable. Where

there is a rationale for change, the changes can be accommodated for, but there was a question about how to justify the effort required to make the changes in data reporting systems in the absence of compelling information indicating that the change makes things better or more accurate."

Although currently a disease of incompletely understood aetiopathogenesis, active research will inform decisions about potential chapter relocation or whether to assign multiple parents. For now, current scientific evidence of neurological impairment and WHO/ICD Revision's position on precedence supports retention of chronic fatigue syndrome and myalgic encephalomyelitis in *Diseases of the nervous system*.

References:

1 Fourth Meeting of the JLMMS Task Force, Queensland, Australia, 11-14 July 2016

http://www.who.int/entity/classifications/icd/revision/2016.07.11-14_iSummaryMeetingReportQueensland.pdf

3.3 Consideration of creating a sub class under: *Other disorders of the nervous system*: Until such time that further research supports the creation of, or assignment to a more specific parent class, either within *Diseases of the nervous system*, or under another chapter, or assignment to multiple parents, the recommendation is to retain chronic fatigue syndrome and myalgic encephalomyelitis as siblings under *Other disorders of the nervous system*.

3.4 Assigning unique codes for chronic fatigue syndrome (CFS) and myalgic encephalomyelitis (ME): In ICD-10, all three terms are coded or indexed to the same code. The IOM Report, the AHRQ Evidence Report, the IACFS/ME Primer for Clinical Practitioners [1] and studies on exercise testing [2] all highlight the importance of post exertional malaise (PEM) as a hallmark symptom, both clinically and in research.

As a result, the IOM specified a clinical criteria that requires PEM, a feature not required for CFS criteria. In addition, researchers internationally are increasingly using the Canadian Consensus Criteria (CCC) [3] or the ME International Consensus Criteria (ME-ICC) [4] – both of which require PEM – to progress research into disease pathology, subtypes, diagnostics, and treatments.

Notably, the IOM Report compared the CFS definitions with the CCC and the ME-ICC and as noted previously, concluded that a CFS diagnosis is not equivalent to an ME diagnosis.

Therefore, the recommendation is to place both chronic fatigue syndrome and myalgic encephalomyelitis in the same location under parent class: *Other disorders of the nervous system*, and to assign a unique code to each.

The authors would not support precedence being given to chronic fatigue syndrome as the new concept title, with myalgic encephalomyelitis as the inclusion term, synonym term, or consigned to the Index.

References:

1 ME/CFS: A Primer for Clinical Practitioners 2014.

http://iacfsme.org/portals/0/pdf/Primer_Post_2014_conference.pdf

2 Keller B, Pryor J, Giloteaux, L. Inability of myalgic encephalomyelitis/chronic fatigue syndrome patients to reproduce VO₂peak indicates functional impairment. *Journal of Translational Medicine* April 2014, 12:104. PMID: 24755065. <http://dx.doi.org/10.1186/1479-5876-12-104>

3 Carruthers BM, Jain AK, De Meirleir KL, Peterson DL, Klimas NG, Lerner AM, Bested AC, Flor-Henry P, Joshi P, Powles et al. Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Clinical Working Case Definition, Diagnostic and Treatment Protocols. *Journal of Chronic Fatigue Syndrome* 2003; 11(1): 7-117.

4 Carruthers BM, van de Sande MI, De Meirleir KL, Klimas NG, Broderick G, Mitchell T, Staines D, Powles ACP, Speight N, Vallings R et al. Myalgic Encephalomyelitis: International Consensus Criteria. *Journal of Internal Medicine* October 2011; 270(4): 327–338. [PMID: 2177306]

3.5 Consideration of the IOM Report's recommendation for a new case definition and change of nomenclature: The IOM expert panel members were charged with developing clinical diagnostic criteria and making recommendations for a new disease name. The IOM recommended that the term, "chronic fatigue syndrome" should not be used for those patients who meet the IOM's diagnostic criteria and instead, proposed that the term be replaced with "*Systemic Exertion Intolerance Disease (SEID)*."

Experts and patients have raised concerns over the suggested new name [1].

No proposals have been submitted to the U.S. Coordination and Maintenance Committee to add "*Systemic Exertion Intolerance Disease (SEID)*" to the U.S. specific ICD-10-CM. Instead, the CDC has begun to use the hybrid term "ME/CFS" [2] and intends to use that term as it implements the IOM clinical diagnostic criteria. Other agencies within the U.S. Department of Health and Human Services, including the National Institutes of Health, are already using this term and not "*SEID*" [3].

Therefore, the authors consider there is currently insufficient evidence or support for incorporating the proposed "*Systemic Exertion Intolerance Disease (SEID)*" definition into ICD-11, either as a replacement for one or more of the G93.3 legacy terms or for insertion as an inclusion term, synonym term or index term.

References:

1 Jason LA, Sunnquist M, Brown A, McManimen S, & Furst J. (2015). Reflections on the Institute of Medicine's systemic exertion intolerance disease. *Polskie Archiwum Medycyny Wewnętrznej*. 125(7-8), 576–581. [PMID: 26176405]

2 Unger E, Lin J, Brimmer D, Lapp C, Komaroff A, Nath A, Laird S, Iskander J. CDC Grand Rounds: Chronic Fatigue Syndrome — Advancing Research and Clinical Education. *MMWR Morb Mortal Wkly Rep* 2016. <http://dx.doi.org/10.15585/mmwr.mm655051a4>

3 A Report from the Federal Partners Meeting of the National Institutes of Health Pathways to Prevention Workshop: Advancing the Research on Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). May 2016. <https://prevention.nih.gov/docs/programs/p2p/mecfs-federal-partners-report.pdf>

4. Definitions: There are 20 or more CFS and ME definitions, which have been conflated into a single evidence base, with evidence from one definition being assumed to apply to patients meeting any definition [1][2].

PDF: An overview of definitions used for Myalgic Encephalomyelitis and Chronic fatigue syndrome
<http://bit.ly/2niiKfu>

Yet, as noted in published research and by U.S. government reports published in 2015-2016, these definitions have significant differences in inclusion and exclusion criteria [2][3][4].

The CFS definitions all require medically unexplained chronic fatigue lasting 6 or more months and either do not require other symptoms or else require one additional or any combination of 4 of 8 common symptoms. As a result, the CFS definitions do not require symptoms recognized by the IOM Report as hallmark symptoms for this disease while allowing the inclusion of primary psychological illness.

The 1991 Oxford definition has most often been used in studies based on a psychogenic disease model. The 1994 Fukuda definition has more often been used for biomedical research. As noted above, U.S. government reports stated that the Oxford CFS definition included patients with other fatiguing illnesses and noted that not all Fukuda CFS patients will meet the IOM's new clinical diagnostic criteria.

The ME definitions (the 2003 Canadian Consensus Criteria (CCC) uses the hybrid term ME/CFS) and the 2011 ME International Consensus Criteria (ME-ICC) both require hallmark symptoms of the disease such as PEM, sleep dysfunction and neurological/cognitive manifestations and also highlight immunological impairment [3].

Expert clinicians use the CCC in clinical practice; researchers have increasingly used the CCC or the ME-ICC in published research, and the U.S. National Institutes of Health is using the CCC in its current intramural study.

The Institute of Medicine (now the "The National Academy of Medicine") has published new clinical diagnostic criteria, which are based on the Canadian Consensus Review and also require hallmark symptoms such as PEM. The IOM clinical diagnostic criteria have not been officially implemented in U.S. clinical practice and are not in use in other countries.

At this time, there is no single CFS or ME definition that is used worldwide. However, it is possible to describe the core features specified in the CFS and ME definitions.

Definitions

CFS and ME have been historically treated as synonymous but the case definitions encompass different populations.

CFS Definition Features: According to commonly used CFS definitions, CFS is medically unexplained chronic fatigue that is disabling and lasts six months or more for adults, (3-4 months for pediatric). No other symptoms are specifically required, although some CFS definitions do require an optional combination of other common symptoms. CFS is most often described as fatigue that does not get better with bedrest.

ME Definition Features: According to commonly used ME definitions, ME is a *serious, chronic, complex, and multisystem disease* that causes neurological, cognitive, immunological, autonomic, and energy metabolism impairment. It is characterized by the hallmark post-exertional malaise in which even small amounts of physical and mental exertion causes an often-delayed exacerbation of all symptoms that can last for days, weeks or even months. Onset can follow an infectious trigger, which is often but not always viral.

References:

1 Brurberg K, Fønhus A, Larun L, Flottorp S, Malterud K. Case definitions for chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a systematic review. *BMJ Open*. February 7, 2014; 4(2): e003973. <http://dx.doi.org/10.1136/bmjopen-2013-003973>

2 Jason LA, So S, Evans M, Brown A, Sunnquist M, Im Y, Schafer C. An overview of operationalizing criteria for ME, ME/CFS, and CFS case definitions. *Prev Interv Community*. 2015;43(1):1-4. [PMID: 25584523]

3 National Academy of Medicine. Beyond Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Redefining an Illness. *The National Academies Press*; May 2015. <https://www.nap.edu/catalog/19012/beyond-myalgic-encephalomyelitischronic-fatigue-syndrome-redefining-an-illness>

4 U.S. Agency for Healthcare Quality and Research. Research Review. Diagnosis and Treatment of Myalgic Encephalomyelitis/ Chronic Fatigue Syndrome. Evidence Report/Technology Assessment Number 219. U.S. Agency for Healthcare Quality and Research. December 9, 2014. Addendum July, 2016. AHRQ Publication No. 15-E001-EF. <https://effectivehealthcare.ahrq.gov/ehc/products/586/2004/chronic-fatigue-report-160728.pdf>

5 Overview of more commonly used myalgic encephalomyelitis and chronic fatigue syndrome definitions. <http://bit.ly/2niiKfu>

[Ends]

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You can include references to papers, reports etc in support of your comments but you won't be able to upload files – and it's a plain text field only.

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If you have any queries about submitting comments please contact one of us below, and we'll do our best to get back to you quickly.

Mary Dimmock: medimmock@gmail.com

Suzy Chapman: dxrevisionwatch@page1.myzen.co.uk

A copy of this proposal can also be read in this post on *Dx Revision Watch*: <http://wp.me/pKrrB-4dV>