Tom Kindlon's Written Testimony: CFSAC Meeting October 2009

My name is Tom Kindlon. I have had CFS (or ME or ME/CFS, the terms I prefer) for over 20 years, having previously been healthy (I used to play various sports competitively). Unfortunately it took me over 5 years to get diagnosed. By the time I was diagnosed I was virtually bedbound and I have only improved a small bit since then i.e. I have been housebound with CFS for over 15 years.

I have been on the committee of the Irish ME/CFS Association (formerly the Irish ME/CFS Support Group) since 1996 and have been Assistant Chairperson since 1997. I have been active in the ME community internationally in various ways.

I believe I have a lot of useful knowledge and experience in the area. In the last twelve months, I have had three letters on the subject of CFS published in four peer-reviewed journals (British Medical Journal, Brain (a neurology journal), Bulletin of the IACFS/ME and Pain Medicine) and have two more "in press" (Psychological Medicine and Journal of Rehabilitation Medicine (this one was co-written with Ellen Goudsmit PhD)).

I want to make three points in my testimony:

1) I am very concerned about the "empirical" definition (Reeves, 2005) the CDC has adopted for CFS research in recent years

2) I think the CDC CFS program should have to cut its ties with Peter White, according to its own rules regarding external reviewers

3) There is potential that the individuals who the CDC invites to its upcoming workshops may not be representative of the spectrum of opinion amongst experts in the field, based on the make up of, for example, some International CFS Study Groups previously. I think other bodies such as the CFSAC should get to nominate people for these committees.

1) I am very concerned about the "empirical" definition (Reeves, 2005) the CDC has adopted for CFS research in recent years

I set up a petition on the issue on the 15th of April, 2009. This petition is summarized in 10 words as,

"CDC CFS Research should not involve the empirical definition (2005)"

http://www.ipetitions.com/petition/empirical_defn_and_CFS_research/index.html

The petition

We call on the Centers for Disease Control and Prevention (CDC) to stop using the "empirical" definition[1] (also known as the Reeves 2005 definition) to define Chronic Fatigue Syndrome (CFS) patients in CFS research.

The CDC claim it is simply a way of operationalizing the Fukuda (1994) definition[2]. However the prevalence rates suggest otherwise: the "empirical" definition gives a prevalence rate of 2.54% of the adult population[3] compared to 0.235% (95% confidence interval, 0.142%-0.327%) and 0.422% (95% confidence interval, 0.29%-0.56%) when the Fukuda definition was used in previous population studies in the US[4,5].

The definition lacks specificity. For example, one research study[6] found that 38% of those with a diagnosis of a Major Depressive Disorder were misclassified as having CFS using the empirical/Reeves definition.

References:

[1] Reeves WC, Wagner D, Nisenbaum R, Jones JF, Gurbaxani B, Solomon L, Papanicolaou DA, Unger ER, Vernon SD, Heim C. Chronic fatigue syndrome--a clinically empirical approach to its definition and study. BMC Med. 2005 Dec 15;3:19. Link: http://www.biomedcentral.com/1741-7015/3/19

[2] Fukuda K, Straus SE, Hickie I, Sharpe MC, Dobbins JG, Komaroff A. The chronic fatigue syndrome; a comprehensive approach to its definition and study. Ann Int Med 1994, 121:953-959.

[3] Reeves WC, Jones JF, Maloney E, Heim C, Hoaglin DC, Boneva RS, Morrissey M, Devlin R. Prevalence of chronic fatigue syndrome in metropolitan, urban, and rural Georgia. Popul Health Metr. 2007 Jun 8;5:5.

[4] Reyes M, Nisenbaum R, Hoaglin DC, Unger ER, Emmons C, Randall B, Stewart JA, Abbey S, Jones JF, Gantz N, Minden S, Reeves WC: Prevalence and incidence of chronic fatigue syndrome in Wichita, Kansas. Arch Int Med 2003, 163:1530-1536.

[5] Jason LA, Richman JA, Rademaker AW, Jordan KM, Plioplys AV, Taylor RR, McCready W, Huang CF, Plioplys S. A community-based study of chronic fatigue syndrome. Arch Intern Med. 1999 Oct 11;159(18):2129-37.

[6] Jason, LA, Najar N, Porter N, Reh C. Evaluating the Centers for Disease Control's empirical chronic fatigue syndrome case definition. Journal of Disability Policy Studies 2008, doi:10.1177/1044207308325995.

Further reading: Leonard Jason, Ph.D., DePaul University. Problems with the New CDC CFS Prevalence Estimates tinyurl.com/2qdgu4 i.e. http://www.iacfsme.org/IssueswithCDCEmpiricalCaseDefinitionandPrev/tabid/105/Default.aspx

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I'm the first to admit that this isn't exactly the "catchiest" petition that has ever been created. One might think it would be lucky to get a few dozen responses.

However already, **1641 people have signed** (at the time of writing). Many have left comments which can be read on the site:
http://www.ipetitions.com/petition/empirical_defn_and_CFS_research/index.html
[Aside: other people have also left comments but for some reasons the comments have not gone up].

I believe this shows the depth of feeling there is on this issue.

As I said in my last submission, if one looks at the CFSAC function, it is clear that the issues relating to the definition are fairly central.

I listed numerous problems regarding the definition in my submission to the May 2009 CFSAC meeting (http://www.hhs.gov/advcomcfs/meetings/presentations/kindlon_0509.pdf) so I'm not going to repeat them now.

I do not believe that Dr Bill Reeves adequately dealt with the concerns about the Reeves 2005 criteria in the last meeting. He said that the difference between the prevalence rates they found in Georgia (2540 per 100,000) compared to previous estimates (235 and 422 per 100,000) were down to two issues:
- the different methodology in the Georgia where they brought in people who did not complain of fatigue on the telephone screening. He said that "20-30 percent of people who did not complain about fatigue endorsed the Fukuda criteria." However, the paper for which he is the corresponding author actually gives a lower figure of 11.5% ["*In other words, 11.5% of subjects with CFS would not have been detected in previous studies that queried participants only for fatigue"].* It should also be remembered that some of these people might not have satisfied the criteria for Fukuda as it is normally applied – the Reeves criteria make it easier to satisfy the criteria. So the real figure could well be less than 11.5%. But even if one takes the figure of 11.5%, that would only bring the figures of 235 and 422 per 100,000 up to 266 and 479 per 100,000 which are still dwarfed by the 2540 per 100,000 prevalence rate from the Reeves criteria (2005).

- The other point he starts talking about in this section is criteria regarding major depressive disorder so he may have been trying to make a point with regard to this. Personally I agree with him and see this as an important area also! First a quick aside: there are various forms of depression e.g. dysthymia, atypical depression, etc. In the past, apart from bipolar, the main one excluded was MDDm (melancholic Major Depressive Disorder), a severe type of depression. Many people still had depression but were included as they satisfied the criteria.

With the Reeves (2005) criteria, it says: *"Following recommendations of the International CFS Study Group, only current MDDm was considered exclusionary for CFS."* However, part of the specific recommendations of the International CFS Study Group [1] that (Reeves claims his definition is based on) was that MDDm had to have been resolved for more than 5 years:
"The 1994 case definition stated that any past or current diagnosis of major depressive disorder with psychotic or melancholic features, anorexia nervosa, or bulimia permanently excluded a subject from the classification of CFS ... we now recommend that if these conditions have been resolved for more than 5 years before the onset of the current chronically fatiguing illness, they should not be considered exclusionary."

It might not be important to point this out for definitions for some illnesses: however if one looks at table 2 of the 2005 paper, 6 of the 16 who are said to have CFS using the "current classification" of CFS, had been diagnosed with MDDm at a previous assessment which suggests it is important in this context.

Also Leonard Jason published a study which found that 38% of those who have Major Depressive Disorder but not CFS would satisfy the symptom, fatigue, etc criteria in the Reeves definition.

Also the Nater et al. (2009) study found that 57% had current psychiatric disorders and 89% had lifetime psychiatric disorders, suggesting the definition is picking up a group with a lot of psychopathology.

[Aside: A lot of people have made suggestions to me speculating why the CDC broadened the criteria in the way they have done. I do not know the answer. The most plausible theory to me is the following: The CDC followed patients in the community in 1997, 1998, 1999 and 2000. Between December 2002 and July 2003, they were brought in for intensive testing. In total, 227 people were invited in, including 70 who had previously been diagnosed with CFS. These people went through very expensive testing – the whole exercise cost $2m. However, unfortunately, only 6 out of the 70 cases of CFS satisfied the Fukuda definition when they were brought in. Also 4 more of the other individuals also satisfied the definition. If one only excludes people who currently have Melancholic Major Depressive Disorder (MDDm) (which was not the recommendation of the International CFS Study group), one can get the numbers who satisfy the Fukuda definition up to 16. The CDC admit this in their paper (Reeves, 2005). However 10 (or 16 if one allows all the MDDm cases) people with CFS would not be enough for the CDC to publish CFS studies with a lot of the data they have. For some of the experiments, people would not have been suitable for one reason or another e.g. they were on medication. Also, often data is not complete or tests become corrupted so a percentage is lost. For some of the experiments, gender might make a difference and one may end up excluding the men as there might not be enough patients. So 10 or 16 CFS patients is not enough to publish CFS papers using this data. But $2m of the CFS fund had been spent on this experiment and it might look like a waste of taxpayers' money if papers were not published. The CDC had already gotten into trouble for misusing the CFS budget in the past. So the definition of CFS was expanded so that CFS papers could be published. So that's one plausible theory although one does not need to accept that to believe that the empirical definition is flawed].

Even if for some reason, the CFSAC do not want to recommend against the definition, it would be good if you pressed the CDC to make clear in each and every paper they write that they use the empirical criteria, that they were used. The reference for the empirical criteria is often not being put in the list of references. I know the patients were selected using the empirical criteria because they are part of the 2-day Wichita study cohort or from the Georgia study but most people reading the papers will not know this.

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2) I think the CDC CFS program should have to cut its ties with Peter White, according to its own rules regarding external reviewers

At the May 2008 CFSAC meeting, the following information was given on the CDC External Peer Review of CFS Program http://www.hhs.gov/advcomcfs/meetings/minutes/cfsac080505min_pdf.pdf

"CDC plans to conduct an external peer-review of the CFS program in late summer/early fall 2008. This review will be conducted by a panel composed of national and international experts that is to include representatives from the Coordinating Center for Infectious Diseases Board of Scientific Counselors and CFSAC. CDC is requesting that CFSAC members recommend names of experts with no conflict of interest (direct funding from CDC)"

and

Dr. Miller:

*"The panel will be external experts in the field who have no conflict of interest-they are not receiving CDC funding and ***would not have a direct impact on the program in its development in stages other than the recommendations.***"*

One of the external review panel (which was small – only 4 people wrote the report), was Dr Peter White. At the May 2008 CFSAC meeting, Dr Bill Reeves said: *"We talk to Dr. White fairly regularly."*

It is unclear who nominated Dr. White to the panel of external reviewers – perhaps the CFSAC could ask this. It was not the CFSAC as the minutes show. Dr. Reeves talked as if they might have suggested Dr. White be involved because he was an *"expert on autonomic nervous system function."* (which is a curious statement to make given Dr White is a psychiatrist, whose PubMed-listed articles do not suggest he is an expert in this field).

Anyway, the external review panel made the following recommendations:

"The panelists recommend that the CDC program urgently consider intervention studies to help to elucidate the direction of causality in the several pathophysiologies identified by the CDC. This strategy was not articulated clearly. For example, since both cognitive behavior therapy and graded exercise therapies are known to address some of the

abnormalities found, and since both these therapies have been shown to be efficacious for CFS, these behavioral interventions should be seriously considered. Collaborations with providers and medical schools practised in randomised controlled trials might provide the best means to achieve this."

A summary of strategic recommendations
[..]
5. Clinical guidelines on management should be developed for use in the USA, by the CDC team in collaboration with others, and disseminated for CFS.

6. The team needs to consider studies that test the direction of causality of pathophysiology, such as using interventions."

At the May 2009 meeting, Dr Reeves said:
""Peter White, the psychiatrist that we work with at Emory,"

*"We are in the process of planning a cognitive behavioral therapy (CBT) and graded exercise (GET) trial as part of the provider registry population in Macon. We're going to do that in collaboration with the providers in Macon, with Mercer Medical School, ***with the U.K. group***, and with Mayo Clinic."*

- "International Workshop - Research, Clinical, and Pediatric Definitions of CFS - I would like to try to get together by the winter of 2009. I know the IACFS/ME is interested in this. We want to include countries such as UK that have CFS care completely integrated into their healthcare system."

- "Dr. Reeves: An excellent comment. Our focus is obviously on the United States. There are three important reasons for international collaboration. One of them I alluded to. There are countries that have put CFS evaluation, diagnosis, and management into their national health systems. The UK is one of those. An international meeting provides the chance to learn from another government that has embraced this illness- perhaps not to the extent that everybody would like-but is trying to work with it as a national health service."

Given that the only representative from the UK that the CDC has invited to its CFS meetings since around 2001/2002 is Peter White, it looks very likely that they have him in mind for both of these workshops. Also it looks like he is involved in their Emory research and may be involved in the CBT/GET. Both for the CDC's reputation and Dr White's, it would be better if the CDC cuts its ties with him given he took part in the external peer-review.

3) There is potential that the individuals who the CDC invites to its upcoming workshops may not be representative of the spectrum of opinion amongst experts in the field, based on the make up of, for example, some International CFS Study Groups previously. I think other bodies such as the CFSAC should get to nominate people for these committees.

The CDC are planning to have three workshops on CFS (according to their draft plans):

- International Workshop - Clinical Management of CFS
- International Workshop - CFS Case Definition
- Workshop International - CFS Study Group (Research priorities)

However, it should be remembered that, for example, what is considered good management of CFS is a highly disputed area. Many professionals believe that Graded Exercise Therapy (GET) and Cognitive Behavioural Therapy (CBT) based on GET are basically all that patients need. Symptoms are seen as largely due to deconditioning and maladaptive beliefs and behaviours rather than an ongoing disease process. I will call these the people of the "CBT School of Thought."

A few professionals go further and claim that GET and CBT based on GET can lead to full recovery. This is a small group but it includes Peter White (mentioned above) and the psychologist, Gijs Bleijenberg PhD from the Netherlands. Both of these professionals, who many would consider to have extreme views, have been the sole representatives from their countries at workshops the CDC have organised on the illness (see for example http://www.cdc.gov/cfs/cfsmeetingsHCP.htm).

The CDC was involved in a paper this year, *"Are chronic fatigue and chronic fatigue syndrome valid clinical entities across countries and healthcare settings?"* by Hickie I, Davenport T, Vernon SD, Nisenbaum R, Reeves WC, Hadzi-Pavlovic D, Lloyd A and International Chronic Fatigue Syndrome Study Group (28 collaborators). Of the 35 individuals involved, apart from the CDC team members, virtually all could be said to be of the CBT School of Thought with regard to CFS.

However, a meta-analysis (Malouff et al., 2008) found that the average Cohen's d effect size for Cognitive Behavioural Interventions (include GET) was 0.48 which does not reach the threshold of 0.5 for something to have a moderate effect! Leonard Jason published a large NIH-funded study in 2007 which found that an intervention based around encouraging patients to pace activities did better than interventions that assessed CBT or exercise programmes. Prof. Jason subsequently published a paper which found that within this trial, "Those who were able to stay within their energy envelope had significant improvements in physical functioning and fatigue severity."

Is the CDC going to ensure that there are a reasonable numbers of individuals at these workshops who believe that pacing is a good management strategy for CFS? Some/many in the CBT School of Thought are against pacing and will not recommend it. Are the CDC going to ensure there will be proponents of Energy Envelope Theory at these workshops? Also I don't think one person is sufficient given group dynamics.

An even more important issue is the high rate of adverse reactions reported by people with CFS who have done exercise programmes (and CBT based on exercise programmes). Unlike drugs, generally there is no easy way for professionals or individual patients with CFS to report adverse reactions to non-pharmacological interventions such as GET. So formal data is not systematically collected by statutory agencies in countries around the world. Surveys on the issue are the next best source of information it would seem. I sent information on 10 such surveys to the CDC in my submission on their draft plans – see http://tinyurl.com/adversereactionsinCFS , i.e. http://sacfs.asn.au/download/Tom%20Kindlon's%20Submissio%20on%20CDC%20Draft%205-year%20Strategic%20Plan%20for%20CFS%20-%20June%202009.pdf

These are surveys from various countries (the UK, US, the Netherlands and Norway) and show the high rates of adverse reactions that are reported. The latest survey was from the UK, by the ME Association: 906 replies: Made much worse: 33.1% (300 individuals), Slightly worse: 23.4%, No change: 21.4%. Improved: 18.7% and Greatly improved: 3.4%. These represent very high rates of adverse reactions. If a drug made 33.1% "much worse", it would probably be taken off the market until they worked out if there were certain groups of patients for whom it was, and was not, appropriate. Dosages might be changed.

Some proponents of GET for CFS claim that it is simply because the GET was not done under a suitable professional. However, in the UK, where CFS clinics have been set up around the country, this was investigated in a survey by AYME/AfME (May 2008). They asked about experiences of GET in the three previous years. This was after the specialist services had been set up. There was no statistical difference between the rate of adverse reactions in those who did GET under an "NHS specialist" and the people who did GET under other individuals or by themselves.

Even if it was the case that GET is only unsafe when not done under an appropriate professional, GET is available "over the counter" so if guidelines from the CDC and others recommend it, many patients will try this treatment.

Many proponents of GET and CBT based on GET do not impart information on the high rates of adverse reactions to either the patients themselves or even other professionals when they are educating them about the interventions. Some use the "catch phrase" that they are "safe and effective." The CFSAC should insist that any guidelines should give information on adverse reactions either with specific information or simply generally points about the high rates of adverse reactions that have been reported.

Perhaps the CFSAC (and indeed other groups) could have a role in recommending names for these workshops to ensure these workshops are balanced e.g. the CFSAC get to recommend 25% of the groups, the IACFS/ME another 25%, a patient group such as the CAA 10% and the CDC 40%. (Groups could give alternates if some of their picks were already used).

Suggestions for professionals from the UK who I would think would give balance to any workshops are: (i) Charles Shepherd MD charles.c.shepherd@btinternet.com; (ii) Ellen Goudsmit C.Psychol. PhD FBPsS (Health Psychologist and Visiting Research Fellow, University of East London) ellengoudsmit@hotmail.com; (iii) Abhijit Chaudhuri DM MD PhD FACP FRCP (a consultant neurologist) chaudhuria@gmail.com; (iv) Neil Abbot MSc PhD (Operations Director, ME Research UK) Neil.Abbot@pkavs.org.uk and (v) William Weir MD (an infectious disease consultant who ran an NHS clinic for ME for a number of years) wrcweir@hotmail.com. All of these five professionals have published in the area and been in the area for over 10 years – Dr William Weir is in the area for approximately 20 years and Drs Shepherd and Goudsmit for over 20 years. Drs Chaudhuri and Goudsmit did their PhDs in the area.