

Severely Overlooked by Science

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An Overview of Research on Severely-ill People with M.E.

By

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Severely ill are severely overlooked; just ignored and invisible” (CMO report 2002, Section 2.3.1)

Ignored and invisible! When the authors of the Chief Medical Officer's report of 2002 coined that phrase they were referring to the exclusion of the most severely ill people with M.E. from community and social care provision. However, the same description also holds true for mainstream scientific research.

A cursory glance at the existing scientific literature on M.E. (largely held in electronic databases, mainly MEDLINE, and specialist resources like the downloadable database of some 3000 abstracts at the MERGE website:

<http://www.mereseearch.org.uk/melibrary/publications/researchdatabase/index.html> reveals the virtual absence of information on the most severely affected people.

"M.E. is a Cinderella illness compared with other comparable chronic conditions"

The Table gives the number of articles (loosely defined) published for some randomly-chosen illnesses, and it shows two things. First, that M.E. is a Cinderella illness compared with other comparable chronic conditions in terms of volume of research publications; and second, that research on the severely ill is a rarity in most illnesses, including M.E..

Table. Number of MEDLINE entries to May 2004 for a range of illnesses including ME/CFS. The percentage of these relating to severe illness (variously defined) is also shown. These crude ballpark figures illustrate well enough the paucity of research into ME/CFS, and on severely ill people in particular.

Illness	Total number of articles	Estimated number of "clinical trials"	Estimated trials on the severely ill (as % of total)
Diabetes	221828	10236	0.27%
Rheumatoid arthritis	78589	4351	0.38%
Multiple sclerosis	29032	1426	0.32%
Low back pain	9649	969	0.57%
Irritable bowel syndrome	2978	519	0.47%
ME/CFS	2841	146	0.49%*

* In practice, very few these studies deal *specifically* with the most severely ill people with ME/CFS (i.e., the housebound, bedbound or immobile).

The point is that severely affected people with M.E. are *doubly* disadvantaged: not only is this illness under-researched compared with other chronic conditions, but the most severely ill group of patients is under represented in what little research is done. In fact, very few studies exist, and all define “severe illness” in different ways, complicating interpretation of the findings. And specific laboratory-based or experimental studies on severe sufferers are as rare as hen’s teeth.

"Experimental studies on severe sufferers are as rare as hen’s teeth"

The findings so far...

For the record, the studies in question that present some kind of patient data (albeit with varying definitions of "severe" illness) include: </

a) *Effect of specialist hospital programmes* – The CFS team at Oldchurch Hospital in Essex surveyed the 72 most severely affected CFS patients admitted 1990–98. They found that 46% had actually been discharged with an alternative diagnosis to CFS, that patients with a symptom duration greater than five years appeared to improve, and that the level of severity did not preclude improvement (Cox and Findlay, 2000). In a subsequent quasi-experimental study, this team found that their occupational therapy intervention significantly improved perception of health and ‘length of time tired’ in patients compared to waiting list control patients (Cox, 2002).

"46% had actually been discharged with an alternative diagnosis to CFS"

The Oldchurch team have continued to audit the outcomes of their work, and the most recent of these (December 2003) examines 24 severely affected patients following an inpatient stay. While two-thirds saw their severity rating improve by one or two grades on a scale of one to five, a third saw no change in their level of severity. However, 50% reported a positive shift in mood and 87% described an increase in their quality of life, post-admission. Using a patient feedback questionnaire, 39% rated their satisfaction with the CFS service as 10/10, with just 4% giving a score of less than five.

Two similar, smaller outcome studies (Chalder et al, 1996; and Essame et al, 1998) also reported appropriate multidisciplinary inpatient rehabilitation to be beneficial, at least in terms of ‘functional ability’, to the majority of severely affected patients. (Five out of six patients ‘functionally improved’ in the Chalder study and 17 out of the 19 followed up in the Essame study).

b) **An experimental study of cardiac output.** (Peckerman et al, 2003). Researchers examining 38 patients found that participants with 'severe' CFS had significantly lower cardiac output than the controls and less ill patients. Post-exertional fatigue and flu-like symptoms of infection clearly differentiated the patients with severe CFS from those with a less severe presentation, and were predictive of lower cardiac output. These results, say the researchers, "provide a preliminary indication of reduced circulation in patients with severe CFS".

c) **Investigating longer-term outcomes.** One study has evaluated the natural history of CFS in a severely ill group of 24 patients at three points in time (Hill et al, 1999). Over the four years of the study, thirteen patients remained severely ill, nine improved but still fulfilled the 1994 case definition for CFS, and one recovered. Illness duration, mode of onset, psychiatric status/depressed mood at intake, or chemical sensitivity did not appear to predict illness outcome. Not surprisingly, mood improved for those patients whose illness lessened. The researchers concluded that the prognosis for full recovery was extremely poor for the most severely ill subset of CFS patients.

Another outcome study of severely affected children (Rangel et al, 2000) followed up 25 children using child-parent interviews. After nearly four years, two-thirds of the children had recovered, and none had developed any other medical conditions, allowing tentative conclusions that severe illness can cause severe handicap but that most children recover.

In addition, one report has detailed outcomes for two wheelchair-bound CFS patients treated by a "pragmatic intervention" consisting of more than 50 face-to-face or telephone contacts with a therapist over approximately two years. By the end of the intervention, both patients were reported to be free of their wheelchairs and leading "relatively independent existences" (Powell et al, 1999). And two reports have also been published giving results from the Case History Research on Myalgic Encephalomyelitis (CHROME) database (Gibbons et al, 1996 and 1998).

Why is there so little research?

The CMO report defined the severely affected as those *"patients whose physical disability is most severe, leading to serious restrictions in mobility and functioning. In many, these restrictions are accompanied by other markers of severity, such as cognitive impairment or prolonged course"* (Section 3.4.3). Clearly, anyone who is severely affected would struggle to attend hospital-based investigations, which often require multiple visits.

However, even if they could attend, they might well be excluded for other reasons, such as the presence of "co-morbid" illnesses which often accompany severe M.E. and its consequences (e.g., long term immobility with accompanying de-conditioning, susceptibility to infection, etc.), or their inability to fulfill the requirements of a trial (e.g., perform graded exercise or stop current medications). Sensible though these restrictions might seem to healthy young researchers, they are little comfort to severely ill people who wish to see scientific progress within their own lifetime! Of course, it is feasible to conduct a "pragmatic" study in which a "treatment" is given to a large group of diverse patients in their own homes, and one of these – the FINE trial – has just begun.

The FINE Trial - thanks a £million?

Heralded as offering a "promising new treatment" for people with severe M.E., the FINE (Fatigue Intervention by Nurses Evaluation) Trial is presently recruiting staff and will report its conclusions in 2008 or even later. Costing £1,147,000, the trial is funded by the UK's Medical Research Council with a grant to Dr Alison Wearden, a psychologist based in the Department of Psychology, University of Manchester, and colleagues in Liverpool (Department of Psychiatry) and Manchester (Dept of Psychiatry). In the preliminary supporting documentation, the FINE Trial is described as a "randomised controlled trial of nurse-led, self-help treatment for patients in primary care....Referred patients will be randomly allocated to one of three treatment groups (a) nurse-led self-help; (b) supportive listening; or (c) GP treatment as usual"Patients will be visited in their own homes, and before "treatment" commences qualitative interviews will be conducted to explore, "patient views on illness causation, beliefs about chronic fatigue, expectations of intervention, and previous experience of treatment and doctor-patient relationships". At the same time, the patients' GPs will be asked about their experiences of and attitudes towards patients with M.E. After 20 weeks of "treatment" patients will be assessed for a variety of outcomes, and again after one year.

"Pragmatic rehabilitation challenges dysfunctional illness beliefs"

What is the "promising new treatment" on offer to the severely-ill patients? Called, "nurse-led self-help" or "pragmatic rehabilitation", the approach "is designed to increase activity and challenge dysfunctional illness beliefs" (Powell et al 1999), and includes elements of the cognitive behavioural and graded exercise therapy championed by those psychiatrists and psychologists who promote the "biopsychosocial" model of M.E. The basis of this model is that "once an illness has started, its expression is affected by beliefs, coping styles, and behaviours, while consequential physiological and psychological effects act in some ways to maintain and/or modify the disease process" (CMO Report 2002). Pragmatic rehabilitation, we are told, will help patients to understand their symptoms and, jointly with the nurse, agree a programme of rehabilitation. In support of its usefulness for the most severely ill patients, a single report in the scientific literature (Powell et al 1999) describes two wheelchair-bound patients who had dramatic improvements in health following the pragmatic rehabilitation regimen now being rolled out to larger groups of patients as a full-scale MRC-funded trial.

This treatment is not new and hardly promising on the basis of two case reports. But will some people benefit and report improvement of a sort? Well, probably – given that the quality of life of us all (well or unwell) can be improved by changing some of our beliefs and coping behaviour, and increasing our activity levels. But as the authors of the new Canadian definition of CFS/ME make clear, the question is whether such treatments (generally recognised not to be a cure for patients' physical illnesses or suitable for everyone with M.E.) add anything to what is available in the general medical setting, and hence whether the taxpayer-spend of £1,147,000 (including £411,000 in NHS costs, very useful for oiling the

wheels of academic departments) is value for money. And furthermore, there are considerable doubts about whether the trial will address the central problem of M.E.

"Nurses steeped in the biopsychosocial culture of their paymasters?"

For instance, will each severely-ill person on the FINE Trial be given a comprehensive medical assessment to identify somatic (physical) symptoms and signs? Autonomic disturbances, seizures, frank muscle weakness, neuroendocrine disturbances (like sweating episodes), recurrent flu-like symptoms – will they be recorded over the 70 weeks? Symptoms like musculoskeletal pain, neurocognitive problems and sleep dysfunction – will they be comprehensively assessed? Will patients receive treatment for any of these? Or will these signs and symptoms of M.E. be ignored while the patient's beliefs are explored by nurses steeped in the biopsychosocial culture of their paymasters? Because the full protocol for this trial has not been made publicly available, despite being publicly funded, it is impossible to know....

But one thing we do know. The FINE trial is recorded under the "Mental Health in Primary Care" programme in the National Research Register 2004. And there's the rub. Given the expanding core of evidence for a biological pathology for this illness (see article at <http://www.mererearch.org.uk/melibrary/publications/advances.html>), it is widely felt by patients, support groups, and their political representatives that scarce research funding would be better targeted at biomedical investigation and treatment of the physical basis of M.E.

A scandalous situation overall

In truth, there is overall a serious mismatch between published biomedical research and the extent of the human problem. While we know very little about the incidence and prevalence of M.E. generally, the proportion of patients with severe illness has been variously estimated at 25% (hence, the "25% ME Group for Severe Sufferers"), one third who experience "a severe and debilitating downhill course" (Dr Melvin Ramsay), and 34% as reported by Action for ME's Members Survey of November 2000. This evidence, conjoined with findings from the CMO's report that "a minority...remain permanently, severely disabled and dependent on others .." illustrates the scale of the problem that still needs to be addressed.

"There is a serious mismatch between published biomedical research and the extent of the human problem"

To put it bluntly, if 30% of M.E. patients in the UK are severely affected at any one time, this means that between 36,000 and 72,000 people are severely ill. For such numbers to be so under-investigated by scientists, albeit for practical reasons, is surely scandalous – yet this is the situation. The CMO's Report concludes that: "Current provision of services falls well below what is needed for the vast majority of severely and very severely affected patients" (Section 3.4.3.1).

"For such numbers to be so under-investigated by scientists...is surely scandalous"

Stabbing in the dark

It's sobering to consider that in 2004 we still understand very little about the origin and outcome of severe illness in M.E.. Yes, we know that severe illness (and the other medical conditions that accompany it) complicates matters. We know that the prospects for recovery > tend to be worse for those most severely affected, whether adults or children; and that specific viral triggers, duration of illness and socioeconomic status have all been associated with the severity of the clinical picture. Most importantly, we know that the cumulative impact of severe illness over many years, where there is no sense of improvement, is profound.

Yet, even these rather unsurprising findings are based on a relatively small number of investigations, and as such cannot be called definitive. The truth is that after some stabbing in the dark, the complexity, severity, and longevity of the illness are still only dimly perceived. The most meaningful information often comes from the dedicated efforts of specialist groups that have collected data on their severely ill members or clients (see table below).

Sources of community-based information on severely affected M.E. patients

Organisation	Most recent	Example areas of concern raised by reports
25% M.E. Group for Severe Sufferers	Severely affected analysis report, March 2004	<ul style="list-style-type: none"> · community care provision either non-existent or inadequate · Most patients unable to attend GP, yet minority get GP home visit · Unhelpful psychological strategies, e.g., cognitive behavioural therapy (93% unhelpful) and psychotherapy (90% unhelpful) · Worsening of condition with graded exercise therapy (tried by 39% of members, and 82% made worse by it). · More than half waited longer than two years for formal diagnosis
Action for M.E.	Report: <i>Severely Neglected: M.E. in the UK</i> , March 2001	<ul style="list-style-type: none"> · 41% reported having been bedridden now or in the past · More than half reported to have felt suicidal because of their illness (especially those with severe pain and late diagnosis) · 80% suffered severe pain as a result of their illness

		15% had more than one close family member who had also had M.E.
Case History Research on Myalgic Encephalomyelitis (CHROME)	Database providing ongoing monitoring and progress of adults and children severely affected by M.E. via regular questionnaires	

Soft data and hard experience

Clearly, community-based surveys can be very useful for describing the experiences of people with severe M.E., and might be important for hypothesis generation, i.e., they may uncover areas of concern (such as the lack of community care provision), and highlight areas where new research is needed (such as the urgent need for pain relief). In short, they can provide a systematic record of individual suffering, and point to ways to alleviate it.

However, there is a very real problem about the meaning of survey data generally to medical/scientific professionals outside of M.E. patient circles. Strange as it may seem, surveys come low (grade III or lower) in the hierarchy of research designs, since they are not valuable for determining causation, or the "specific effect" of treatment.

In addition, charities' "in-house" patient surveys have many limitations. First, most of the data has usually not been collected using validated, standardised outcome questionnaires that can be used for comparison with other studies or illnesses. Then, there is the problem of poor response rates that range from 66% down to 31% in recent M.E. group surveys, raising the whole question of the meaning of non-responses, a statistical minefield (fortunately) beyond the scope of this article.

The "Christine Keeler" effect - "they would say that, wouldn't they"

But, the greatest flaw in the eyes of suspicious outsiders is the "Christine Keeler" effect - "they would say that, wouldn't they". Since the survey data emanates from a so-called self-selecting group of people with self-reported symptoms, a question mark hangs over the veracity of the data, especially if – as some psychosocial professionals maintain – claiming to be severely ill can help maintain a sickness role and acquire state benefits.

A good example of the difficulties of getting such information published came in 2002 when the 25% ME Group and MERGE tried to publish a small table of data as a letter in the Journal of the American Medical Association:

<http://www.mereseearch.org.uk/research/reviews/experiences.html> . To say there was a lack of interest is an understatement: in the end, the data was presented in MERGE's report "Unhelpful

Counsel" <http://www.25megroup.org/Information/Medical/Unhelpful%20Counsel> , and so was seen by – at most – a few hundred people instead of the 200,000+ members of the American Medical Association, the sort of audience the most severely affected patients, and the data, deserved. These problems with survey data are not specific to M.E. by the way, but

this illness – with its peculiar combination of public scepticism and professional uncertainty or outright disdain – is probably more at risk than most.

Preparing to climb the mountain

Given that surveys are things that patient charities are well-positioned to undertake, there are in fact some simple things that groups representing the severely ill can do to facilitate the acquisition of valid information. One is to include with their custom-designed questionnaires at least one recognised validated outcome measure, such as the Medical Outcomes Study SF36, a short, easily completed measure of quality of life that allows direct comparison with other illnesses and other types of M.E. patients. Again, groups could be willing to supply data for analysis by independent organizations though, of course, the ideal situation is for a university department or other professional group to be involved from the outset.

"The most useful advance would be a national epidemiological investigation of the true impact of severe M.E."

However, a most useful advance would be a national epidemiological investigation of the true prevalence and impact of severe M.E. Indeed, as the CMO report made clear, the organisation of primary care services in the UK offers a unique opportunity to undertake prevalence studies on the national scale needed to generate the requisite data.

To end where we began, the same report stated in 2002 that "care of people who are severely affected is an urgent challenge". Scientific investigation of the severely affected – their clinical status, experience of illness, and treatment – is also a challenge that should be swiftly met.

Ignored and invisible, maybe - but it doesn't have to be like that. Energy, vision and funding can transform any situation.>

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