Institution: The University of Edinburgh

Unit of Assessment: 4

Title of case study: F: Medically unexplained symptoms including chronic fatigue syndrome can be accurately identified and treated

1. Summary of the impact (indicative maximum 100 words)

Impact: By showing the benefits of accurate identification and targeted treatment of chronic fatigue syndrome, UoE research has influenced worldwide medical practice and stimulated public and governmental debate.

Significance: Guidelines and policy debate have resulted in improved patient treatment, with associated economic benefit.

Beneficiaries: Patients with medically unexplained symptoms, policy-makers, clinicians.

Attribution: Work conducted at UoE in a team led by Carson and Sharpe.

Reach: The research affects the more than 25% of all GP presentations who have unexplained symptoms / chronic fatigue syndrome (40% in gastroenterology and neurology). Guidelines have been changed internationally including UK, USA, Australasia.

2. Underpinning research (indicative maximum 500 words)

Up to 1 in 300 people in the UK have chronic fatigue syndrome (CFS). Moreover, more than a quarter of all individuals presenting to a GP in the UK—in excess of 100 million consultations per year—have pain, paralysis, bowel symptoms or chronic fatigue for which no adequate medical explanation can be found [3.1]. These medically unexplained symptoms are also prevalent in secondary care (e.g., neurology, where they account for more than 33% of consultations), and cost the NHS £14K per annum per patient. The cost to the UK economy is up to £3.5B p.a. for chronic fatigue syndrome (CFS) alone [3.2]. In spite of the considerable costs and associated suffering, the management of these conditions has, until recently, been neglected [3.1].

Epidemiology of CFS and medically unexplained symptoms

The Edinburgh team (Professor Michael Sharpe, Professor of Psychological Medicine, UoE, 1997–2012; now honorary Professor, University of Oxford; Dr Alan Carson, Senior Lecturer, UoE, 2011–present; Dr Jon Stone, Honorary Clinical Senior Lecturer, UoE, 2005–present) demonstrated in large prospective cohort studies of referrals to neurology clinics in the UK that 30% were explained by functional ‘medically unexplained’ symptoms [3.1, 3.3]. Patients with a higher number of individual symptoms ($p<0.005$) or depression ($p<0.005$; 70% of individuals with completely unexplained symptoms) were more likely to be ultimately diagnosed as being without organic disorder [3.1]. The team showed that individuals with medically unexplained symptoms had higher mean inpatient (£3,539 difference), outpatient (£778 difference) and emergency (£99 difference) patient costs [3.2] compared with patients presenting without these symptoms, and that their repeated assessment had little or no benefit [3.3]. Moreover, the Edinburgh team showed that the diagnosis of ‘medically unexplained’ was rarely changed at 18 months follow-up (0.4% of the original sample) [3.3].

Management of individuals with medically unexplained symptoms

From 2006–2010, the Edinburgh team conducted a randomised controlled trial of guided self-help for medically unexplained symptoms at NHS neurology clinics in Edinburgh and Glasgow. The guided self-help was superior to the comparator treatment (odds ratio=2.36, p=0.02; number needed to treat=8), with efficacy maintained at 6 months follow-up [3.4]. In 2011, Sharpe and colleagues published the first definitive randomised controlled study (n=641) showing superior efficacy of cognitive behaviour therapy (CBT) for CFS compared with specialist care alone (rating scale score difference=3.4, *p*=0.0001), and inefficacy of the very widely recommended (at the time) intervention of 'pacing' at 52 weeks follow-up (the Pacing, graded Activity and Cognitive behaviour therapy: a randomised Evaluation (PACE) trial) [5.5]. Finally, in 2012, Edinburgh and Aarhus Universities together published a study of CBT in a range of medically unexplained syndromes, conducted across both primary and secondary care showing efficacy (mean difference=4.0; *p*=0.002 for the primary outcome measure) over enhanced standard care [3.6].

3. References to the research (indicative maximum of six references)

3.1 Carson A, Ringbauer B, Stone J, McKenzie L, Warlow C, Sharpe M. Do medically unexplained symptoms matter? A prospective cohort study of 300 new referrals to neurology outpatient clinics. J Neurol Neurosurg Psychiatry. 2000;68:207–10. DOI:10.1136/jnnp.68.2.207.

3.2 Burtona C, McGorm K, Richardson G, Weller D, Sharpe M. Healthcare costs incurred by patients repeatedly referred to secondary medical care with medically unexplained symptoms: A cost of illness study J Psychosom Res. 2012;72:242–7. DOI: 10.1016/j.jpsychores.2011.12.009.

3.3 Stone J, Carson A, Duncan R,…Sharpe M. Symptoms 'unexplained by organic disease' in 1144 new neurology out-patients: how often does the diagnosis change at follow-up? Brain. 2009;132:2878–88. DOI: 10.1093/brain/awp220.

3.4 Sharpe M, Walker J, Williams C, et al. Guided self-help for functional (psychogenic) symptoms: a randomized controlled efficacy trial. Neurology. 2011;77:564–72. DOI: 10.1212/WNL.0b013e318228c0c7.

3.5 White P, Goldsmith K, Johnson AL,…Sharpe M. Comparison of adaptive pacing therapy, cognitive behaviour therapy, graded exercise therapy, and specialist medical care for chronic fatigue syndrome (PACE): a randomised trial. Lancet. 2011;377:823–36. DOI: 10.1016/S0140-6736(11)60096-2

3.6 Schröder A, Rehfeld E, Ørnbøl E, Sharpe M, Licht R, Fink P. Cognitive-behavioural group treatment for a range of functional somatic syndromes: randomised trial. Br J Psychiatry. 2012;200:499–507. DOI: 10.1192/bjp.bp.111.098681.

4. Details of the impact (indicative maximum 750 words)

The UoE work challenged the once popularly held view that 1. CFS is an organic disorder for which assessment and treatment are inappropriate or ineffective; 2. 'functional' neurological symptoms are often eventually explained by organic disease; and 3. functional 'medically unexplained' symptoms are completely explained by life events, are often short-lived and the patients can be neither engaged nor treated.

Pathways to impact

The work has been presented at international meetings, and published in high-impact medical journals with global reach accompanied by UoE and Medical Research Council press releases and by extensive commentaries on the importance of the research on the websites of the funding bodies (e.g., http://www.mrc.ac.uk/Newspublications/News/MRC007706, Feb 2011).

Impact on public policy and clinical practice

The UoE research has led to changes in national and international guidelines on the management of medically unexplained symptoms and CFS/myalgic encephalomyelitis (ME), e.g., in the UK (Chief Scientist Office guidance on CFS was endorsed by The Royal College of General Practitioners in 2010), the USA [5.1] and Australia [5.2]. Professor Sharpe was on the guideline working group for the USA guidelines.

The work has also led specifically to individual service developments across the UK (e.g., Yorkshire [5.3], Lothians (2008), Oxford (2013) and Nottingham (2011)), and directly to changes in what is considered best clinical practice [5.4].

The work has fed into the development of the International Classification of Diseases (ICD-11) and the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-V) [5.5].

Reference has been made to the UoE research in both the House of Commons and the House of Lords, which has led to political pressure to provide better services for people with medically unexplained symptoms (e.g., House of Commons Early Day Motion 405, July 2010 [5.6]).

Impact on public engagement
Edinburgh work on CFS and medically unexplained symptoms has been widely disseminated to the public, for instance by coverage on national and international news (e.g., BBC news, Feb 2011 [5.7]; USA National Public Radio broadcast by R Knox, Feb 2011; ABC News Australia, Aug 2012) and articles on the websites of patient organisations [e.g., 5.8].

The Edinburgh group also set up a website for the community of individuals with medically unexplained symptoms (http://www.neurosymptoms.org). This site receives an average of 30,000 hits per month; it has had 466,061 unique hits since its creation in 2009 and has been translated by neurologists into 10 languages. It is widely used by clinicians and the public in the USA (41% of hits) and UK (38% of hits), and is linked from the Movement Disorders Society, Royal College of Psychiatrists and MS Society websites, in addition to the BBC.

Impact on the economy
CFS costs the NHS £14K per annum per patient and the annual cost to the UK economy is up to £3.5B [3.2]. It is clear that enormous savings can be made by effective management of this condition.

A Dutch study suggested that up to 3.6% of the workforce suffers from CFS. The UoE research has led to national changes in the occupational management of individuals with medically unexplained symptoms, demonstrating effective strategies to reduce absence from work (e.g., NHS/Royal College of Physicians Guidance [5.9]).

5. Sources to corroborate the impact (indicative maximum of 10 references)

5.1 US Department of Veterans Affairs. VA/DoD clinical practice guidelines for the management of medically unexplained symptoms: chronic pain and fatigue (2002). http://www.healthquality.va.gov/mus/mus_fulltext.pdf. *[USA guidelines. N.B. These remain the current guidelines from 2008–present.]*

5.2 Government of South Australia. A guideline for the diagnosis and management of ME/CFS in the community or primary care setting. Management guidelines for General Practitioners (2004); http://sacfs.asn.au/download/guidelines.pdf *[Australian guidelines. N.B. These remain the current guidelines from 2008–present].*

5.3 Leeds & West Yorkshire CFS/ME service. http://www.bacme.info/document_uploads/POD_Docs/MancfsinPrimCare.pdf *[Corroborates establishment of specialist CFS/ME services.]*

5.4 Scottish Good Practice Statement on ME-CFS (2010) http://www.show.scot.nhs.uk/App_Shared/docs/MainDoc.pdf. *[Corroborates change to clinical practice regarding CFS/ME.]*

5.5 APA DSM-5 Work Group Member Disclosure Report (2012). http://www.dsm5.org/MeetUs/Documents/Somatic%202012/Sharpe-Disclosure-2012.pdf. *[Corroborates Sharpe's membership of Somatic Distress DSM-V Work Group.]*

5.6 House of Commons Early Day Motion on Chronic Fatigue Syndrome / Myalgic Encephalomyelitis (2010). http://www.parliament.uk/edm/2010-12/405. *[Corroborates debate of CFS/ME in the House of Commons.]*

5.7 “Brain and body training treats ME, UK study says” (2011). http://www.bbc.co.uk/news/health-12493009. *[BBC news coverage of clinical trials contributing to public engagement.]*

5.8 “Professor Sharpe and Richard Horton talk about the PACE trial on ABC National Radio, Australia: 18 April 2011”. Article on UK ME Association website (2011): http://www.meassociation.org.uk/?p=5703. *[Article on patient website contributing to public engagement.]*

5.9 NHS Plus. Occupational Aspects of the Management of Chronic Fatigue Syndrome: a National Guideline (2006). http://www.anhops.com/docs/92_8_273539_CFSyndrome_full_review.pdf. *[Evidence that the research has altered guidelines for occupational management. N.B. These remain the current guidelines from 2008–present.]*