Institution: University of the West of England (UWE), Bristol

Unit of Assessment: 3 – Allied Health Professions, Dentistry, Nursing and Pharmacy

Title of case study: Addressing a priority of people with rheumatoid arthritis: Managing fatigue

1. Summary of the impact

Quality of life for people with rheumatoid arthritis (RA) has improved, responding to their stated major priority for help with fatigue. Their self-management of fatigue has improved using our cognitive-behavioural therapy intervention. Over 30,000 patients and healthcare professionals a year request our resulting self-management booklet, distributed via Arthritis Research UK.

This group's research spearheaded a new international patient/professional consensus that fatigue must be measured in all clinical trials. Along with the Bristol RA Fatigue scales, which we developed (translated into 35 languages) this has helped to place fatigue at the centre of drug development by changing the way the pharmaceutical industry performs multi-national drug trials.

Nursing management has now improved demonstrably. Fatigue evaluation and intervention have now been recommended in national guidelines.

2. Underpinning research

Context: Prior to Hewlett *et al.*'s research, rheumatoid arthritis (RA) fatigue was ignored and considered unimportant by professionals, who had no valid RA fatigue measure, conceptualised fatigue as just reflecting inflammation or depression, and consequently did not support patients with their fatigue. In 2002, we invited patients to join us for the first time at the biennial international OMERACT conference (Outcome Measures in Rheumatology). This collaboration developed throughout 2003-10. The OMERACT patients highlighted fatigue as an important, daily problem that they struggle to manage, which led to our research.

The research group comprises Sarah Hewlett, Arthritis Research UK Professor of Rheumatology Nursing (joined UWE 2005); Jon Pollock, Associate Professor Epidemiology (joined UWE 2001); Fiona Cramp, Associate Professor Musculoskeletal Conditions (joined UWE 2005); Dr Tessa Sanderson (PhD student 2006-09; MRC/ESRC Research Fellow 2009-13); Dr Emma Dures (Research/Leverhulme Fellow 2009-15); Dr Jo Nicklin (PhD student 2006-09; Research Fellow 2012-14); Karen Kitchen, volunteer fatigue patient research partner.

A) Research identifying the importance of RA fatigue. Fatigue was not included in the 1993 international consensus of core outcomes to be measured in RA clinical trials agreed by professionals of OMERACT. Our first novel findings were that patients consider fatigue to be a significant and unmanageable problem that was at that time ignored by professionals (2003-2007, ref 1, grant G1). Building on these ground-breaking findings that challenged clinicians' beliefs and practices, we showed for the first time that patients consider fatigue to be a crucial treatment outcome for quality of life when judging medication efficacy (2006-11, grant G2) and disease flares (2010-13). Indeed, patients often rated fatigue as more severe and more important than RA pain. This resulted in international agreement by OMERACT patients and professionals together that fatigue must now be measured as a core outcome in all RA clinical studies (ref 2) and form part of disease flare definitions (2013).

B) Research to develop a valid measure of RA fatigue. Building on this, we developed and validated the Bristol RA Fatigue scales (BRAFs) (2006-2013, grants G3, G4). The BRAFs measure fatigue severity and separate out for the first time, dimensions of coping, impact, life with fatigue, emotional fatigue and cognitive fatigue (ref 3). This was previously impossible and, crucially, provides potential for creating individualised interventions based on the combination of dimensions affected. During 2011-13, the BRAFs were further validated in 6 EU countries (grant G5) and were used by other research groups in the UK and Europe.

C) Conceptual mechanisms of RA fatigue. During 2008-13, we reviewed the RA fatigue literature, developing and publishing a novel conceptual framework of mechanisms, challenging professionals' beliefs that RA fatigue is driven entirely by inflammation or depression. Our 2013 Cochrane review identified potential for self-management interventions (ref 4).

D) Research into self-management of RA fatigue: Building on our conceptual proposal, our RCT of group cognitive behavioural therapy (CBT) was the first intervention that specifically aimed to reduce the impact of RA fatigue by enhancing self-management (2006-2011, grant G6). The intervention reduced the impact and severity of fatigue, and improved patients' ability to cope with it as well as their physical and psychological wellbeing (ref 5). In our qualitative evaluation patients spontaneously raised the key elements of CBT as being crucial to improving their self-management (ref 6). As few rheumatology teams have a clinical psychologist, in 2011-12 we manualised the 6-week programme for use by rheumatology clinical teams after brief CBT training. Following our pilot and in direct response to our research, HTA issued a commissioned call to test widespread delivery of psychological interventions for RA fatigue across the NHS, and awarded us the grant (2013-2018; grant G7).

3. References to the research

1. **Hewlett, S.,** Cockshott, Z., Byron, M., Kitchen, K., Tipler, S., Pope, D. and Hehir, M. (2005). Patients' perceptions of fatigue in rheumatoid arthritis: Overwhelming, uncontrollable, ignored. *Arthritis & Rheumatism*, 53 (5) pp. 697-702. ISSN 0004-3591, http://dx.doi.org/10.1002/art.21450 (Grant G1)
2. Kirwan, J. R., Minnock, P., Adebajo, A., Bresnihan, B., Choy, E., De Wit, M., Hazes, M., Richards, P., Saag, K., Suarez-Almazor, M., Wells, G. and **Hewlett, S**. (2007). Patient perspective workshop: fatigue as a recommended patient-centred outcome measure in rheumatoid arthritis. *Journal of Rheumatology*, 34 (5) pp. 1174-1177. ISSN 0315-162X, http://jrheum.org/content/34/5/1174.short (Grant G1)
3. **Nicklin, J., Cramp, F.,** Kirwan, J., Urban, M., **Hewlett, S**. (2010). Measuring fatigue in rheumatoid arthritis: A cross-sectional study to evaluate the Bristol Rheumatoid Arthritis Fatigue Multi-Dimensional questionnaire, visual analog scales, and numerical rating scales. *Arthritis Care and Research*, 62 (11) pp.1559-68. http://dx.doi.org/10.1002/acr.20282 (Grants G3, G4)
4. **Cramp F., Hewlett S.,** Almeida C., Kirwan J.R., Choy E.H.S., Chalder T., **Pollock J.** and Christensen R. (2013). Non-pharmacological interventions for fatigue in rheumatoid arthritis. *Cochrane Database of Systematic Reviews* 2013, Issue 8. Art. No.: CD008322. DOI: 10.1002/14651858.CD008322.pub2. http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008322.pub2/pdf
5. **Hewlett, S.,** Ambler, N., Almeida, C., Cliss, A., Hammond, A., Kitchen, K., Knops, B., Pope, D., Spears, M. and Swinkels, A. (2011). Self-management of fatigue in rheumatoid arthritis: A randomised controlled trial of group cognitive-behavioural therapy. *Annals of Rheumatic Disease*, 70 (6) pp. 1060-1067. ISSN 0003-4967, http://dx.doi.org/10.1136/ard.2010.144691 (Grant G6)
6. **Dures, E.,** Kitchen, K., Almeida, C., Ambler, N., Cliss, A., Hammond, A., Knops, B., Morris, M., Swinkels, A. and **Hewlett, S**. (2012). "They didn't tell us, they made us work it out ourselves": Patient perspectives of a cognitive–behavioural programme for rheumatoid arthritis fatigue. *Arthritis Care and Research*, 64 (4) pp. 494-501. ISSN 2151-4658, http://dx.doi.org/10.1002/acr.21562 (Grant G6)

Grants underpinning the research
(Hewlett is PI on all except G2, where she is sponsor for Sanderson)

G1 **Hewlett S.** ARC Academic Fellowship (Allied Health Professionals). Academic Sponsors: Kirwan, Hollander, Dieppe (University of Bristol), **Means (UWE)**. *Arthritis Research Campaign* 2002-2007 (£242,126)

G2 **Sanderson T, Hewlett S,** Calnan M, Morris M. Understanding RA patients' prioritisation of treatment outcomes. *MRC/ESRC Interdisciplinary Postgraduate Fellowship.* 2009-11 (£161,157)

G3 **Hewlett S**, Kirwan J. Fatigue measurement in RA (J Nicklin appointed as clinical doctoral fellow). *Glaxo Smith Kline* and *Above and Beyond, Charitable Trust*. 2006-09 (£85,000)

G4 **Hewlett S**, Ambler N, Pope D, Hammond A, Robinson F. Fatigue in people with RA: Validation of the Bristol RA Fatigue scales and development and pilot of a clinician-led intervention. *Above and Beyond, Charitable Trust* (£61,181) and *UWE developmental funding*. 2009-11 (£43,960, total £105,141)

G5 **Hewlett S,** Gossec L, Kirwan J**, Cramp F, Dures E,** Von Krause G, Davis B. Cross-cultural validation of patient-reported outcome measures in RA (BRAF & RAID). *European League Against Rheumatism.* 2011-14 (€150,000)
G6 **Hewlett S**, Hammond A, Swinkels A, Hehir M, Ambler N. Self-management of fatigue in rheumatoid arthritis. *Arthritis Research Campaign.* 2006-09 (£148,671)
G7 **Hewlett S**, **Pollock J**, Blair P, Ambler N, Hollingworth W, **Dures E**, Kirwan J, Hammond A, Choy E, Creamer P, Viner N, Green S, Hughes R, Thompson P, Rooke R, Robinson R. **R**educing **A**rthritis **F**atigue: Clinical **T**eams using cognitive-behavioural approaches. *HTA*. 2013-18 (£1,315,470 + NHS costs £112,372, total £1,427,842)

4. Details of the impact

People with rheumatoid arthritis (RA) have learned how to self-manage fatigue; rheumatology healthcare professionals have read or heard the research findings and used them to enhance their clinical practice in supporting self-management.

Impact on patient self-management. Our cognitive behavioural therapy (CBT) programme for fatigue self-management led to reduced fatigue impact and severity, improvements in physical and mood states, increased social participation and a return to lost leisure activities. Local patients have indicated their improvement in quality of life since receiving this CBT intervention, describing the effects as “long-lasting”, “life-changing”, and with “reduced hospital appointments” (source T1). Similar findings have been demonstrated in clinical practice in Scotland, where Occupational Therapists are utilising the programme with “improvements in outcome measures and patient experience” (source T2). To disseminate these approaches to patients, the trial funders (Arthritis Research UK) asked to us to write a patient booklet for fatigue self-management. The booklet contains self-help information, activities and materials based on our trial (source S1). It is displayed in most UK rheumatology clinics, many GP surgeries and can also be ordered by patients. In the 16 months since publication in January 2012, over 30,000 hard copies have been requested (still averaging 1100/month). The National RA Society (a patient organization) utilised it to include a fatigue session in their general self-management programme.

Impact on clinician awareness and treatment guidelines. Our research into fatigue is cited in the standards for UK service provision, the 2006 British Society of Rheumatology and British Health Professional in Rheumatology Guidelines for managing RA, which states that fatigue must be addressed (source S2). Our 2008 Fatigue Topic Review commissioned by Arthritis Research UK is a publication series distributed nationally to all UK rheumatologists, rheumatology health professionals and GPs, to inform care. Following the development of our BRAF scales (2010), the joint working party of pharmaceutical agencies and the USA Federal Drug Administration looking at rheumatology outcomes invited Hewlett to submit information to a policy meeting (2012) considering fatigue as a key RA treatment target for patients, in support of the industry’s need to evaluate fatigue as a drug licensing claim (source S3), and the possible use of the BRAFs to do this. The FDA was broadly supportive and talks continue; meanwhile the BRAFs have been translated into 35 languages, and are being used in drug trials worldwide with 2000 patients. The pharmaceutical industry has highlighted how our work has helped place fatigue at the centre of drug development: one company has described this “breakthrough” and “major advancement” as “critical in the drug development process” (source T3).

Impact on clinical practice: Following our successful RCT of CBT for fatigue self management, a rheumatology Occupational Therapist and a consultant nurse (Hewlett) supported patients in fatigue self-management using materials and approaches from the CBT course, with Hewlett receiving an average 2 new referrals per week from the local team, and occasionally another Trust. Our use of CBT approaches has altered local practice, with 3 health professionals deciding to attend CBT skills courses and using these in clinic. During 2003-2013, 15 NHS clinical rheumatology teams and professional bodies throughout the UK requested presentations on RA fatigue and its management. Following these, our 2013 repeat survey of UK rheumatology nurse specialists showed that 82% are now using our booklet to deliver support for fatigue self-management, 98% find it helpful for patients, and 83% do not require more RA fatigue information (compared to 35% in 2007). Many clinical teams say they have decided to use our methods: a rheumatology unit in Scotland that has used our materials for their fatigue self-management

programme has reported significant improvement in fatigue impact, and also that uptake is spreading as other units have visited to observe, resulting in "NHS Glasgow and Clyde starting their [programmes] this year" (source T2). Seven NHS teams across England and Wales have offered to be trained in the manualised CBT course. The OMERACT patient panel (see section 2 above) has testified to improvements in clinical practice internationally, describing them as "groundbreaking… fatigue is no longer denied, dismissed or neglected" (source T4).

During 2003-2013, 10 presentations to rheumatology clinicians were requested across USA, Europe and Asia, together with a series of presentations in Iceland, including a public lecture. Following these presentations, clinical rheumatology teams from the Netherlands, Finland, Denmark and Canada have requested the manualized CBT course. In 2012, Hewlett's presentation of our CBT research transmitted to 15 hospitals across British Columbia in Canada, led to their staff changing their clinical practice in the management of fatigue by "using the work of Dr Hewlett's team to better assist clients" helped by provision of "tangible resources" (source T5). The Arthritis Society of Canada has used our fatigue self-management materials to develop an online fatigue module for Canadians living with arthritis ("very grateful for Dr Hewlett's support and the ability to make use of her work"). The content, which was based directly on Hewlett's research, completed online testing in July 2013 ready for launch in autumn 2013.

Impact on fatigue in other long-term conditions: Hewlett was invited to present the fatigue work to the patient conferences of the National Ankylosing Spondylitis Society and the quality of life group LifePsychol, where patients expressed considerable interest in adopting some self-management aspects. Keynote Lectures were given to the British Association of Cognitive and Behavioural Therapists and the British Pain Society to help clinicians understand links between fatigue, thoughts, feelings and pain; after the BPS presentation, the Chair asked the clinician delegates how many would now address fatigue with patients, and approximately 50% indicated they would.

5. Sources to corroborate the impact

S1 Arthritis Research UK: Self-help and daily living: Fatigue and Arthritis. *A self-management booklet for patients, written by and based on the research by the Hewlett group:* http://www.arthritisresearchuk.org/arthritis-information/arthritis-and-daily-life/fatigue.aspx

S2 British Society of Rheumatology guidelines for the management of RA: Luqmani R et al. *Rheumatology* 2006. *Clinicians use these guidelines as benchmarks for delivering care* http://rheumatology.oxfordjournals.org/content/45/9/1167/suppl/DC1

S3 Fatigue must be measured in all clinical RA trials. Kirwan J, Minnock P, Adebajo A, Bresnihan B, Choy E, De Wit M, Hazes M, Richards P, Saag K, Suarez-Almazor M, Wells G, **Hewlett S.** *Journal of Rheumatology* 2007 . *Clinicians, drug developers and drug licensing authorites use these guidelines as benchmarks.* http://jrheum.org/content/34/5/1174.full.pdf+html

Testimonials (held by UWE)

T1 Patient, University Hospitals Bristol NHS Foundation Trust:
Impact on quality of life from the intervention

T2 Occupational therapist, Scottish Rheumatic Diseases Unit:
Impact on patient quality of life from the intervention, and increasing uptake by other units

T3 Pharmaceutical Industry:
Impact on drug development/testing for fatigue

T4 Patient group, OMERACT:
Impact of the group's research on fatigue care internationally

T5 Provider of arthritis rehabilitation services for British Columbia:
Impact of the research on clinician practice