Group cognitive–behavioural programme to reduce the impact of rheumatoid arthritis fatigue: the RAFT RCT with economic and qualitative evaluations

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Disclaimer: This report contains transcripts of interviews conducted in the course of the research and contains language that may offend some readers.

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Scientific summary

The RAFT RCT

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Scientific summary

Background

Fatigue is a major problem in rheumatoid arthritis (RA). Group cognitive–behavioural therapy (CBT) delivered by a clinical psychologist reduces the impact of RA fatigue on patients' lives, but few rheumatology units have psychologists.

Objectives

1. To compare the clinical effectiveness and cost-effectiveness of a group programme for RA fatigue [named RAFT, i.e. Reducing Arthritis Fatigue by clinical Teams using cognitive–behavioural (CB) approaches], delivered by the rheumatology team in addition to usual care, with usual care alone. The primary outcomes were fatigue impact at 6 months (followed up for 24 months), and
2. an evaluation of tutors' experiences of the RAFT programme.

Design

A randomised controlled trial (RCT) with a nested qualitative evaluation.

Setting

Seven rheumatology units in England and Wales.

Interventions

The RAFT programme consists of group CBT co-delivered by pairs of rheumatology nurses and/or occupational therapists (tutors), using reflective questioning to enable patients to identify links between thoughts, feelings, behaviours and fatigue. The group provides role models/peer support for legitimising fatigue, goal-setting and problem-solving. The RAFT programme comprises six 2-hour sessions (weeks 1–6) and a 1-hour consolidation session (week 14), covering fatigue validation, pacing, how thoughts drive boom-and-bust cycles, energisers/drainers, sleep, stress and communication. Patients monitor their activity, rest and fatigue with charts, which are reviewed in the group sessions to support goal-setting towards personal priorities for improving quality of life. Tutors were trained together over 4 days and provided with a RAFT programme manual/material, before delivering a practice programme locally (observed by a trainer). Tutors delivered four RAFT programmes with clinical supervision for one session in alternate programmes.

Usual care was a short discussion with the research nurse of the Versus Arthritis (formerly Arthritis Research UK) fatigue self-management booklet, in routine use in UK rheumatology units (written by the RAFT programme trainers based on an original RCT of the intervention delivered by a psychologist).

Participants

Adults aged $\geq$ 18 years with RA and fatigue severity score of $\geq$ 6 [out of 10, as measured by the Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale (BRAF-NRS)], which patients considered recurrent. Any patients who had a recent change in major RA medication or glucocorticoids were excluded.

Recruitment

Each centre (hospital) delivered four consecutive RAFT programmes over 2 years. In order to randomise 5–7 patients to a RAFT programme, each centre recruited 10–14 patients and then closed that 'cohort'. Over a 2-week period, those patients then attended for informed consent and baseline assessment and received usual care for fatigue. When all visits for patients in that cohort were completed, randomisation occurred and recruitment commenced for the next cohort.

Randomisation, concealment and blinding

Once a centre completed all baseline visits for a cohort, the clinical trials unit conducted the randomisation for that centre's cohort (concealed from the RAFT programme study team and the local research nurse). Computer-generated randomisation was stratified by the seven centres and by cohort within centres (four cohorts recruited consecutively over 2 years). Allocation was 1 : 1 within cohorts but, in the event of an odd number, the CB arm received the extra patient. Patients randomised to the RAFT programme but unable to attend maintained their allocation and were offered subsequent local RAFT programmes. If they accepted, the patients had a new baseline assessment performed with that cohort. Blinding of RAFT programme tutors and patients was not possible, but analysis was performed blind to allocation.

Outcome assessment

Primary clinical outcome

Fatigue impact [measured by the Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale (BRAF-NRS) for impact] was measured at 26 weeks.

Secondary clinical outcomes

Fatigue assessments included impact, severity, coping (BRAF-NRS), and overall fatigue impact, physical fatigue, living with fatigue, emotional fatigue and cognitive fatigue [as measured by the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ)]. Clinical assessment included mood, pain, disability, disease activity, quality of life, sleep, valued leisure activities and self-efficacy (belief in ability to achieve an action), using validated scales. All data were collected at weeks 0, 6, 26, 52, 78 and 104. In addition, fatigue data were collected at weeks 10 and 18 (i.e. 4 weeks before and 4 weeks after the consolidation session).

Economic outcomes

The primary economic outcome was quality-adjusted life-years (QALYs) at 26 weeks, using the EuroQol-5 Dimensions, five-level version (EQ-5D-5L) questionnaire (BRAF-NRS impact was a secondary outcome). Resource use data were collected for RA-related costs, including RAFT programme training and delivery; RA medications; primary, community and secondary medical and health professional appointments/care; rheumatology telephone helpline usage; social care; work productivity and patient-incurred expenses for travelling to appointments and the RAFT programme sessions. Data were collected through staff logs, hospital computer records and patient questionnaires (at weeks 0, 6, 26, 52, 78 and 104).

Tutor experiences

Individual face-to-face interviews were used to capture tutors' diverse experiences and a focus group discussion allowed tutors to discuss clinical implementation. Interviews and focus groups were audio-recorded and guided by a broad, neutral discussion schedule.

Sample size

The RAFT programme is delivered by clinical teams rather than psychologists; therefore, the RCT was powered to be able to demonstrate a difference of 1.46 units on a 0–10 fatigue impact scale (i.e. 75% of that previously demonstrated by a psychologist). For a two-sided significance of 0.05 and a power of 90%, 73 patients per trial arm were required; allowing for potential clustering of groups within and between centres increased this to 75 patients per trial arm. Allowing for 50% attrition at 2 years, recruitment aimed for 150 patients per trial arm.

Analysis methods

Clinical analysis

Descriptive statistics of baseline clinical and sociodemographic characteristics were used to describe the study sample and ascertain comparability of randomisation arms. The primary analysis of effectiveness was carried out under the intention-to-treat (ITT) principle and used linear regression to estimate an adjusted mean difference, comparing fatigue impact at 26 weeks (the primary outcome) between arms as randomised, adjusted for baseline values of the outcome and recruitment centre. Sensitivity of the primary analysis to the effect of missing data was explored by imputing missing primary outcome data and repeating the primary analysis model. A secondary analysis compared arms at follow-up across 26, 52, 78 and 104 weeks using mixed-effects repeated measures regression. Further secondary analyses of the primary outcome included repeating the primary analysis model restricted to only baseline-eligible participants (some patients had dropped below their screening fatigue severity of 6 out of 10 during the time it took to build cohorts); a complier-average causal-effect analysis to investigate the efficacy of the intervention (based on treatment compliance status), for comparison with the ITT estimate of the offer of the arm; and investigation of potential clustering by centre and cohort. The effect of the arm on secondary outcomes, collected at 26 weeks, was also examined using appropriate regression models (i.e. linear regression for continuous outcomes, logistic regression for binary outcomes, etc.), adjusted for baseline values of the outcome being investigated and centre. The secondary outcomes were also subject to repeated measures analysis using data collected at 26, 52, 78 and 104 weeks' follow-up. Exploratory/subgroup analyses explored further RA fatigue-related questions.

Health economics analyses

The primary economic analysis used QALYs at 26 weeks as the outcome measure and was conducted from the societal perspective. Secondary analyses investigated the BRAF-NRS impact outcome measure, NHS and Personal Social Services perspectives, and a 2-year follow-up. All costs are reported in 2015/16 pounds sterling. Costs and QALYs in the second year of follow-up were discounted at 3.5%.

All analyses were conducted using ITT principles, comparing the trial arms as randomised and including all patients. Missing data were imputed by the predictive mean-matching method. The incremental mean differences in total costs and QALYs (adjusted for baseline utility) were estimated between the two arms of the trial and 95% confidence intervals (CIs) derived. Cost and QALY data were combined to calculate the incremental cost-effectiveness ratio (ICER) and net monetary benefit statistics. Calculations were made to investigate whether or not the RAFT programme is cost-effective at the established National Institute for Health and Care Excellence (NICE) thresholds of £20,000 and £30,000 per QALY gained. One-way sensitivity analyses were used to judge the potential impact of sources of uncertainty.

Qualitative analyses

Interview and focus group audio-recordings were transcribed and anonymised. All transcripts were analysed by the qualitative researcher using inductive thematic analysis, with subsets independently analysed by three co-applicants (two professionals and one patient). Items of interest and their related text were coded, then patterns of codes identified and their supporting text collated. Related clusters of coded text formed subthemes, which were then grouped together to form themes. The three independent analyses were

incorporated into the final analysis, as there were no substantial differences. The focus group transcript was analysed by two researchers and used to confirm, challenge or elaborate the themes (triangulation).

Patient and public involvement

Two patient co-applicants brought experiential knowledge of RA fatigue and had undertaken the original CBT intervention facilitated by a psychologist. The patient co-applicants suggested improvements to the RAFT programme patient materials, advised on trial outcomes, questionnaire packs and recruitment, talked with the tutors about fatigue and the intervention, and analysed qualitative data.

Results

Clinical results

A total of 333 participants were recruited (175 participants were randomised to the RAFT programme and 158 participants to the control arm), and participant characteristics were well balanced between the trial arms at baseline. The RAFT programme participants attended a mean of 5.85 sessions out of their 7 RAFT sessions (standard deviation 1.63 sessions). Of those participants randomised, 308 participants (92%) provided primary outcome data. Both trial arms had improved fatigue impact at 26 weeks; however, there was evidence of a difference between trial arms, with those in the RAFT arm having a BRAF-NRS impact score that was –0.59 units lower (i.e. better) than those receiving usual care (95% CI –1.11 to –0.06 units; $p = 0.03$, effect size 0.36). Repeated measures analysis suggested a sustained effect of the intervention over the 2 years' follow-up (adjusted mean difference –0.49 units, 95%CI –0.83 to –0.14 units; $p = 0.01$). When restricting analyses to the 262 baseline-eligible participants, a slightly larger effect was observed both at 26 weeks (adjusted mean difference –0.82 units, 95% CI –1.40 to –0.24; $p = 0.01$) and over 2 years (adjusted mean difference –0.58 units, 95% CI –0.95 to –0.22 units; $p = 0.002$). Analysis of secondary outcomes provided evidence of a between-arm difference in favour of the RAFT programme in BRAF-MDQ fatigue impact, living with fatigue and emotional fatigue, at both 26 weeks and over 2 years. There was also evidence of a difference in self-efficacy at 26 weeks and BRAF-NRS coping over 2 years in favour of the RAFT programme. Fatigue severity and other outcomes were similar between arms at 26 weeks and over 2 years. There were relatively few missing data and the analysis of imputed data differed very little to complete-case analysis. No harms were reported. The RAFT programme satisfaction was rated ≥ 8 (out of 10) by 89% of patients, compared with 54% of patients in the control arm rating the booklet ($p < 0.0001$).

Health economic results

Participants were relatively low users of primary care and community services, but were regular attenders in secondary care for RA-related appointments and high users of RA-related medications. At baseline, 76 participants (22.8%) were in work, with no difference between trial arms. There was no statistically significant difference between trial arms for total societal costs, including the RAFT programme training and delivery (mean difference £434, 95% CI –£389 to £1258), nor in QALYs gained (mean difference 0.008, 95% CI –0.008 to 0.023). The point estimate of the incremental cost per QALY gained was £55,202 and the net monetary benefit was –£277 (95% CI –£1212 to £657) at a societal willingness-to-pay threshold of £20,000 per QALY. The probability that the intervention is cost-effective at the same threshold is 0.28. The sensitivity analysis without training costs gave an ICER of £31,578 per QALY and a cost-effectiveness probability of 0.42 at the £20,000 per QALY threshold. Up to 30% of health economics data were missing at the 2-year follow-up; therefore, imputed data were used throughout (although complete-case analysis did not alter the primary analysis results). The primary analysis was repeated excluding those individuals who had fallen below the eligibility criterion of BRAF-NRS severity score of ≥ 6 (out of 10) between screening and baseline (control, $n/N = 24/158$; RAFT, $n/N = 28/175$). For baseline-eligible patients, the ICER was £17,214 per QALY and the probability of cost-effectiveness was 0.52 at the £20,000 NICE threshold. Cost-effectiveness analysis using the primary effectiveness outcome gave an ICER of £455 per unit of

improvement in BRAF-NRS impact, giving a probability of cost-effectiveness of, for example, 0.78, if society is willing to pay £1000 per unit improvement in BRAF-NRS impact.

Qualitative results

Among the 15 RAFT programme tutors, 14 participated in interviews and eight participated in the focus group. The following five themes were identified. First, 'the RAFT programme was a daunting but exciting undertaking', as CB approaches and 'ask don't tell' differed from the tutors' usual advice-giving and problem-solving approaches. Becoming confident required time and effort. Second, 'skills practice and demonstrations were essential', and training together and expert demonstrations were helpful. Role play was invaluable, but uncomfortable. Third, 'developing an individual approach to a standardised intervention' came through personalising their RAFT programme manuals by paraphrasing sample text. Clinical supervision helped and tutors developed the dynamics of pair work. Fourth, 'enhanced clinical practice beyond the RAFT programme' was demonstrated as tutors described working with the patient as a whole person in clinic; their new 'ask don't tell' skills helped them listen, draw things out and confidently discuss fatigue utilising the RAFT programme material. Fifth, 'delivering the RAFT programme in clinical practice' was what tutors wanted but would require buy-in from managers/colleagues, and NHS restraints mean that models of training and support need to be explored, perhaps blending online learning with reduced face-to-face training. Tutors considered the RAFT programme to be life-changing for patients.

Conclusions

The RAFT programme, delivered by clinical rheumatology teams, improved fatigue impact beyond usual care alone, as well as emotional fatigue, living with fatigue, coping with fatigue and self-efficacy, sustained over 2 years. Although costs were not statistically significantly different between trial arms, the primary economic evaluation using QALYs based on EQ-5D-5L suggested that the RAFT programme was unlikely to be cost-effective at conventional NICE thresholds. Rheumatology clinicians delivering the RAFT programme acquired new skills that they utilised in patient care beyond the RAFT programme.

Strengths and limitations

Multiple hospitals and tutors were involved in a pragmatic trial, with broad entry criteria incorporating usual RA management, natural variations in patient attendance and staff ability to deliver clinical services. In addition, evaluations aimed to capture all relevant outcomes and costs for 2 years, plus qualitative analysis by multiple researchers.

However, controlling for any social effects of the RAFT programme groups was impractical; seven didactic information sessions would not reflect usual care and risk high attrition. There were no follow-up data on 25 patients who withdrew before week 26; the economic evaluation had 30% missing data and the EuroQol-5 Dimensions questionnaire may not capture RA fatigue.

Implications for health care

Although cost-effectiveness was not demonstrated, findings must be reviewed in the context of a low-cost intervention with sustained clinical effect and no harms, for an important symptom with few treatment options; analysis of patients with a fatigue severity score of ≥ 6 at baseline and discounting one-off RAFT programme training costs demonstrated greater effectiveness. Rheumatology teams without clinical psychologists might thus consider implementation. Increasing RAFT programme groups to 8–10 patients could be feasible and economically beneficial.

Implications for future research

The RAFT programme co-delivery by a rheumatology professional–patient tutor pair (combining professional and experiential knowledge) could be tested, as could delivery to people with physical long-term conditions with fatigue. The number of RAFT programme sessions required, and contribution of the consolidation session, could be tested. The amount of change in BRAF-NRS impact that is meaningful for patients needs clarifying, along with patient values for fatigue (for QALY calculations).

Trial registration

This trial is registered as ISRCTN52709998.

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