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A pragmatic multi-centred randomised controlled trial of yoga for chronic low back pain: Trial protocol

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Abstract

A systematic review revealed three small randomised controlled trials of yoga for low back pain, all of which showed effects on back pain that favoured the yoga group. To build on these studies a larger trial, with longer term follow-up, and a number of different yoga teachers delivering the intervention is required. This study protocol describes the details of a randomised controlled trial (RCT) to determine the effectiveness and cost-effectiveness of Yoga for chronic Low Back Pain, which is funded by Arthritis Research Campaign (arc) and is being conducted by the University of York. 262 patients will be recruited from GP practices in 5 centres in England. Patients will be randomised to receive usual care or 12 weekly classes of yoga. A yoga programme will be devised that can be delivered by yoga teachers of the two main national yoga organisations in the UK (British Wheel of Yoga and Iyengar Yoga Association (UK)).

Trial registration: Current controlled trials registry ISRCTN81079604 (date registered 30/03/2007).

Keywords

Randomised; Trial; RCT; Yoga; Back; Pain

1 Background

Back pain is an extremely common and costly condition and treatments for low back pain (LBP) tend to be unsatisfactory. Exercise treatment, though widely used and recommended,

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has only a small effect on back pain, and manipulation treatments, delivered either by a physiotherapist, chiropractor or osteopath, are better than exercise alone but are not widely available on the NHS and are more expensive than group exercise sessions. An alternative approach to the treatment of low back pain may be the use of yoga. Yoga offers a combination of physical exercise with mental focus that may make it a suitable therapy for the treatment of low back pain. A randomised controlled trial (RCT) undertaken in the USA has shown that LBP patients allocated to yoga classes had significantly less pain after 12 weeks compared with those allocated to an exercise control group. The improvement in back pain at 12 weeks was 3.4 points on the Roland and Morris back pain scale, which was more than twice as much as that noted for manipulation in the recent UK BEAM study among a similar group of patients and at a similar follow-up time.

We have undertaken a systematic review of the Cochrane database and the relevant research registers and at this time found no ongoing RCTs of yoga therapy of low back pain. We did, however, identify a total of three small published RCTs of yoga therapy for low back pain. All three studies showed effects on back pain that favoured the yoga group and this was statistically significant in two of the studies (yoga versus written material $P < 0.001$, yoga versus exercise $P = 0.034$; yoga versus educational control $P = 0.003$).

Despite these encouraging results there is still need for another trial. The main limitation with existing trials is that only one yoga teacher delivered the intervention which makes the trial's results unrepresentative of all yoga teachers, therefore it is important that several yoga teachers deliver treatment. In order to develop an intervention with the widest possible applicability, it is also important to gain the agreement of yoga practitioners of the most prominent schools of yoga operating in the UK on a package of movements that all would be willing to deliver to patients with low back pain. An agreed package would allow the results to be generalisable across all yoga practitioners. Existing trials as well as being small also have short-term follow-up. It would be useful to see whether the effects of yoga are longer lasting. The potential for yoga to have a longer term influence is more likely than, for example, manipulation, as yoga participants will be encouraged to practise the technique at home between classes, and to continue with home practice after the classes have been completed. It is reasonable therefore to suppose that if participants do continue with home practice, initial yoga training may have long-term benefits on back pain making it important that we should follow-up a cohort of low back pain patients, after having had yoga treatment, for at least a year to ascertain whether or not any long-term benefits are seen.

Because back pain is an excessive burden on society and is associated with high costs, it is important that we should evaluate any treatment that may reduce this problem. Yoga is potentially a very cost-effective treatment as it can be delivered in group sessions, which substantially reduces the cost per treatment for each individual, when compared to a treatment delivered on a one-to-one basis such as physiotherapy.

2 Trial objectives

The primary objectives of this study are to test the effectiveness and cost-effectiveness of yoga for LBP in primary care. This will be achieved by:

1. Producing a package of yoga care agreed by a cross-section of yoga practitioners from different Yoga traditions, including a written manual for yoga teachers and their students.
2. Undertake a large multi-centre RCT of the agreed yoga care package versus usual care on patients with low back pain to evaluate if the yoga intervention is more effective in reducing disability due to back pain.

3. Undertaking a cost-effectiveness analysis of yoga treatment and usual care in relation to usual care alone for LBP.

3 Methods

3.1 Trial design

This study is a multi-centred pragmatic two-arm RCT which will collect patient preference data before all patients are randomised. Randomisation will be at the patient level and patients will be randomly allocated to receive yoga or usual care. We will recruit approximately twenty yoga teachers at five sites (Cornwall, North London, West London, Manchester and York). These yoga teachers will be trained in the agreed package of care.

3.2 Recruitment and participants

We plan to use a 'database' recruitment method as this method has been shown to recruit large numbers of patients in a relatively short space of time. We will recruit GP practices local to each site by mailing out to them an invitation letter and an information sheet detailing the process of the trial and what would be required of the practice if they agreed to participate. GP practices will be compensated for the time taken on the research and all stationary and postage costs will be provided. Participating GP practices will search their databases using Read Codes and mail out a recruitment pack to all patients aged between 18 and 65 who have had a consultation with low back pain in the last 18 months. Patients will be asked to consider taking part in a trial of yoga therapy for LBP. Those patients who agree will be asked to complete an eligibility questionnaire containing the Roland and Morris back pain scale and to return this to the York Trials Unit at the University of York. The trial co-ordinator will then assess eligibility. Patients who score 4 or more on the measure, and meet other inclusion criteria will be eligible to participate. One back pain trial based in Manchester used the database recruitment method and found 2068 LBP patients from 9 GP practices. Out of these 234 (11.3%) met the inclusion criteria and were randomised. This trial used the database method of recruitment and recruited its sample size on time. In this study we propose to recruit 20 GP practices in case of differential recruitment rates across the different geographical areas, and we anticipate recruitment will take 6 months.

3.3 Inclusion and exclusion criteria

The inclusion criteria will be: aged 18–65; presented to their GP with low back pain in the previous 18 months; a score of 4 or more on the Roland & Morris Disability Questionnaire (RDQ); must be physically mobile (i.e. able to climb up and down stairs, and able to get off the floor unaided); and, indicated that they are able to attend at least one of the yoga classes on offer.

The exclusion criteria will be: patients over 65 as they are more likely to have serious spinal pathology; clinical indications of serious spinal or neurological pathology as indicated by 'warning signs'; pregnant women; previous spinal surgery, and; history of psychosis or alcohol abuse (due to difficulty in assessing outcomes).

3.4 Randomisation and allocation

Eligible patients will be randomised remotely to either yoga or usual care. In the trial eligibility questionnaire, participants will be asked to specify their availability to attend yoga classes in different regions from a list of dates and times available. Once the total number of participants wanting to attend each yoga class is known, then the randomisation will be undertaken. To ensure that each yoga class does not exceed its maximum capacity, but still ensure balance in the overall number of participants in each trial arm, unequal allocation may be used for some classes. For example, if 24 participants specified their availability as

being the yoga class in Manchester on Monday and the maximum capacity for this class was 15, then a allocation ratio of 1:1.7 (9 to the control group and 15 to the yoga group) could be used. Allocation ratios will need to be amended to ensure balance overall and thus it is possible that some classes will not reach their maximum capacity. The randomisation and allocation will be conducted by an independent data manager in the York Trials Unit, University of York, using a computer program. The trial co-ordinator will write to the participants informing them of their treatment allocation.

3.5 Interventions

The yoga intervention will consist of 12 weekly 75-min classes (with a one or two week break at mid-course), plus education and information for home practice. There are a number of recommended yoga practices for people with low back pain, which are delivered by teachers of different yoga traditions. Among the co-applicants are representatives of the two largest yoga associations within the UK: British Wheel of Yoga and Iyengar Yoga Association (UK). Within the first three months of the study, whilst we gain ethics permission and NHS Research and Development approval, we will conduct a series of meetings between experienced yoga practitioners in order to agree on a basic package of yoga that can be delivered by yoga teachers of these two national organisations. Yoga teachers taking part in the study will be trained in this package of care over two intensive training weekends. As part of the study we will also develop a manual for yoga teachers and a manual and relaxation CD for patients. The manuals will describe the agreed series of yoga techniques that can be readily used by experienced yoga teachers and can be practised at home by patients receiving yoga. A yoga mat will be given to patients. Intervention patients will also receive any normal ongoing treatments if these are deemed necessary.

The patients allocated to the control group will receive any ongoing treatment (i.e. usual care) that they would normally receive plus the offer of one yoga class in twelve months time after the final 12 month questionnaire has been completed. Both groups will receive ‘The Back Book’ which is an evidenced-based booklet written by a group of international back pain experts and is aimed at patients who have chronic low back pain.

3.6 Outcomes

Clinical outcome measures will be collected via postal questionnaires at baseline, 3 months, 6 months, and 12 months follow-up. The primary outcome measure will be functional limitations and disability as measured by the Roland & Morris Disability Questionnaire (RDQ). The RDQ consists of a 24 point scale asking questions relating to the patients back pain and dysfunction on that day. The minimum clinically significant difference on the RDQ has been estimated to range between 2 and 3 points. This scale has been found to be sensitive to change, reliable and valid.

Secondary outcome measures will include: Clinical status as measured by the Aberdeen Back Pain Scale (ABPS); general health status measured using the SF-12; the EQ-5D health index; pain self-efficacy as measured by the Pain Self-Efficacy Questionnaire (PSEQ); HADS; simple quantifying measures of (i) number of days spent in bed due to back pain, (ii) number of days with restricted activity attributed to back pain, and (iii) whether medication was used for back pain over the previous four weeks; economic data; preference for treatment at baseline; and, for the yoga group, class attendance and continued use of yoga at home or elsewhere.

3.7 Bias

Randomisation eliminates selection bias. However there are other sources of bias we need to avoid. When patients do not receive their preferred treatment in randomised trials there may

be difficulties with patient recruitment and scientific problems with bias. For example, bias may occur when patients are aware of a treatment not available to them and comply poorly with the standard treatment or withdraw from the trial completely, commonly known as resentful demoralisation. The absence of these patients from trials may restrict generalisation of the results as participants may not be representative. To control for patient preferences we propose to ask the participants at baseline their treatment preferences. This design allows us to control for the impact of patient preference in the analysis. In addition, we will offer the control participants a one-off yoga class at the end of the study to help minimise resentful demoralisation.

Loss to follow-up is likely to lead to biased estimates of intervention effect. We will try to avoid bias due to attrition by carefully following up the participants in both groups. We will phone participants who fail to complete questionnaires after a second reminder to ask if they would be willing to complete the RDQ over the phone. The final follow-up questionnaire will be accompanied by a £5 incentive to complete the questionnaire in order to reduce attrition rates. We anticipate a 20% loss to follow-up in this trial, and will implement procedures to minimise loss to follow-up and patient withdrawal, and where possible we will collect information on reasons for patient withdrawal.

Non-adherence to the intervention is likely to reduce its potential effectiveness, and provide a conservative estimate of intervention effect compared to what would be expected if there was full compliance. In the UK BEAM trial compliance was 92% for manipulation and 63% for exercise. We anticipate that compliance in this trial will lie somewhere between these. In the Sherman trial of yoga for LBP, the median attendance was 9/12 classes. Furthermore, attendance to yoga was greater than attendance to exercise classes.

3.8 Sample size

The UK BEAM trial found that a change in the RDQ score of 1.57 points was a cost-effective difference. Assuming a standard deviation of 4 points, (the UK BEAM sample size was based on an assumed population standard deviation of 4 points for this questionnaire) this results in a standardised effect size (difference in means/standard deviation) of 0.39. To detect this effect size, assuming 80% power, an independent samples *t*-test and a 2-sided 5% significance level would require 105 participants per group, 210 in total. Allowing for 20% loss to follow-up we require a total of 262 participants (131 per group).

4 Analysis

4.1 Statistical analysis plan

All analyses will be conducted on an intention to treat basis, including all randomised patients in the groups to which they were randomised. Analyses will be conducted using 2-sided significance tests at the 5% significance level. The statistician conducting the analyses will remain blind to treatment group and data will only be unblinded once all data summaries and analyses are completed.

4.2 Baseline data

All baseline data will be summarised by treatment group. Baseline data will be described descriptively. No formal statistical comparisons will be undertaken.

4.3 Follow-up data

The primary outcome will be the RDQ scores. These will be summarised descriptively (mean, SD, median, minimum and maximum) at each time point by treatment group. The primary analysis will compare the yoga and control groups at 3 months. This time point has

been chosen as it corresponds to the end of the yoga classes. A secondary analysis will compare the two groups at 12 months to assess if any differences between groups have been maintained over time. Reasons for missing outcome data will be explored by descriptively comparing the baseline characteristics of participants who do and do not return their 3, 6 or 12 month questionnaires.

A repeated measures mixed model (SAS proc mixed) will be used to compare the treatment groups. This will treat yoga classes as a random effect to account for clustering effects within centres. The outcome modelled will be the Roland Morris score at 3, 6 and 12 months and the model will include the baseline score, age, gender, duration of back pain, treatment group, and time. An interaction term assessing whether the difference between the treatment groups changes over time will also be assessed for inclusion in the model.

Different covariance patterns for the repeated outcome measures will be explored and the most appropriate structure will be used. The difference in mean scores between the treatment groups (yoga versus standard care) at 3 months and corresponding 95% confidence interval (CI) will be estimated from this model. Estimates of the difference between treatment group means at 12 months and corresponding 95% CI will also be obtained from this model. Model assumptions will be checked (normal distribution and constant variance) and, if necessary, data will be transformed prior to analysis if this improves the model fit.

An additional exploratory analysis will be used to investigate the effect of compliance with treatment using a CACE (complier average causal effect) analysis. Participants complying with the yoga course will be defined as those who attend at least 3 out of the first 6 classes and at least any other 3 classes (at least 6 in total). The numbers of compliant participants using these criteria, and further details of attendance (numbers attending each class, reported by centre) will be summarised.

Secondary outcomes will be summarised and analysed in the same way as the primary outcome. The SF-12 will be summarised for all components. To minimise multiple testing, only the overall physical component score and mental component score will be analysed, using the same analysis methods as for the primary outcome.

4.4 Adverse events

The number of adverse events experienced by each participant and total number of events overall will be summarised for each treatment group. The severity of the event and whether or not it was considered related to treatment will also be summarised.

4.5 Economic analysis plan

The economic analysis will compare the costs and outcomes in terms of quality adjusted life years (QALYs) as weighted by the EQ-5D. Costs will be assessed from the viewpoint of both the NHS and society. We will undertake a cost-effectiveness analysis by comparing costs associated to resource use between the two groups and setting this against any treatment benefit. The time horizon for the analysis is 1 year after recruitment. This way, costs or QALYs will not be discounted. There will be a baseline assessment followed by an assessment at 3 months, 6 months and 12 months that will collect data on quality of life, resource use data and, for the yoga group, continued use of yoga at home or elsewhere.

Data for the resource use component of the economic analysis will be collected from the patients, such as visits to their GP and visits to other health providers (e.g. physiotherapy), both private and within the NHS and whether related to back pain or not. Unit costs will be assigned to resource use observed for each individual, in order to estimate total costs. Unit

costs will come from a variety of national sources including published sources e.g. GP visits from the Personal Social Services Research Unit (PSSRU).

The EQ-5D profiles generated for each patient will be scored using the set of UK 'social preference weights' supplied by the EuroQol group, based on the general population scores for the health states defined. Mean scores and measures of dispersion will be calculated for both groups. QALYs will be calculated using area under the curve analysis based on the social preference weights. To avoid bias we will adjust for differences in baseline EQ-5D scores as a measure of baseline severity to account for any differential recruitment.

To meet the needs of decision-makers, the focus will be on estimating expected values for costs and outcomes (QALY) of the health technologies. The use of a regression method for CEA has many advantages: possible heterogeneity sources can be evaluated through the incorporation of stratification or prognostic variables and the hierarchical nature of the data in relation to multi-centre data collection or different carers applying the treatment can be accounted for. Moreover, it allows the identification and quantification of subgroup effects (e.g. socio-demographic variables as sex, age or ethnic group; or prognostic factors as length of illness).

As the recruitment will be based on different yoga teachers at five sites (Cornwall, North London, West London, Manchester and York) a multilevel net benefit regression approach will be used. The net monetary benefit for each participant is calculated by subtracting the additional cost from the additional effect valued in pounds. Relevant covariates (those that will be included in the statistical analysis, including baseline utility score) will be considered in the regression. Subgroup analysis focussing on compliance will be undertaken as specified in the clinical analysis plan. Additionally, if deemed necessary, the impact of missing data will be evaluated in sensitivity analysis.

4.6 Uncertainty assessment and sensitivity analysis

Due to sampling, costs and QALYs are estimated with uncertainty. This uncertainty will be interpreted through both bootstrap and graphical methods. For such, cost-effectiveness planes and cost-effectiveness acceptability curves (CEAC) will be plotted. The CEAC will show the probability of the low back pain management including yoga being cost-effective in relation to the reference management strategy, for different thresholds the decision maker may be willing to pay for additional benefit (QALY). A series of sensitivity analysis will be conducted to explore the variability in estimating cost-effectiveness. For instance, alternative imputation methods for missing data and various assumptions of costs.

5 Ethical review

Ethical approval for this trial was obtained from Leeds East Research Ethics Committee, UK. The investigators will ensure that the trial will be conducted in compliance with ethical guidelines as set out by this committee, and in line with recommended good clinical practice (GCP) guidelines.

Conflict of interest statement

None declared.

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References

1. UK BEAM Investigators. United Kingdom back pain exercise and manipulation (UK BEAM) randomised trial: effectiveness of physical treatments for back pain in primary care. BMJ 2004;329:1377–1384. [PubMed: 15556955]
2. Sherman K.J. Cherkin D.C. Erro J. Miglioretti D.L. Deyo R.A. Comparing yoga, exercise, and a self-care book for chronic low back pain: a randomised controlled trial. Ann Intern Med 2005;143:849–856. [PubMed: 16365466]
3. Williams K.A. Petronis J. Smith D. Goodrich D. Wu J. Ravi N. Effect of Iyengar yoga therapy for chronic low back pain. Pain 2005;115:107–117. [PubMed: 15836974]
4. Galantino M.L. Bzdewka T.M. Eissler-Russo J.L. Holbrook M.L. Mogck E.P. Geigle P. The impact of modified hatha yoga on chronic low back pain: a pilot study. Altern Ther Health Med 2004;10:56–59. [PubMed: 15055095]
5. Johnson R.E. Jones G.T. Wiles N.J. Chaddock C. Potter R.G. Roberts C. Active exercise, education and cognitive behavioural therapy for persistent disabling low back pain: a randomised controlled trial. Spine 2007;32(15):1578–1585. [PubMed: 17621203]
6. Burton, K.; Klaber-Moffett, J.; Main, C.; Roland, M.; Waddell, G. 2nd ed.. TSO Publishers; Norwich: 2002. The back book.
7. Roland M. Morris R. A study of the natural history of back pain. Part I: development of a reliable and sensitive measure of disability in low back pain. Spine 1983;8:141–144. [PubMed: 6222486]
8. Patrick D.L. Deyo R.A. Atlas S.J. Singer D.E. Chapin A. Keller R.B. Assessing health-related quality of life in patients with sciatica. Spine 1995;20:1899–1908. [PubMed: 8560339]
9. Roland M. Fairbank J. The Roland-Morris disability questionnaire and the Oswestry disability questionnaire. Spine 2000;25:3115–3124. [PubMed: 11124727]
10. Bombardier C. Hayden J. Beaton D.E. Minimal clinically important difference. Low back pain: outcome measures. J Rheumatol 2001;28:431–438. [PubMed: 11246692]
11. Deyo R.A. Measuring the functional status of patients with low back pain. Arch Phys Med Rehabil 1988;69:1044–1053. [PubMed: 2975164]
12. Ruta D.A. Garratt A.M. Wardlaw D. Developing a valid and reliable measure of health outcome for patients with low back pain. Spine 1994;19:1887–1896. [PubMed: 7997920]
13. Jenkinson C. Layte R. Development and testing of the UK SF-12. J Health Serv Res Policy 1997;2:14–18. [PubMed: 10180648]
14. Nicholas MK. Self-efficacy and chronic pain. Paper presented at the annual conference of the British Psychological Society. St. Andrews; 1989.
15. Torgerson D.J. Sibbald B. What is a patient preference design? BMJ 1998;316:36.
16. Personal Social Service Research Unit (PSSRU). University of Kent; Canterbury: 2008. Unit costs of health and social care 2008.
17. Kind, P.; Hardman, G.; Macran, S. Centre for Health Economics, University of York; York: 1999. UK population norms for EQ-5D. Centre for Health Economics Discussion Paper 172
18. Manca A. Hawkins N. Sculpher M.J. Estimating mean QALYs in trial-based cost-effectiveness analysis: the importance of controlling for baseline utility. Health Econ 2005 May;14(5):487–496. [PubMed: 15497198]
19. Hoch J. Briggs A.H. Willan A.R. Something old, something new, something borrowed, something BLUE: a framework for the marriage of health econometrics and cost-effectiveness analysis. Health Econ 2002;11:415–430. [PubMed: 12112491]
20. Willan A.R. Briggs A.H. Hoch J. Regression methods for covariate adjustment and subgroup analysis for non-censored cost-effectiveness data. Health Econ 2004;13:461–475. [PubMed: 15127426]

21. Manca A. Rice N. Sculpher M.J. Briggs A.H. Assessing generalisability by location in trial-based cost-effectiveness analysis: the use of multilevel model. Health Econ 2005;14:471–485. [PubMed: 15386662]

22. Van Hout B.A. Al M.J. Gordon G.S. Rutten F.F. Costs, effects and c/e-ratios alongside a clinical trial. Health Econ 1994;3:309–319. [PubMed: 7827647]

23. Fenwick E. O'Brien B.J. Briggs A. Cost-effectiveness acceptability curves – facts, fallacies and frequently asked questions. Health Econ 2004;13(5):405–415. [PubMed: 15127421]