Physiotherapy Rehabilitation for Osteoporotic Vertebral Fracture (PROVE): an adaptive design randomised controlled trial

An adaptive design randomised controlled trial evaluating the effectiveness and cost-effectiveness of Exercise Therapy Intervention and Manual Therapy Intervention in people with osteoporosis and a clinically diagnosed vertebral fracture

ISRCTN 49117867

Data Monitoring Committee Charter

Version 1, 14th October 2013

Prepared and Authorised by:

Name:	Karen L Barker	Role:	Chief Investigator
Signature:		Date:	14th October 2013

A) Details of the Study

Study Title	Physiotherapy Rehabilitation for Osteoporotic Vertebral Fracture (PROVE): an adaptive design randomised controlled trial
Funder Number	NIHR HTA programme under the commissioned research programme HTA 10/99/01
R&D Number	107863
ISRCTN Number	ISRCTN 49117867
Sponsor	University of Oxford
Ethical Approval	The study protocol was approved by South Central Research Ethics Committee (Reference 12/SC/0411).
Version of the Document	1
Date of the Document	14/10/2013

B) Introduction

This Charter is for the Data Monitoring Committee for the commissioned HTA project 10/99/01, an adaptive design RCT evaluating the effectiveness and cost-effectiveness of Exercise Therapy Intervention and Manual Therapy Intervention in people with osteoporosis and a clinically diagnosed vertebral fracture. The Charter defines the primary responsibilities of the DMC, its membership, its relationship with the TSC, guidance on the meetings and the trial documentation which will be considered at meetings.

C) Terms of Reference of DMC

- It is the only body involved in a trial that has access to the unblinded comparative data
- The role of its members is to monitor these data and make recommendations to the Trial Steering Committee (TSC) on whether there are any ethical or safety reasons why the trial should not continue
- The safety, rights and well-being of the trial participants are paramount
- The DMC will oversee the interim analysis, advising the TSC on whether the trial should continue with both the Exercise Therapy Intervention and Manual Therapy Intervention or one of the interventions
- The DMC may be asked by the TSC, Trial Sponsor or Trial Funder to consider data emerging from other related studies
- If funding is required above the level originally requested, the DMC may be asked by the Chief Investigator, TSC, Trial Sponsor or Trial Funder to provide advice and, where appropriate, information on the data gathered to date in a way that will not compromise the trial
- Membership of the DMC should be completely independent, small (3- 4 members) and comprise experts in the field, e.g. a clinician with experience in the relevant area and expert trial statistician

D) Membership of DMC (approved by the HTA)

Membership of the DMC should be completely independent, small (3- 4 members) and comprise experts in the field, e.g. a clinician with experience in the relevant area and expert trial statistician.

Professor David Torgeson, University of York (Chair)
Professor Helen Dawes, Oxford Brookes University
Professor Susan Todd, University of Reading

E) DMC Guidance for Meeting Structure

(adapted from MRC Guidelines for Good Clinical Practice in Clinical Trials 1998 & NIHR HTA Guidance)

- Responsibility for calling and organising DMC meetings lies with the Chief Investigator, in association with the Chair of the DMC. The project team should provide the DMC with a comprehensive report, the content of which should be agreed in advance by the Chair of the DMC
- The DMC should meet at least annually, or more often as appropriate, and meetings should be timed so that reports can be fed into the TSC
- Dates for DMC meetings should be agreed in advance and only altered with agreement of all members.
- The trial statistician may be invited by the Chairman to attend part of the meeting to present the data; otherwise no-one involved with the trial or TSC should be present to see the unblinded data.
- All significant communications between the CI and the DMC should be in writing, or if they have to be oral, they should be backed up by written records.
- Minutes of meeting should be sent to all members, the sponsor, the funder, the TSC and the trial master file. It should be noted that the minutes may have 'in camera' items redacted from some copies

- A full confidential report should be made in writing by the Chairman of the DMC providing advice to the Trial Steering Committee on whether the trial should continue or not. If the DMC recommends that the trial should be stopped at any point, then funding body should be notified. It will be the responsibility of the TSC to decide whether or not to act upon the information received from the DMC.
- If an extension to the grant is needed the DMC will provide information on the data gathered to date (from this and other studies) and then advise on the likelihood that continuation of the trial will allow detection of an important effect. This should be done using methods that do not unblind the trial.
- Information provided by the DMC is likely to fall into two categories, both based on accumulating data from the study or on the basis of information available from other sources:
  (a) Information that might lead to the TSC stopping the trial early in the event of a clear outcome.
  (b) Information that might lead to the TSC modifying the design of the trial.

F) Trial Documentation

(a) Material Available in Open Sessions

Accumulating information related to the total number of patients recruited in the trial. Information from on-going or published external trials. Attendance data to the follow-up visits will also be presented.

(b) Material Available in Closed Sessions

Baseline characteristics and outcome data categorised by intervention group. Data for baseline, 4-months and 12 months follow-up will be presented.

The trial statistician will know the groups as ‘A’, ‘B’ and ‘C’, but have an envelope for the DMC members to open to indicate the intervention groups.

Appendix I: Agreement and competing interests form for independent members

PROVE trial Data Monitoring Committee: Agreement to join the Data Monitoring Committee as an independent member and disclosure of potential competing interests

Please complete the following form and return to the Trial Administrator.

(Please initial box to agree)

	I have read and understood the DMC Charter version 1, dated 14/10/2013
	I agree to continue as an independent member of the Data Monitoring and Ethics Committee for this trial
	I agree to treat all sensitive trial data and discussions confidentially

The avoidance of any perception that independent members of a DMC may be biased in some fashion is important for the credibility of the decisions made by the DMC and for the integrity of the trial.

Potential competing interests should be disclosed. In many cases simple disclosure up front should be sufficient. Otherwise, the (potential) independent DMC member should remove the conflict or stop participating in the DMC. **Table 1** lists potential competing interests.

	No, I have no potential competing interests to declare
	Yes, I have potential competing interests to declare (please detail below)

Please provide details of any potential competing interests:

_____

_____

_____

Name: _____

Signed: _____ Date: _____

Table 1: Potential competing interests for independent members

- Stock ownership in any commercial companies involved
- Stock transaction in any commercial company involved (if previously holding stock)
- Consulting arrangements with the Sponsor/Funder
- Frequent speaking engagements on behalf of the intervention
- Career tied up in a product or technique assessed by trial
- Hands-on participation in the trial
- Involvement in the running of the trial
- Emotional involvement in the trial
- Intellectual conflict e.g. strong prior belief in the trial's experimental arm
- Involvement in the writing up of the main trial results in the form of authorship