Research question: How does frequency of manual therapy treatment influence outcome for people with knee osteoarthritis?

Specific objectives:
a. To investigate the feasibility of conducting a randomized controlled trial (RCT) to determine if frequency of manual therapy treatment alters outcome for people with knee OA.

Background:
Osteoarthritis is well-recognized as a global health problem, with hip and knee OA being the 11th highest contributor to disability worldwide [1]. The lifetime risk for knee OA is estimated to be 45% and is continuing to rise with ageing populations [2]. A number of physiotherapy interventions, including manual therapy have been strongly recommended by international guidelines as appropriate for management of knee OA [3]. Manual therapy is the application of physiotherapist generated forces to body structures to produce several beneficial therapeutic effects [4]. Studies investigating manual therapy to increase knee extension, a common problem in individuals with knee OA, have produced encouraging short and long-term results [5-9]. Complex interactions between neurophysiological, biomechanical and psychological effects are proposed mechanisms of action for manual therapy, which may be mediated through varying the dose [10, 11]. However, the optimal dose of manual therapy is yet to be determined for patients with knee OA [4].

Frequency of treatment is one aspect of dosage which lacks evidence to support decision-making by physiotherapists; instead practical considerations such as cost, convenience, access to services, and size of caseloads may outweigh limited scientific evidence..

Ultimately, an RCT will be necessary to determine if frequency of manual therapy treatment affects clinical outcome for patients with knee OA. However, an RCT with sufficient power to detect a significant difference in outcome between two doses of manual therapy is likely to need a large sample size, and therefore be expensive and lengthy. A feasibility study is an important preliminary step to evaluate trial protocols and procedures, thereby determining whether a fully powered RCT is justifiable [12] [13]. Therefore, the aim of the proposed research is to evaluate the feasibility of a future RCT determining if frequency of manual therapy treatment for individuals with knee OA influences outcome.

Potential significance of project:
The proposed project will be an essential preliminary step towards a fully powered RCT which will investigate if frequency of treatment influences outcome following manual therapy in individuals with knee OA.
Findings will add to the current body of evidence about use of manual therapy for people with knee OA. They have the potential to directly influence physiotherapy practice and patient outcomes.

Methods

Study design: A feasibility study will be conducted as a preliminary step for investigating how the frequency of manual therapy influences treatment outcome for people with knee OA. This will be a three-arm intervention study with two intervention groups and one control group.

Study setting: School of Physiotherapy, University of Otago, Dunedin, NZ.

Ethical considerations: Ethics approval for this project will be obtained from the Southern Health and Disability Ethics Committee (HDEC), and Ngai Tahu research consultation will be undertaken.

Inclusion criteria: Adults (≥ 18yrs) with persistent knee pain meeting the clinical classification criteria for knee OA [14] . In addition the nominated knee must lack full extension (≥ 5 degrees loss).

Exclusion criteria: Previous lower limb joint arthroplasty, lower limb injury/surgery/knee OA treatment in previous 12 months, consultation with orthopaedic specialist for knee OA, or commencement of new medication for OA (previous 1 month); other forms of arthritis, plus comorbidities that will preclude safe application of manual therapy.

Sample size: 10 participants in each of three groups. Total 30 participants.

Recruitment: Individuals will be recruited from the Otago region by community advertising between February 2015 and July 2015.

Randomization: Participants will be assigned to groups by concealed allocation, using an on-line randomization service.

- Group A: standardized intervention, one 45 minute session per week for six weeks, at a target treatment interval of seven days (Six treatments). Two further treatment sessions of 45 minutes each, to teach an individualised home exercise programme, and to progress the programme. These will take place after the follow-up assessments at six weeks and six months.
- Group B: standardized intervention, two 45 minute sessions per week for 3 weeks. Treatment interval will be three days ideally, but not more than four days (Six treatments). Two further treatment sessions of 45 minutes each, to teach an individualised home exercise programme, and to progress the programme. These will take place after the follow-up assessments at three weeks and six months.
- Group C (control): Two treatment sessions of 45 minutes each, to teach an individualised home exercise programme, and to progress the programme. These will take place after the follow-up assessments at six weeks and six months. Standardized intervention (minus manual therapy) will also be delivered in these two sessions.

Interventions: Both manual therapy groups (A and B) will receive standardized manual therapy treatment based on a proven study protocol and delivered by a NZ registered physiotherapist [8]. They will be taught a home stretching programme intended to maintain treatment gains. During treatment sessions physiotherapists will deliver uniform generic advice and education about OA. The same standardized advice will be delivered to the control group. All participants will record their physical activity and exercise from baseline to six-week assessment. Intervention groups will receive a total of eight treatments, and the control group a total of two treatments, across the 6-month study period.

Researchers: Blinded assessors will be experienced in working with patients. They will be trained in administration of questionnaires, measuring knee range of motion (ROM), and conducting Physical Performance Measures (PPM). NZ registered physiotherapists will deliver all interventions. They will undergo two hours training in study interventions, to ensure standardized application of methods, and to understand the scope allowed to tailor interventions to individual participants. Analysis will be performed by researchers blind to group allocation.

Outcome measures: Primary: Knee injury and Osteoarthritis Outcome Score (KOOS) [15] to evaluate pain, function, joint stiffness and quality of life; knee ROM using goniometry. Secondary: PPM (30-second sit to stand, stair climb, 40 metre self-paced walk); patient global assessment; physiotherapist and patient compliance with study protocols. Feasibility data will include monitoring success of participant recruitment/retention, reporting and management of adverse events, missing data, suitability of inclusion/exclusion criteria, and analysis procedures. Semi-structured interviews will be conducted with physiotherapists to evaluate satisfaction with study protocols. A question will be included in the 6-month follow-up to determine satisfaction with study protocols. It will ask how satisfied the participant was with the study protocols, with response on a 5-point Likert scale, and an option for free text comments.

Procedures: Respondents to community advertising will receive study information, give signed consent and be screened for eligibility. Following baseline assessment, a research administrator will randomize patients and book appointments according to group allocation. Follow-up assessments will be conducted by a blinded assessor at three weeks, six weeks and six months following commencement of treatment. Given OA is a chronic disease, long term follow-up is justified. To maintain assessor blinding all participants will be followed up at the same time points. Participants will be assigned coded identification numbers and investigators will be blinded to group allocation during data analysis.

Data analysis
For the feasibility study the main emphasis will be on gathering information to inform sample size calculation for a subsequent fully powered RCT. Thus identification of variance, consideration of the

minimal clinically important difference (MCID) of outcome measures, and the attrition rate of participants are all important factors [13]. Repeated measures ANOVA analysis will be performed to detect changes in primary outcome over the multiple time-points. Descriptive stats will be used to present baseline characteristics, investigate comparability of groups. report secondary outcome measures and feasibility data. Data from the individual interviews with physiotherapists about satisfaction with trial protocols will be transcribed and analysed for common themes using a general inductive approach [16]. As this is a feasibility study, and hence does not have statistical power to detect between-group differences, little emphasis will be placed on whether a significant difference is detected between the groups.

Study time line

	Sep-Dec 2015	Feb 2016	Mar 2016	April - Jun 2016	July 2016	Aug - Feb 2017	April - Jun 2017
NGT Feasibility	Ethics & Maori Consultation		Training	Recruitment & Intervention		Final assessment	Data analysis & draft manuscript

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