

Biennial report

Study Groups

Title of the study group: OA Trial Bank

Study Group Leader's name: Sita Bierma-Zeinstra

Date of annual report submission: 14 March 2018

Summary of last year's activities

Half-yearly steering committee meetings have been organised in which steering committee members participated, but also the leading investigators of the ongoing initiatives in the OA Trial Bank (further described in detail below).

Finished project

Subgroup analysis on the effectiveness of glucosamine in patients with knee or hip osteoarthritis using individual patient data meta-analysis.

The primary aim of this project was to evaluate the effectiveness of glucosamine in subgroups of knee and hip osteoarthritis patients. We were able to include data of five trials (all independent of industry, n=1625) which compared glucosamine with placebo, representing 55% of the total number of participants in all published placebo-controlled RCTs. Based on this, we concluded that although proposed and debated for several years, open trial data are not widely made available for studies of glucosamine for OA, especially those sponsored by industry. Currently, there is no good evidence to support the use of glucosamine for hip or knee OA and an absence of evidence to support specific consideration of glucosamine for any clinically relevant OA subgroup according to baseline pain severity, BMI, sex, structural abnormalities or presence of inflammation.

Status of project:

Results have been published:

Runhaar J, Rozendaal RM, van Middelkoop M, Bijlsma HJW, Doherty M, Dziedzic KS, Lohmander LS, McAlindon T, Zhang W, Bierma Zeinstra S. Subgroup analyses of the effectiveness of oral glucosamine for knee and hip osteoarthritis: a systematic review and individual patient data meta-analysis from the OA trial bank. Ann Rheum Dis. 2017 Nov;76(11):1862-1869.

Leading role: Erasmus MC University Medical Center Rotterdam, Jos Runhaar, PhD; Sita Bierma-Zeinstra, PhD.

Ongoing initiatives

Relative efficacy of topical non-steroidal anti-inflammatory drugs and topical capsaicin in osteoarthritis: protocol for an individual patient data meta-analysis

The primary aim for this study is to investigate the relative treatment effects of topical NSAIDs and topical capsaicin in OA and to identify patient-level predictors of treatment response.

Status of project:

So far, authors of 16 trials have agreed to participate and data collection is ongoing.

Protocol has been published:

Persson MS, Fu Y, Bhattacharya A, Goh SL, van Middelkoop M, Bierma-Zeinstra SM, Walsh D, Doherty M, Zhang W; OA Trial Bank Consortium. Relative efficacy of topical non-steroidal anti-inflammatory drugs and topical capsaicin in osteoarthritis: protocol for an individual patient data meta-analysis. Syst Rev. 2016 Sep 29;5(1):165.

Leading role: University of Nottingham, Monica Persson, PhD; Weiya Zhang, PhD

Identifying placebo responders and predictors in osteoarthritis

The overall aim of this project is to identify placebo responders and to examine predictors of placebo response in patients with OA. The key objectives are:

- 1) To identify placebo responders in the OA Trial Bank data for topical non-steroidal anti-inflammatory drugs (NSAIDs), topical capsaicin, intra-articular (i.a.) glucocorticoid injections, and glucosamine/chondroitin products.
- 2) To compare characteristics of placebo responders and non-responders;
- 3) To explore predictors of placebo response.

Status of project:

Data collection is complete and results will be available within 6 months.

Protocol has been published:

Fu Y, Persson MS, Bhattacharya A, Goh SL, Stocks J, van Middelkoop M, Bierma-Zeinstra SM, Walsh D, Doherty M, Zhang W. Identifying placebo responders and predictors of response in osteoarthritis: a protocol for individual patient data meta-analysis. Syst Rev. 2016 Oct 28;5(1):183.

Leading role: University of Nottingham, Yu Fu, PhD; Weiya Zhang, PhD

Subgrouping and targeted exercise programmes for knee and hip osteoarthritis: A systematic review update and individual participant data meta-analysis

The primary study aims are to identify: (1) subgroups of people with knee and hip OA that do/do not respond to therapeutic exercise and to different types of exercise and (2) mediators of the effect of therapeutic exercise for reducing pain and improving physical function. This will enable optimal targeting and refining the content of future exercise interventions

Status of project:

By systematically reviewing the literature, 114 trials have been identified on hip and/or knee osteoarthritis. Authors of trials are now approached, and 62 have provisionally agreed to participate so far.

Protocol has been published:

*Holden MA, Burke DL, Runhaar J, van Der Windt D, Riley RD, Dziedzic K, Legha A, Evans AL, Abbott JH, Baker K, Brown J, Bennell KL, Bossen D, Brosseau L, Chaipinyo K, Christensen R, Cochrane T, de Rooij M, Doherty M, French HP, Hickson S, Hinman RS, Hopman-Rock M, Hurley MV, Ingram C, Knoop J, Krauss I, McCarthy C, Messier SP, Patrick DL, Sahin N, Talbot LA, Taylor R, Teirlinck CH, van Middelkoop M, Walker C, Foster NE; OA Trial Bank. Subgrouping and TargetEd Exercise pROgrammes for knee and hip OsteoArthritis (STEER OA): a systematic review update and individual participant data meta-analysis protocol. *BMJ Open*. 2017 Dec 22;7(12):e018971.*

Leading role: Keele University UK, MA Holden, PhD

Subgroup analysis on the effectiveness of bisphosphonates on clinical and structural outcomes in patients with knee osteoarthritis

Primary study aims are:

1. To perform subgroup analyses in trials investigating the effectiveness of bisphosphonates on clinical and structural outcomes in patients with knee osteoarthritis to identify predictors of treatment response (treatment effect modifiers).

The initial selection of characteristics that we consider to investigate are: 1) bone mineral density (BMD); if BMD is unavailable in the trials, only clinical characteristics will be used; 2) presence of osteoporosis and osteopaenia; 3) menopausal status; 4) gender; 5) body mass index; 6) smoking status; 7) use of corticosteroid; 8) disease stage (Kellgren Lawrence grade and duration of symptomatic knee OA); 9) presence of moderate to large bone marrow lesions, if there are enough trials with MRIs available; 10) baseline levels of systemic markers of bone turnover (e.g., CTX-I, CTX-II and NTX-I), if there are enough trials with these data available.

2. To determine whether there is a difference in treatment response by bisphosphonate type (oral vs intravenous; and nitrogenous vs non-nitrogenous).

Status of project:

Protocol is in development.

Leading role: University of Sydney, D Hunter, PhD

Predictors of placebo responses after intra-articular therapies and the identification of baseline pain thresholds for the prediction of clinically important treatment response of intra-articular injections in patients with

Primary study aims are:

1. To identify patient-level predictors of placebo response in intra-articular injection trials in patients with knee osteoarthritis
2. To identify the threshold of baseline pain in patients with knee and hip osteoarthritis that will predict a clinically significant treatment response in intra-articular injections

Status of project:

Protocol is in development.

Leading role: University of Sydney, D Hunter, PhD