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GLUCOSAMINE AND CHONDROITIN FOR KNEE OSTEOARTHRITIS: A DOUBLE BLIND RANDOMISED CONTROLLED CLINICAL TRIAL EVALUATING SINGLE AND COMBINATION REGIMENS

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Purpose: Glucosamine and chondroitin are dietary supplements frequently utilised by people with chronic joint pain. Evidence for symptomatic or structural benefit is inconclusive.

Methods: A double-blind randomised placebo-controlled clinical trial. A total of 605 people aged 45 to 75 years with chronic knee pain and medial tibio-femoral compartment narrowing were randomised to take once daily: glucosamine sulfate potassium chloride 1500 mg ($n = 152$), low molecular weight bovine-derived chondroitin sulfate 800 mg ($n = 151$), both dietary supplements ($n = 151$) or matching placebo capsules ($n = 151$) for two years. The primary hypotheses were that these dietary supplements would result in reduced joint space narrowing at two years and reduced knee pain over one year, compared to placebo. Joint space width was measured from digitised radiographs. Knee pain (0-10) was reported daily in a Participant Diary for seven days every two months.

Results: The mean (sd) age and BMI of this study sample was 60.5 (8.1) years and 29.0 (5.5). At baseline, the mean (sd) medial joint space width was 3.8 (1.0) mm and knee pain 4.7 (2.4); most evaluated knees (52%) had early radiographic disease (Kellgren and Lawrence grade <2). Two-year follow-up in each of the allocation groups ranged from 81-85%. At two years, mean (sd) medial joint space narrowing in the placebo group was 0.22 (0.33) mm. After adjusting for gender, BMI, structural disease severity and Heberdens nodes, allocation to the glucosamine-chondroitin combination resulted in a significantly reduced two year joint space narrowing compared to placebo [mean difference 0.10 mm (95% confidence interval: 0.002 to 0.20 mm); no significant structural effect for the single treatment allocations was detected. All allocation groups demonstrated reduced knee pain over the first year, with no significant between-group differences ($p = 0.93$). However, our study appeared to demonstrate a trend for a slightly greater knee pain reduction for the active treatment allocations during the second year, compared to placebo. There were no significant effects demonstrated for any of the secondary outcome measures. Only 34 (6%) participants withdrew from study treatment due to adverse medical events; these events were balanced between the allocation groups.

Conclusion: The combination of glucosamine sulfate with chondroitin sulfate for two years resulted in a significantly reduced joint space narrowing among these study participants with mostly mild structural disease severity. While all allocation groups demonstrated reduced knee pain over the study period, none of the treatment allocation groups demonstrated significant symptomatic benefit above placebo.

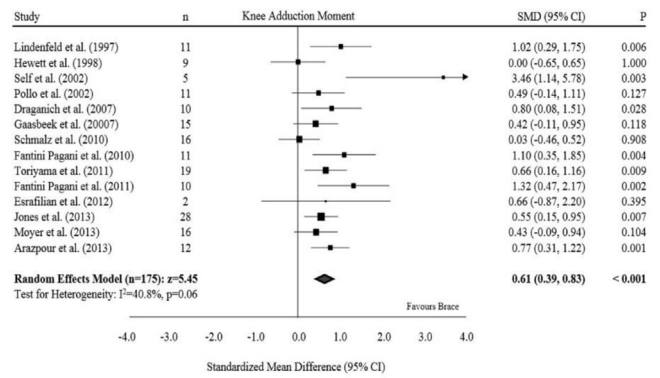
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A SYSTEMATIC REVIEW AND META-ANALYSIS OF BIOMECHANICAL AND CLINICAL EFFECTS OF VALGUS KNEE BRACING

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Purpose: Clinical practice guidelines include knee braces designed to redistribute loads across the knee, decrease pain and improve function for patients with lower limb malalignment and knee osteoarthritis (OA). Despite reviewing the same literature, some guidelines support the use of valgus knee bracing as an appropriate treatment for medial knee OA, while others suggest inconclusive evidence to support brace use. The objective of this systematic review and meta-analysis was to investigate the biomechanical effects, patient-reported outcomes, complications and compliance with valgus brace use for medial compartment knee OA.

Methods: Adhering to the PRISMA guidelines for systematic reviews, five electronic databases were searched from their inception to



February 2013. Two reviewers independently determined study eligibility, rated study quality and extracted data. Articles were first categorized as being primarily biomechanical or clinical. We defined biomechanical articles as laboratory studies that repeated tests with and without wearing a valgus brace. Clinical studies were further categorized by study design including observational cohorts and randomized clinical trials. Pooled estimates for each meta-analysis were obtained using a random effects model. Heterogeneity was tested using I^2 . For biomechanical outcome measures, standardized mean differences (SMD) and 95% confidence intervals (95%CI) were calculated for paired samples using within-patient pre-intervention and post-intervention means and standard deviations. For patient-reported outcome measures in high quality randomized trials that compared a valgus knee brace treatment group to a control group, SMD and 95%CI were calculated using post-intervention means, standard deviations and/or effect sizes.

Results: Thirty-eight studies were included ($n = 1098$). Data from 16 studies were pooled in meta-analyses. Biomechanical studies suggested a moderate, significant decrease in the external knee adduction moment (SMD=0.61; 95%CI: 0.39, 0.83; $p < 0.001$; $I^2=40.8$, $p = 0.06$) (Figure 1) and knee adduction angular impulse during walking (SMD=0.77; 95%CI: 0.32, 1.23; $p < 0.001$; $I^2=56.3$, $p = 0.08$). Randomized clinical trials suggested moderate, significant improvements in pain (SMD=0.46; 95%CI: 0.09, 0.83; $p = 0.014$; $I^2=35.5$, $p = 0.21$) and function (SMD=0.39; 95%CI: 0.10, 0.68; $p = 0.008$; $I^2=0.0$, $p = 0.44$). Studies that reported brace parameters influencing dosage were inconsistent and unclear. No studies evaluated structural measures of disease progression or cost of bracing. Significant heterogeneity prevented pooling of complications data. Complications reported during brace use were slipping, discomfort and poor fit, mechanical brace problems, heat, heaviness, skin irritation, blisters and swelling. Patient-reported brace use varied considerably between studies, but consistently decreased over time.

Conclusions: This systematic review and meta-analysis of the published literature is the first to quantify effect sizes for valgus knee braces. Results on biomechanical effects and clinical outcomes supports the use of valgus knee braces in the management of medial knee OA; however, issues related to their appropriate dosage, patient comfort and compliance remain as substantial challenges to long-term use. Identified gaps in the literature include optimal dosage, characteristics of those who respond best, effects on disease progression, and economic evaluations.

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GOOD LIFE WITH ARTHRITIS IN DENMARK (GLA:D) - IMPLEMENTATION OF EVIDENCE-BASED CARE FOR KNEE AND HIP OSTEOARTHRITIS IN CLINICAL PRACTICE

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Purpose: To introduce a nationwide initiative in Denmark (Good Life with Arthritis in Denmark (GLA:D)) aimed at implementing international guidelines for knee and hip osteoarthritis (OA) and evaluate the short-term and long-term effectiveness of a pilot study.