Table 1. Hypothesis 1

| % denuded bone, analyzed at: | Increase* in median pain score, per 10% increase in denuded bone, adjusted for age, gender, BMI, bone edema score (95% CI) |
|---|---|
| Medial tibial surface | 4.46 (1.45, 7.47) |
| Weightbearing medial femoral surface | 5.24 (3.19, 7.28) |
| Medial tibial + weightbearing medial femoral surface | 6.35 (3.10, 9.59) |
| Medial tibial + weightbearing medial femoral + patellar | 6.19 (1.28, 11.10) |

*significant if 95% CI excludes 0.

Table 2. Hypothesis 2

| % denuded bone, analyzed at: | Age, gender, BMI, K/L grade, bone edema score-adjusted OR* per 10% increase in denuded bone (95% CI) |
|---|---|
| Medial tibial surface | 1.61 (1.07, 2.42) |
| Weightbearing medial femoral surface | 1.49 (1.13, 1.95) |
| Medial tibial + weightbearing femoral | 1.61 (1.15, 2.26) |
| Medial tibial + weightbearing medial femoral + patellar | 2.44 (1.50, 3.96) |

*significant if 95% CI excludes 1.

## A44 THE EFFECT OF CHONDROITIN SULFATE ON STRUCTURE MODIFICATION IN PATIENTS WITH KNEE OSTEOARTHRITIS: A META-ANALYSIS OF RANDOMIZED PLACEBO-CONTROLLED TRIALS

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**Purpose:** To determine the effect of chondroitin sulfate on structure modification, as measured by change in the rate of decline in minimum joint space width, in patients with osteoarthritis (OA) of the knee.
**Methods:** The authors searched MEDLINE from 1996 to 2007 to identify articles on the effect of chondroitin sulfate on structure modification in patients with knee OA. The reference lists of systematic reviews and meta-analyses were searched and authors were contacted to identify additional studies. The primary outcome was the change in minimal joint space width over one year. One person abstracted data on the change in minimum joint space width in the placebo-treated and chondroitin sulfate-treated groups. Whenever possible, we used data from the intention-to-treat analyses for pooling. For studies of two years in duration, we assumed that the change was linear over time. Results were summarized for both the absolute difference between the chondroitin sulfate and placebo-treated groups as well as the standardized mean difference (effect size) using the pooled standard deviations. Fixed effects models were used as the Q and I2 statistics showed no evidence of between-trial heterogeneity. Sensitivity analyses were also performed.

Meta-analysis of randomized controlled trials of chondroitin sulfate for structure modification

| Author (Year) | Chondroitin Sulfate | | | Placebo | | | Difference (mm/year) | Effect Size |
|---|---|---|---|---|---|---|---|---|
| | No. of patients | Mean decline | SD | No. of patients | Mean decline | SD | Mean (95% CI) | SMD (95% CI) |
| Uebelhart (1998) | 14 | −0.1 | 1.24 | 12 | 0.4 | 1.00 | −0.50 (−1.36, 0.36) | −0.43 (−1.21, 0.36) |
| Uebelhart (2004) | 39 | 0.04 | 0.83 | 39 | 0.32 | 1.12 | −0.28 (−0.72, 0.16) | −0.28 (−0.73, 0.16) |
| Michel (2006) | 150 | −0.02 | 0.24 | 150 | 0.04 | 0.28 | −0.06 (−0.12, 0.00) | −0.23 (−0.46, 0.00) |
| Reginster (2007) | 309 | 0.05 | 0.26 | 313 | 0.12 | 0.27 | −0.07 (−0.11, −0.03) | −0.26 (−0.42, −0.11) |
| Summary | 512 | | | 514 | | | −0.07 (−0.10, −0.03) | −0.26 (−0.38, −0.l4) |

**Results:** Six reports of 4 placebo-controlled trials of chondroitin sulfate in patients with knee OA that reported changes in joint space width were identified, including 5 articles (3 that reported on the same trial) and 1 conference abstract. Two trials each were of one and two years in duration. Overall, the 4 trials enrolled a total of 1026 patients (512 randomized to chondroitin sulfate and 514 to placebo) (see Table). One pilot study, including only 26 patients, was published in 1998; the remaining three trials were published in 2004 or later.
The meta-analysis of all 4 trials found a mean difference of 0.07 mm per year (95% confidence intervals [CI] 0.03, 0.10) in favor of chondroitin sulfate for retarding the decline in minimal joint space width ($P < 0.0001$). This corresponds to an effect size of 0.26 (95% CI: 0.14, 0.38). Sensitivity analyses excluding the trial published only in abstract form (Reginster et al [2007]) or excluding the two small trials of only one year in duration (Uebelhart et al [1998 and 2004]) showed similar significant results.
**Conclusions:** This meta-analysis demonstrates a significant small-to-moderate effect of chondroitin sulfate as a structure modifying drug for treatment of patients with knee OA as measured by slowing the rate of decline in minimum joint space width. These results support recent OARSI treatment recommendations for use of chondroitin sulfate in patients with knee OA.

## A45 INDIRECT COMPARISON OF CLINICAL EFFICACY ACROSS COCHRANE REVIEWED PHYSIOTHERAPY INTERVENTIONS FOR PATIENTS WITH OSTEOARTHRITIS: A META-ANALYSIS WITH MIXED TREATMENT COMPARISONS

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**Purpose:** There have been numerous of systematic reviews of interventions designed to diminish pain and improve function for patients with OA, but the comparable effectiveness of such interventions is unclear. To assess the clinical efficacy of physiotherapeutic (PT) modalities and interventions available in library of Cochrane reviews, on the pain and disability in patients with osteoarthritis (OA), applying data from published systematic Cochrane reviews of RCTs would be a useful method.
**Methods:** The Cochrane Library was searched for Cochrane reviews considering patients with OA and different physiotherapeutic interventions with the aim of reducing pain, and disability. A meta-regression analysis was applied, for the mixed treatment comparisons, applying the individual study's standardized mean difference (SMD) as outcome measure, for pain and disability, respectively. The statistical random-effects model was based on a restricted maximum likelihood (REML), mixed-effects model procedure with intervention as fixed- and trial as random-factor, respectively. The within study variance was considered known for each published RCT, based on the explicit SD's presented in each of the original Cochrane reviews. A negative SMD favors the intervention on trial.
**Results:** The search with "osteoarthritis" in the title resulted in 35 reviews. Reasons for exclusion was protocols ($K = 12$), pharmacological treatments and surgery ($K = 15$), withdrawn ($K = 1$) and 1 study compared two different kinds of treatment ($K = 1$). Thus, 6 Systematic Cochrane Reviews were included in the meta-regression model (patients included, $N = 3{,}016$): Lateral wedged insoles (LWI, pain $k = 1$; disability $k = 1$), electromagnetic field therapy (EMF, pain $k = 2$; disability $k = 2$), exercise (EXE, pain $k = 17$; disability $k = 18$), ultrasonic therapy (UST, pain $k = 1$; disability $k = 0$), thermotherapy (THT, pain $k = 1$; disability $k = 1$), and transcutaneous electrical nerve stimulation (TENS, pain $k = 6$, disability $k = 1$).
Based on the indirect meta-analysis we were able to rank these 6 mutually independent interventions according to the published efficacy on pain; data are presented in descending efficacy (SMD) order with the corresponding p-value: EMF (SMD: −1.13, $p = 0.003$); THT[cold] (SMD: −0.69, $p = 0.21$); TENS (SMD: −0.45, $p = 0.003$); EXE (SMD: −0.43, $p = 0.0001$); LWI (SMD: 0.31, $p = 0.45$); UST (SMD: 0.43, $p = 0.34$). According to the published efficacy on disability: THT[cold] (SMD: −1.96, $p < 0.0001$); EMF (SMD: −0.81, $p = 0.002$); TENS (SMD: −0.60, $p = 0.08$); EXE (SMD: −0.34, $p < 0.0001$); LWI (SMD: 0.30, $p = 0.24$).
**Conclusions:** Based on this mixed treatment comparison, we provide quantitative evidence-based efficacy ranking of the PT interventions currently available as an updated Cochrane review. Based on the reported pain and disability reduction, it is highly evident ($p < 0.0001$) that exercise therapy does benefit the patient; although not necessarily with the largest magnitude of efficacy. Of the other therapies tested, both EMF and TENS showed a relevant effect size of moderate statistical significance ($p = 0.003$ respectively $p = 0.03$) on pain. In addition, THT and EMF showed a clinically relevant effect size on disability reduction ($p < 0.0001$ respectively $p = 0.002$). The present indirect-comparison provide the clinician a review of the modalities to choose, accordingly LWI, UST might not be effective in the treatment of osteoarthritis.

## A46 TAI CHI IS EFFECTIVE IN TREATING KNEE OSTEOARTHRITIS: A RANDOMIZED CONTROLLED TRIAL

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**Purpose:** Knee osteoarthritis (KOA) is a major cause of pain and functional impairment among elders and has no medical remedy. The