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The Rotterdam Study

Annals of the Rheumatic Diseases 2007 July 66(7):916–20

Changes in pain, stiffness and physical function in patients with osteoarthritis
waiting for hip or knee joint replacement surgery

Osteoarthritis and Cartilage, 2007 July; 15(7): 837–43

Efficacy and safety of etoricoxib 30 mg and celecoxib 200 mg
in the treatment of osteoarthritis in two identically designed, randomized,
placebo-controlled, non-inferiority studies

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osteoarthritis: a preliminary study

Osteoarthritis and Cartilage, 2007 June 8; [Epub ahead of print]

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138-week randomised studies of patients with osteoarthritis

Annals of Rheumatic Diseases, 2007 July; 66(7):945–51

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DO METABOLIC FACTORS ADD TO THE EFFECT OF OVERWEIGHT ON HAND OSTEOARTHRITIS? THE ROTTERDAM STUDY

Annals of the Rheumatic Diseases 2007 July 66(7):916–20

AUTHORS: DAHAGHIN S, BIERMA-ZEINSTRAS SM, KOES BW, HAZES JMW, POLS HAP

CENTERS: DEPARTMENTS OF GENERAL PRACTICE, INTERNAL MEDICINE, RHEUMATOLOGY, AND EPIDEMIOLOGY AND BIOSTATISTICS, ERASMUS MEDICAL CENTRE, ROTTERDAM, THE NETHERLANDS

BACKGROUND AND AIM: Osteoarthritis (OA), a slowly progressive degenerative disease of cartilage and bone, is the most common form of arthritis and much effort has been invested in identifying potential risk factors. Overweight may contribute to the development of OA by increasing load across weight-bearing joints and subsequent cartilage breakdown. However, this mechanism does not explain the association between overweight and OA in non weight-bearing joints such as the hand, and it has been speculated that metabolic factors associated with overweight may play a role. Diabetes, hypertension, high triglyceride levels, and high total cholesterol:high-density lipoprotein (HDL)-cholesterol ratios have all been suggested as potential risk factors for the development of OA. The aim of this study was to evaluate the association between overweight and hand OA, and to investigate the potential influence of metabolic factors.

STUDY DESIGN: Cross-sectional data analysis of a population-based cohort study.

ENDPOINT: Kellgren–Lawrence OA score.

METHODS: Cross-sectional data were obtained for 3585 patients aged 55 years and older included in the Rotterdam Study. Baseline demographic and medical characteristics were recorded, and metabolic variables (e.g., diabetes, hypertension, and

total cholesterol:HDL-cholesterol) were analyzed. Hand radiographs were taken at baseline and at 6-year follow up. Hand OA was defined as a Kellgren–Lawrence score of 2 or more. Data were analyzed by univariate and multivariate logistic regression analysis.

RESULTS: Overweight (body mass index, BMI, >27.4 kg/m²) was significantly associated with hand OA (odds ratio, OR, 1.4, 95% confidence interval, CI, 1.2–1.7), independent of other metabolic factors. Diabetes was associated with hand OA only in people aged 55–62 years (OR 1.9, 95% CI 1.0–3.8), hypertension was weakly associated with hand OA but the association disappeared after adjustment for BMI, and the total:HDL-cholesterol ratio was not significantly associated with hand OA. However, the prevalence of hand OA was higher in patients with concurrent overweight, diabetes, and hypertension than in patients with none of these conditions (OR 2.3, 95% CI 1.3–3.9). This increased prevalence was most pronounced in patients aged 55–62 years (OR 3.2, 95% CI 1.1–8.8).

CONCLUSIONS: Overweight is associated with hand OA, independent of other metabolic factors. The concurrent presence of overweight with diabetes and hypertension has an additive effect on the prevalence of hand OA.

MANAGING COMPLEX MEDICATION REGIMENS: PERSPECTIVES OF CONSUMERS WITH OSTEOARTHRITIS AND HEALTHCARE PROFESSIONALS

The Annals of Pharmacotherapy, 2007 May; 41(5):764–71

AUTHORS: MANIAS E, CLAYDON-PLATT K, MCCOLL GJ, BUCKNALL TK, BRAND CA

CENTERS: SCHOOL OF NURSING AND SCHOOL OF MEDICINE, FACULTY OF MEDICINE, DENTISTRY AND HEALTH SCIENCES, THE UNIVERSITY OF MELBOURNE, MELBOURNE; AND CLINICAL EPIDEMIOLOGY AND HEALTH CARE EVALUATION UNIT, THE ROYAL MELBOURNE HOSPITAL, MELBOURNE, AUSTRALIA

BACKGROUND & AIM: Osteoarthritis (OA) has an unpredictable course and many patients have one or more comorbid conditions, often necessitating polypharmacy. However, complex medication regimens are often difficult to manage, and failure to manage medications appropriately can result in inadequate symptom relief, with its associated personal, health, and economic consequences. The aim of this study was to examine medication management in OA and other chronic conditions from the perspective of community-dwelling consumers and healthcare professionals, using a qualitative approach.

STUDY DESIGN: Exploratory research study.

ENDPOINTS: Medication consumption; provision of information; perceived role of healthcare professionals.

METHOD: Thirty-four consumers with OA and at least one other chronic condition and 19 healthcare professionals provided information about their perceptions and experiences with managing medication regimens.

RESULTS: In addition to OA, common chronic conditions included hypertension (53%), ischemic heart disease (47%), and peptic ulcer disease, hypercholesterolemia, or diabetes mellitus (each 32%). Consumers were taking an average of 7 medications daily (range 3–16). Despite the use of

practical strategies to remind them to take their medication correctly, many consumers were dissatisfied about the complexity of their medication regimens. Consumers also did not understand why they had been prescribed certain medications and how to take them effectively. Financial constraints affected consumers' consumption of medications, such that patients omitted to take what they perceived as lower-priority medications (e.g., pain-relieving therapies). Prescription instructions to take analgesics "as needed" meant that consumers rarely took analgesics regularly. Although healthcare professionals mentioned the importance of using nonpharmacological measures to improve symptoms, consumers stated that physicians encouraged them to continue using medications, often for prolonged periods, even when the agents were not helpful.

CONCLUSIONS: Consumers are often dissatisfied with the complexity of their medication regimens. Thus healthcare professionals should take the necessary time during medical consultations to provide consumers with information about medications, and pharmacists should communicate regularly with physicians about consumers' medication needs to help avoid potential problems. Instructions should be revised so that "as needed" directions provide more explicit advice about when and how to use medications.

CHANGES IN PAIN, STIFFNESS AND PHYSICAL FUNCTION IN PATIENTS WITH OSTEOARTHRITIS WAITING FOR HIP OR KNEE JOINT REPLACEMENT SURGERY

Osteoarthritis and Cartilage, 2007 July; 15(7): 837–43

AUTHORS: KAPSTAD H, RUSTØEN T, HANESTAD BR, MOUM T, LANGELAND N, STAVEM K

CENTER FOR CORRESPONDENCE: DEPARTMENT OF ORTHOPAEDICS, RIKSHOSPITALET-RADIUMHOSPITALET MEDICAL CENTRE, OSLO, NORWAY

BACKGROUND & AIM: Patients with osteoarthritis (OA) of the hip and knee experience increasing pain and progressive loss of function. Joint replacement is an effective intervention for severe OA, but the waiting list for surgery may be considerable and many patients may experience a deterioration of their condition while they are waiting. The aim of this study was to assess self-reported changes in pain, stiffness, and physical function in patients with OA of the hip or knee from when patients decided to have surgery up to 14 days before surgery.

STUDY DESIGN: Prospective multicenter study.

ENDPOINTS: Changes in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores.

METHOD: Patients with OA of the hip or knee scheduled for joint replacement completed the WOMAC as soon as they were

put on the waiting list and about 2 weeks before scheduled surgery if they had waited at least 30 days for surgery. Changes in WOMAC scores were analyzed using the paired *t* test.

RESULTS: The WOMAC was completed on both occasions by 120 patients with hip OA and 50 patients with knee OA. Patients with knee OA waited longer for surgery (median 102 days versus 71 days) and reported a longer duration of pain (median 11.4 years versus 6.3 years) than patients with hip OA. While patients with hip OA did not report changes in pain, stiffness, or physical function during the waiting period, patients with knee OA reported deterioration in physical function ($p=0.03$) and stiffness ($p=0.15$) (see Table). In both patient groups, higher baseline WOMAC scores were associated with smaller changes on all subscales and the total score, and female sex was associated with deterioration on the pain subscale.

CONCLUSIONS: Unlike patients with OA of the hip, patients with OA of the knee report worsening stiffness and physical function while waiting for joint replacement surgery. This could be due to differences in the disease processes or may be related to differences in patient selection or timing of referral to surgery.

WOMAC subscale and total score at baseline and 2 weeks before scheduled surgery in patients with osteoarthritis of the hip (hip OA) or knee (knee OA)

	Hip OA			Knee OA		
	Baseline	Before surgery	<i>p</i>	Baseline	Before surgery	<i>p</i>
Pain	5.2±1.7	5.4±1.6	0.40	5.5±1.6	5.5±1.3	0.62
Stiffness	6.1±1.8	6.1±1.8	0.70	5.9±1.7	6.2±1.4	0.15
Physical function	5.5±1.5	5.6±1.7	0.35	5.1±1.5	5.4±1.3	0.03
Total	5.6±1.4	5.7±1.4	0.59	5.5±1.3	5.7±1.1	0.16

THE EFFICACY, SAFETY AND CARRY-OVER EFFECT OF DIACEREIN IN THE TREATMENT OF PAINFUL KNEE OSTEOARTHRITIS: A RANDOMISED, DOUBLE-BLIND, NSAID-CONTROLLED STUDY

Osteoarthritis and Cartilage, 2007 June; 15(6):605–14

AUTHORS: LOUTHRENOO W, NILGANUWONG S, AKSARANUGRAHA S, ASAVATANABODEE P, SAENGNIPANTHKUL S, FOR THE THAI STUDY GROUP

CENTER FOR CORRESPONDENCE: DIVISION OF RHEUMATOLOGY, DEPARTMENT OF INTERNAL MEDICINE, FACULTY OF MEDICINE, CHIANG MAI UNIVERSITY, CHIANG MAI, THAILAND

BACKGROUND & AIM: Current pharmacological agents available for the treatment of osteoarthritis (OA) are mainly palliative and include analgesics and nonsteroidal anti-inflammatory drugs (NSAIDs). The cytokine interleukin-1 β (IL-1 β) has been found to play a key role in cartilage degradation, subchondral bone remodeling, and joint inflammation, processes that characterize OA. Diacerein, an IL-1 β inhibitor, is now available for the treatment of OA in Thailand. The drug has a slow onset of efficacy and a long carry-over effect when treatment is discontinued or interrupted. The aim of this study was to compare the efficacy, safety, and carry-over effects of diacerein and the NSAID piroxicam in Thai patients with painful OA of the knee.

STUDY DESIGN: Double-blind, randomized, controlled, parallel-group study.

ENDPOINTS: Pain; joint stiffness; physical function; paracetamol intake.

METHOD: After a 7-day NSAID washout period, patients (mean age 54 years) were randomized to receive either diacerein (100 mg/day; $n=82$) or piroxicam (20 mg/day; $n=79$) for 16 weeks, followed by an 8-week treatment-free observation period. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) subscales were used and data expressed as mean

percent change from baseline. The medical relevance of the differences between groups was quantified using the Mann–Whitney superiority measure and its one-sided 97.5% confidence interval.

RESULTS: Joint pain had decreased to a similar extent in both groups at week 16 (diacerein $-69.7\pm 31.5\%$, piroxicam $-74.1\pm 26.2\%$). While diacerein was not inferior to piroxicam in reducing joint pain between weeks 8 and 16, it was superior to piroxicam between weeks 20 and 24. On treatment discontinuation, patients treated with piroxicam reported an increase in pain at weeks 20 ($-47\pm 47.8\%$) and 24 ($-26.8\pm 60.6\%$) whereas the patients treated with diacerein did not ($-66.9\pm 35.9\%$ and $-69.5\pm 33.7\%$ at weeks 20 and 24, respectively). The changes seen in joint stiffness, physical function, total WOMAC score, and paracetamol intake were similar to those seen for joint pain. Both treatments showed good tolerability. The incidence of adverse events was similar in both groups, although more severe events were observed in the piroxicam-treated patients.

CONCLUSIONS: Diacerein appears to be as effective as piroxicam in reducing pain and improving function, and has a similar tolerability. However, diacerein has a long carry-over effect and a better safety profile.

KNEE OSTEOARTHRITIS IN COMMUNITY-DWELLING OLDER ADULTS: ARE THERE CHARACTERISTIC PATTERNS OF PAIN LOCATION?

Osteoarthritis and Cartilage, 2007 June; 15(6):615–23

AUTHORS: WOOD LRJ, PEAT G, THOMAS E, DUNCAN R

CENTER: KEELE UNIVERSITY, PRIMARY CARE MUSCULOSKELETAL RESEARCH CENTRE, KEELE, UNITED KINGDOM

BACKGROUND & AIM: Knee pain is one of the commonest regional pains and the most frequently encountered pain problem among older adults in primary care settings. Knee osteoarthritis (OA) is the most likely underlying cause although definitive attribution is difficult. The aim of this study was to determine whether there are characteristic patterns of pain locations associated with knee OA among community-dwelling older adults.

STUDY DESIGN: Population-based, cross-sectional survey.

ENDPOINT: Pain location.

METHOD: A total of 697 adults aged 50 years and older reporting knee pain within the past 6 months were recruited from three health centers. Subjects completed a two-stage postal survey, consisting of a general health questionnaire and a regional pain questionnaire. Pain at 13 individual sites at or around the knee was coded. Pain locations in participants with and without “symptomatic knee OA” (defined as symptoms on most days in the past month, at least a definite osteophyte on plain radiographs, and current pain intensity of 2 or more on an 11-point numerical rating scale) were compared. Participants were then

grouped by knee pain location pattern and their clinical and radiographic characteristics were compared.

RESULTS: The most frequent individual sites of knee pain were the medial tibiofemoral joint line (69%) and the infrapatellar region (69%). The most common pain pattern was whole-knee pain (medial and lateral and peripatellar) without radiation (33%), followed by whole-knee pain with either proximal or distal radiation (12%). Patients with symptomatic knee OA were at greater risk of having medial knee pain (risk difference +13.9%; 95% confidence interval, CI, 6.0–20.9) and radiating pain (risk difference +12.3%, 95% CI 3.9–20.9), but not peripatellar or lateral knee pain, than patients without symptomatic knee OA. Individuals with whole-knee pain with distal radiation had more persistent, severe pain, and a relatively high proportion had moderate or severe radiographic disease.

CONCLUSIONS: Pain location patterns differ in older people with knee pain, so that no single pattern of pain location is pathognomonic for knee OA. However, medial knee pain and distally radiating pain occur more often among older adults with symptomatic knee OA than among patients with early disease or other causes of knee pain.

LONGITUDINAL PERFORMANCE EVALUATION AND VALIDATION OF FIXED-FLEXION RADIOGRAPHY OF THE KNEE FOR DETECTION OF JOINT SPACE LOSS

Arthritis & Rheumatism, 2007 May; 56(5):1512–20

AUTHORS: NEVITT MC, PETERFY C, GUERMAZI A, FELSON DT, DURYEY J, WOODWORTH T, CHEN H, KWON K, HARRIS TB

CENTER FOR CORRESPONDENCE: DEPARTMENT OF EPIDEMIOLOGY AND BIostatISTICS, UNIVERSITY OF CALIFORNIA, SAN FRANCISCO, CALIFORNIA, USA

BACKGROUND & AIM: The measurement of joint space loss using serial radiography is the gold standard method for assessing cartilage loss in osteoarthritis (OA) of the knee, and is a key index of disease progression. Fluoroscopic guidance is often used to standardize and reproduce knee positioning, but can be associated with technical and logistic difficulties, and is not always available. As an alternative, nonfluoroscopically guided knee radiography protocols have been developed that fix the radioanatomic position of the knee in a manner designed to be reproducible between examinations. The aim of this study was to evaluate the precision and sensitivity of this method for detecting joint space loss.

STUDY DESIGN: Cohort study.

ENDPOINT: Joint space width.

METHOD: The study included 80 patients (aged 70–79 years) with knee pain who were participating in the longitudinal Health, Aging, and Body Composition Study investigating weight-related dis-

eases. A total of 153 knees were assessed. Bilateral posteroanterior knee radiography films were obtained between 23 and 47 months apart, with the patient standing, knees flexed to 20–30°, and feet internally rotated 10°. Baseline radiographic OA was assessed, and joint space width was measured using a computerized algorithm. Serial knee magnetic resonance imaging was performed at the same time to evaluate cartilage lesions.

RESULTS: The mean joint space loss for all knees over the 3-year follow-up was 0.24 ± 0.59 mm ($p < 0.001$). A total of 35% of knees had radiographic evidence of OA at baseline, and in these knees the joint space loss was 0.43 ± 0.66 mm ($p < 0.001$). Joint space loss increased with increasing severity of joint space narrowing at baseline (see Table). While joint space loss was insignificant in knees without cartilage lesions at baseline (0.08 ± 0.49 mm), it was intermediate in knees with baseline cartilage lesions that did not worsen during follow-up (0.30 ± 0.64 mm) and greatest in knees with baseline lesions that worsened during follow-up (0.42 ± 0.86 mm).

CONCLUSION: Fixed-flexion radiography of the knee provides a sensitive and valid measure of joint space loss over 3 years.

Grade of baseline medial compartment joint space narrowing and medial tibiofemoral joint space loss over 3 years

Baseline joint space Narrowing	Joint space loss (mm)	<i>p</i>
Grade 0	0.14 ± 0.53	0.010
Grade 1	0.36 ± 0.76	0.014
Grade 2	0.63 ± 0.66	<0.001

EFFICACY AND SAFETY OF ETORICOXIB 30 MG AND CELECOXIB 200 MG IN THE TREATMENT OF OSTEOARTHRITIS IN TWO IDENTICALLY DESIGNED, RANDOMIZED, PLACEBO-CONTROLLED, NON-INFERIORITY STUDIES

Rheumatology, 2007 March; 46(3):496–507

AUTHORS: BINGHAM CO III, SEBBA AI, RUBIN BR, RUOFF GE, KREMER J, BIRD S, SMUGAR SS, FITZGERALD BJ, O'BRIEN K, TERSHAKOVIC AM

CENTERS: JOHNS HOPKINS UNIVERSITY, BALTIMORE, MARYLAND; ARTHRITIS ASSOCIATES, PALM HARBOR, FLORIDA; UNIVERSITY OF NORTH TEXAS, FORT WORTH, TEXAS; WESTSIDE FAMILY MEDICAL CENTER, KALAMAZOO, MICHIGAN; AND THE CENTER FOR RHEUMATOLOGY, ALBANY, NEW YORK; AND MERCK & CO, INC, WEST POINT, PENNSYLVANIA, USA

BACKGROUND & AIM: Osteoarthritis (OA) affects approximately 21 million people in the USA alone, and its prevalence increases with age. Nonsteroidal anti-inflammatory drugs (NSAIDs) are effective analgesic and anti-inflammatory agents but have considerable toxicity, particularly gastrointestinal. As patients with OA are typically at high risk for NSAID gastropathy, cyclo-oxygenase (COX)-2 inhibitors, which have similar efficacy to NSAIDs but improved gastrointestinal toxicity, offer a valuable alternative therapy. Etoricoxib is a selective COX-2 inhibitor that is widely available in Europe, Latin America, and Asia, and which is currently under development in the USA. The aim of this study was to compare the safety and efficacy of etoricoxib and celecoxib, a COX-2 inhibitor registered in the USA, for the treatment of OA.

STUDY DESIGN: Multicenter, double-blind, placebo-controlled studies.

ENDPOINTS: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale, WOMAC physical function subscale, and Patient Global Assessment of Disease Status (PGADS) scores.

METHOD: Two multicenter studies with an identical design enrolled patients with OA

who were prior users of NSAIDs or acetaminophen. After withdrawal of NSAIDs (but not acetaminophen), patients were randomized 4:4:1:1 to receive etoricoxib (30 mg once daily), celecoxib (200 mg once daily), or one of two placebos for 12 weeks. After 12 weeks, placebo-treated patients were evenly distributed to receive etoricoxib or celecoxib for a further 14 weeks. Patients completed the WOMAC pain and physical function subscales and the PGADS scale after 2, 4, 8, 12, 16, and 26 weeks of treatment.

RESULTS: In total, 468 (69.6%) and 474 (68.9%) patients in the two studies completed the full 26-week treatment period. In both studies, etoricoxib was as effective as celecoxib in improving physical function and global health status and in reducing pain over 12 and 26 weeks; both had a superior efficacy compared with placebo over 12 weeks ($p < 0.001$). The safety and tolerability of etoricoxib and celecoxib were similar over 12 and 26 weeks; both treatments increased mean systolic blood pressure and mean diastolic blood pressure to a similar extent.

CONCLUSION: Etoricoxib (30 mg once daily) is at least as effective as celecoxib (200 mg once daily) in the treatment of knee and hip OA and has a similar safety profile. Both drugs are superior to placebo.

VALIDITY AND FACTOR STRUCTURE OF THE AUSCAN OSTEOARTHRITIS HAND INDEX IN A COMMUNITY-BASED SAMPLE

Osteoarthritis and Cartilage, 2007 July; 15(7):830–6

AUTHORS: ALLEN KD, DEVELLIS RE, RENNER JB, KRAUS VB, JORDAN JM

CENTER FOR CORRESPONDENCE: VETERANS AFFAIRS MEDICAL CENTER, DURHAM, NORTH CAROLINA, USA

BACKGROUND & AIM: The AUStralian CANadian Osteoarthritis Hand Index (AUSCAN) is a 15-item self-report scale measuring pain (5 items), stiffness (1 item), and function (9 items) in the previous 48 hours, with items rated on a score from 0 (none) to 4 (extreme). Various studies have shown its reliability, construct validity, and responsiveness in small clinical samples and family-based samples. The aim of this study was to assess the properties of the AUSCAN in a large, community-based sample.

STUDY DESIGN: Cohort study.

ENDPOINTS: Internal consistency; construct validity; factor structure.

METHOD: The study included 1730 participants (mean age 61 years, 65% female, 30% African American) enrolled in the Johnston County Osteoarthritis Project, a prospective study of osteoarthritis (OA) in the hand and knee. The participants completed the AUSCAN questionnaire about 5 to 7 years after their baseline assessment. Objective measures of pinch and grip strength were recorded, and hand radiographs were taken to diagnose hand OA, defined as a Kellgren–Lawrence grade 2 or greater, OA in at least one distal interphalangeal joint, as well as in at least two other interphalangeal or carpometacarpal

joints. Subgroups were formed on the basis of gender, age, race, presence of hand pain, and presence of radiographic hand OA.

RESULTS: The median AUSCAN score was 20, indicative of mild pain and functional difficulty. The median scores for the different subgroups were men=16, women=23, Caucasians=20, African Americans=19, hand OA=24, no hand OA=17, hand pain=31, no hand pain=15. Internal consistency was high for the total scale (Cronbach's alpha 0.96, average inter-item correlation 0.64), for the pain and function subscales (Cronbach's alphas 0.94 and 0.95, respectively; average inter-item correlations were 0.74 and 0.67), and for all subgroups. Grip and pinch strength were more strongly correlated with the AUSCAN function subscale than with the pain and stiffness subscales. In addition, for the full sample and most subgroups, all pain items loaded on one factor (standardized regression coefficients 0.59–0.81), and all function items loaded on another (standardized regression coefficients 0.61–0.78). A different factor pattern was observed for African Americans.

CONCLUSION: The AUSCAN is a valid instrument to assess hand OA in the general population, as well as in demographic and clinical subgroups.

ASSOCIATION BETWEEN VALGUS AND VARUS ALIGNMENT AND THE DEVELOPMENT AND PROGRESSION OF RADIOGRAPHIC OSTEOARTHRITIS OF THE KNEE

Arthritis & Rheumatism 2007 April 56(4):1204–11

AUTHORS: BROUWER GM, VAN TOL AW, BERGINK AP, BELO JN, BERNSEN RMD, REIJMAN M, POLS HA, BIERMA-ZEINSTRAS SM

CENTER FOR CORRESPONDENCE: DEPARTMENT OF GENERAL PRACTICE, ERASMUS MEDICAL CENTER, ROTTERDAM, THE NETHERLANDS

BACKGROUND AND AIM: It is not known whether malalignment (varus and valgus) of the knee precedes, follows, or is bidirectionally associated with the development of osteoarthritis (OA) of the knee. While malalignment is mainly measured as the hip–knee–ankle angle on full-limb radiographs, the method is cumbersome and expensive. More recently, the femorotibial (FT) angle, measured on anteroposterior radiographs of the knee, has been used as a valid alternative to the hip–knee–ankle angle for determining frontal plane knee alignment. It has not yet been used to assess the influence of malalignment on the development of knee OA. The aim of this study was to determine whether malalignment (FT angle on anteroposterior radiographs) is associated with the development or progression of knee OA in individuals without or with knee OA at baseline.

STUDY DESIGN: Prospective cohort study.

ENDPOINTS: FT angle; knee OA.

METHODS: Knee OA at baseline and at follow-up (mean 6.6 years) was scored with the Kellgren–Lawrence scale in 1501 randomly selected participants of the Rotterdam study. Alignment was measured as the FT angle on radiographs at baseline. Multivariable logistic regression for

repeated measurements was used to analyze the association between malalignment and the development and/or progression of OA.

RESULTS: Of 2664 knees, 1012 (38%) had normal, 693 (26%) varus, and 959 (36%) valgus alignment. Compared with normal alignment, valgus alignment was associated with a borderline significant increase in the development of knee OA (odds ratio, OR, 1.54, 95% confidence interval, CI, 0.97–2.44) and varus alignment was associated with a twofold-increased risk (OR 2.06, 95% CI 1.28–3.32). Stratification by body mass index showed this effect to be greater in overweight/obese individuals and absent in non-overweight individuals. The risk of OA progression was significantly increased in the individuals with varus alignment compared with the individuals with normal alignment (OR 2.90, 95% CI 1.07–7.88).

CONCLUSIONS: Malalignment predates knee OA, with varus alignment being a risk factor for the development of knee OA and positively associated with disease progression. This relationship is stronger in overweight/obese individuals than in individuals of normal weight. There is a need to evaluate preventive interventions to reduce the risk of varus load, especially in overweight individuals.

PATIENT KNOWLEDGE AND MISCONCEPTIONS OF OSTEOARTHRITIS ASSESSED BY A VALIDATED SELF-COMPLETED KNOWLEDGE QUESTIONNAIRE (PKQ-OA)

Rheumatology, 2007 May; 46(5):796–800

AUTHORS: HILL J, BIRD H

CENTERS: ACUMEN AND UNIVERSITY OF LEEDS, CHAPEL ALLERTON HOSPITAL, LEEDS, UK

BACKGROUND & AIM: Education is particularly important for patients who have a chronic disease such as osteoarthritis (OA), because effective management relies on patients' willingness and ability to adhere with long-term treatments and to cope with the side effects of such therapy. The aims of this study were to develop a reliable OA patient knowledge questionnaire (PKQ-OA) and to use it to assess patients' knowledge of OA and its treatment.

STUDY DESIGN: Questionnaire design and validation study.

ENDPOINTS: PKQ-OA readability (Flesch Reading Index); understanding; reliability (Kuder–Richardson Formula 20); reproducibility (test/retest).

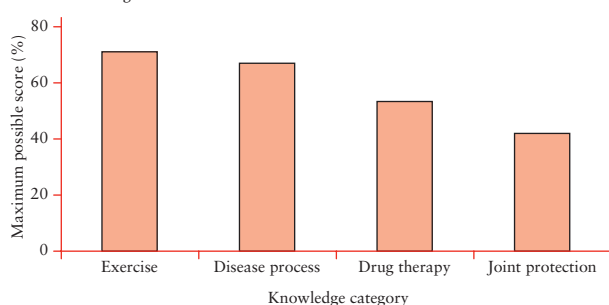
METHOD: The PKQ-OA consists of 16 multiple-choice questions on disease process (etiology, symptoms, and diagnostic tests), drug therapy (effects of commonly prescribed medications, side effects, and how

to take medications), exercise and rest (suitable methods of exercise and ways to get a good night's sleep), and joint protection (most suitable methods of joint protection and energy conservation, pain relief, and complementary therapies). It was completed by 83 patients (median age 62 years) with established disease.

RESULTS: The PKQ-OA was fairly easy to read and understand, reliable ($r=0.75$), reproducible ($r=0.81$, $p<0.01$), quick (5–10 min) and physically easy for patients to complete, and quick for practitioners to score. The median score was 19 (range 8–26) but was higher in higher-educated patients ($p<0.005$). Patients' knowledge of OA and its treatment was variable (see Figure). While patients knew about the symptoms of OA and exercise, they knew less about prophylactic analgesia and the side effects of nonsteroidal anti-inflammatory drugs (NSAIDs): only 31% knew that analgesics could be taken prophylactically, 70% did not know that they should be taken when pain starts to increase, and 34% did not know that NSAIDs should be taken with or following food. Many patients were unaware of the gastrointestinal side effects of NSAID therapy.

CONCLUSION: The PKQ-OA is a readable, easy to complete and score, reliable, and reproducible questionnaire to assess patients' knowledge of OA.

Patient knowledge



DISPARITIES IN TOTAL KNEE REPLACEMENTS: A REVIEW

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AUTHORS: KANE RL, WILT T, SUAREZ-ALMAZOR ME, FU SS

CENTERS: MINNESOTA EVIDENCE-BASED PRACTICE CENTER, MINNEAPOLIS, MINNESOTA; UNIVERSITY OF MINNESOTA CLINICAL OUTCOMES RESEARCH CENTER, MINNEAPOLIS, MINNESOTA; MINNEAPOLIS VA CENTER FOR CHRONIC DISEASE AND OUTCOMES RESEARCH, MINNEAPOLIS, MINNESOTA; AND BAYLOR COLLEGE OF MEDICINE AND HOUSTON CENTER FOR QUALITY OF CARE AND UTILIZATION STUDIES, HOUSTON, TEXAS, USA

BACKGROUND & AIM: Differences in total knee replacement (TKR) utilization in specific population subgroups have been noted in the literature, with women and white patients being more likely to undergo TKR than men and African American and Hispanic patients. This difference in TKR utilization may be due to a lack of access to health care (e.g., no insurance or regular healthcare provider), physician bias, and patient-level factors (e.g., patients' values and preferences, sociocultural beliefs or trust in physicians, making them more or less likely to accept TKR); however, it may also be due to differences in the prevalence and severity of osteoarthritis (OA) in different subgroups of patients. Moreover, the complex relationships between race/ethnicity and socioeconomic status may contribute to disparities in healthcare access and use. The aim of this study was to determine whether the observed differences in TKR utilization in population subgroups are due to healthcare disparities or to variations in disease prevalence/severity.

STUDY DESIGN: Systematic review.

RESULTS: PUBMED was searched to assess racial/ethnic or sex disparities in TKR in the years 1995–2003. Most studies reported women to be more likely to receive TKR replacement on a 2:1 ratio, after controlling

for OA prevalence and severity. One study described opposite results after restricting the population to patients with arthritis. On the basis of the severity of joint symptoms, radiographic findings, and willingness to undergo TKR, men had a higher rate of meeting criteria for TKR than women. The rate of TKR was lower among African Americans, even among African Americans eligible for Medicaid, and despite a higher prevalence of OA in this group. Surveys conducted among primary care physicians and orthopedic surgeons showed disagreement in indications for TKR, suggesting the absence of consensus: primary care physicians were more likely to suggest TKR. Race or sex was not specified as indication or contraindication for TKR.

CONCLUSIONS: No specific conclusions can be drawn from this literature review on differences in TKR utilization according to patients' sex, race, or ethnic group. There does, however, appear to be underutilization of TKR. Careful studies with a broad range of methodologies are needed to address this sensitive issue. Improved understanding of the factors underlying healthcare disparities may help narrow the inequality gap in vulnerable population subgroups.

GLUCOSAMINE/CHONDROITIN COMBINED WITH EXERCISE FOR THE TREATMENT OF KNEE OSTEOARTHRITIS:

A PRELIMINARY STUDY

Osteoarthritis and Cartilage, 2007 June 8; [Epub ahead of print]

AUTHORS: MESSIER SP, MIHALKO S, LOESER RF, LEGAULT C, JOLLA J, PFRUENDER J, PROSSER B, ADRIAN A, WILLIAMSON JD

CENTERS: DEPARTMENT OF HEALTH AND EXERCISE SCIENCE, AND SECTIONS ON MOLECULAR MEDICINE, BIostatISTICS, AND GERONTOLOGY AND GERIATRIC MEDICINE, WAKE FOREST UNIVERSITY, WINSTON-SALEM, NORTH CAROLINA, USA

BACKGROUND & AIM: The use of glucosamine and chondroitin for the treatment of osteoarthritis (OA) has increased over the past few years. Although the results of placebo-controlled studies of glucosamine sulfate for reducing pain and other symptoms of OA have been contradictory, some studies have shown the combination of glucosamine and chondroitin to have beneficial effects on OA joint pain. Exercise has been shown to produce clinically significant improvements in function, pain, and strength in patients with OA. The aim of this study was to investigate the effects of glucosamine hydrochloride plus chondroitin sulfate (GH/CS) alone or combined with exercise on physical function, pain, strength, balance, and mobility in older adults with OA of the knee.

STUDY DESIGN: Two-phase, double-blind, placebo-controlled, randomized, clinical trial.

ENDPOINTS: Physical function; pain; mobility; balance; knee strength.

METHOD: After a 2-week washout period, patients (aged 52–95 years) with OA of the knee were randomized to receive either GH/CS ($n=45$) or placebo ($n=44$) for 6 months in phase I of the study. In phase II, exercise was added to both groups for

a further 6 months. Physical function and pain were assessed using the appropriate subscales of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC); mobility was assessed using the 6-min walk test.

RESULTS: There were no significant differences between the two groups with regard to physical function, pain, mobility, or knee strength after 6 or 12 months; however, balance was better in the placebo group than in the GH/CS group at both 6 ($p=0.01$) and 12 months ($p<0.05$). Median medication compliance was 94% and 95% in phase I, and 97% and 91% in phase II for the GH/CS and placebo groups, respectively. Median exercise compliance during phase II was 77% for the GH/CS group and 78% for the placebo group. *Post-hoc* analysis showed that patients who were more compliant with GH/CS medication showed greater improvements in pain, mobility, and knee strength at 12 months than less compliant participants; however, the less compliant participants had a better balance than the more compliant participants at 6 months.

CONCLUSION: GH/CS does not appear to be better than placebo in improving function, pain, mobility, or knee strength in patients with knee OA.

EVALUATION OF THE EFFICACY AND SAFETY OF ETORICOXIB COMPARED WITH NAPROXEN IN TWO, 138-WEEK RANDOMISED STUDIES OF PATIENTS WITH OSTEOARTHRITIS

Annals of the Rheumatic Diseases, 2007 July; 66(7):945–51

AUTHORS: REGINSTER JY, MALMSTROM K, MEHTA A, BERGMAN G, KO AT, CURTIS SP, REICIN AS
CENTERS: SERVICES DE MEDECINE DE L'APPAREIL LOCOMOTEUR, POLYCLINIQUES UNIVERSITAIRES L BRULL, LIEGE, BELGIUM; AND CLINICAL IMMUNOLOGY AND ANALGESIA, MERCK RESEARCH LABORATORIES, RAHWAY, NEW JERSEY, USA

BACKGROUND & AIM: Nonsteroidal anti-inflammatory drugs (NSAIDs) and selective cyclo-oxygenase (COX)-2 inhibitors are often used in the treatment of osteoarthritis (OA). Although NSAIDs (e.g., naproxen) and selective COX-2 inhibitors (e.g., etoricoxib) have been found to exhibit comparable pain relief, COX-2 inhibitors are associated with a significantly better gastrointestinal tolerability. However, both types of drug are suggested to increase the risk of cardiovascular events in comparison with placebo. The aim of this study was to compare the efficacy and tolerability of etoricoxib and naproxen in patients with OA.

STUDY DESIGN: Randomized, double-blind, parallel-group, two-part studies.

ENDPOINTS: Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain and physical function subscales (100-mm visual analog scale) scores; disease status (patient global assessment); adverse events.

METHOD: Patients with knee or hip OA from 80 clinical centers (19 countries) were randomized to receive etoricoxib (60 mg once daily), naproxen (500 mg twice daily), or placebo for 12 weeks (part I). At the end of part I, patients taking etoricoxib or naproxen continued with their medica-

tion for a further 40 weeks; those receiving placebo were randomized (1:1) to receive either etoricoxib or naproxen. At the end of part II, patients were eligible to enter an 86-week extension in which they continued with their existing medication.

RESULTS: Of 997 patients (mean age 63 years) randomized, 615 completed parts I and II, of whom 463 entered the extension (246 receiving etoricoxib and 217 receiving naproxen). Both etoricoxib and naproxen produced similar and significantly greater improvements than placebo in all efficacy endpoints in all phases of the study. WOMAC pain assessments were 67 mm, 28 mm, and 34 mm at baseline, 52 weeks, and 138 weeks, respectively, for etoricoxib, and 67 mm, 29 mm, and 33 mm, respectively, for naproxen. Both etoricoxib and naproxen were generally well tolerated, with hypertension and upper respiratory tract infection being the most common adverse events. Safety data suggested that while etoricoxib had a more favorable gastrointestinal safety and tolerability profile than naproxen, naproxen was associated with a lower incidence of thrombotic cardiovascular events.

CONCLUSION: Etoricoxib and naproxen have a similar long-term clinical efficacy as treatment for OA and are generally well tolerated.

AGREEMENT BETWEEN CLINICAL AND RADIOLOGICAL METHODS OF DIAGNOSING KNEE OSTEOARTHRITIS

Scandinavian Journal of Rheumatology, 2007 January-February; 36(1):58–63

AUTHORS: TOIVANEN AT, AROKOSKI JP, MANNINEN PS, HELIÖVAARA M, HAARA MM, TYRVÄINEN E, NIEMITUKIA L, KRÖGER H

CENTERS: DEPARTMENT OF ORTHOPAEDICS, TRAUMATOLOGY, AND HAND SURGERY; DEPARTMENT OF PHYSICAL AND REHABILITATION MEDICINE; DEPARTMENT OF CLINICAL RADIOLOGY; BONE AND CARTILAGE RESEARCH UNIT; AND INSTITUTE OF CLINICAL MEDICINE, UNIVERSITY OF KUOPIO, KUOPIO; FINNISH INSTITUTE OF OCCUPATIONAL HEALTH, KUOPIO; AND FINNISH PUBLIC HEALTH INSTITUTE, HELSINKI, FINLAND

BACKGROUND & AIM: Knee osteoarthritis (OA) is a common joint disease among the aged population and causes pain and stiffness and reduces physical activity and quality of life. There are many radiological scales and clinical criteria for evaluating knee OA but none is considered a gold standard. The aim of this study was to determine the agreement between clinical diagnosis and different radiological grading scales of knee OA in an epidemiological study.

STUDY DESIGN: Re-examination of a randomized subgroup of the Health 2000 Survey.

ENDPOINT: Agreement between clinical diagnosis and different radiological grading scales of knee OA.

METHOD: The Health 2000 survey is an extensive population study focusing on major health problems in a representative sample of 8028 Finns older than 30 years. In the survey, knee OA was diagnosed on the basis of physical status, symptoms, and medical history. A total of 130 participants

(mean age 60 years, 68% female) were re-examined 1 year later (Kuopio OA 2000 Study), to determine the agreement between clinical and radiological diagnoses and between three different radiological grading scales (Kellgren–Lawrence, Ahlbäck, and Piperno). Weight-bearing knee radiographs were taken and scored. The history of knee symptoms was obtained using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Lequesne questionnaire.

RESULTS: Knee OA was diagnosed clinically in 17.7% and radiologically in 24.6–30% of participants (see Table). The highest prevalence was obtained with the Piperno scale, but there was no significant difference in diagnostic sensitivity between the grading scales. The agreement between the clinical and radiological diagnoses was moderate (kappa values of 0.54, 0.35, and 0.34 for the Kellgren–Lawrence, Piperno, and Ahlbäck scales, respectively), but there was substantial agreement (0.62–0.78) between the different radiological scales. Irrespective of the method used to diagnose OA, patients with OA reported significantly more symptoms and disability than patients without OA.

CONCLUSIONS: There appears to be only moderate agreement between clinical diagnosis and radiological diagnosis of OA. In contrast, the agreement between different radiological grading scales is substantial.

Prevalence of osteoarthritis of the knee by diagnostic method

Diagnostic method	Women (%)	Men (%)	Total (%)
Clinical diagnosis	19.1	14.6	17.7
Kellgren–Lawrence (grade ≥ 2)	23.6	26.8	24.6
Ahlbäck (grade ≥ 1)	24.7	24.3	24.6
Piperno (grade ≥ 2)	28.1	34.1	30.0

RETROSPECTIVE ANALYSIS OF TRANSIENT ELEVATIONS IN ALANINE AMINOTRANSFERASE DURING LONG-TERM TREATMENT WITH ACETAMINOPHEN IN OSTEOARTHRITIS CLINICAL TRIALS

Current Medical Research and Opinion, 2006 November; 22(11):2137–48

AUTHORS: KUFFNER EK, TEMPLE AR, COOPER KM, BAGGISH JS, PARENTI DL

CENTERS: McNEIL CONSUMER HEALTHCARE, DIVISION OF McNEIL-PPC, INC, FORT WASHINGTON, PHILADELPHIA, USA

BACKGROUND & AIM: Acetaminophen is currently recommended as the first-choice oral analgesic for the acute and long-term management of osteoarthritic pain of the hip and knee, having a good long-term safety and tolerability. However, two recent osteoarthritis trials reported levels of alanine aminotransferase (ALT) to be raised more often in patients receiving acetaminophen than in those receiving placebo. The aim of this study was to determine the proportion of patients with any elevation of ALT, the magnitude of the ALT elevation, and the rate of ALT resolution while patients remained on acetaminophen treatment in McNeil-sponsored clinical studies of acetaminophen in patients with osteoarthritis.

STUDY DESIGN: Retrospective analysis.

ENDPOINTS: ALT levels; adverse events.

METHOD: Seven of nine controlled clinical trials that included acetaminophen alone as a treatment met inclusion criteria, namely, availability of ALT and aspartate aminotransferase (AST) data at baseline and at least one ALT value at an additional visit. Patients with ALT and/or AST values above the upper limit of the reference range (ULRR) at baseline were excluded. Patients

had received acetaminophen 1950–4000 mg/day for 4 weeks up to 12 months.

RESULTS: In the seven trials reviewed, 181 (17.4%) of 1039 patients (mean age 60.6 years) had an ALT value that exceeded the ULRR during long-term acetaminophen treatment. Subsequent ALT data were available for 139 of these patients: ALT levels normalized (\leq ULRR) in 102 (73.4%) and decreased in 26 (18.7%) patients while on treatment. Forty-four (4.2%) patients had an on-treatment ALT level more than 1.5 times the ULRR. Subsequent ALT data were available for 31 of these patients: ALT levels normalized or decreased in 29 (93.5%) of these patients while on treatment. Ten patients (0.96%) had an on-treatment ALT level more than 3 times the ULRR (levels subsequently decreased), and no patients had an ALT level higher than 10 times the ULRR. Hepatotoxicity or hepatic failure was not reported in any of the acetaminophen-treated patients.

CONCLUSION: Low-level increases in ALT concentrations are relatively common during long-term acetaminophen treatment but usually resolve or decrease with continued therapy and are not accompanied by clinically relevant signs or symptoms of liver injury.

EFFECTS OF A SELF-MANAGEMENT ARTHRITIS PROGRAMME WITH AN ADDED EXERCISE COMPONENT FOR OSTEOARTHRITIC KNEE: RANDOMIZED CONTROLLED TRIAL

Journal of Advanced Nursing, 2007 July; 59(1):20–8

AUTHORS: YIP YB, SIT JWH, FUNG KKY, WONG DYS, CHONG SYC, CHUNG LH, NG TP

CENTERS: SCHOOL OF NURSING, THE HONG KONG POLYTECHNIC UNIVERSITY, HUNG HOM, HONG KONG, CHINA; QUEEN MARY HOSPITAL, HONG KONG; KWONG WAH HOSPITAL, HONG KONG; AND ORTHOPEDICS SURGICAL DEPARTMENT, QUEEN MARY HOSPITAL, HONG KONG, CHINA

BACKGROUND & AIM: Osteoarthritis (OA) is a prevalent disorder that occurs predominantly after the fifth decade of life. Treatment of OA is mostly symptomatic. Some evidence suggests that increasing a patient's ability to cope with the disease and related symptoms (self-efficacy enhancement) may improve health outcomes. The aim of this study was to investigate the effect of an arthritis self-management program with an exercise component in increasing arthritis self-efficacy (ASE).

STUDY DESIGN: Randomized controlled study.

ENDPOINT: ASE

METHOD: Patients with knee OA ($n=182$) were randomized to a control group or to an arthritis self-management program (2-hour classes a week for 6 weeks). In these classes, patients were taught how to manage pain and other circumstances associated with OA, such as fatigue, physical limitations, and stress, using self-management techniques such as use of cold and hot compresses for pain relief, joint protection methods, and exercises (stretching, walking, and Tai Chi-like movements). Routine conventional treatment was continued for the intervention group and was the sole therapy for the control group. An ASE scale was used to measure a patient's ability to control pain (ASE:pain) and other symp-

toms (ASE:OS) related to OA. Assessments took place at baseline and at 1 week and 16 weeks after the intervention.

RESULTS: Sixty-seven patients in the intervention group and 53 in the control group completed the study. At 16 weeks, mean ASE:pain and ASE:OS had improved significantly in the intervention group but not in controls (between-group comparison $p=0.0001$). Patients in the intervention group, but not patients in the control group, showed a statistically significant improvement from baseline in self-management skills, such as using hot and cold compresses (34.10% at baseline versus 58.0% at 16 weeks; $p=0.0001$) and joint protective methods (e.g., sharing load over various joints, 83.0% versus 96.6%; $p=0.0001$), and could perform light exercise for significantly longer (5.60 ± 4.48 hours versus 7.17 ± 5.18 hours; $p=0.0001$). Compared with the control group, the intervention group showed a greater reduction in current arthritis pain (mean score change -11.88 versus -1.76 , respectively) and more favorable daily activities outcomes (mean score change -0.85 versus -0.60 , respectively) at 16 weeks.

CONCLUSION: An arthritis self-management program with an exercise component improves ASE, pain, and ability to perform daily activities in patients with OA.

PREDICTORS OF DEPRESSION IN A SAMPLE OF 1,021 PRIMARY CARE PATIENTS WITH OSTEOARTHRITIS

Arthritis & Rheumatism, 2007 April 15; 57(3):415–422

AUTHORS: ROSEMANN T, BACKENSTRASS M, JOEST K, ROSEMANN A, SZECSENYI J, LAUX G

CENTERS: UNIVERSITY HOSPITAL OF HEIDELBERG, HEIDELBERG; AND ACADEMIC HOSPITAL OF THE LUDWIG-MAXIMILIANS UNIVERSITY MUNICH, ROSENHEIM, GERMANY

BACKGROUND & AIM: Osteoarthritis (OA) and depression are both highly prevalent in the older population. Depression has a substantial impact on OA because of its effects on the two main symptoms of OA, namely, pain and disability. Depressed patients with OA are more likely to have an increased sensitivity to pain and less effective coping with the illness. Thus treatment of depression may improve the health status and functional ability of patients with OA. It is therefore important to identify patients with OA who are at risk of depression. The aim of this study was to determine the prevalence of depression and to identify risk factors for depression in patients with OA.

STUDY DESIGN: Cross-sectional study.

ENDPOINTS: Prevalence of depression; risk factors for depression.

METHOD: In total 1250 patients were sent a set of self-administered questionnaires assessing general information (sociodemographic data, education level, and presence of associated comorbidities), depression, and the health impact of OA. Depression was evaluated with the Patient Health Questionnaire (PHQ-9), and a validated and adapted German version of the Arthritis Impact Measurement Scales Short Form (AIMS2-SF) was used to evaluate aspects of functional health associ-

ated with OA, such as physical limitation (upper or lower body), perceived pain, mood, and patient social and work-related characteristics.

RESULTS: Of the 1021 patients who returned the questionnaires, 66% were women and 92% were white. Fewer than 9% of the patients used antidepressants. PHQ-9 scores showed that 100 men and 233 women were classified as not depressed, whereas 181 women and 107 men were depressed (PHQ-9 score ≥ 10); of these, 52 men and 99 women were moderately severely depressed (PHQ-9 score 15–19). Bivariate correlation showed a linear relationship between PHQ-9 scores and all components of the AIMS2-SF, OA duration, age, number of comorbidities, and body mass index. On multiple regression analysis, age was inversely associated with depression. Perceived pain was the strongest predictor of depression severity, followed by restricted social contacts and physical limitations.

CONCLUSIONS: Depression is highly prevalent among patients with OA, with pain, few social contacts, and physical limitations being the strongest predictors of depression severity. Modification of these and other predictors may help decrease the prevalence of depression in this population.

RELATIONSHIP OF HEIGHT, WEIGHT AND BODY MASS INDEX TO THE RISK OF HIP AND KNEE REPLACEMENTS IN MIDDLE-AGED WOMEN

Rheumatology, 2007 May; 46(5):861–7

AUTHORS: LIU B, BALKWILL A, BANKS E, COOPER C, GREEN J, BERAL V, ON BEHALF OF THE MILLION WOMEN STUDY
COLLABORATORS
CENTERS: CANCER RESEARCH UK EPIDEMIOLOGY UNIT, UNIVERSITY OF OXFORD, OXFORD, UK; NATIONAL CENTRE FOR EPIDEMIOLOGY AND PUBLIC HEALTH, AUSTRALIAN NATIONAL UNIVERSITY, CANBERRA, AUSTRALIA; AND MRC EPIDEMIOLOGY RESOURCE CENTRE, UNIVERSITY OF SOUTHAMPTON, SOUTHAMPTON, UK

BACKGROUND & AIM: Rates of primary hip and knee joint replacement are rising in many developed countries. While joint replacement surgery is more common among women and people older than 60 years, little is known about risk factors for such surgery. Studies have shown body mass index (BMI) to be predictive of total hip replacement for osteoarthritis, and adult height to be associated with hip replacement. Little is known about the relationship between height and knee replacement. The aim of this study was to investigate whether height, weight, and BMI affect the risk of primary hip and knee joint replacement in middle-aged women.

STUDY DESIGN: Prospective cohort study.

ENDPOINT: Relation between BMI and knee or hip replacement.

METHOD: Women aged 50–69 years recruited into the Million Women Study in UK in 1996–2001 were followed up for 2.9 years ($n=490,532$ women) to determine the rate of hip or knee replacement due to osteoarthritis. Relative risks for the relationship between height, weight, and BMI and first incident hip or knee replacement were calculated using a Cox regression model.

RESULTS: In total, 1917 women had a hip replacement and 974 had a knee replacement (rates of 1.4 and 0.7 per 1000 person-years, respectively). Height (≥ 170 cm), weight (≥ 75 kg), and BMI (≥ 30 kg/m²) were associated with an increased risk of hip or knee replacement (see Table). These effects did not vary with age, education, alcohol and tobacco consumption, frequency of strenuous activity, parity, or use of hormone therapy.

CONCLUSIONS: In middle-aged women, the risk of having a hip or knee replacement increases with increasing height, weight, and BMI. Even relatively small increases in average BMI are likely to have a substantial impact on rates of joint replacement.

Relative risk of hip and knee joint replacement according to height, weight, and body mass index (BMI)

	Risk of hip replacement (95% CI)	Risk of knee replacement (95% CI)
Height (cm)		
<155	1.00 (0.84–1.19)	1.00 (0.81–1.23)
155–159	1.22 (1.11–1.36)	1.04 (0.91–1.19)
160–164	1.28 (1.17–1.39)	1.17 (1.04–1.32)
165–169	1.64 (1.50–1.79)	1.27 (1.11–1.45)
>170	1.90 (1.71–2.10)	1.55 (1.32–1.80)
<i>p</i> value (trend)	<0.0001	<0.0001
Weight (kg)		
<60	1.00 (0.88–1.44)	1.00 (0.77–1.29)
60–64	1.19 (1.06–1.34)	1.89 (1.55–2.32)
65–69	1.51 (1.35–1.69)	2.38 (1.95–2.92)
70–74	1.92 (1.73–2.14)	4.27 (3.63–5.02)
>75	2.37 (2.19–2.56)	9.71 (8.88–10.62)
<i>p</i> value (trend)	<0.0001	<0.0001
BMI (kg/m ²)		
<22.5	1.00 (0.88–1.13)	1.00 (0.76–1.32)
22.5–24.9	1.31 (1.19–1.44)	1.65 (1.37–1.98)
25–27.4	1.52 (1.38–1.67)	3.19 (2.75–3.69)
27.5–29.9	1.64 (1.46–1.85)	5.53 (4.88–6.48)
>30	2.47 (2.25–2.71)	10.51 (9.52–11.62)
<i>p</i> value (trend)	<0.0001	<0.0001

META-ANALYSIS: ACUPUNCTURE FOR OSTEOARTHRITIS OF THE KNEE

Annals of Internal Medicine, 2007 June 19; 146(12):868–77

AUTHORS: MANHEIMER E, LINDE K, LAO L, BOUTER LM, BERMAN BM

CENTERS: CENTER FOR INTEGRATIVE MEDICINE, UNIVERSITY OF MARYLAND SCHOOL OF MEDICINE, KERNAN HOSPITAL MANSION, BALTIMORE, MARYLAND, USA; CENTRE FOR COMPLEMENTARY MEDICINE RESEARCH, DEPARTMENT OF INTERNAL MEDICINE II, TECHNISCHE UNIVERSITÄT MÜNCHEN, MUNICH, GERMANY; AND VU UNIVERSITY, EXECUTIVE BOARD, VU-WINDESHEIM, AMSTERDAM, THE NETHERLANDS

BACKGROUND & AIM: The evidence for nonpharmacological treatments for osteoarthritis (OA) of the knee is generally sparse and inconclusive, although weight loss and exercise have proved effective. However, because not all patients are able to lose weight or exercise, there is a need for additional safe and effective treatments. While acupuncture is a safe treatment, its efficacy in OA is not known. The aim of this study was to conduct a systematic review and meta-analysis of the effects of acupuncture for treating knee OA.

STUDY DESIGN: Meta-analysis.

ENDPOINTS: Standardized mean differences (SMD) in pain and function.

METHOD: The MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials databases were searched to January 2007 to identify randomized, controlled trials (RCTs) of acupuncture with at least 6 weeks of observation. The RCTs were classified according to control groups, which were sham, usual care, and waiting list. Short-term follow-up was defined as the measurement point closest to 8 weeks, but no longer than 3 months after randomization. Long-term outcome was defined as the measurement point closest to 6 months but longer than 3 months after randomiza-

tion. SMD were calculated using differences in improvements from baseline between patients assigned to acupuncture or control groups. Clinically relevant improvement was defined as an SMD of 0.39 for pain and 0.37 for function.

RESULTS: Eleven trials met the selection criteria, and nine reported sufficient data for pooling. Patients treated with acupuncture reported clinically relevant short-term improvements in pain (SMD -0.96) and function (SMD -0.93) compared with waiting list controls and clinically relevant short- and long-term improvements in pain (SMD -0.62 and -0.52 , respectively) and function (SMD -0.56 and -0.45 , respectively) compared with usual care controls. However, when compared with a sham control, acupuncture failed to produce clinically relevant improvements in pain and function in either the short (pain SMD -0.35 ; function SMD -0.35) or long (pain SMD -0.13 ; function SMD -0.14) term.

CONCLUSIONS: Acupuncture does not have a clinically relevant effect on pain or function when compared with sham acupuncture in patients with OA of the knee. The clinically relevant effects of acupuncture compared with a waiting list or usual care control group are probably due to placebo or expectation effects.

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