



Figure. Study cohort three-dimensional knee kinematic curve measurements.

Frequency of mechanical factors linked to knee OA in the study cohort	
Varus alignment at initial contact	42 (70%)
Varus alignment during stance	42 (70%)
Knee flexion at initial contact	46 (76.7%)
Limited flexion excursion during loading	60 (100%)
Fixed flexion during stance	48 (80.0%)
Decreased sagittal plane range of motion	50 (83.3%)

485 SKIN PENTOSIDINE IN VERY EARLY HIP/KNEE OSTEOARTHRITIS (CHECK) IS NOT A STRONG INDEPENDENT PREDICTOR OF RADIOGRAPHIC PROGRESSION OVER 5 YEARS FOLLOW-UP

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Purpose: Age-related changes in articular cartilage are likely to play a role in the aetiology of osteoarthritis (OA). One of the major age-related changes in cartilage is the accumulation of advanced-glycation-endproducts (AGEs). The present study evaluates whether pentosidine can predict radiographic progression and/or burden over 5 years follow-up in a cohort of early knee and/or hip OA.

Methods: The Cohort Hip and Cohort Knee (CHECK) is a cohort of participants with very early OA. In this study data of 5 years follow-up were used. Radiographic progression and burden were assessed by X-rays of both knees and hips (K&L and Altman scores). Radiographic OA burden was expressed as the summed K&L grade or Altman scores of both hips and knees. Radiographic OA progression was expressed as the area under the curve (AUC) of the summed K&L grade over the 5 years minus the baseline value over 5 years. The burden of radiographic joint

damage was expressed as the AUC over 5 years. For the summed Altman scores for JSN and osteophyte formation the same approaches were used to determine progression and burden scores per patient.

Baseline skin pentosidine levels (and urinary CTXII as a comparator) were measured by HPLC (and ELISA). Univariate and multivariate associations including baseline radiographic damage, age, gender, BMI and kidney function were performed.

Results: Of 183 participants all data were available. At 5-year follow-up radiographic progression of OA was seen (sum K&L score 1.69 ± 1.13 at T0 versus 3.30 ± 1.81 at T5). Both pentosidine and uCTXII correlated with this radiographic progression and burden (ie progression AUC sum K&L score $R=0.167$ $p=0.024$ and $R=0.323$ and $p=0.000$ for skin pentosidine and urine CTXII, respectively). In multivariate analysis, in general pentosidine did not have an added predictive value to uCTXII for progression nor burden of the disease. The best prediction was obtained for burden of radiographic damage ($R^2=0.60-0.88$), but this was predominantly determined by baseline radiographic damage (without this parameter $R^2=0.07-0.17$). Interestingly, pentosidine significantly added to prediction of osteophyte formation, whereas uCTXII significantly added to prediction of JSN in multivariate analysis.

Conclusion: Pentosidine adds to prediction of radiographic progression and burden of osteophyte formation and uCTXII to radiographic progression and burden of JSN, but overall skin pentosidine did not perform better than uCTXII in predicting radiographic progression or burden. Burden of damage over 5 year is mainly determined by radiographic joint damage at baseline.

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OSTEOARTHRITIS OF THE KNEE AT 6-YEAR FOLLOW-UP AND THEIR PROGNOSTIC FACTORS IN PATIENTS WITH TRAUMATIC KNEE COMPLAINTS IN GENERAL PRACTICE

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Purpose: To identify degenerative abnormalities of the knee on magnetic resonance imaging (MRI) and radiography 6 years after knee trauma, and their relation with persistent knee complaints and prognostic factors at baseline (including MRI findings).

Methods: Adults (18–65 years) with incident traumatic knee complaints who visited their general practitioner were followed for 6 years. To identify degenerative abnormalities, an MRI was made at baseline and at 6-year follow-up, and a radiograph was made at 6-year follow-up. Logistic regression analysis was used to calculate associations between the various degenerative abnormalities on the 6-year MRI and the 6-year radiograph, their relation with persistent knee complaints, and to identify baseline prognostic factors associated with knee osteoarthritis (OA) at the 6-year MRI.

Results: On the 6-year radiograph, 60% of the patients showed no OA, 28% OA with a Kellgren & Lawrence (K&L) grade 1 and 13% had a K&L grade 2. On the 6-year MRI, 55% of the patients showed cartilage defect(s), 45% osteophyte(s), 36% subchondral cyst(s), 40% bone marrow edema, 21% meniscal subluxation, 83% meniscal degeneration, 11% effusion and 11% a Baker's cyst. Most degenerative abnormalities on the 6-year MRI were significantly related with the K&L score on the 6-year radiograph. Only a few abnormalities [lateral cartilage defect(s), medial osteophyte(s) and medial meniscal subluxation] were also significantly related with persistent knee complaints at 6-year follow-up. For knee OA seen on the 6-year MRI, 32% of the patients showed new onset or progressive knee OA. Age, history of non-traumatic knee complaints and bone marrow edema on the baseline MRI were independently related with new onset or progressive knee OA on the 6-year MRI.

Conclusions: Degenerative abnormalities on MRI of the knee are related to the K&L score on knee radiography; however, not all abnormalities are reflected in clinical outcome. Six years after knee trauma, knee OA is present in 32% of the patients. Age, history of non-traumatic knee complaints and bone marrow edema are possible predictors for new onset or progressive knee OA 6 years after knee trauma.

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BIOMECHANICAL MECHANISMS UNDERLYING TREATMENT EFFECTS OF EXERCISE THERAPY IN PATIENTS WITH KNEE OSTEOARTHRITIS: DATA FROM A RANDOMIZED CONTROLLED TRIAL

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Purpose: To evaluate longitudinal associations between changes in biomechanical functions and changes in pain and activity limitations in knee OA patients treated with exercise therapy.

Methods. Data were used from a randomized controlled trial (NTR1475) in which two exercise programs of 12 weeks were compared. One hundred forty nine patients with knee OA, who completed the exercise program, were measured at baseline and at 6-, 12- and 38-week follow-up. Generalized Estimating Equations (GEE) analyses were used to determine longitudinal associations of changes in biomechanical functions (upper leg muscle strength, knee joint proprioceptive accuracy, self-reported knee instability and knee flexion and extension range of motion) with changes in pain severity (numeric rating scale) and activity limitations (WOMAC, physical function and Get up and go test) over time. Univariable and multivariable associations, analyzing all biomechanical functions together, were performed.

Results. Improvements in upper leg muscle strength (both quadriceps and hamstrings strength) and self-reported knee stability were longitudinally associated with outcome of exercise therapy, i.e. improvements in pain and activity limitations, while improvements in proprioceptive accuracy or knee range of motion were not.

Conclusions. Muscle strengthening and knee stabilization were consistently associated with outcome of exercise therapy in knee OA patients. These findings provide better insight in underlying biomechanical mechanisms of exercising in OA, which may help optimizing exercise effects.

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MANAGING CHRONIC KNEE SYMPTOMS: "WE'RE ALL LOOKING FOR SOLUTIONS"

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Purpose: The prevalence of osteoarthritis (OA) increases with age and as a result, much of the focus of OA has been on older adults. However, the first signs of OA begin in the fourth or fifth decade or even sooner. The estimated incidence of OA increases exponentially in adults aged 20-50 years and there is also evidence that OA is progressing to severe disease in people of younger ages as demonstrated by a 311% increase in the number of total knee replacements in 45-54 year olds. To date, policy efforts and interventions have focused largely on older adults and end stage disease. There is an opportunity for earlier intervention in the working age population to support management of knee symptoms or even halt or delay progression of OA and its concomitant morbidity. Currently, there is inadequate knowledge about younger adults with knee symptoms to target their needs with interventions. We aimed to explore how people aged 35-65 years manage their knee symptoms including how they make decisions about management.

Methods: The research design was qualitative, using grounded theory methods. We included individuals aged 35-65 who self-reported a diagnosis of OA or reported knee symptoms (i.e. pain, aching or stiffness) on most days of the past month. Purposive sampling was used, in particular seeking variation in age and sex. Data were collected using focus groups; participants were organized into focus groups based on two age groups (35-49 years and 50-65 years). All focus groups were audio recorded and transcribed verbatim. Data were analyzed using

a constant comparative method. The three main steps in analysis were open coding, axial coding and progressively conceptualizing and categorizing the data.

Results: Six focus groups were conducted with 41 participants. The mean age was 50.9 years (range 38-65 years) and 63.0% were female. Our analysis identified three main themes. 1. *The Work of Managing Knees: Tactical Responses and Long Term Solutions:* Participants made considerable efforts to try a range of strategies to manage their knee symptoms (e.g exercise, weight loss, medications, diet). They also described adaptations in their daily life, such as modifications or restriction of activities. While some strategies were used to address immediate symptoms, participants were also interested in a longer term solution which would fix the problem or delay progression. 2. *The Work of Decision Making:* Participants described how they made decisions about management of their knee symptoms. Their actions included consulting others, researching available options, evaluating the trustworthiness of information and then using trial and error. 3. *The Work of Navigating Health Care:* Participants' experiences indicated that navigating the health care system added to the work of managing their knees. They commonly expressed perceptions that the health care system didn't offer much for them. This resulted in expressions of frustration, particularly for younger adults. These categories are inextricably interwoven into a core category, *Working Hard but Still Seeking Solutions.* Participants' accounts suggest that people are making efforts to manage their knee problems and, in many cases, are still seeking better solutions for their knee symptoms.

Conclusions: We found that people with knee symptoms are making considerable efforts to learn about and execute a range of management strategies even at earlier ages and stages of disease, often with little support as they navigate through the health care system. These findings suggest there is opportunity for earlier intervention to provide support for people with knee symptoms to ensure people are engaging in best practices for their knee that are likely to make a difference in the short and long term.

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A SYSTEMATIC REVIEW OF THE LITERATURE ON BEST PRACTICE AND QUALITY OF CARE FOR PATIENTS WITH OSTEOARTHRITIS IN THE SETTING OF DIABETES OR CARDIOVASCULAR DISEASE

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Purpose: The management of osteoarthritis (OA) is challenging in patients who also have other medical conditions, which may be perceived as precluding the safe use of OA therapies. We conducted a systematic review of the literature to identify and evaluate studies that addressed best practice or quality of OA care in the setting of diabetes (DM) and/or cardiovascular disease (CVD).

Methods: Two reviewers independently reviewed titles and abstracts of publications identified via a comprehensive search of electronic databases (MEDLINE, EMBASE, and CINAHL) between January 2000 and February 2011 and citation lists. Articles addressing the management of OA in the presence of DM or CVD (or vice versa) were included.

Results: 8334 articles were identified through the search process, 41 were selected for full-text review and 32 were included after discussion. Only 10 of the 32 identified studies (31%) discussed strategies to improve OA management in the setting of comorbid DM and/or CVD. Five studies recommended cautious prescribing of non-steroidal anti-inflammatory drugs (NSAIDs) and cyclo-oxygenase (COX)-2 inhibitors in patients with CVD or CV risk factors. One study recommended naproxen for treatment of OA in the setting of DM and CVD; another recommended acetaminophen with or without codeine in the setting of hypertension (HTN). Three studies recommended only non-pharmacological approaches. Six of 32 studies (19%) documented pharmacological under-treatment of one condition in the presence of another (use of NSAIDs and overall treatment for OA in CVD/DM; treatment of HTN in OA). 3 studies showed no differences in prescribing patterns. Eight studies (25%) documented a negative impact of OA on outcomes for CVD/DM (recovery from stroke, hospitalization for congestive heart failure and physical activity/self-management). Three qualitative studies identified comorbid OA as a barrier to care for CVD/DM. Three studies documented the non-applicability of single-disease clinical practice guidelines to the management of patients with multiple conditions, including OA guidelines in the setting of CVD/DM. Only one study evaluated the influence of either DM or CVD on quality of care for