incident osteophytes at 30 months, respectively, using Poisson regression with GEE in knee-based analyses. We performed additional analyses on a subregion-basis. Given the systemic effects of vitamin K, we also performed person-based analyses examining the relation of vitamin K deficiency with risk for having incident OA in 1 or 2 knees. All analyses were adjusted for age, sex, BMI, BMD and 25(OH)-vitamin D.

Results: Among 1180 participants (62% women, mean age 62.7±9.9 years, mean BMI 30.1±5.1 kg/m², median vitamin K 1.2 nm), 21% developed incident knee OA over 30 month follow-up and 9.2% were vitamin K deficient at baseline. In the knee-based analyses, compared with those who were not vitamin K deficient, those who were deficient had 1.43 times higher risk of incident radiographic OA (95% CI 0.99-2.09) and 2.82 times higher risk of incident cartilage abnormality (95% CI 1.26-6.30). Vitamin K deficiency was not statistically significantly associated with incident osteophytes in the knee-based analyses (RR 1.77, 95% CI 0.41-7.55), although this sample was small as most knees had some osteophytes at baseline and were therefore excluded. The risk of incident osteophytes on a subregion basis was similar to the knee-based analyses (RR 1.61, 95% CI 0.71-3.66). In the person-based analyses, those who were vitamin K deficient were more likely to develop incident OA in 2 knees versus 0 knees (RR 2.07, 95% CI 1.28-3.36), 2 knees versus 1 knee (RR 2.76, 95% CI 0.99-7.69) and 1 knee versus 0 knees (RR 1.23, 95% CI 1.01-1.50).

Conclusions: In this first longitudinal study of vitamin K in OA, we found that vitamin K deficiency was associated with an increased risk of incident knee OA, extending prior cross-sectional findings, as well as with incident cartilage abnormalities. We could not detect an association with incident osteophytes but most knees had osteophytes at baseline, limiting sample size for this analysis. Further study of vitamin K is warranted given its potential to be a simple and effective preventive agent.

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USING OAI CLINICAL DATA TO STUDY THE PROGNOSTIC ROLE OF MENTAL HEALTH
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Purpose: The Osteoarthritis Initiative provides an excellent source of public use data for the study of prognostic factors that may influence pain and functional status of patients with knee osteoarthritis. An extensive literature has examined various prognostic factors but little research has been done to determine if mental health constructs impact future knee pain or function. The goals of this study were to determine whether baseline depression (measured with the CESD), knee related confidence (measured on a Likert scale) and general psychological distress (measured with the SF-12) influenced change in pain and functional status outcomes during two years of follow up.

Methods: To define the sampling frame we included only persons who reported baseline pain of 1 or greater on a 0 to 10 scale in at least one knee and had no knee or hip surgery during the two-year follow-up (n=3407). The four outcome variables of interest included performance-based measures of repeated chair standing and the 20 meter walk test, and self report measures of pain and disability (WOMAC) where the worst of the two knees was used as a person-level measurement. Linear mixed effects models were used to assess the association of each mental health variable with the change of each outcome measure over time. Examination of the descriptive data for the entire sample indicated that little change occurred in the outcome measures. As importantly, change was highly dependent on baseline outcome score. For example, persons scoring in the lowest quartile (least pain) on WOMAC Pain at baseline increased their mean score by 0.2 WOMAC points at 1 year while persons in the highest quartile (worst pain) had reductions in their mean 1 year scores of 6.6 WOMAC points. Because change was highly dependent on baseline outcome, we adjusted for the baseline score for all analyses. All variables prognostic of pain or function identified in previously published large sample cohort studies were considered, and covariates significantly associated with the change in outcome at significance level 0.10 were included in the multivariate analyses to determine the independent role of each of the mental health variables on outcome.

Results: Depression was significantly predictive of the change in WOMAC Pain and Disability outcomes, 20 meter walk time and repeated chair stand time. However, given the very small changes overall in the outcomes, the magnitude of change predicted for each year was very small. For example, for WOMAC pain, each point increase in depression at baseline resulted in a 0.02 point increase in WOMAC Pain scores each year. This finding was highly significant (p<0.0008) and very robust (Estimate = 0.02, Standard error = 0.006). Knee confidence was not predictive of change for any outcome. General psychological distress as measured with the SF-12 Mental Health score was predictive of change in 20 meter walk times and WOMAC Pain.

Conclusions: The most consistent psychological predictor of the change in WOMAC and performance outcomes during the two-year follow up was depression. Although depression in particular appears to be a statistically robust predictor of outcome, given that change is very small and highly dependent on baseline status, our results indicate that a considerable degree of depression would be required to have a meaningful effect on future function.

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URINARY MARKERS, ALPHA CTX AND CTXII, ARE INDICATIVE OF OA SEVERITY AND BONE TURNOVER
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Purpose: Biological markers have the potential to aid in the identification of people in the earliest stage of osteoarthritis (OA), prior to any evidence of radiographic disease, when interventions would be most efficacious. We have recently shown that bone scintigraphy is a sensitive indicator of symptomatic knee OA and may be a useful marker of early OA events related to bone turnover. Urinary ALPHA CTX, a marker specific for localized high bone turnover, reflecting bone resorption of newly formed type I collagen by osteoclasts, has shown a strong correlation to the number of bone metastases determined by scintigraphy in patients with breast and prostate cancers. A similar pattern of local high bone turnover has been observed by scintigraphy in patients with OA, thus ALPHA CTX was investigated as a potential OA marker. Urinary CTXII, a well studied marker which detects the C-telopeptide of type II collagen, has previously been shown to be associated with radiographic disease and OA progression. We hypothesize that urinary biomarkers related to degradation of types I and II collagen, ALPHA CTX and CTXII, may be indicative of OA severity and correlate to amount of high bone turnover determined by bone scan.

Methods: A total of 159 participants (118 women, 41 men) were included who met ACR criteria for symptomatic OA and had the presence of Kellgren Lawrence grade 1-4 radiographic OA in at least one knee. In addition to KL grade, which represents global OA severity, compartmental OA severity, based on scoring of osteophytes and joint space narrowing (range of 0-3 for each knee), was determined using the standardized OARSI radiographic atlas. Late phase bone scan images, indicative of bone turnover, were obtained 2 hours after administration of 99mTc-MDP. Four views of each knee (anterior, posterior, medial, and lateral) were obtained to precisely localize intensity and site of uptake. Bone scan images were scored semi-quantitatively by two readers at 16 joint sites, each of which was scored on a scale of 0-3, where 0=normal, 1= mild, 2=moderate, and 3=intense. Urine samples were obtained and stored at ~40C until analysis. Concentrations of urinary markers, ALPHA CTX and CTXII (Nordic Biosciences) were determined by ELISA and normalized to creatinine concentration. All data were transformed logarithmically to obtain normality. All aspects of this study were approved by the Institutional Review Board.

Results: Urinary ALPHA CTX did not correlate with severity of knee OA based on the static radiographic features (OST and JSN) but did correlate with the dynamic measure of bone turnover based on intensity of bone scintigraphic uptake in the medial knee compartment. Concentrations of urinary CTXII were strongly correlated with knee OA severity based on osteophyte (medial > lateral OST, Table 1), but not degree of joint space narrowing. Urinary CTXII also correlated with the dynamic measure of bone turnover showing a correlation with intensity of bone scintigraphic uptake in the knee (medial > lateral compartment but not the patellofemoral compartment, Table 2).

Discussion: Urinary ALPHA CTX and CTXII are sensitive markers capable of reflecting accelerated bone turnover in patients with knee OA. Both markers correlated with active bone turnover in the knee. In addition, uCTXII correlated with radiographic OST scores. It has been suggested that the main source of uCTXII is remodeling of type II collagen of mineralized tissue including osteophytes and the mineralized interface between cartilage and bone. Given the systemic effects of vitamin K, we also performed person-based analyses examining the relation of vitamin K deficiency with risk for having incident OA in 1 or 2 knees. All analyses were adjusted for age, sex, BMI, BMD and 25(OH)-vitamin D.

Results: Among 1180 participants (62% women, mean age 62.7±9.9 years, mean BMI 30.1±5.1 kg/m², median vitamin K 1.2 nm), 21% developed incident knee OA over 30 month follow-up and 9.2% were vitamin K deficient at baseline. In the knee-based analyses, compared with those who were not vitamin K deficient, those who were deficient had 1.43 times higher risk of incident radiographic OA (95% CI 0.99-2.09) and 2.82 times higher risk of incident cartilage abnormality (95% CI 1.26-6.30). Vitamin K deficiency was not statistically significantly associated with incident osteophytes in the knee-based analyses (RR 1.77, 95% CI 0.41-7.55), although this sample was small as most knees had some osteophytes at baseline and were therefore excluded. The risk of incident osteophytes on a subregion basis was similar to the knee-based analyses (RR 1.61, 95% CI 0.71-3.66). In the person-based analyses, those who were vitamin K deficient were more likely to develop incident OA in 2 knees versus 0 knees (RR 2.07, 95% CI 1.28-3.36), 2 knees versus 1 knee (RR 2.76, 95% CI 0.99-7.69) and 1 knee versus 0 knees (RR 1.23, 95% CI 1.01-1.50).

Conclusions: In this first longitudinal study of vitamin K in OA, we found that vitamin K deficiency was associated with an increased risk of incident knee OA, extending prior cross-sectional findings, as well as with incident cartilage abnormalities. We could not detect an association with incident osteophytes but most knees had osteophytes at baseline, limiting sample size for this analysis. Further study of vitamin K is warranted given its potential to be a simple and effective preventive agent.