were used to assess which parameters (age, sex, BMI >30, prescription of opioids or physical therapy, WOMAC, whether the OA was mainly treated by an orthopaedist) were associated with having discussed a TJR.

Results: Of 2352 persons with knee or hip OA, 932 had symptomatic OA of the knee, 478 of the hip, 94 of both, and 848 did not report pain in the relevant joint(s). Mean age was 64 to 67 years, 63% to 68% were female and mean BMI was high, especially in patients with knee OA (29 kg/m²). 54%–74% had considerable impairment (WOMAC>39). 72%–83% had any pain medication, 12%–25% opioids and 33%–46% physical therapy. 63%–72% were treated by orthopaedists and 45%–50% had discussed TJR. In knee as well as hip and knee OA male sex and an orthopaedist as main treating physician was associated with having discussed a TJR (table 1). Age, WOMAC and opioid prescription was only associated with a higher OR of discussing a TJR in knee OA.

Abstract FRI0526 – Table 1. Results from multivariable logistic regression models showing parameters associated with having discussed TJR.

	OR for knee and hip OA (n=94), 95% CI	OR for hip OA (n=478), 95% CI	OR for knee OA (n=932), 95% CI
Orthopaedist is treating	7.2 (1.9,26.8)	1.6 (0.9,2.8)	1.7 (1.1,2.6)
Age, per 10 years	1.0 (0.56,1.8)	1.0 (0.8,1.3)	1.2 (1.1,1.5)
BMI≤30 vs>30	0.9 (0.2,3.6)	1.0 (0.6,1.8)	1.3 (0.9,2.0)
Male vs female	5.3 (1.3,21.8)	1.1 (0.6,1.8)	1.5 (1.1,2.2)
WOMAC, per 10%	1.3 (0.8,1.9)	1.1 (0.9,1.3)	1.3 (1.2,1.5)
Opioids	0.8 (0.1,6.1)	0.5 (0.2,1.2)	1.9 (1.0,3.3)
Physical therapy	1.1 (0.3,3.3)	1.1 (0.6,2.0)	1.2 (0.8,1.7)

Conclusions: Disease burden is highest in persons with concomitant knee and hip OA. Men are more likely to discuss TJR with their physician, but not in hip OA. Disease burden and treatment recommendations were only weakly associated. Therefore, other factors may be more important when considering surgery in knee and hip OA.

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FRI0527 EFFICACY OF BIO-OPTIMISED CURCUMA EXTRACT (FLEXOFYTOL®) FOR PAINFUL KNEE OSTEOARTHRITIS: DATA FROM COPRA, A MULTICENTER RANDOMISED CONTROLLED STUDY

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Background: Flexofytol is a Curcuma Longa extract with an increased bioavailability (bio-optimised) by mixing curcuma extract with polysorbate.

Objectives: To demonstrate the effects of Flexofytol on OA symptoms and soluble biomarkers.

Methods: 141 patients with symptomatic knee OA (mean age 61.8 years [min.45–max.86]; 80.1% female; mean K and L grade of the knee 2.4; mean BMI 29.7 kg/m²) were randomised in a prospective double blinded, 3 parallel groups, comparative and multicenter, study (NCT02909621). At inclusion, all patients took pain killers or anti-inflammatory drugs which were authorised during the study. Patients received 6 months continuous treatment with either high dose Flexofytol (n=49, 140.01 mg Curcuma longa L. extract/treatment), low dose Flexofytol (n=47, 93.34 mg Curcuma longa L. extract/treatment) or placebo (n=45, Sunflower seed oil fill ingredient). Each treatment corresponded to 3 oral capsules two

times a day to respect the blinding. All patients had clinical assessment (knee pain, knee function and patient global assessment of disease activity [PGADA]) and blood sampling for biomarkers measurements (usCRP and sColl2–1) at baseline (T0), 1 month (T1), 3 months (T3) and 6 months (T6). Additionally, patient compliance, satisfaction and tolerance were assessed at each timepoint following baseline. Primary outcome was the change at 3 months versus baseline in type II collagen degradation-specific biomarker sColl2–1 and VAS PGADA.

Results: Comparison of time evolution curves showed that sColl2–1 levels were lower in the treated groups but differences were not significant. The decrease in PGADA overtime was significantly more important in low dose group than in placebo group only at the 1 month evaluation timepoint (low dose Δ T1-T0, –12.5 mm vs placebo Δ T1-T0, –2 mm, p=0.035). Further, the knee pain relief was significantly higher in low dose group at T1 and T3 than in placebo (low dose Δ T1-T0, –16.5 mm vs placebo Δ T1-T0, –4 mm p=0.046; low dose Δ T3-T0, –36.5 mm vs placebo Δ T3-T0, –8 mm p=0.043). No difference was observed at T6. No differences were seen for any parameter when the high dose group was compared with the placebo group at any time point. The global KOOS score and its subscales significantly decreased overtime but changes were comparable in each group. Additionally, patient compliance was good and patient satisfaction remained stable overtime in each group. The ratio of patients with adverse events (AE) related to the product were similar in placebo and treated groups but the number of AE linked to the product was higher in the high dose group than in placebo (p=0.012).

Conclusions: Flexofytol, at a low dose, induced a rapid symptomatic relief on knee pain and a beneficial effect on the patient assessment of disease. This study also provides information on the dose to use and the design of a larger phase III clinical trial.

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FRI0528 LONG-TERM EFFECTS OF VITAMIN D SUPPLEMENTATION AND MAINTAINING VITAMIN D SUFFICIENCY ON KNEE OSTEOARTHRITIS OVER 5 YEARS

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Background: Epidemiological studies suggest that vitamin D deficiency is associated with knee symptoms and structural progression of knee osteoarthritis (OA). However, randomised controlled trials (RCTs) failed to demonstrate a significant effect of vitamin D supplementation on OA, probably due to selecting OA participants with and without vitamin D deficiency, short duration of follow-up and a large proportion of participants in the placebo group reaching vitamin D sufficiency (61.3% of patients in the placebo group achieved a serum 25(OH)D level of >60 nmol/L at 3 months of a clinical trial).

Objectives: To examine whether those maintaining sufficient serum vitamin D levels over 5 years had reduced knee symptoms compared with those who did not maintain adequate vitamin D levels in patients with knee OA. We also explored the effect of 2 year vitamin D supplementation on knee symptoms compared to placebo after 3 years of cessation of treatment.

Methods: Participants with symptomatic knee OA and low 25-hydroxyvitamin D [25(OH)D] (12.5–60 nmol/L) were randomly assigned to receive monthly treatment with oral vitamin D3 (50 000 IU; n=209) or an identical placebo (n=204) for 2 years. 172 participants who enrolled in the study from Hobart were followed up after 3 years (5 years from baseline) of the cessation of the treatment to assess knee symptoms and vitamin D levels. Participants were classified as maintaining sufficient vitamin D group if they maintained serum 25(OH)D>50 nmol/L at month 3, 24 and 60 (n=79), and not maintaining sufficient vitamin D group (25(OH)D≤50 nmol/L at month 3, 26 and 60, n=62) groups. Knee symptoms were assessed at baseline, 3, 6, 12, 24 and 60 month using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

Results: The level of 25(OH)D dropped in the vitamin D group (87.0 nmol/L to 53.3 nmol/L) and slightly increased (53.3 nmol/L to 61.7 nmol/L) in the placebo group 3 years after the cessation of the treatment. Knee pain increased from the end of the study to 5 years of follow-up in the treatment (81.8 to 91.7) and placebo (75.8 to 101.1) groups. 16.7% of the participants in vitamin D and 18.5% of the participants in placebo group underwent total knee replacement (TKR) surgery. There were no significant differences in WOMAC symptoms, TKR rates or change in symptoms between Vitamin D and placebo groups after 3 years of cessation of the supplementation.

Participants who maintained adequate vitamin D levels over 5 years had significantly less WOMAC knee pain (β : -38.4, 95% CI: -69.2, -7.7) and physical dysfunction (β : -98.5, 95% CI: -193.8, -3.1) than participants with vitamin D deficiency over 5 years in multivariable analyses.

Conclusions: Vitamin D supplementation over 2 years did not result in significant differences in change in knee symptom score over 5 years compared to placebo. However, knee OA patients maintaining sufficient serum vitamin D levels over long-term had more improvement in knee pain and physical function than those who did not maintain adequate vitamin D levels, suggesting a beneficial effect of maintaining sufficient serum vitamin D for knee OA.

Disclosure of Interest: None declared

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FRI0529 PREOPERATIVE PAIN SEEMS TO MODIFY THE EFFECT OF RADIOGRAPHIC OSTEOARTHRITIS SEVERITY ON POSTOPERATIVE PAIN AND FUNCTION 1 YEAR AFTER TOTAL KNEE ARTHROPLASTY

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Background: Radiographic osteoarthritis (OA) severity and pain play an important role in the indication for total knee arthroplasty (TKA). It is however unknown whether preoperative self-reported clinical pain modifies the effect of radiographic OA severity on postoperative pain and function in OA patients 1 year after TKA.

Objectives: To investigate whether preoperative self-reported clinical pain modified the effect of radiographic OA severity on postoperative pain and function in OA patients 1 year after TKA.

Methods: Data from the Longitudinal Leiden Orthopaedics Outcomes of Osteoarthritis Study (LOAS), a multicentre cohort study on outcomes after TKA were used. Radiographic OA severity was assessed with the Kellgren and Lawrence (KL) score (0–4). Pain and function were evaluated with the Knee Injury and Osteoarthritis Outcome Score (KOOS). After adjustment for confounders (BMI, age, gender and Mental Health Component Scores from the Short Form-12), multivariate linear regression analyses with an interaction term between KL-score and preoperative pain were performed.

Results: 560 patients were included. Both KL-score and preoperative pain were associated with postoperative pain (β : 6.1, 95% CI: 1.7–10.5 and β : 0.4, 95% CI 0.1–0.7) and function (β : 8.0, 95% CI: 3.7–12.3 and β 0.5, 95% CI 0.2–0.8). A trend towards effect modification of preoperative pain on the association between KL-score and postoperative pain (β -0.1, 95% CI -0.2–0.0) and function (β -0.1, 95% CI -0.2–0.0) was found indicating that effect of preoperative pain on postoperative pain and function seems to become less important when more severe radiographic severity is present.

Conclusions: Patients with less preoperative pain and higher KL grades have better function and pain outcomes 12 months after TKA. However preoperative pain seems less important in patients with more severe radiographic OA.

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FRI0530 TOTAL JOINT REPLACEMENT (TJR) AS CLINICAL ENDPOINT IN OA; PREVALENCE AND INCIDENCE RATES OF TJRS FROM THE PROSPECTIVE EPIDEMIOLOGIC RISK FACTOR (PERF I) STUDY

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Background: Osteoarthritis (OA) is a heterogeneous disease described by a combination of joint pain, physical disability and radiographic alterations leading to joint failure and total joint replacement (TJR). Commonly used endpoints in OA trials are worsening of pain and joint space narrowing. TJR is normally not considered an endpoint. Age and female gender are considered as major risk factors for developing OA.

Objectives: We hypothesise that TJR can be used as an endpoint in OA outcome studies within reasonable time frame. To investigate the basis for this hypothesis, we explored the prevalence and incidence of TJR as a reflection of joint failure in the Prospective Epidemiologic Risk Factor (PERF I) study.

Methods: A total of 5,855 Danish postmenopausal women aged 49–88 enrolled in the Prospective Epidemiologic Risk Factor (PERF I) study during 1999–2001 (baseline). Three, six and twelve year follow-up data from the Danish National registry was collected in end of 2014, including occurrence of TJR, OA and other relevant diagnosis. Also, women where at baseline and in 2014 asked whether they had a TJR or OA. The biomarker C1M was measured in baseline serum samples. The PERF I study was carried out in accordance with ICH-GCP and the study protocol was approved by the local ethics committees.

Results: There were 798 women that had their first TJR between baseline and 12 year follow-up; giving an incidence proportion of 13.6%. The TJR women were on average 1 year older ($p=0.010$) and heavier (1.7 kg/cm², $p<0.0001$), compared to women with no TJR in the follow-up period. The incidence after three and six years, of first ever TJRs, were 171 and 362 corresponding to an incidence proportions of 2.9% and 6.2%. Next we investigated the TJR incidence rates at 3, 6 and 12 years in different subgroup of women: 1) All, PERF I women that experience their first ever TJR (5855); 2) Prior TJR, had a TJR before baseline (266); 3) OA diagnosis at baseline but no prior TJR (1757) and 4) OA diagnosis at baseline and high C1M (>40 ng/mL, median) that after baseline underwent their first ever TJR (841). Group 1 is as described above. The 3, 6 and 12 incidence rates were 9.0, 17.3% and 29.7% for the prior TJR group, 6.2, 12.1% and 23.3% for the OA group, and 7.6, 13.6% and 25.1% for the OA +C1M group. The age-dependent prevalence and incidence for the first TJR. The prevalence was insignificant for the age group younger than 60 years old ($<0.1\%$). The prevalence increased steadily from the age group 60 to age group 85; from 0.1% to 13.2%.

Conclusions: Within a timeframe of 3, 6 or 12 years TJR incidence for women with an OA diagnosis reached 6, 12% and 23%, which was a doubling compared to the All population. The incidence increased by adding a single diagnostic measure. This reflects that TJRs are frequent amongst elderly women and that if designed minutiously, such as including specific diagnostic criteria (e.g. biomarker, OA diagnose), it may be feasible to conduct clinical studies with TJR as an endpoint. However, special attention must be directed to the objectiveness of the criteria for TJR. This may build a case for design of outcome studies (joint failure) for developing drugs in OA.

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