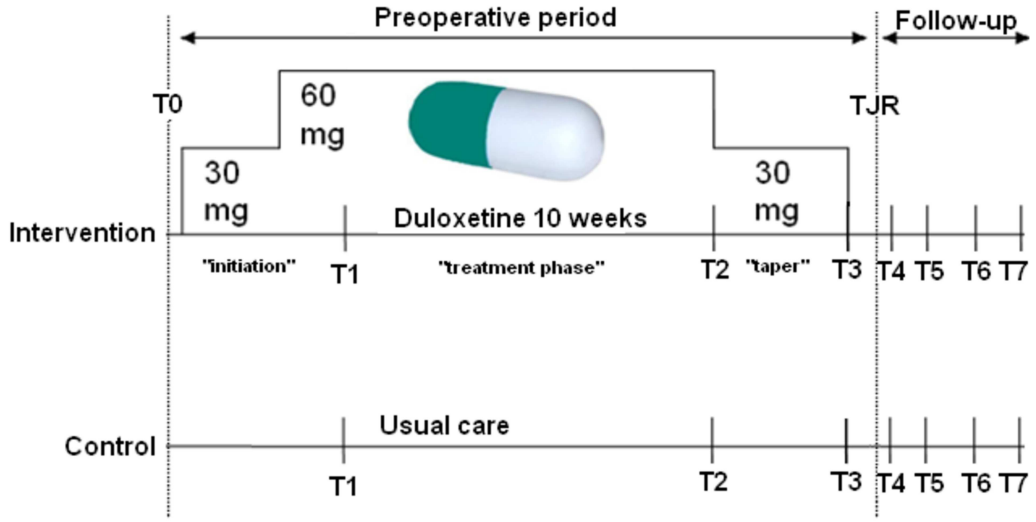
Supplementary 1/3: Scheme of the DOA trial



Supplementary 2/3. Detailed description of questionnaires used

HOOS/KOOS

The KOOS and the HOOS are self-administered, disease-specific questionnaires designed to assess patients' opinion about their knee or hip symptoms and associated problems. Both scores consist of five subscales: pain, other symptoms, activities of daily living (ADL), sport and recreational function, and hip/knee related quality of life (QOL). Answers are given on a 0-4 Likert scale. For each subscale a normalised 0-100 score is calculated. These 0-100 scores were transformed so that 0 represents extreme symptoms and 100 represents no symptoms. To our knowledge, there is no validated cut-off score on the KOOS/HOOS pain subscale indicating categories of light, moderate or severe pain. We considered a KOOS/HOOS pain subscale score <70 points as moderate to severe pain. The validity and reliability of the Dutch version of the KOOS and HOOS have been assessed quite extensively in previous literature.[13,49,50] Missing items in the KOOS/HOOS were imputed according to the KOOS/HOOS manual.[51,52]

Dutch Modified PainDETECT Questionnaire (m-PDQ)

The m-PDQ is a self-administered questionnaire consisting of 12 items on neuropathic pain symptoms in the left/right knee or hip during the past week. The first item concerns the presence of pain radiation using a body map. The second item concerns pain patterns, where patients have to choose between four figures representing distinctly described (and visually illustrated) pain patterns. Seven items concern pain quality on a 0-5 Likert scale, 0 representing 'never' and 5 representing 'very strongly': burning sensation, tingling or prickling sensation, pain at light touch, sudden pain attacks, pain at cold or warm stimulus, numbness, and pain at light pressure. The total score ranges from -1 to 38 points. Analogously to the original PainDETECT Questionnaire, a score ≤12 indicates a nociceptive pain profile, 13-18 a

possible neuropathic pain profile, and ≥19 a likely neuropathic pain profile.[43,53] m-PDQ scores >12.0 were associated with greater odds of having signs of sensitisation. Correcting for age, knee OA patients with m-PDQ scores >12.0 were almost six times more likely to have signs of sensitisation (on Quantitative Sensory Testing) than those with scores ≤12.[43] Gwilym et al. found significant positive correlations between PainDETECT scores and functional MRI activity, indicating central sensitisation among hip OA patients.[14] The Dutch version of the m-PDQ is considered to be a reliable and valid self-report instrument in patients with hip and knee OA.[44,45]

Visual Analogue Scale Pain (VAS pain)

Visual Analogue Scales (VAS) are widely used to measure pain. Patients place a marking on a 100-mm horizontal line that represents their pain. The left ending of the line represents 'no pain at all' and the right ending 'worst pain imaginable'. The distance between the marking and the left ending of the line is measured in whole millimetres and represents the pain score. Patients were asked to note their present pain status and their mean pain status over the last week, at rest (VAS-R: defined as pain at rest while sitting, standing or lying down) and during movement (VAS-M defined as pain during regular walking). VAS have been reported as valid and reliable measures for pain intensity.[54]

Supplementary 3/3: Sub-analysis of knee vs hip patients

As a sub-analysis, another mixed model for repeated measures was constructed adding a fixed variable for joint to the above-mentioned model. In this way, the difference explained by whether the hip or knee was the affected joint could be taken in consideration. In addition to the variable 'joint' interaction, terms were added between the joint, time, piece-wise and treatment allocation variables. Also, a three-way interaction term between time, treatment allocation and joint were added. Considering the fit of this model, the Akaike Corrected Information Criterion improved to 4839.136, and the Bayesian Information Criterion improved to 4847.770.

Results of sub-analysis:

Sub-analysis mixed model for repeated measures including joint as a fixed variable.

The study group consisted of 61 knee OA patients and 50 hip OA patients. Table 4 presents estimated means and differences based on the mixed model for repeated measures using a piece-wise design that includes joint as a fixed variable. Figure 3 shows the course of the KOOS/HOOS pain subscale for the different treatment groups based on the mixed model for repeated measures, including joint groups.

Rienstra W, *et al. BMJ Open* 2022; 11:e052944. doi: 10.1136/bmjopen-2021-052944

Table 3. Estimated means (95% CI) and Estimated difference (95% CI) on the mixed model for repeated measures using a piece-wise design with joint as a fixed variable.

KOOS/HOOS pain subscale		Intervention (57)	Control (54)	Difference	Significance
After 7 weeks targeted treatment	Hip	39.9 (14.0-65.7)	38.0 (12.3-63.7)	1.8 (-8.0-11.7)	0.714
	Knee	47.2 (21.6-72.8)	33.9 (8.3-59.5)	13.3 (4.4-22.3)	0.004
6 weeks post-arthroplasty	Hip	70.8 (45.1-96.6)	78.0 (52.2-103.9)	7.2 (-3.0-17.4)	0.165
	Knee	56.5 (30.7-82.2)	60.0 (34.4-85.6)	3.6 (-5.8-12.9)	0.455
6 months post-arthroplasty	Hip	82.9 (57.1-108.8)	87.0 (61.2-112.9)	4.1 (-6.1-14.3)	0.432
	Knee	66.7 (40.9-92.4)	67.1 (41.5-92.8)	0.5 (-9.1-10.0)	0.924
12 months post-arthroplasty	Hip	84.6 (58.8-110.4)	88.8 (63.0-114.7)	4.2 (-6.0-14.4)	0.418
	Knee	75.5 (49.8-101.2)	75.9 (50.3-101.5)	0.4 (-9.0-9.8)	0.936

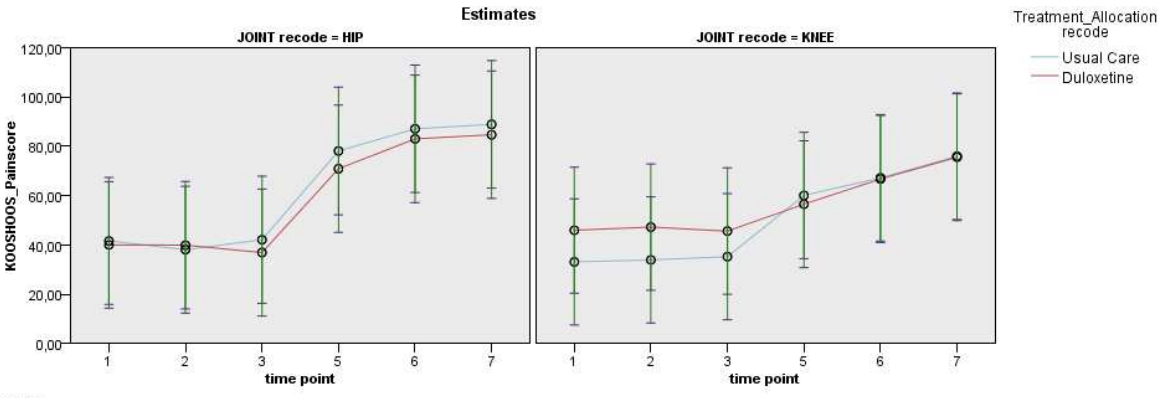


Figure 3. Course of KOOS/HOOS pain subscale per treatment group for hip and knee patients.