Knee arthroscopic surgery is beneficial to middle-aged patients with meniscal symptoms: a prospective, randomised, single-blinded study

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Knee arthroscopy is beneficial to middle-aged patients with meniscal symptoms:

A prospective, randomised, single-blinded study

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Running headline: Knee arthroscopy

ABSTRACT

Objective: There is no evidence that a knee arthroscopy is more beneficial to middle-aged patients with meniscal symptoms compared to other treatments. This randomised controlled trial aimed to determine whether an arthroscopic intervention combined with a structured exercise programme would provide more benefit than a structured exercise programme alone for middle-aged patients with meniscal symptoms that have undergone physiotherapy.

Method: 150 out of 179 eligible patients, aged 45 to 64 (mean:54±5), symptom duration more than 3 months and standing x-ray with Ahlbäck grade 0, were randomised to: (1) a physiotherapy appointment within 2 weeks of inclusion that included instructions for a 3-month exercise programme (non-surgery group); or (2) the same as (1) plus, within 4 weeks of inclusion, knee arthroscopy for resection of any significant meniscal injuries (surgery group). The primary outcome was change in pain at 12 months, assessed with the Knee Injury and Osteoarthritis Outcome Score ($KOOS_{PAIN}$).

Results: In the Intention-To-Treat analysis, pain at 12 months was significantly lower in the surgery than in the non-surgery group. The change in $KOOS_{PAIN}$ was significantly larger in the surgery than in the non-surgery group (between-group difference was 10.6 points of change; 95% CI: 3.4 to 17.7, p=0.004). The As-Treated analysis results were consistent with the Intention-To-Treat analysis results.

Conclusion: Middle-aged patients with meniscal symptoms may benefit from arthroscopic surgery in addition to a structured exercise programme. Patients´ age or symptom history (i.e. mechanical symptoms or acute onset of symptoms) didn´t affect the outcome.

Trial registration: NCT01288768

Keywords: Knee arthroscopy, menisci, meniscectomi

INTRODUCTION

Meniscal lesions are frequent incidental findings on knee MRIs from middle-aged patients; most of these lesions are not associated with knee pain, aching, or stiffness. Meniscal lesions with degenerative changes might be the first sign of osteoarthritis (OA) of the knee joint, because meniscal damage is common in individuals with radiographic evidence of tibiofemoral OA.[1] A high level of evidence has suggested that exercise has at least short term benefits; it reduces knee pain and improves physical function in individuals with knee OA.[2-4] According to the present clinical praxis, patients should undergo physiotherapy for at least 2-3 months before they can be referred to an orthopaedic surgeon and a possible knee arthroscopy.

Many non-randomised studies have shown good results after a partial meniscectomy.[5, 6] However, no randomised study has been able to show that knee arthroscopy had a significant positive effect in middle-aged patients with meniscal symptoms, when it was performed in addition to a structured rehabilitation program[7-10] or compared to sham surgery.[11, 12] Moreover, substantial disability occurs for three months after an arthroscopic partial meniscectomy.[13] Nevertheless, knee arthroscopy is one of the most common orthopaedic procedures performed.[14, 15]

The aim of this study was to evaluate whether an arthroscopic intervention provided additional benefit when combined with a structured exercise program, compared to that provided with a structured exercise programme alone, in middle-aged patients with meniscal symptoms. A secondary objective was to assess whether age and symptom history (onset of pain, daily joint catching, and joint locking) had any effect on the outcome, after controlling for the intervention.

METHODS

Study design and participants

Subjects were recruited between 4th March 2010 and 5th April 2012 from the orthopaedic department at the Linköping University hospital, which had a catchment area of 172 316 inhabitants. The clinical routine is that middle-aged patients with pain from the knee joint where the general practitioner suspects a meniscal injury, receive standing x-rays and physiotherapy for at least 3 months, before they are referred to the orthopaedic department. In Sweden, more than 95% of the population is directed to the public medical service. Accordingly, the majority of middle-aged patients with suspected meniscal injury were eligible for the present study.

For this study, all referrals for consideration for arthroscopy because of a suspected meniscal injury were evaluated for eligibility by one orthopaedic surgeon (HG). Inclusion criteria were: age 45-64, symptom duration more than 3 months, standing x-ray with Ahlbäck 0 (less than 50% reduction of the joint space, without consideration of possible osteophytes), had undergone prior physiotherapy, and could understand the Swedish language. Patients were excluded when they had a locked knee or joint lockings for more than 2 seconds more often than once a week, rheumatic or neurological disease, fibromyalgia, replacement of hip- or knee joints, or a contraindication for day-surgery at the current unit (BMI > 35 or a serious medical illness).

> PLEASE INSERT FIGURE 1 <

A total of 179 subjects were assessed during the inclusion period. The same orthopaedic surgeon (HG) assessed and informed all except 4 subjects. Twenty-four subjects were excluded and five declined participation (Figure 1). The subjects provided written informed consent. Patients were informed that they had the opportunity to cross over to knee arthroscopy or to decline arthroscopy, according to their preferences.

The participants were randomly allocated to one of two parallel intervention groups. One group (non-surgery) received a physiotherapy appointment within 2 weeks, with a functional assessment and instructions for an exercise programme; the other group (surgery) received the same treatment as the non-surgery group, plus a knee arthroscopy within 4 weeks. Any significant meniscal injuries were to be resected during the arthroscopy.

The allocation sequence was concealed from the orthopaedic surgeon that enrolled and assessed participants. The allocations were placed in sequentially numbered, opaque, sealed envelopes in 15 blocks, block size 10. Envelopes were opened after the enrolment by the patient and a nurse.

Interventions

Exercise programme

At an independent clinic, five physiotherapists experienced in knee rehabilitation, gave individual instructions for the exercise programme. Physiotherapists were blinded to the patient group; however, some patients revealed their group. The exercise programme aimed to increase muscle function and postural control and lasted three months (Table 1, Supplementary Appendix). Participants were asked to perform the exercise programme in the gym, without supervision from a physiotherapist. A home-based exercise programme was provided as an alternative. The exercise program should be performed twice per week. Compliance was monitored with self-reported exercise diaries.

Surgery

All operations were performed with full or local anaesthetics by one of two experienced arthroscopists at an independent day-care clinic. During the arthroscopy, after the arthroscope was inserted in the joint and the joint was visually inspected, the surgeon judged, according to their experience, whether a meniscal resection or any other surgical treatment was indicated. After surgery, all patients were allowed immediate, full weight-bearing activity. The patients were advised to resume the exercise programme according to phase 1 for 1 week, and then switch to phase 2.

Assessment

Before randomisation, the orthopaedic surgeon assessed the symptom history; onset of pain (e.g., sudden onset, the patient could tell that the pain started during a particular activity); daily joint catching; and joint locking for more than 2 seconds over the past month. Also, at the orthopaedic clinic directly after the surgeons assessment, the patients sat alone to complete the Knee Injury and Osteoarthritis Outcome Score (KOOS),[16] the EuroQol (EQ5D),[17] the Physical Activity Scale (PAS),[18] and the symptom satisfaction scale.[19] Immediately after randomisation, when the participants were aware of the treatment they would receive, patients were asked to report their expectation of the treatment. The same questionnaires were sent to the patients at 3 and 12 months after baseline. The x-rays were re-evaluated by a radiologist or an orthopaedic surgeon according to the original description of Kellgren-Lawrence classification for comparison reasons.[20] A 3-year follow-up is planned.

The KOOS is used to assess subjective knee function, based on five subscales that cover pain ($KOOS_{PAIN}$), symptoms ($KOOS_{SYMPTOM}$), function in daily life ($KOOS_{ADL}$), function in sports and recreational activities ($KOOS_{SPORTS}$), and knee-related quality of life ($KOOS_{QOL}$). The score for each subscale ranges from 0 to 100, where 100 indicates good knee function.[16]

The EQ5D assesses health-related quality of life, and consists of an index and a vertical visual analogue scale (VAS) where overall health is rated.[17]

The PAS assesses physical activity in a six-point Likert scale that ranges from “1: no physical activity” to “6: heavy physical activity several times a week”.[18] Symptom satisfaction was analysed with a six-point Likert scale that ranged from “delighted” to “terrible”.[19] Patient expectations about recovery were analysed with a four-point Likert scale that ranged from “no recovery” to “full recovery”.

The functional assessments were performed by the five physiotherapists at the physiotherapy clinic and included; pain during maximum squatting, 30-s chair stand test on one leg, and standing on one

leg with eyes closed test. The same physiotherapist repeated the assessments at 3 months follow-up.

The primary outcome was the change between baseline and the 12-month follow-up, based on the KOOS subscale of pain ($KOOS_{PAIN}$).

Adverse events

We checked the electronic medical charts at one-year follow-up. One patient had undergone a new arthroscopy 10 months after the initial one. No other adverse events were reported.

STATISTICAL ANALYSIS

Intention-To-Treat and, for patients crossing over between the groups (figure 1), the As-Treated analyses were used.

The Student's t-test was used for between-group comparisons. Categorical data were analysed with Pearson's chi-square or Fisher's exact test and McNemar´s-test for within-group changes over time. Effect size was calculated with Cohen´s d ($d=(M1-M2)/ \sqrt{[(SD_1^2+ SD_2^2)/2]}$).

Two-factor analysis of variance was used to analyse whether the intervention and the predefined factors had any effects on the change in $KOOS_{PAIN}$. Based on Levene´s test, homogeneity of variance was assumed. Four separate full factorial models were conducted; each model included the intervention plus one predefined factor and a two-way interaction between these binary variables.

A minimal clinically-important change of 8-10 is considered appropriate for the $KOOS_{PAIN.}$ A 10 points change was used as the cut off indicating improvement.[21] To detect a between-group difference of 10 points (SD19)[21] in the $KOOS_{PAIN}$ (false positive error rate (alpha) =0.05, false negative error rate (beta) =0.2), we included 75 subjects in each group; this accounted for a dropout rate of 33%.

RESULTS

Study participants

Participants were randomly assigned to either the surgery (N=75, age mean: 54, SD:5) or non-surgery (N=75, age mean: 54, SD:6) group. Patient baseline characteristics and OA severity according to the Kellgren-Lawrence are presented in Table 1. Eleven patients had Kellgren-Lawrence grade 2 and the rest were equally distributed to grade 1 (46%) or grade 0 (46%). Recovery expectations were similar between groups; 97% of patients in the surgery group and 92% in the non-surgery group expected dramatic or full recovery (p=0.275).

A total of 149 out of 150 patients completed the baseline questionnaires. The 3-month questionnaires were completed by 137 (91%) patients. However, 14 of these patients completed the questionnaire more than 5 months after baseline, and these were excluded from the analysis. Accordingly, 123 patients (82%) were included in the 3-month analysis. The 12-month questionnaire was completed by 130 patients (87%). Sixteen patients crossed over from the non-surgery group to receive an operation (21%), but only two (3%) crossed over before the 3-month questionnaire. Nine patients (12%) that were allocated to the surgery group did not go through with the operation (Figure 1).

The number of patients included in the functional assessment is presented in Table 2 in the Supplementary Appendix. Seventy-nine participants (53%) completed the exercise diary. In both groups, participants performed an average of 19 training sessions, either at home or at the gym, during approximately 3 months. No difference was observed between groups.

Of the 75 patients who initially were randomised to surgery, 66 had surgery (56 had partial meniscal resection, 2 had removal of degenerated joint cartilage fragments, 1 had resection of loose bodies, 1 had synovectomy, 1 had partial resection of ACL-remnants and 8 were judged not to need a surgical treatment). Of the 75 patients who initially were randomised to non-surgical treatment, 16 crossed

over and had surgery (11 had partial meniscal resection, 1 had resection of loose bodies, 1 had microfracture, 1 had partial resection of ACL-remnants, 1 was judged not to need a surgical treatment and there was missing information for 2 patients). As a standard, shaver was not used at meniscal resection. At the arthroscopic surgery, 3 patients (2 initially randomised to surgery and 1 cross-over) were diagnosed to have a total rupture of the anterior cruciate ligament.

> PLEASE INSERT TABLE 1 <

Patient characteristics and baseline data

In the Intention-To-Treat analysis, there were no differences in patient characteristics or KOOS at inclusion (Table 1 and 2A). In the As-Treated analysis, the surgery group had a higher proportion of females (Table 1) and scored worse than the non-surgery group in the four out of five KOOS subscales at baseline (Table 2B).

> PLEASE INSERT TABLE 2 <

Primary outcome

In the Intention-To-Treat analysis, both treatment groups improved significantly in $KOOS_{PAIN}$, at 12-month follow-up ($p<0.001$). The change in $KOOS_{PAIN}$ was significantly larger in the surgery group than the non-surgery group (between-group difference in change: 10.6 points, 95% CI: 3.4 to 17.7; $p=0.004$) (Table 3A and Figure 2A). The effect size was 0.51.

The results of the As-Treated analyses were consistent with the Intention-To-Treat analyses (Table 3B and Figure 2B).

> PLEASE INSERT TABLE 3 <

> PLEASE INSERT FIGURE 2 <

Figure 3 shows the percentage of patients with the indicated changes in $KOOS_{PAIN}$ from baseline to the 12-month follow-up.

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Both interventions had a significant, main effect on the change in $KOOS_{PAIN}$. None of the factors; sudden onset of pain, daily joint catching, or joint locking for more than 2 s in the past month, had any significant main or interaction effect on the change in $KOOS_{PAIN}$. Age, categorised as 'under 55 years' or '55 and older', had a significant main effect on $KOOS_{PAIN}$, after controlling for the intervention. In both groups, older patients exhibited larger improvements than younger patients did. The interaction effect between age and intervention was not significant; thus, the older patients showed similar improvements in both groups (Table 4).

> PLEASE INSERT TABLE 4 <

Secondary outcome

In the Intention-To-Treat analysis, the surgery group had less pain (higher $KOOS_{PAIN}$) at both the 3 and 12-month follow-ups ($p<0.05$) (Table 2A). The changes in scores, from baseline to the 3-month follow-up, were significantly larger in the surgery group compared to the non-surgery group, for all KOOS subscales. From baseline to 12-month follow-up, the change in score was larger in the surgery group in $KOOS_{PAIN}$ and $KOOS_{ADL}$ (Table 3A)

In the As-Treated analysis, the surgery group had significantly less pain (higher $KOOS_{PAIN}$) at 3-months and less pain and fewer symptoms (higher $KOOS_{PAIN}$ and $KOOS_{SYMPTOM}$) than the non-surgery group at the 12-month follow-up ($p<0.05$) (Table 2B). The changes in scores from baseline to both 3 and 12 months were significantly larger in the surgery group than in the non-surgery group in all secondary subscales (Table 3B).

In the Intention-To-Treat analysis, both groups reported higher symptom satisfaction and higher activity levels at 12 months compared to baseline (Table 2, Supplementary Appendix). The changes in functional assessments were not significantly different between the groups (Table 5).

> PLEASE INSERT TABLE 5 <

DISCUSSION

Arthroscopic surgery could provide more benefit to middle-aged patients with meniscal symptoms compared to no surgery. The change in $KOOS_{PAIN}$ from baseline to 12 months was larger in the surgery group compared to the non-surgery group, with a medium effect size of 0.51. The difference in improvement between the groups was clinically relevant, because it exceeded the suggested level for a minimally important clinical change.[22] These results were valid for both the Intention-To-Treat and the As-Treated analyses. Previous RCTs have not shown any benefit of surgical treatment for this group of patients compared to sham surgery or physiotherapy alone.[7-12] To our knowledge, this is the first RCT to show that arthroscopic surgery may be beneficial to middle-aged patients with meniscal symptoms.

Our study differed from previous studies in at least two aspects. Our patients had a milder degree of OA compared to some other studies.[7-9, 12] In addition, we had a higher participation rate. The majority of patients with meniscal symptoms in the geographical catchment area were eligible, and only five patients declined participation. Thus, we were able to recruit sufficient patients over a short period of time without changing the clinical praxis. In other studies, many patients declined participation.[7-10] In addition, many studies had long inclusion periods or large catchment areas in order to reach sufficient sample size.[8, 9, 11, 23]

Surgery may involve a greater placebo effect compared to other treatments.[11, 12, 24] Accordingly, the placebo effect may have been greater in the surgery group. Participating in a clinical trial gives rise to placebo effects, due to the therapeutic milieu and increased caregiver contact.[25] In our study, both groups had high expectations of partial or full recovery, with no difference between groups. In addition, both groups had equal contact with caregivers, except during the surgery.

Despite the superior results for the arthroscopic surgery group, both intervention groups showed clinically-relevant improvements. The non-operative regimen in our study was designed to be structured but not excessive to the clinical routine as the aim of the study was to examine the effect

of arthroscopic surgery and not the effect of exercise therapy. The exercise therapy may have been of too low dose since only 53% of the patients completed the exercise diary and in average, the patients performed 19 out of the 24 suggested training sessions. Consistent with our results, many studies have shown that exercise therapy had beneficial effects in patients with meniscal symptoms[7-10] or knee OA.[2, 22] In our study, arthroscopic surgery in addition to a structured exercise programme had a larger effect compared to a structured exercise programme alone. On the other hand, previous studies have suggested that arthroscopy might increase the risk for future OA,[26, 27] and exercise therapy may decrease that risk.[28] Therefore, exercise therapy should be the first intervention, as recommended by the guidelines.[3, 4]

With the predefined predictive factors, we aimed to determine whether surgery might provide more benefit to young patients or to patients with an acute onset of symptoms; e.g., related to trauma. It was previously suggested that an arthroscopy would have a less favourable outcome in older individuals. However, previous studies were inconclusive about the effect of age on the outcome after a meniscectomy.[26] In our study, older age was the only factor associated with a better result, but the effect was similar for both interventions. One explanation for the observed age effect may be that the older patients started with higher pain, and ended with a score similar to that of the younger patients. In contrast to previous studies, we chose to include patients with sudden onset of symptoms to elucidate whether these patients gained more benefit than other patients from arthroscopic surgery. However, our results did not show a difference between these groups, which may be due to the low sample size in these analyses. For example, the group of patients that reported joint locking was small by design, because the study design excluded patients that reported joint locking more than once a week. Like previous studies,[9, 11] we were not able to identify a subgroup of patients that might benefit more from surgery.

Our study had several strengths. It was a single centre study; it had access to the majority of the population, a limited drop-out rate, and highly trained surgeons and physiotherapists at two

independent centres. Moreover, almost all eligible patients agreed to participate in the study. In previous studies, 15-45% patients declined participation.[7-10, 12, 23] One reason for the high willingness to participate in the present RCT may be that, during the study period, the Swedish Board of Health and Welfare stated that surgical treatment may provide no benefit for this patient group. This statement had a major impact on the media. In addition, one orthopaedic surgeon assessed almost all the patients; thus, all the patients received the same information; namely, that there is no evidence that surgery is more beneficial than training.

This study also had some limitations. The cross-over rate was 17%. Also, only 82% and 87% of patients completed the questionnaires at the 3- and 12-month follow-ups, respectively, indicating a small number of patients who were lost to follow-up that may have influenced the results. The small variations in surgical treatment (only two highly-trained arthroscopists) may have limited the generalisation of results. Only adverse effects reported in the medical records were identified and milder adverse effects may have been missed. Moreover, not all patients attended physiotherapy during the study, and only half the patients in both groups reported how much they had exercised. In addition, the exercise therapy may have been of too low dose, which may have biased the comparisons. However, both groups performed a similar amount of exercise training during the study.

In summary, this study showed that middle-aged patients with meniscal symptoms and no radiographic OA, may benefit from arthroscopic surgery in addition to a structured exercise programme. We were not able to show that age or symptom history (i.e. mechanical symptoms or acute onset of symptoms) affected the outcome.

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Author contributors

HG, ST, AM, and JK were responsible for the study design and protocol. HG recruited patients. HG, ST, HM, and JK were responsible for the statistical analyses and interpreting the data. HG, ST, and JK wrote the manuscript, and all authors commented and approved the final version. All authors had full access to all data.

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Conflict of interest

The authors declare no conflict of interest.

Ethics approval

The study was approved by the ethics committee at Linköping University (dnr: M2010/6-31).

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Figure legends

Figure 1. Patient enrolment and randomisation.

At the 12-month follow=up, the cross-over boxes show the number that crossed over between 3 and 12 months, and the total number of crossovers. Groups analysed in the Intention-To-Treat analysis: Surgery group=a+b, Non-surgery group=c+d. Groups analysed in the As-Treated analysis: Surgery group=a+c, Non-surgery group=b+d.

Figure 2. Mean $KOOS_{PAIN}$ scores at baseline, 3, and 12 months according to treatment group.

A: Intention-To-Treat analysis (baseline n surgery group 74, non-surgery group 74; 3 months n surgery group 66, non-surgery group 57; 12 months surgery group 70, non-surgery group 60) ,

B: As-Treated analysis (baseline n surgery group 81, non-surgery group 67; 3 months n surgery group 52, non-surgery group 55; 12 months surgery group 74, non-surgery group 56).

Figure 3. Percent of patients in each group that showed the indicated change of 10-points, i.e. minimal clinically-important change (dotted horizontal line), in $KOOS_{PAIN}$ score from baseline at 12 months. Each bar include % of patients with 2-point change in $KOOS_{PAIN}$.

A: Intention-To-Treat analysis. 57 out of 70 (81%) patients in the surgery group, compared to 41 out of 60 (68%) patients in the non-surgery group, improved by more than 10 points on the KOOSPAIN score at the 12 month follow-up (p=0.039).

B: As-Treated analysis. 62 out of 74 (84%) patients in the surgery group, compared to 36 out of 56 (64%) patients in the non-surgery group, improved by more than 10 points on the KOOSPAIN score (p=0.010).

Table 1. Patient characteristics at baseline

	Intention-To-Treat			As-Treated		
	Surgery (n=75)	Non-surgery (n=75)	p-value	Surgery (n=82)	Non-surgery (n=68)	p-value
Age, years, mean (SD)	54 (5)	54 (6)	0.725	55 (5)	54 (6)	0.624
Sex (male/female)	53/22	56/19	0.583	54/28	55/13	0.040
Duration of knee pain (months)[a]	7 (8)	7 (7)	0.641	7 (8)	7 (8)	0.838
Expectations of treatment (dramatic or full recovery)	70 (97%)	67 (92%)	0.275	*NA*	*NA*	
Kellgren & Lawrence grade			0.539			0.155
0	37 (49%)	32 (43%)		43 (52%)	26 (38%)	
1	34 (45%)	36 (48%)		35 (43%)	35 (51%)	
2	4 (5%)	7 (9%)		4 (5%)	7 (10%)	
Sudden onset of pain	45 (61%)	34 (47%)	0.099	46 (58%)	33 (50%)	0.365
Daily joint catching	45 (61%)	41 (56%)	0.568	50 (62%)	36 (55%)	0.379
Joint locking for >2 s	18 (24%)	11 (15%)	0.159	19 (24%)	10 (15%)	0.208
Age <55	36 (48%)	39 (52%)	0.624	41 (50%)	30 (50%)	1.000
Moderate to high physical activity level (PAS 4-6)	23 (32%)	23 (32%)	0.954	26 (33%)	20 (31%)	0.833

Values represent number of patients (percentage of the indicated group), unless stated otherwise

PAS = Physical Activity Scale

[a] median and interquartile range

Table 2. Primary and secondary outcomes at baseline, 3, and 12 months.

A. Intention-To-Treat analysis

	Baseline			3 months			12 m onths		
	Surgery	Non-surgery	p-value	Surgery	Non-surgery	p-value	Surgery	Non-surgery	p-value
KOOS									
Pain	55 (51 to 59) n=74	58 (54 to 62) n=74	0.241	77 (73 to 81) n=66	69 (64 to 75) n=57	*0.023*	84 (81 to 88) n=70	78 (73 to 83) n=60	*0.029*
Symptoms	59 (55 to 62) n=74	62 (57 to 66) n=73	0.298	74 (70 to 78) n=66	69 (64 to 74) n=57	0.148	82 (78 to 85) n=70	78 (73 to 83) n=60	0.210
ADL	65 (61 to 69) n=73	68 (63 to 73) n=73	0.319	81 (77 to 86) n=65	76 (71 to 82) n=57	0.157	86 (82 to 90) n=70	83 (79 to 88) n=60	0.370
Sports	29 (25 to 34) n=73	31 (26 to 37) n=73	0.577	53 (46 to 59) n=65	46 (38 to 53) n=57	0.159	59 (52 to 65) n=70	55 (48 to 62) n=60	0.450
QoL	34 (30 to 37) n=74	35 (31 to 39) n=73	0.762	56 (51 to 61) n=66	49 (43 to 55) n=56	0.066	66 (60 to 71) n=70	59 (53 to 65) n=60	0.090

EQ5D									
Index	0.63 (0.57 to 0.68) n=74	0.62 (0.56 to 0.68) n=72	0.913	0.78 (0.73 to 0.83) n=64	0.75 (0.70 to 0.79) n=56	0.362	0.82 (0.78 to 0.87) n=70	0.82 (0.78 to 0.86) n=60	0.968
VAS	62 (58 to 67) n=72	64 (59 to 69) n=72	0.631	76 (72 to 80) n=63	72 (67 to 77) n=56	0.211	78 (74 to 82) n=69	75 (70 to 80) n=59	0.809

B. As-Treated analysis

	Baseline			3 months			12 months		
	Surgery	Non-surgery	p-value	Surgery	Non-surgery	p-value	Surgery	Non-surgery	p-value
KOOS									
Pain	54 (50 to 57) n=81	60 (55 to 64) n=67	*0.028*	80 (76 to 84) n=52	72 (67 to 78) n=55	*0.031*	85 (81 to 88) n=74	77 (72 to 82) n=56	*0.009*
Symptoms	58 (55 to 62) n=80	62 (58 to 67) n=67	0.170	75 (71 to 79) n=52	71 (66 to 77) n=55	0.294	83 (79 to 86) n=74	77 (72 to 82) n=56	*0.042*
ADL	64 (59 to 68) n=80	70 (65 to 75) n=66	*0.036*	83 (78 to 88) n=51	78 (73 to 84) n=55	0.188	87 (83 to 91) n=74	82 (77 to 87) n=56	0.091
Sports	27 (23 to 31) n=80	35 (28 to 41) n=66	*0.031*	53 (46 to 60) n=51	50 (42 to 57) n=55	0.506	58 (52 to 64) n=74	56 (49 to 64) n=56	0.728
QoL	32 (28 to 35) n=81	38 (33 to 42) n=66	*0.034*	58 (53 to 63) n=52	53 (47 to 59) n=54	0.209	65 (60 to 70) n=74	59 (53 to 65) n=56	0.146

EQ5D									
Index	0.60 (0.55 to 0.65) n=80	0.65 (0.59 to 0.71) n=66	0.195	0.80 (0.76 to 0.84) n=51	0.76 (0.71 to 0.81) n=53	0.195	0.83 (0.78 to 0.87) n=74	0.82 (0.78 to 0.86) n=56	0.883
VAS	61 (56 to 65) n=79	65 (60 to 71) n=65	0.192	78 (73 to 83) n=49	73 (68 to 78) n=54	0.129	78 (74 to 82) n=73	74 (70 to 79) n=55	0.238

Table 3. Change scores for primary and secondary outcomes between baseline and 3 months, and between baseline and 12 months.

A. Intention-To-Treat analysis

	Difference baseline to 3 months				Difference baseline to 12 months			
	Surgery	Non-surgery	Between group difference	p-value	Surgery	Non-surgery	Between group difference	p-value
KOOS								
Pain	22.2 (17.3 to 27.2) n=66	10.6 (5.9 to 15.4) n=56	11.6 (4.7 to 18.5)	*0.001*	29.4 (25.0 to 33.8) n=70	18.8 (12.9 to 24.8) n=60	10.6 (3.4 to 17.7)	*0.004*
Symptoms	15.3 (11.4 to 19.2) n=66	6.7 (2.5 to 10.8) n=55	8.6 (2.9 to 14.3)	*0.003*	23.2 (19.2 to 27.2) n=70	17.3 (12.3 to 22.2) n=59	5.9 (-0.3 to 12.2)	0.063
ADL	15.8 (11.1 to 20.4) n=64	8.0 (3.5 to 12.4) n=56	7.8 (1.4 to 14.2)	*0.018*	21.0 (16.8 to 25.2) n=69	14.2 (8.9 to 19.4) n=59	6.8 (0.2 to 13.4)	*0.044*
Sports	23.9 (17.7 to 30.2) n=64	12.2 (6.5 to 17.9) n=55	11.7 (3.2 to 20.2)	*0.007*	29.2 (22.9 to 35.6) n=69	22.9 (15.5 to 30.3) n=60	6.3 (-3.3 to 15.9)	0.198
QoL	22.4 (17.1 to 27.7) n=66	10.8 (5.2 to 16.5) n=54	11.6 (3.9 to 19.2)	*0.003*	31.4 (25.1 to 37.7) n=70	23.8 (17.5 to 30.0) n=60	7.6 (-1.2 to 16.5)	0.091

EQ5D								
Index	0.16 (0.09 to 0.22) n=64	0.13 (0.07 to 0.20) n=53	0.02 (-0.07 to 0.12)	0.626	0.21 (0.15 to 0.26) n=70	0.19 (0.12 to 0.26) n=57	0.02 (-0.07 to 0.11)	0.719
VAS	12.7 (7.5 to 17.9) n=62	6.7 (1.2 to 12.2) n=53	6.0 (-1.5 to 13.5)	0.116	15.4 (10.9 to 19.9) n=67	10.3 (5.2 to 15.5) n=56	5.0 (-1.7 to 11.8)	0.142

B. As-Treated analysis

	Difference baseline to 3 months				Difference baseline to 12 months			
	Surgery	Non-surgery	Between group difference	p-value	Surgery	Non-surgery	Between group difference	p-value
KOOS								
Pain	25.7 (20.9 to 30.5) n=52	12.9 (8.0 to 17.7) n=54	12.9 (6.1 to 19.6)	*<0.001*	30.1 (26.3 to 34.7) n=74	16.6 (10.6 to 22.6) n=56	13.9 (6.9 to 21.0)	*<0.001*
Symptoms	16.8 (12.6 to 20.9) n=52	9.5 (5.4 to 13.7) n=54	7.2 (1.4 to 13.0)	*0.015*	24.7 (21.0 to 28.5) n=73	15.0 (9.8 to 20.0) n=56	9.8 (3.7 to 16.0)	*0.002*
ADL	19.2 (14.4 to 23.9) n=51	8.5 (4.3 to 12.7) n=53	10.6 (4.4 to 16.9)	*0.001*	22.5 (18.4 to 26.6) n=73	11.7 (6.5 to 16.9) n=55	10.8 (4.3 to 17.3)	*0.001*
Sports	26.5 (20.0 to 33.0) n=50	14.5 (8.5 to 20.6) n=53	12.0 (0.6 to 17.0)	*0.008*	30.3 (24.2 to 36.4) n=73	21.1 (13.4 to 28.8) n=56	9.2 (-0.4 to 18.8)	0.06
QoL	27.1 (21.7 to 32.5) n=52	12.9 (7.4 to 18.5) n=52	14.2 (6.6 to 21.9)	*<0.001*	32.4 (26.4 to 38.4) n=74	21.9 (15.4 to 28.4) n=56	10.5 (1.7 to 19.3)	*0.020*

EQ5D								
Index	0.21 (0.14 to 0.29) n=51	0.12 (0.06 to 0.18) n=51	0.10 (0.00 to 0.19)	*0.043*	0.23 (0.17 to 0.29) n=73	0.16 (0.10 to 0.23) n=54	0.06 (-0.03 to 0.15)	0.171
VAS	16.5 (10.9 to 22.0) n=48	7.0 (1.8 to 12.3) n=51	9.4 (1.9 to 17.0)	*0.015*	16.0 (11.1 to 21.0) n=71	9.1 (4.8 to 13.4) n=52	7.0 (0.5 to 13.4)	*0.044*

Table 4. Summary of the separate full factorial analysis of variance models for testing the effect of the intervention and the four predefined factors (age <55, sudden onset of pain, daily joint catching, joint locking for >2 s) on changes in the primary outcome $KOOS_{PAIN}$ score. Each model included the intervention plus one predefined factor and a two-way interaction between these binary variables. (Intention-To-Treat analysis)

	df	F	p-value	Partial Eta Squared	R^2
Model 1 (n=130)					0.107
Intervention	1	7.7	0.006	0.058	
Age <55	1	4.4	0.037	0.034	
Interaction	1	1.5	0.231	0.011	
Model 2 (n=129)					0.058
Intervention	1	6.8	0.010	0.051	
Sudden onset of pain	1	0.2	0.692	0.001	
Interaction	1	0.2	0.657	0.002	
Model 3 (n=129)					0.068
Intervention	1	8.5	0.004	0.064	
Daily joint catching	1	0.1	0.725	0.001	
Interaction	1	1.5	0.216	0.012	
Model 4 (n=129)					0.058
Intervention	1	4.3	0.040	0.033	
Joint locking for >2 s	1	0.4	0.550	0.003	
Interaction	1	0.0	0.964	0.000	

Table 5.Functional assessments at baseline and at the 3-month follow up (Intention-To-Treat analysis).

	Baseline		3 months		Between group difference in change
	Surgery	Non-surgery	Surgery	Non-surgery	
Squatting	n=51	n=44	n=45	n=36	
Able without pain	22%	9%	36%	39%	
Able with pain	31%	41%	38%	39%	
Not able	47%	50%	27%	22%	
30-s chair stand test on one leg (maximum number of repetitions)	7.2 (5.6 to 8.9) n=52	8.1 (6.2 to 10.0) n=44	9.2 (7.1 to 11.3) n=45	10.1 (7.9 to 12.4) n=36	0.2 (-1.8 to 2.1)
SOLEC (s)	11.8 (9.3 to 14.2) n=53	15.0 (12.0 to 18.1) n=44	15.4 (12.4 to 18.4) n=45	19.2 (15.3 to 23.0) n=36	-0.7 (-5.0 to 3.6)

Values represent the number of patients (percentage of the indicated group) for the squatting, and the mean (95% CI) for standing up from a chair (number of repetition) and the SOLEC (s).

SOLEC = standing on one leg, eyes closed; mean duration (s) and 95%CI of the duration.

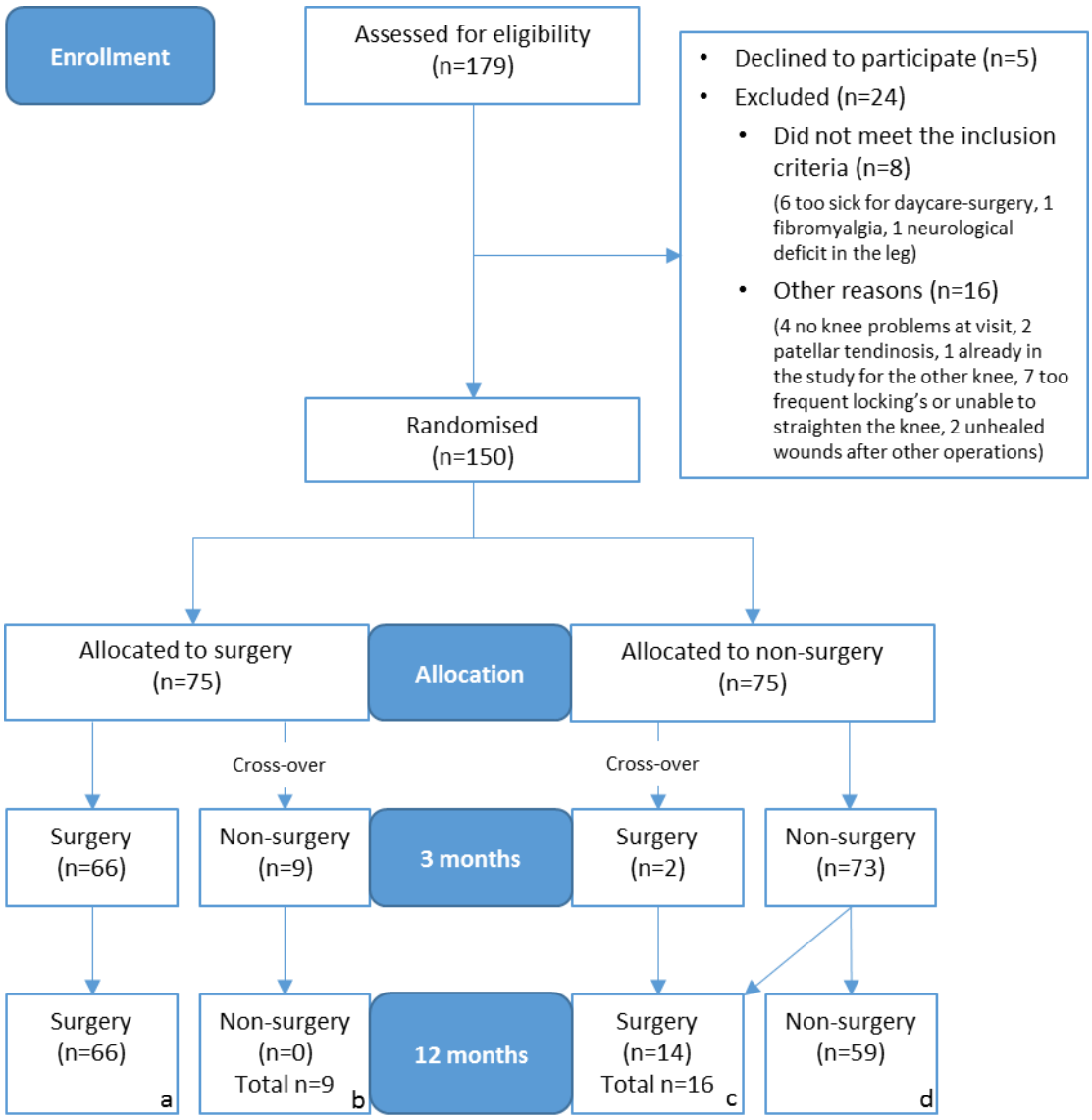
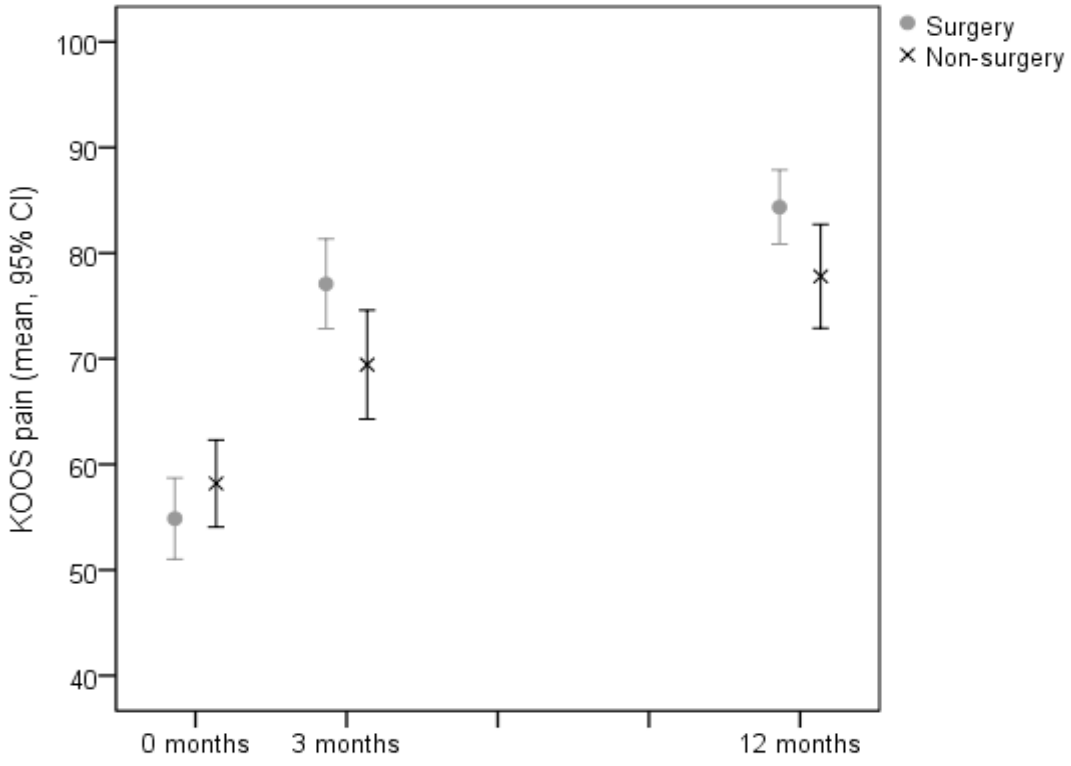
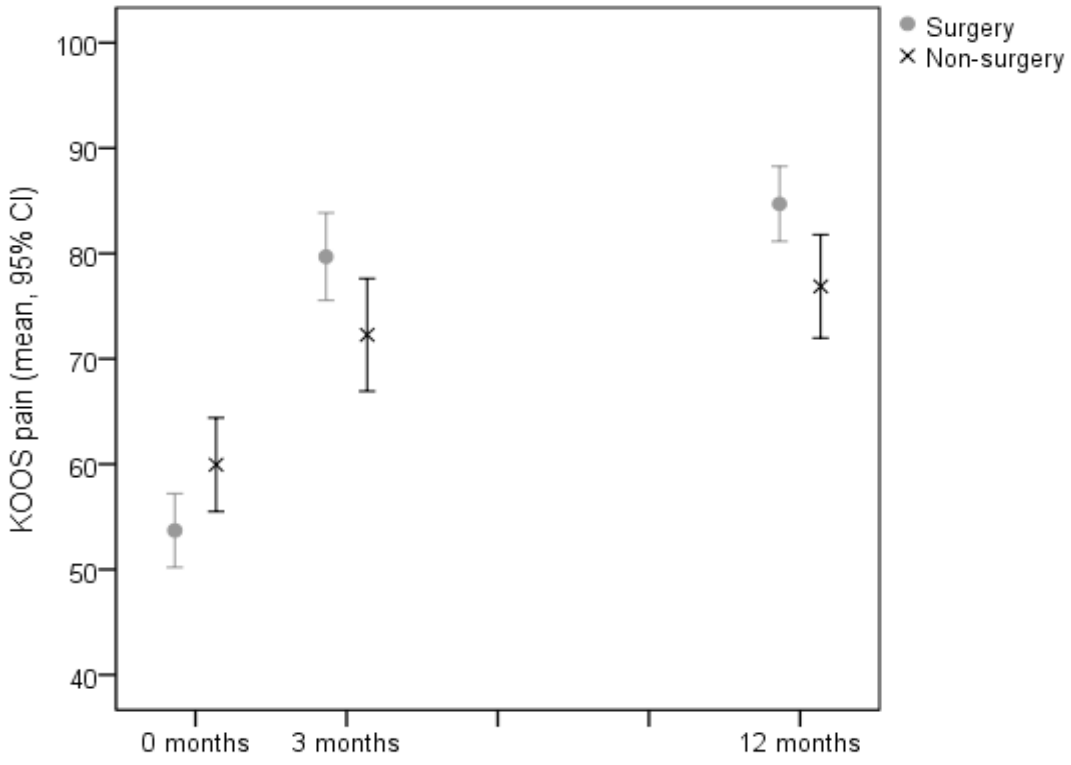

Enrollment
Assessed for eligibility (n=179)
Declined to participate (n=5)
Excluded (n=24)
Did not meet the inclusion criteria (n=8)
(6 too sick for daycare-surgery, 1 fibromyalgia, 1 neurological deficit in the leg)
Other reasons (n=16)
(4 no knee problems at visit, 2 patellar tendinosis, 1 already in the study for the other knee, 7 too frequent locking's or unable to straighten the knee, 2 unhealed wounds after other operations)
Randomised (n=150)
Allocated to surgery (n=75)
Allocation
Allocated to non-surgery (n=75)
Cross-over
Cross-over
Surgery (n=66)
Non-surgery (n=9)
3 months
Surgery (n=2)
Non-surgery (n=73)
Surgery (n=66)
a
Non-surgery (n=0) Total n=9
b
12 months
Surgery (n=14) Total n=16
c
Non-surgery (n=59)
d

Figure 1.

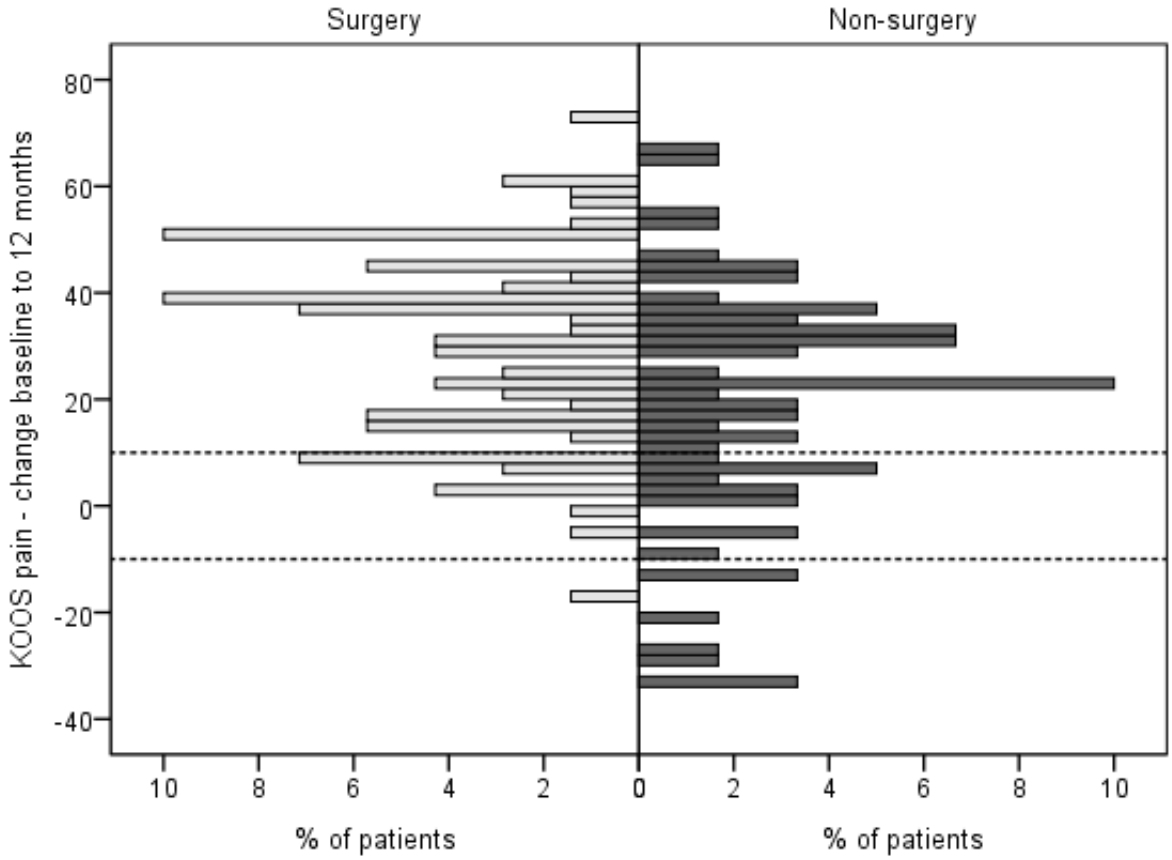


2A.

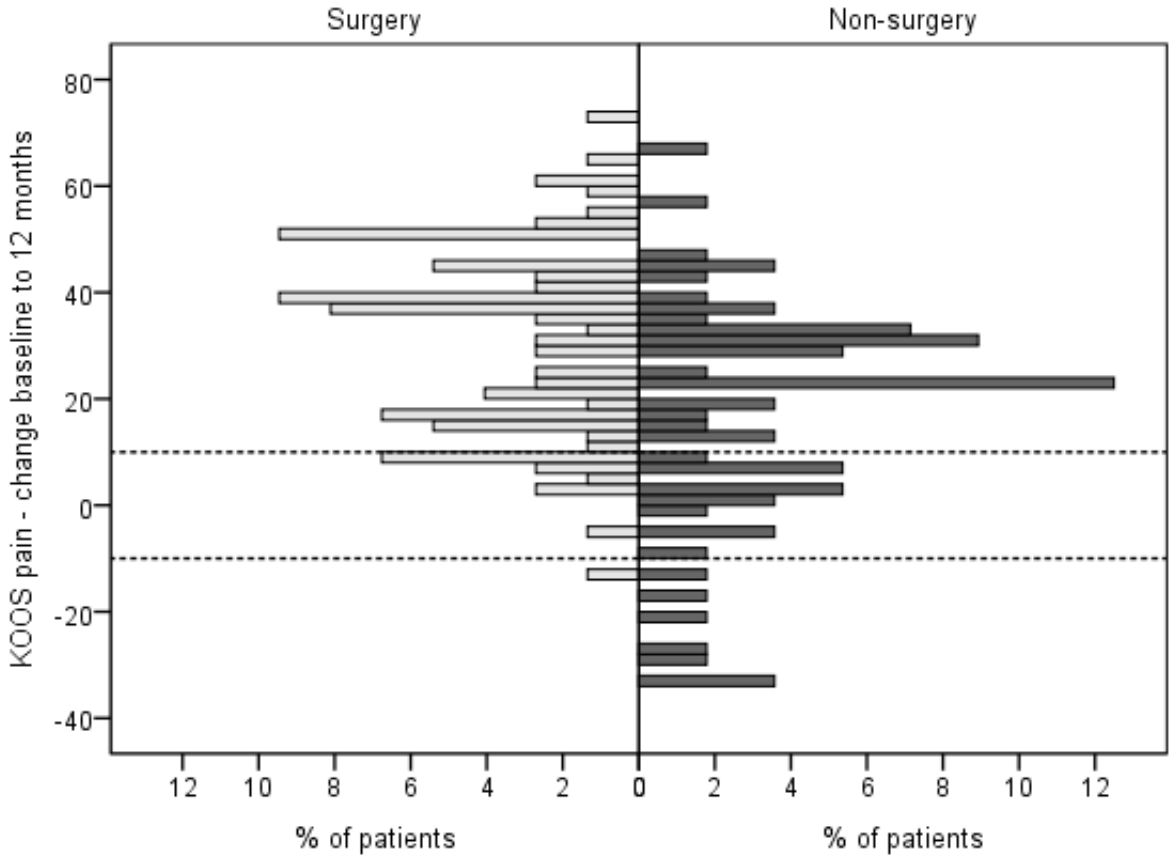


2B.

Figure 2.


Surgery
Non-surgery
KOOS pain - change baseline to 12 months
80
60
40
20
0
-20
-40
10
8
6
4
2
0
2
4
6
8
10
% of patients
% of patients

3A.


Surgery
Non-surgery
KOOS pain - change baseline to 12 months
80
60
40
20
0
-20
-40
12
10
8
6
4
2
0
2
4
6
8
10
12
% of patients
% of patients

3B.

Figure 3.