Postprint Version	1.0
Journal website	http://linkinghub.elsevier.com/retrieve/pii/S1063-4584(10)00161-5
Pubmed link	http://www.ncbi.nlm.nih.gov/pubmed/20488250
DOI	10.1016/j.joca.2010.05.008

Long-term effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized controlled trial comparing two different physical therapy interventions

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SUMMARY

Objective: To determine if behavioral graded activity (BGA) results in better long-term effectiveness (5 years after inclusion) than usual exercise therapy (UC; usual care) in patients with osteoarthritis (OA) of the hip or knee.

Method: Long-term follow-up study of a single blind cluster randomized trial comparing BGA and UC. One hundred and forty-nine patients out of the 200 included were followed until 60 months' follow-up. Primary outcome measures were pain, physical function, and patient global assessment. Furthermore, patient-oriented physical function, physical performance, health care utilization and the number of joint replacement surgeries were assessed. Assessments took place at 3, 9, 15 and 60 months' follow-up. Data were analyzed according to intent-to-treat principle.

Results: Both treatments showed beneficial within-groups effects in the long-term. In patients with knee OA no differences between treatments were found on the short-, mid-long and long-term. In patients with hip OA significant differences in favor of BGA were found at 3 months' (pain and physical performance) and 9 months' follow-up (pain, physical function, patients global assessment and patient-oriented physical function). Furthermore, UC resulted in patients with hip OA in more joint replacement surgeries compared to BGA (hazard ratio [HR], 2.87; 95% confidence interval [CI], 1.1; 7.3).

Conclusion: No differences between treatment groups were found in the long-term on the primary outcome measures. Although more research is needed to confirm the study findings, the results indicate that BGA reduces the risk for joint replacement surgeries compared to UC in patients with hip OA, which probably can be explained by better outcome in favor of BGA in the short- and mid-long-term.

Randomized controlled trial *Trial Registration*: ClinicalTrials.gov, identifier: NCT00522106.

INTRODUCTION

Osteoarthritis (OA) of the hip or knee is a common chronic and degenerative musculoskeletal disorder with a high prevalence increasing with age[1]. OA causes impairments in body functions and physical functioning, which often leads to moderate to severe limitations in participation and a decreased quality of life[2], [3] and [4]. In several guidelines for the medical management of OA of the hip or knee the use of pharmacologic agents (e.g., simple analgesic or anti-inflammatory drugs) and non-pharmacologic modalities (e.g., patient education and exercise therapy) are recommended[5], [6] and [7]. In advanced disease, partial or total replacement of joints often becomes unavoidable. In earlier stages of disease patients are often referred for physical therapy treatment to reduce impairments and improve overall physical function, so that individuals can meet the demands of daily living as long as possible.

Several studies have demonstrated beneficial short-term effect of exercise therapy on pain, physical functioning and patients' self perceived effect[8], [9] and [10]. So far, only a few studies investigated the long-term effectiveness of exercise therapy and the studies that do exist used relatively short follow-up periods, varying from 6 to 15 months after discharge. The positive effects of exercise therapy seem to decline over time after discharge and finally disappear in the long-term[11]. Low exercise adherence rates after discharge are seen as one of the main reasons to explain poor long-term effectiveness of exercise therapy[12] and [13]. Furthermore, stimulation of a physically active lifestyle seems important, because a lack of regular physical activity is an important risk factor for functional decline in patients with OA[14]. In most existing studies investigating the effectiveness of exercise therapy, the exercise programs consisted primarily of muscle strengthening exercises. To stimulate exercise adherence and a more physically active lifestyle post-treatment, it is suggested that exercise programs should become more functional and task-oriented, including additional booster sessions and strategies to improve exercise behavior and self-regulation skills[15].

Veenhof *et al.* developed and evaluated an exercise program integrating operant behavioral principles, self-regulation principles and additional booster sessions called the 'behavioral graded activity' (BGA) program[16]. The BGA treatment is an individually tailored exercise program in which patients' most problematic physical activities are gradually increased in a time-contingent way. Furthermore, the intervention includes individually tailored exercises to improve impairments limiting the performance of these activities. The ultimate goal is integration of these exercises and activities in patients' daily living, so that patients get a more physically active lifestyle. In additional booster sessions patients are supported and stimulated to sustain their physically active lifestyle and integrate exercises and activities in their daily life. Earlier research has shown no significant differences between BGA and usual exercise therapy according to the Dutch guideline (usual care; UC) on pain, self-reported physical function and patient global assessment (PGA). However, significant differences in favor of BGA were found on physical performance, patient-oriented physical functioning, and patients' physical activity level[16]. Furthermore, patients treated with BGA were significantly more adherent to advised exercises compared to patients treated with usual exercise therapy, namely 75% vs 44% in the short-term and 59% vs 34% in the mid-long-term[17]. Because of the better results in patients treated with BGA on exercise adherence and patients' physical activity level, it is expected that BGA results in better long-term effectiveness than UC. Therefore, the objective of the current study was to compare the long-term effectiveness (5 years after inclusion) between UC and BGA in patients with OA on the hip and/or knee.

METHODS

This article reports a follow-up study (5 years after inclusion) of a single blind cluster randomized trial comparing BGA and UC in 200 patients with hip or knee OA[16] and [18]. The study was approved by the medical ethics committee of the VU University Medical Center, Amsterdam and performed in compliance with the Declaration of Helsinki. Full details of the trial protocol (in Dutch) are available on request from the authors.

Setting and participants

Eighty-seven physiotherapists (working in 72 practices) from the region of Utrecht were willing to participate in the study. Patients with OA of the hip or knee were recruited (November 2001–May 2003) by participating physiotherapist and by articles about the study in local newspapers[18]. Inclusion criteria were

OA of hip or knee according to the clinical criteria of the American College of Rheumatology[19] and [20]. Exclusion criteria were: other pathology explaining the complaints; complaints in less than 10 out of 30 days; treatment for these complaints with exercise therapy in the preceding 6 months; under 50 or over 80 years of age; indication for hip or knee replacement within 1 year; contraindication for exercise; inability to understand the Dutch language; and a low level of limitations in activities, defined as: a score < 2 on the sections walking ability and physical function of the Algofunctional index[21] and [22]. All patients completed written informed consent.

Randomization

To avoid contamination of interventions, cluster randomization was performed at the level of the participating physiotherapy practices. The participating practices were randomly assigned to one of the two treatment groups by means of a computer generated random sequence table. Allocation was concealed.

Interventions

BGA

BGA is a behavioral treatment integrating the concepts of operant conditioning with exercise therapy comprising booster sessions. BGA was based on the time-contingency management as described by Fordyce[23] and applied by Lindström[24]. In this individually tailored treatment patients' most problematic activities were gradually increased in a time-contingent way. Furthermore, the intervention included individually tailored exercises to improve impairments limiting the performance of these activities. The treatment consisted of a 12-week period with a maximum of 18 sessions, followed by five pre-set booster moments with a maximum of seven sessions (respectively in week 18, 25, 34, 42, and 55). After the 12-week treatment period physiotherapists advised patients to maintain exercising and performing the activities at home. The additional booster sessions consisted of evaluating, motivating (stimulating exercise adherence) and repeating the main treatment message.

UC

The physical therapists in the UC group were requested to treat the patients according to the Dutch physical therapy guideline for patients with hip and/or knee OA[25]. This guideline consists of general recommendations, emphasizing provision of information and advice, exercise therapy, and encouragement of a positive coping with the complaints. Furthermore, it is recommended to advise patients to maintain exercising at home after discharge. The treatment consisted of a maximum of 18 sessions within a period of 12 weeks.

More specific information on the interventions has been published elsewhere[16] and [26]. Both BGA and UC were given individually by physical therapists in primary care. To avoid contamination of interventions, participating practices were randomly assigned to one of the two treatment groups by means of a computer generated random sequence table. Physical therapists in both treatment groups received a training on the allocated treatment.

Outcome measures

Demographics and clinical data

Demographic and clinical data were collected for each patient including age, gender, height, weight, location of complaints, and duration of complaints. X-rays of the hip and/or knee were scored by a rheumatologist following a standardized procedure according to the Kellgren and Lawrence (K&L) scale; consisting of five degrees: 0, no OA; 1, doubtful OA; 2, minimal OA; 3, moderate OA and; 4, severe OA[27] and [28].

Primary outcome measures

Pain in the last 48 h and physical function was assessed with the WOMAC questionnaire[29] and [30]. PGA was assessed by patients on a eight-point scale (1 = vastly worsened; 8 = completely recovered)[31].

Secondary outcome measures

Patient-oriented physical functioning was assessed with the MACTAR Questionnaire[32]. This functional index measures change in impaired activities selected by each patient in a baseline interview (patients'

priority). Physical performance was measured with the 5 m walking test. Patients' health care utilization for complaints related to OA of the hip and/or knee was assessed, by asking if patients visited health care professionals (general practitioner, medical specialist, physical therapist, occupational therapist or complementary/alternative therapist) in the period from discharge to 60 months' follow-up. Furthermore, patients were asked if they underwent a joint replacement surgery during the study period. If so, the operated joint and operation date were registered.

All primary and secondary outcome measures were obtained at baseline, 3, 9, 15 and 60 months' follow-up, with the exception of physical performance which was not obtained at 9 months' follow-up. All assessments were performed on a test location, in the presence of a research assistant, who was blinded for the assigned treatment. The exception was the assessment at 9 months' follow-up, consisting of only questionnaires, which were sent by mail. Patients were repeatedly instructed not to give information about the allocated treatment to the research assistants. The research assistants were asked to guess the assigned treatment immediately after the measurements at 3, 15 and 60 months' follow-up.

Statistical analyses

The target sample size was 200 patients. This number yields to a power of 80% to detect a 25% difference in PGA and small to medium-sized effects (effect-size = 0.2–0.4) in the outcome measures pain and physical functioning, at two-sided significance level of 0.05 given a maximum loss to follow-up of 20%[33].

The analyses were performed using SPSS 14.0. Descriptive statistics were used to describe the main characteristics of the study population and to explore baseline comparability. The statistical analyses were carried out according to the intention-to-treat principle. Change scores were calculated by subtracting the baseline scores from the post-treatment scores (3, 9, 15 and 60 months, respectively) and were compared for the two intervention groups using Student's *t*-test. The ratings of PGA were dichotomized as improved ("completely recovered", "very much improved" and "much improved") vs not improved ("slightly improved", "not changed", "slightly worsened", "much worsened" and "vastly worsened"). Odds ratios (ORs) with their 95% confidence intervals (CIs) were calculated to test differences between intervention groups. In order to adjust for differences in patients' condition, multiple linear or logistic regression analyses were performed with the change scores as dependent variable and type of intervention as independent variable. The following characteristics were used as covariates in the adjusted analyses: the baseline scores of each outcome measure, duration of symptoms, location of OA (hip, knee, or both), age, sex, and recruitment method (physical therapist or newspaper). To investigate the risk for joint replacement surgery Cox-proportional hazard statistics were used with time at risk in months as underlying time variable. Hazard ratios (HRs) and 95% CIs were calculated to test the difference between treatment groups. Using Kaplan–Meier plots the risk for joint replacement surgery over the 5 years follow-up period for each treatment was illustrated. In all analyses *P* values less than 0.05 were considered statistically significant. In addition, all analyses were also performed on a multi-level basis (using MLwiN) to correct for dependency of observations within subjects and taking into account variation between physiotherapists[34] and [35]. Furthermore, an exploratory per-protocol analysis (not preplanned in research protocol) was performed in which patients who underwent a joint replacement surgery during the study were considered as lost to follow-up from operation date.

RESULTS

A total of 200 patients were included in the trial: 97 patients in the BGA group and 103 patients in the UC group. The BGA group and UC group had similar baseline characteristics and baseline values of outcome measures, as presented in Table I. The 60 months' follow-up (5 years after inclusion) assessment was completed by 76 BGA patients and 73 UC patients. A non-response analysis was performed in which the baseline characteristics of patients who were lost to follow-up were compared with characteristics of patients assessed at 60 months' follow-up. No statistical significant differences were found. Fifty-five physical therapists treated the patients included in this study. Information about the patient flow through the trial is presented in Fig. 1. One patient of the BGA group reported adverse effects (increase of pain) and withdrew at the end of the therapy (after three booster sessions). At 60 months' follow-up 35% UC patients and 28% BGA patients were still adherent to the recommended home exercises (OR = 0.69 [0.3; 1.4]).

[TABLE 1 AND FIGURE 1]

In the long-term (60 months' follow-up), patients in both treatment groups improved on all primary outcome measures. The differences between treatment groups in pain (−0.18 [−1.7; 1.4]), physical function (−1.92 [−6.5; 2.6]) and PGA (OR = 0.67 [0.3; 1.4]) were small and not statistically significant. Similar results were found on most secondary outcome measures at 60 months' follow-up, namely patient-oriented physical functioning, physical performance and health care utilization after discharge. The only significant difference between treatment groups was found in the number of patients that underwent a joint replacement surgery during the study period. Namely, in the BGA treatment group 14 patients (14.4%) underwent a joint replacement surgery during the study period compared to 25 patients (24.3%) in the UC treatment group. Cox-proportional hazard analysis showed that the risk for joint replacement surgery was significantly higher for patients treated with UC compared to BGA (HR [95% CI] = 2.10 [1.1; 4.1]). As indicated by a significant interaction term, the location of OA (hip, knee or both) was a modifier of the relationship between treatment group and the risk for joint replacement surgery. Although it was not preplanned in our research protocol, the data on the long-term effectiveness of BGA and UC were also analyzed separately for patients with hip OA and patients with knee OA, since the location of OA was found to be a significant interaction term. Because Veenhof *et al.*[16] only presented the results for the total group of patients with OA (after 3, 9, and 15 months' follow-up), we also include the results on the short- and mid-long-term for patients with hip and knee OA separately.

Patients with hip OA

In total 70 patients with hip OA were included in the trial: 30 patients in the BGA group and 40 patients in the UC group. In the long-term (60 months' follow-up) no significant differences were found between treatment groups on the primary and most secondary outcomes (patient-oriented physical function and physical performance), see Table II. However, in the BGA treatment group only six patients with hip OA (20.0%) underwent a joint replacement surgery during the study period compared to 18 patients with hip OA (45.0%) in the UC treatment group. Cox-proportional hazard analysis showed that the risk for joint replacement surgery was significantly higher for patients treated with UC compared to BGA (HR = 2.87 [1.1; 7.3]), see Fig. 2.

[TABLE 2. AND FIGURE 2]

Table II also presents the differences between treatment groups on the short-term (3 months' follow-up) and mid-long-term (9 and 15 months' follow-up) for patients with hip OA. At the short-term the differences between treatment groups were mostly not statistically significant. Only on pain and physical performance a significant difference in favor of BGA was found. However, the differences between treatment groups in favor of BGA increased at the mid-long-term (9 months' follow-up) and were statistically significant for pain, physical function, PGA and patient-oriented physical function. At 15 and 60 months no significant differences between treatment groups were found (see Table II). Only on physical performance a significant difference between treatment groups in favor of BGA was found at 15 months' follow-up.

Patients with knee OA

Table III presents the results for patients with knee OA on the primary outcome measures. In total 150 patients with knee OA were included in the trial: 75 patients in the BGA group and 75 patients in the UC group. Although the results were mostly in favor of BGA, the differences between treatment groups on the primary and secondary outcome measures were small and not statistically significant, as well at the short-term, mid-long-term and long-term. Also no differences were found in the risk for joint replacement surgery between treatment groups in patients with knee OA (HR [95% CI] = 1.11 [0.4; 2.8]). In both treatment groups nine patients with knee OA (12.0%) underwent a joint replacement surgery during the study period.

[TABLE 3].

Blinding

The research assistants were asked to guess the assigned treatment immediately after the measurements at 3, 15 and 60 months' follow-up. The research assistants guessed the assigned treatment in 57% of the cases at 3 months' follow-up (Cohen's kappa = 0.14), 46% of the cases at 15 months' follow-up (Cohen's kappa = −0.09), and 51% of the cases at 60 months' follow-up (Cohen's kappa = 0.03).

Additional analyses

In order to correct for dependency of observations within subjects and taking into account variation between physiotherapists all analyses were additionally also performed on a multi-level basis (level: time, patient, and physical therapist). The multi-level analysis yielded similar results (data not presented). To investigate if the differences between treatment groups in the mid-long-term and long-term on primary and secondary outcome measures were biased by the difference in the number of joint replacement surgeries between treatments a exploratory per-protocol analysis (not preplanned in research protocol) was performed. In this per-protocol analysis all patients who underwent a joint replacement surgery during the study period were considered as lost to follow-up from operation date. The differences between treatment groups in patients with hip OA increased considerably in favor of BGA on all outcome measures at 15 months' and 60 months' follow-up. For instance, the differences between treatment groups on physical function in patients with hip OA at 15 and 60 months' follow-up increased respectively from −1.75 [−7.8; 4.3] and −3.26 [−11.0; 4.4] (patients with arthroplasty included) to −3.67 [−9.8; 2.4] and −7.92 [−17.7; 1.9] (patients with arthroplasty considered as lost to follow-up from operation date) (see Fig. 3). However, these differences were not statistically significant. In patients with knee OA the per-protocol analysis yielded similar results compared to the intention-to-treat analyses.

[FIGURE 3]

DISCUSSION

This follow-up study was designed to evaluate whether a BGA results in better long-term effectiveness than UC in patients with OA of the hip and/or knee. Both treatment groups showed beneficial effects in the long-term. No significant differences between treatment groups were found on the primary outcome measures at 5 years follow-up, as well in patients with hip OA as in patients with knee OA. However, in patients with hip OA BGA resulted in the long-term in less joint replacement surgeries than UC.

In the literature it is often suggested that low exercise adherence rates and a lack of regular physical activity post-treatment are important reasons for poor long-term effectiveness of exercise therapy[12] and [13]. Since BGA results in better exercise adherence and a more physically active lifestyle in the short- and mid-long-term[26], the hypothesis was that BGA would result in better long-term effectiveness than UC. Surprisingly, both BGA and UC resulted in beneficial within-groups effects on pain and physical function in the long-term (5 years after inclusion). No significant differences were found between treatment groups. It was expected that UC would only result in short-term effects, because several studies have demonstrated that the beneficial effect of exercise therapy in patients with OA declines after discharge and finally disappears in the mid-long-term[11] and [36]. In patients with hip OA it is likely that the results of UC on pain and physical function at 15 and 60 months' follow-up were biased by patients who underwent joint replacement surgery during the study period. This was confirmed in exploratory per-protocol analysis, in which patients who underwent a joint replacement surgery during the study period were considered as lost to follow-up from operation date. Namely, the exploratory per-protocol analysis demonstrated that the differences increased considerably in favor of BGA on all outcome measures, due to a decline in effectiveness in patients treated with UC in the mid-long-term and long-term. However, these differences between treatment groups at 15 and 60 months' follow-up were not statistically significant, which is probably due to a lack of power.

The reduced risk for joint replacement surgery in BGA patients with hip OA may be due to the beneficial effects of BGA in the short-term and mid-long-term on pain and physical function. In the short-term (3 months' follow-up) a significant difference in favor of BGA was found on pain and physical performance in patients with hip OA. In the mid-long-term (9 months' follow-up) on almost all outcome measures a significant difference was found in favor of BGA in patients with hip OA, namely pain, physical function, PGA, and patient-oriented physical function. Apparently, the beneficial effects of BGA in the short- and mid-long-term are large enough to postpone joint replacement surgery. Comparable results were found in patients with knee OA by Deyle *et al.*, in which was demonstrated that a combination of manual physical therapy and supervised exercise yields functional benefits and may delay or prevent the need for surgical intervention[37]. However, since our study was not specifically designed to investigate the effect of exercise therapy on the risk for joint replacement surgery and the possibility exists that the found difference in the

risk for joint replacement surgery was due to a type-1 error (false positive outcome), further research to confirm our findings is needed.

Several studies in which the effectiveness of exercise therapy in patients with OA was investigated found similar results for patients with hip OA and patients with knee OA[36] and [38]. Surprisingly, the results of our study showed differently. In patients with hip OA the results were in favor of BGA and in patients with knee OA both treatments were equally effective. A possible explanation could be that the biomechanical, psychological or clinical prognostic or risk factors for functional decline are different for patients with hip and knee OA. Because existing studies on prognostic or risk factors are mainly done in patients with knee OA[39], this possibility cannot be fully evaluated. The main goal of exercise therapy is to eliminate potential risk factors for functional decline and improve overall physical function, so that individuals can meet as long as possible the demands of daily living[40]. Due to the positive results in favor of BGA in patients with hip OA, it can be concluded that integrating more functional and task-oriented exercises and strategies directed at behavioral change are in particularly important for patients with hip OA.

There are a few limitations to this study that need to be mentioned. First of all, the lost to follow-up rate at 5 years' follow-up (26%) was higher than expected (20%). The sample of 149 patients which were followed until 5 years' follow-up was smaller than the sample size required by our power analysis. To detect a small to medium effect-size (0.2–0.4) in the outcome measures pain and physical functioning (with a two-sided significance level of 0.05 and power of 80%) in the long-term, the sample size needed to be at least 80 per group. The power calculation was done based on the assumption that both treatments would show similar results in patients with knee and hip OA. Surprisingly, the location of OA seemed to be a modifier of the relationship between the allocated treatment and outcome. For this reason the data needed to be analyzed separately for patients with knee OA and patients with hip OA. Consequently, our study was theoretically underpowered to detect any between-group differences. However, although there was a lack of power, significant and clinically relevant effects were found in patients with hip OA. Secondly, results of our study could be biased by the number of patients which were lost to follow-up, which was 26% at the long-term follow-up (5 years after inclusion). However, the non-response analysis showed similar baseline characteristics for responders and non-responders.

In conclusion, both treatment groups show beneficial within-groups results in the long-term. No significant differences between treatment groups were found in the long-term on pain, physical function and PGA, both in patients with knee and hip OA. Although more research is needed to confirm the study findings, the results indicate that BGA reduces the risk for joint replacement surgeries compared to UC in patients with hip OA, which probably can be explained by better outcome in favor of BGA in the short- and mid-long-term.

AUTHOR CONTRIBUTIONS

The authors declare the following contributions to the preparation of the manuscript: Study conception and design (all authors); collection and assembly of data (Pisters); analysis (Pisters and a professional statistician) and interpretation of data (all authors); drafting of the manuscript (Pisters); critical revision of the manuscript for important intellectual content (Veenhof, Schellevis, De Bakker and Dekker); final approval of the manuscript (all authors); obtaining of funding (Veenhof). All authors take responsibility for the integrity of the work.

CONFLICT OF INTEREST

All authors declare that there are no conflicts of interest.

ACKNOWLEDGMENTS

The authors would like to thank the physiotherapists and patients who participated in the study and Peter Spreeuwenberg (statistician) for performing the multi-level analysis. This project was funded by the Dutch Arthritis Association.

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TABLES AND FIGURES

Table I
Baseline characteristics of both intervention groups

Characteristics	BGA ($n = 97$)	UC ($n = 103$)
Female, n (%)	73 (75)	81 (79)
Age, mean (sd)	65.1 (7.4)	64.5 (8.3)
Location of OA, n (%)		
Knee	67 (69)	63 (61)
Hip	22 (23)	28 (27)
Both	8 (8)	12 (12)
Duration of complaints, n (%)		
<1 year	23 (24)	24 (23)
1–5 years	39 (41)	33 (32)
>5 years	33 (35)	46 (45)
Radiological evidence OA (K&L ≥ 2)		
Knee, n (%)	26 (52)	31 (61)
Hip, n (%)	18 (86)	29 (97)
Body mass index, mean (sd)	28.2 (4.2)	28.8 (4.6)

*Significant difference between-groups ($P < 0.05$).

Figure 1 Flow diagram through study

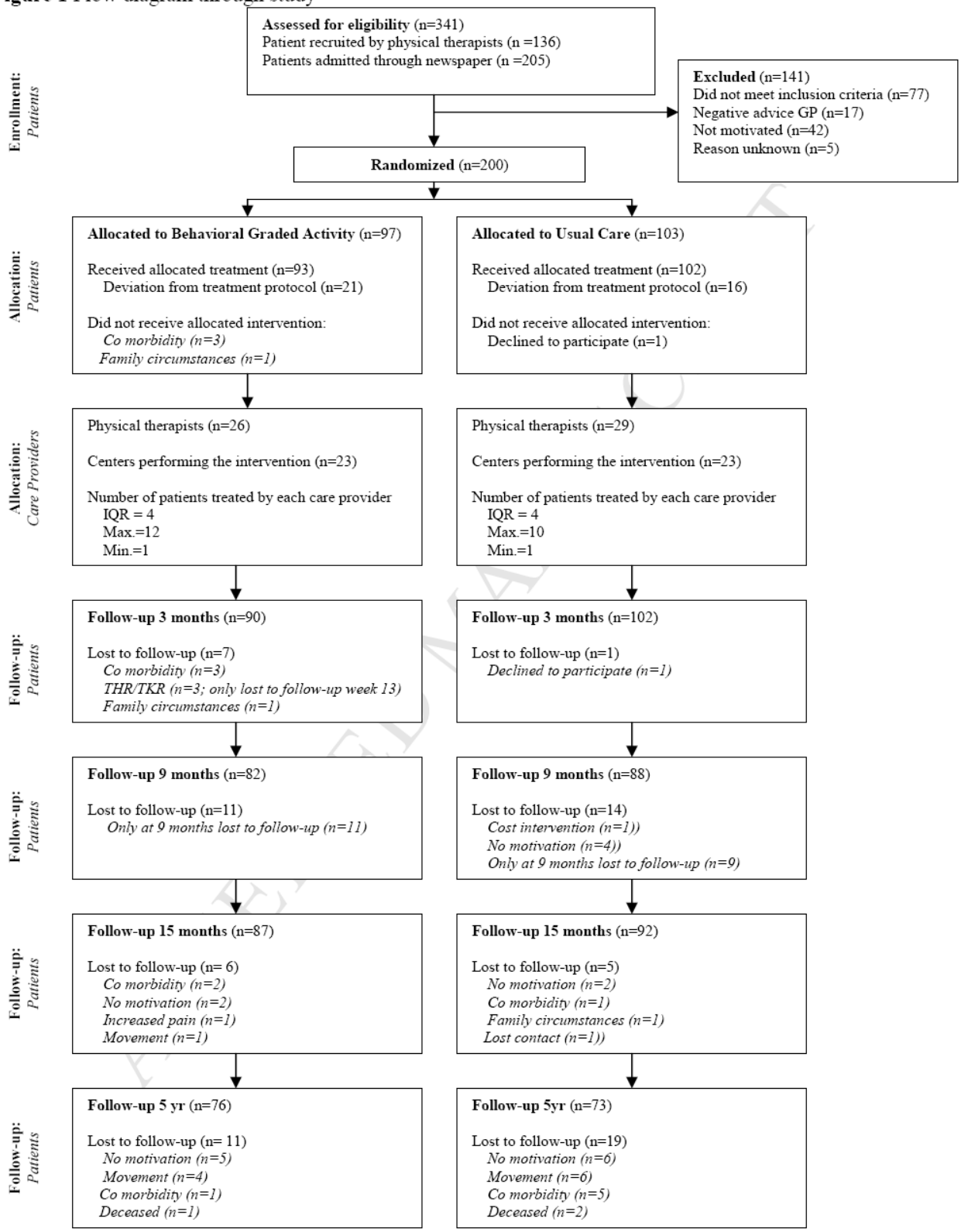


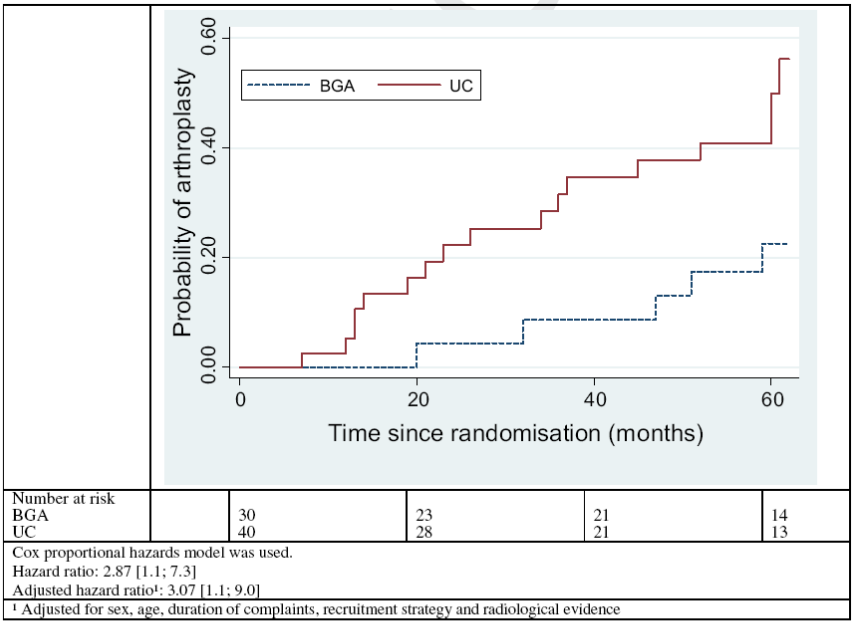
Table II
Outcome in intervention groups in patients with hip OA ($n = 70$)

Outcome measures	BGA		UC		Difference BGA – UC [95% CI]	Adjusted difference [95% CI][†]
	n	Mean [95% CI]	*n*	Mean [95% CI]		
Pain, subscale WOMAC: 0–20						
Baseline, mean (sd)	30	9.9 (2.3)	40	8.4 (2.9)		
Δ 3 Months – baseline	26	−2.57 [−3.6; −1.6]	40	−1.10 [−2.0; −0.2]	−1.46 [−2.8; −0.1][*]	−1.02 [−2.3; 0.3]
Δ 9 Months – baseline	26	−3.12 [−4.8; −1.4]	36	−0.06 [−1.2; 1.1]	−3.05 [−4.9; −1.2][*]	−2.47 [−4.4; −0.5][*]
Δ 15 Months – baseline	25	−3.88 [−5.4; −2.3]	35	−2.54 [−3.6;−1.5]	−1.34 [−3.1; 0.4]	−0.13 [−1.9; 1.7]
Δ 60 Months – baseline	20	−4.70 [−6.6; −2.8]	31	−3.59 [−5.3; −1.9]	−1.10 [−3.6; 1.4]	−0.33 [−3.1; 2.4]
Physical function, subscale WOMAC: 0–68						
Baseline, mean (sd)	30	29.47 (11.3)	40	29.10 (8.5)		
Δ 3 Months – baseline	25	−4.55 [−8.0; −1.1]	40	−3.28 [−5.6;−0.9]	−1.25 [−5.1; 2.7]	−0.61 [−4.7; 3.5]
Δ 9 Months – baseline	24	−6.81 [−11.0; −2.6]	34	−1.64 [−4.4; 1.2]	−5.15 [−9.9; −0.4][*]	−4.10 [−9.0; 0.8]
Δ 15 Months – baseline	24	−6.99 [−12.5; −1.5]	35	−5.23 [−8.8;−1.7]	−1.75 [−7.8; 4.3]	0.45 [−5.2; 6.1]
Δ 60 Months – baseline	21	−13.34 [−19.2; −7.5]	31	−10.06 [−15.3; −4.9]	−3.26 [−11.0; 4.4]	−2.13 [−9.4; 5.2]
PGA					OR	OR
3 Months, % (*n*) improved	26	35 (9)	40	23 (9)	1.94 [0.6; 5.8]	1.41 [0.4; 4.7]
9 Months, % (*n*) improved	25	52 (13)	36	14 (5)	6.72 [2.0; 22.9][*]	5.98 [1.6; 22.0][*]
15 Months, % (*n*) improved	24	58 (14)	32	36 (12)	2.45 [0.8; 7.2]	1.61 [0.5; 5.5]
60 Months, % (*n*) improved	21	57 (12)	28	50 (14)	1.33 [0.4; 4.2]	0.71 [0.2; 2.9]
Patient-oriented physical function, MACTAR: −15 to 15						
Δ 3 Months – baseline	26	6.62 [4.5; 8.8]	40	4.55 [2.3; 6.8]	2.04 [−1.1; 5.2]	1.44 [−1.9; 4.8]
Δ 9 Months – baseline	28	6.96 [3.8; 10.1]	38	−0.97 [−3.6; 1.7]	7.93 [3.9; 11.9][*]	7.26 [3.1; 11.4][*]
Δ 15 Months – baseline	25	5.60 [2.3; 8.9]	35	1.54 [−1.4; 4.5]	4.05 [−0.3; 8.4]	3.69 [−1.1; 8.5]
Δ 60 Months – baseline	20	5.55 [1.4; 9.7]	31	5.32 [1.8; 8.8]	0.23 [−5.1; 5.5]	0.15 [−5.1; 5.4]
Physical performance, 5 m walking in s						
Baseline, mean (sd)	28	4.9 (1.3)	40	4.5 (0.9)		
Δ 3 Months – baseline	25	−0.56 [−1.0; −0.1]	39	0.11 [−0.2; 0.4]	−0.65 [−1.1; −0.2][*]	−0.46 [−0.9; −0.1][*]
Δ 15 Months – baseline	20	−0.71 [−1.4; −0.1]	32	−0.04 [−0.3; 0.3]	−0.66 [−1.3; −0.1][*]	−0.41 [−0.8; 0.0][*]
Δ 60 Months – baseline	19	−0.42 [−1.1; 0.2]	28	0.20 [−0.3; 0.7]	−0.63 [−1.4; 0.2]	−0.37 [−1.0; 0.3]

Negative signs indicate improvement within-groups or improvement in favor of BGA (in case of differences in change between-groups), with the exception of MACTAR. Concerning PGA OR > 1 indicates improvement in favor of BGA.

[*] $P < 0.05$.

[†] Analysis are adjusted for the baseline score of each outcome measure, duration of complaints, age, sex, and recruitment method (physiotherapist or newspaper).



Number at risk					
BGA		30	23	21	14
UC		40	28	21	13

Cox proportional hazards model was used.
Hazard ratio: 2.87 [1.1; 7.3]
Adjusted hazard ratio[1]: 3.07 [1.1; 9.0]
[1] Adjusted for sex, age, duration of complaints, recruitment strategy and radiological evidence

Fig. 2. Kaplan–Meier survival curve for patients with hip OA.

Table III
Outcome in intervention groups in patients with knee OA ($n = 150$)

Outcome measures	BGA		UC		Difference BGA – UC [95% CI]	Adjusted difference [95% CI] *
	n	Mean [95% CI]	*n*	Mean [95% CI]		
Pain, subscale WOMAC: 0–20						
Baseline, mean (sd)	75	9.0 (3.6)	75	8.7 (3.2)		
Δ 3 Months – baseline	69	−2.22 [−3.0; −1.5]	74	−2.47 [−3.3; −1.7]	0.25 [−0.9; 1.4]	0.42 [−0.6; 1.4]
Δ 9 Months – baseline	61	−1.80 [−2.9;−0.7]	62	−1.23 [−2.3; −0.2]	−0.57 [−2.1; 1.0]	−0.32 [−1.8; 1.1]
Δ 15 Months – baseline	66	−3.86 [−4.9;−2.9]	66	−3.39 [−4.2;−2.6]	−0.47 [−1.7; 0.8]	−0.23 [−1.3; 0.9]
Δ 60 Months – baseline	55	−2.27 [−3.7; −0.9]	47	−1.63 [−2.8; −0.5]	−0.63 [−2.5; 1.2]	−0.55 [−2.3; 1.2]
Physical function, subscale, WOMAC: 0–68						
Baseline, mean (sd)	70	28.9 (13.2)	75	28.7 (10.7)		
Δ 3 Months – baseline	63	−6.30 [−8.6; −4.0]	74	−5.99 [−8.2; −3.8]	−0.30 [−3.4; 2.8]	−0.26 [−3.2; 2.6]
Δ 9 Months – baseline	60	−6.36 [−9.5; −3.2]	60	−6.45 [−9.2; −3.7]	0.10 [−4.0; 4.2]	0.37 [−3.5; 4.2]
Δ 15 Months – baseline	60	−7.21 [−10.9; −3.6]	63	−8.23 [−10.5; −5.9]	1.02 [−3.2; 5.2]	1.38 [−2.3; 5.0]
Δ 60 Months – baseline	51	−8.54 [−12.8; −4.3]	45	−5.53 [−9.0; −2.0]	−3.01 [−8.5; 2.5]	−2.87 [−7.7; 2.0]
PGA					OR	OR
3 Months, % (*n*) improved	69	41 (28)	74	39 (29)	1.10 [0.6; 2.2]	1.20 [0.6; 2.4]
9 Months, % (*n*) improved	59	34 (20)	60	32 (19)	1.05 [0.5; 2.3]	1.16 [0.5; 2.6]
15 Months, % (*n*) improved	67	52 (35)	63	51 (32)	1.03 [0.5; 2.1]	1.01 [0.5; 2.1]
60 Months, % (*n*) improved	55	49 (27)	46	35 (16)	1.74 [0.8; 3.9]	1.78 [0.8; 4.1]
Physical function, MACTAR: −15 to 15						
Δ 3 Months – baseline	69	6.09 [4.7; 7.5]	74	5.30 [3.7; 6.9]	0.79 [−1.3; 2.9]	0.89 [−1.2; 3.0]
Δ 9 Months – baseline	72	3.24 [1.2; 5.2]	70	3.33 [1.4; 5.2]	−0.09 [−2.8; 2.7]	0.05 [−2.8; 2.7]
Δ 15 Months – baseline	67	6.18 [4.4; 8.0]	66	4.00 [2.3; 5.7]	2.18 [−0.3; 4.7]	2.25 [−0.2; 4.7]
Δ 60 Months – baseline	54	3.59 [1.0; 6.2]	46	1.70 [−1.1; 4.5]	1.89 [−1.8; 5.6]	2.05 [−1.6; 5.7]
Physical function, 5 m walking in s						
Baseline, mean (sd)	73	4.8 (1.2)	75	4.9 (1.6)		
Δ 3 Months – baseline	68	−0.32 [−0.5; −0.1]	73	−0.31 [−0.5; −0.1]	0.01 [−0.3; 0.3]	−0.05 [−0.3; 0.2]
Δ 15 Months – baseline	61	−0.32 [−0.6; −0.1]	64	−0.15 [−0.4; 0.1]	−0.17 [−0.5; 0.2]	−0.23 [−0.5; 0.0]
Δ 60 Months – baseline	51	0.16 [−0.2; 0.5]	43	0.34 [0.0; 0.6]	−0.18 [−0.7; 0.3]	−0.21 [−0.6; 0.2]

Negative signs indicate improvement within-groups or improvement in favor of BGA (in case of differences in change between-groups), with the exception of MACTAR. Concerning PGA OR > 1 indicates improvement in favor of BGA.

* Analyses are adjusted for the baseline score of each outcome measure, duration of complaints, age, sex, and recruitment method (physiotherapist or newspaper).

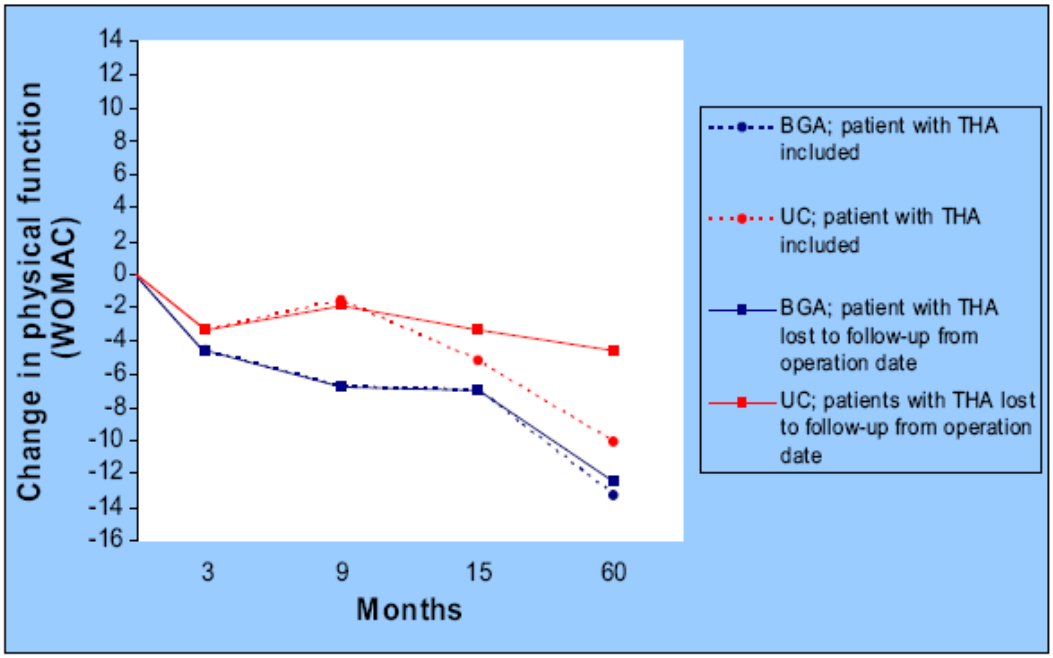


Fig. 3. Change in physical function (WOMAC) in patients with hip OA. Negative signs indicate improvement differences between intention-to-treat and per-protocol analysis (all patients who underwent a joint replacement surgery during the study period were considered lost to follow-up from operation date).