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Are Outcomes From an Exercise Therapy and Patient Education Program for Osteoarthritis Associated With Hip and Knee Replacement Within Two Years? A Register-Based Study of 9,339 Patients With Osteoarthritis

Ilana N. Ackerman,[1] Melker S. Johansson,[2] Dorte T. Grønne,[3] Stine Clausen,[2] Martin Thomsen Ernst,[2] Søren Overgaard,[4] Anders Odgaard,[5] Ewa M. Roos,[2] and Søren T. Skou[3]

Objective. The objective of this study was to determine whether short-term outcomes from exercise therapy and patient education for osteoarthritis (OA) are associated with hip or knee replacement within two years.

Methods. Individual-level data from the Good Life with osteoArthritis in Denmark (GLA:D) Registry were linked to the Danish National Patient Registry and other national registries. Cox proportional hazards models were used to investigate associations between program outcomes (baseline to three-month changes) and time to primary hip or knee replacement. Patients who did not receive joint replacement were censored at two years, time of death, or emigration.

Results. A total of 2,304 and 7,035 patients with clinically diagnosed hip and knee OA, respectively, were included. Of these, 30% with hip OA and 10% with knee OA had joint replacement within two years. Postprogram improvements in hip-related quality of life and arthritis self-efficacy (pain subscale) were associated with a reduced hazard of hip replacement (adjusted hazard ratios [HRs] for a 10-unit improvement: 0.74 [95% confidence interval (CI) 0.69–0.80] and 0.90 [95% CI 0.85–0.96], respectively). Improvements in knee pain, knee-related quality of life, and arthritis self-efficacy (pain subscale) were associated with a lower hazard of knee replacement (adjusted HRs for 10-unit improvement: 0.81 [95% CI 0.76–0.86] to 0.90 [95% CI 0.86–0.95], 0.70 [95% CI 0.63–0.78] to 0.79 [95% CI 0.72–0.86], and 0.89 [95% CI 0.83–0.94], respectively).

Conclusion. The magnitude of improvement in key measures after exercise therapy and education was significantly associated with the likelihood of surgery. Progression to hip replacement was three times higher than progression to knee replacement. This information can guide patient–clinician conversations around anticipated program outcomes.

INTRODUCTION

Contemporary hip and knee osteoarthritis (OA) clinical guidelines recommend that surgery should only be considered once first-line management options have been adequately trialed.[1–3] However, there are reports that many people with hip or knee OA do not receive guideline-recommended care, including education, exercise therapy, and weight management when indicated,[4,5] It is also recognized that some people with OA proceed directly to surgery where first-line options would be

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SIGNIFICANCE & INNOVATIONS

- Although earlier research has examined the influence of patient characteristics, whether the magnitude of improvement after an exercise therapy and education program is associated with short-term progression to joint replacement remains unknown.
- This information could be used to guide clinical conversations with program participants around anticipated outcomes.
- This study examined associations between changes in patient-reported outcomes, as well as changes in measured functional outcomes, after an exercise therapy and education program and the hazard of hip or knee replacement within two years.
- A key study strength was the linkage of large-scale clinical registry data with data from national administrative registries to enable robust analysis of joint replacement outcomes.

appropriate.[6] Current evidence indicates that first-line, nonsurgical management programs (which include appropriately dosed exercise therapy) may delay hip[7] and knee replacement surgery[8,9] for some patients. Whether similar results can be achieved beyond trial settings through real-world implementation of these programs remains unknown.

Two studies have examined whether preprogram factors, including demographic and clinical characteristics and baseline patient-reported scores, are associated with the likelihood of short-term progression to joint replacement surgery. Clausen et al[10] investigated associations between baseline factors and progression to hip replacement within two years among 3,657 people with hip OA who took part in the Good Life with osteoArthritis in Denmark (GLA:D) program. More recently, Gustafsson et al[11] examined associations between baseline factors and progression to hip or knee replacement within five years among 72,069 people in the Better Management of Patients with Osteoarthritis registry in Sweden. We are not aware of studies that have investigated associations between the magnitude of change in patient-reported outcomes or measured functional outcomes after an exercise therapy and education program and progression to surgery. Yet this information would be helpful when discussing possible clinical outcomes with program participants. We aimed to determine whether outcomes from a supervised exercise therapy and patient education program were associated with the likelihood of primary hip replacement or knee replacement within two years.

PATIENTS AND METHODS

Study design. This cohort study was based on data from the GLA:D Registry, linked with national health registry data. It is reported according to the REporting of studies Conducted using Observational Routinely collected health Data (RECORD) statement.[12] Approval for the GLA:D Registry (registration no.: SDU;10.084) and the current analyses (registration no.: SDU;10.124) have been registered at the University of Southern Denmark and the Danish Data Protection Agency. According to Danish legislation, ethics approval for national approved quality databases is not required. Under the Danish Data Protection Act, patient consent was not required because personal data were processed exclusively for research and statistical purposes.

Patient participation in the GLA:D program. The most widely implemented nonsurgical OA management program internationally is the GLA:D program.[13,14] It is grounded in evidence supporting the use of exercise therapy in managing hip and knee OA.[15] GLA:D is a guideline-based supervised exercise therapy and education program that is delivered over 8 to 12 weeks. It is standardized but individualized and incorporates twice-weekly group-based exercise and two intensive education sessions. In Denmark, people with symptoms of hip or knee OA may be referred to a GLA:D physiotherapist by their general practitioner (in which case approximately 40% of the GLA:D cost is reimbursed) or medical specialist (in which case the full cost is reimbursed), or they may be self-referred (in which case individuals must pay the full cost). A physiotherapist trained specifically in clinical diagnosis methods evaluates the inclusion and exclusion criteria for the GLA:D program. People with a clinical diagnosis of hip and/or knee OA are eligible; specifically, the inclusion criterion is "joint problems from knee and/or hip that have resulted in contact with the health care system." The exclusion criteria are a diagnosis other than OA (eg, tumor or inflammatory joint disease) or other pronounced pain symptoms (eg, chronic generalized pain or fibromyalgia). A clinical diagnosis of OA, based on established clinical criteria,[16,17] is made by the physiotherapist after history taking and patient examination. Radiographic examination is not considered; previous analyses have indicated that a high proportion of GLA:D participants have self-reported radiographic hip or knee OA (82% for hip OA and 79% for knee OA),[16,17] although this has not been evaluated against radiographic data. Further detail on the GLA:D program is available elsewhere.[13]

Data sources. We linked data from the Danish GLA:D Registry with individual-level data from the Danish National Patient Registry, the Danish National Prescription Registry, and the Danish Civil Registration System using a unique national civil registration number assigned to all persons living in Denmark. These data sources are briefly summarized in the following sections and in Figure S1.

Danish GLA:D Registry. Individual baseline (at the time of GLA:D enrollment) and three-month postprogram outcomes data were sourced from the Danish GLA:D Registry.[13] Participants

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in the GLA:D program are only registered once in this registry. Clinical characteristics were collected in the baseline questionnaire administered to all participants before commencing the program. Data demonstrating the agreement between self-reported GLA:D Registry data and national administrative data have been reported previously.[18] Body mass index was calculated as weight in kilograms divided by height in meters squared. Follow-up questionnaires were administered via email to all participants approximately three months after program commencement. Scores for average pain intensity in the past month were collected using a visual analog scale (range: 0 [no pain] to 100 [highest pain]). Joint-related quality of life was assessed using the Hip disability and Osteoarthritis Outcome Score (HOOS) and Knee injury and Osteoarthritis Outcome Score (KOOS) quality-of-life scales.[19,20] with scores ranging from 0 (lowest joint-related quality of life) to 100 (highest joint-related quality of life). The Arthritis Self-Efficacy Scale (ASES) pain and ASES other symptoms scales were also collected, with scale scores ranging from 10 (very uncertain) to 100 (very certain).[21] Fear of movement was assessed with the question "Are you afraid that your joints will be damaged from physical activity and exercise?" and response options of "yes" or "no." Participants also completed a 30-second timed chair stand test and a 40-m fast-paced walk test,[13] with results recorded as the number of rises and time in seconds (later converted to speed in m/s), respectively.

Danish National Patient Registry. The Danish National Patient Registry (DNPR) contains information on diagnoses (using the *International Classification of Diseases, 10th Revision* [ICD-10]) and procedures (using the Nordic Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures codes) performed at all hospitals in Denmark.[22] When joint replacement surgery is performed, a surgical code and procedure date are linked to the patient's civil registration number. The following data were extracted from the DNPR: ICD-10 codes within five years before GLA:D (these were used to identify comorbidities for the Charlson comorbidity index) and NOMESCO procedure codes for primary total hip replacement or primary knee replacement before the first program visit (date of surgery and surgery type) and within two years after the program (date of surgery and surgery type). Primary total hip replacement was identified using the surgical codes KNFB20, KNFB30, and KNFB40. Primary knee replacement (total or unicompartmental) was identified using all KNGB* codes (Table S1).

Danish National Prescription Registry. The Danish National Prescription Registry contains individual-level information about all prescriptions dispensed in Danish pharmacies, including but not limited to date of dispensing, Anatomical Therapeutic Chemical (ATC) classification code, number of packages, size of package, strength, defined daily dose, and route of administration.[23] We retrieved data on all prescriptions for opioids (ATC codes N02A*, R05DA04, and N02BA75) that were dispensed within three months before the participant's first program visit.

Danish Civil Registration System. Individual-level data on age, sex, and emigration or death for any reason during the program or within two years after the three-month program follow-up date were obtained from the Danish Civil Registration System.[24] The Danish Civil Registration System is an administrative register that contains individual-level information (eg, name, address, birth, citizenship, civil status, migrations, and others) for all individuals residing in Denmark.

Outcome and predictor variables. The outcome of interest was primary total hip replacement (for the hip cohort) or primary knee replacement (for the knee cohort) performed within two years after the three-month program follow-up date. Predictor variables of interest were baseline to three-month change in hip or knee pain intensity, HOOS or KOOS quality-of-life score, ASES scores (pain and other symptoms), fear of movement, 40-m walk speed, and timed chair stand rises. For continuous variables, change scores were calculated as the difference between three-month and baseline scores. For hip or knee pain intensity, the scales were reversed so that a positive change indicated an improved outcome, consistent with the other continuous variables. For fear of movement (binary outcome), we derived the following four baseline-follow-up groups: no to no (reference), no to yes, yes to no, and yes to yes.

Study cohort. Figure 1 summarizes the establishment of the study cohort. First, we identified people with hip OA and people with knee OA who were enrolled in GLA:D (baseline, based on date of their first visit) between January 1, 2013, and December 31, 2016. The most affected joint was confirmed by the physiotherapist and the patient. Of these people, we excluded those with a history of hip replacement in the index hip and those with a history of knee replacement in the index knee. We also excluded people who received hip or knee replacement before their three-month follow-up, as well as those who completed the three-month questionnaire less than 42 days or more than 183 days after completing the baseline questionnaire. People contributed to either the hip OA or the knee OA analysis according to their index joint. Only those with complete data on all predictor and confounder variables were included in the analyses (57% of all patients in the GLA:D Registry).

Data analysis. GLA:D Registry data were checked for the correct format; no outliers were deleted, and no data were imputed. Data cleaning was not required for the national health registries. Demographic and baseline data were analyzed descriptively for the hip and knee OA cohorts. Descriptive analysis of baseline, three-month, and change score data was also undertaken for individuals who received joint replacement within two years and those who did not.

We described the rate of primary hip and knee replacements over time using Kaplan–Meier curves with 95% confidence

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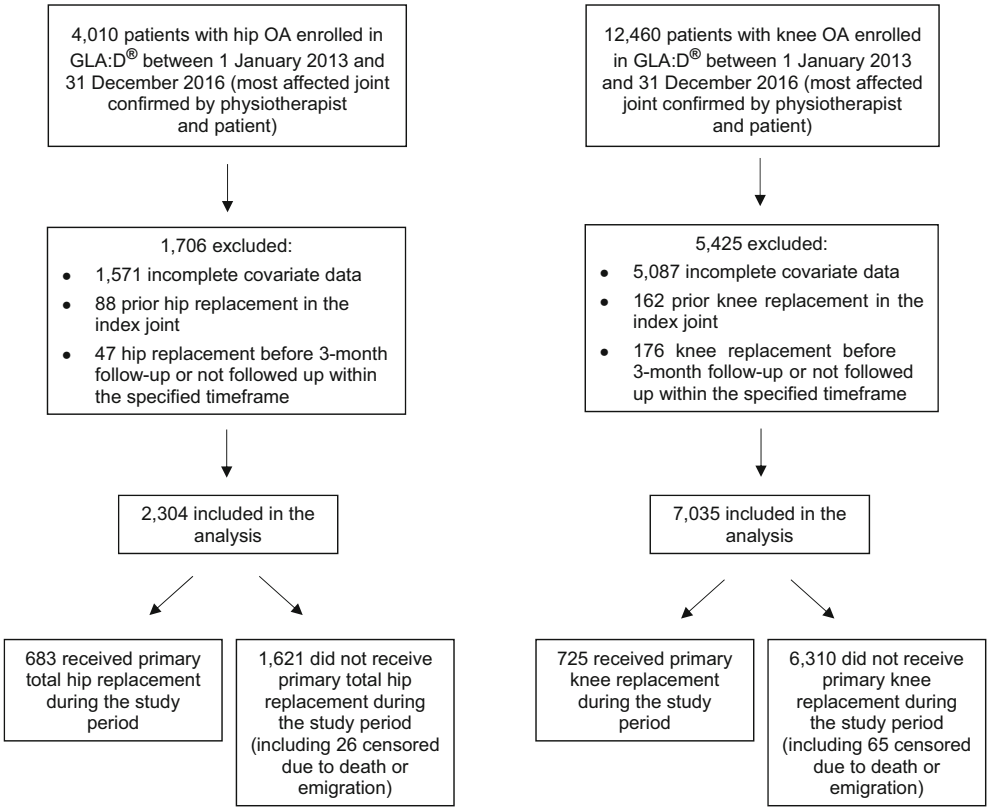

Figure 1. Flowchart of study participants. GLA:D, Good Life with osteoArthritis in Denmark; OA, osteoarthritis.

intervals (CIs), stratified by joint. Time to surgery was calculated as the number of days from the three-month follow-up date to the date of surgery. Study participants who did not receive a hip or knee replacement were censored at two years (730 days) or at the time of death or emigration, whichever occurred first.

Cox proportional hazards models were used to investigate unadjusted and adjusted associations between predictor variables and primary total hip replacement or primary knee replacement. In the adjusted models, we included baseline values of pain intensity (continuous variable), HOOS or KOOS quality-of-life score (continuous), ASES pain subscale score (continuous), ASES other symptoms subscale score (continuous), 40-m walk speed (continuous), and number of chair stands (continuous). We also included the following potential confounders: age (continuous variable), sex (categorical variable), body mass index (continuous), educational level (self-reported, categorical), Charlson comorbidity index (register-based, continuous), wait-listed for surgery status (self-reported, categorical), previous joint replacement in another joint (register-based, categorical), and opioid use (register-based, one or more dispensed opioid prescriptions within three months before the follow-up visit; categorical). To aid interpretation of the results, we report hazard ratios (HRs) for a 10-unit change in each predictor variable (for outcomes reported on a 0–100 scale) and HRs for the observed mean change in each predictor variable. HRs for clinically important improvement, based on published minimal important differences,[25–28] were also calculated.

To assess the proportional hazards assumption, we inspected plots of scaled Schoenfeld residuals versus time, cumulative coefficients from Aalen's additive regression models versus time, and cumulative score (Martingale) residuals from Cox–Aalen regression models versus time and tested for independence between scaled Schoenfeld residuals and time. Furthermore, we assessed (1) influential observations by inspecting deviance residuals, (2) linearity by inspecting Martingale residuals versus continuous variables, (3) correlation, and (4) multicollinearity between the continuous predictors of interest by calculating Spearman's correlation coefficients ($\rho \leq 0.67$ in hip and knee models) and variance inflation factors (<3.0 in the hip model and <2.8 in the knee model). Competing risk analysis for death was conducted but did not alter the results given the relatively few deaths (27 in hip cohort, 43 in knee cohort).

In the hip analyses, we used age as the time scale because of violations of the proportional hazard assumption for this variable. In the knee replacement analyses, we used an extended Cox model with time-varying coefficients because of violations of the proportional hazard assumption for several predictor variables. The coefficients were allowed to vary between days 0 and 200 and days 201 and 730 of the follow-up period. We chose this cut point based on inspection of

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cumulative coefficients from Aalen's additive regression models plotted against time.

RESULTS

Baseline characteristics. In total, 2,304 patients were included in the hip OA analyses and 7,035 patients were included in the knee OA analyses (Figure 1). Key demographic and clinical characteristics are summarized in Table 1. Baseline scores indicated moderate pain, moderately impaired quality of life, and moderate arthritis self-efficacy for the hip OA and knee OA cohorts (Table 1). Relatively few patients were waitlisted for hip or knee replacement surgery (2% each). Attendance at the supervised exercise sessions was high, with >80% of hip and knee OA patients attending at least 10 sessions. Comparison of available data showed that patients with complete data had similar demographic and clinical characteristics, similar exercise session attendance, and similar progression to joint replacement as patients with incomplete data (Table S2).

Progression to hip and knee replacement within two years. Figure 2 shows the rate of progression to joint replacement over the two-year study period. Progression to primary total hip replacement within two years was three times higher (30% of the hip OA cohort) than progression to primary knee replacement (10% of the knee OA cohort). For those who received joint replacement, the median time to surgery after the GLA:D program was 356 days (interquartile range [IQR] 212–524 days) for hip replacement and 357 days (IQR 223–573 days) for knee replacement.

Patients who received hip replacement tended to be older (mean age 67 vs 65 years) and had higher pain, poorer joint-related quality of life, and lower arthritis self-efficacy at baseline and the three-month follow-up than those who did not progress to hip replacement (Table 2). Patients who received hip replacement also reported smaller improvements in pain (mean improvement 6.5 vs 12.8 points) and hip-related quality of life (mean improvement 1.2 vs 6.5 points) after the program, as well as worsening of their ASES scores (compared to improvement in ASES scores for patients who did not receive hip replacement). Attendance at the supervised exercise and patient education sessions was comparable across the two groups.

A similar pattern was observed for patients who received knee replacement. These patients tended to be older (mean age 66 vs 64 years) and had higher pain, poorer joint-related quality of life, and lower arthritis self-efficacy at baseline and the three-month follow-up than patients who did not progress to knee replacement (Table 2). Patients who progressed to knee replacement also reported smaller improvements in pain (mean improvement 7.1 vs 15.3 points) and knee-related quality of life (mean improvement 1.6 vs 6.9 points) and deterioration rather than improvement in their self-efficacy scores. Attendance at the supervised exercise and patient education sessions was similar for the two groups.

Factors associated with progression to hip and knee replacement. After adjustment for potential confounders, improvements in joint-related quality of life and arthritis self-efficacy were the only factors associated with the hazard of hip replacement (Table 3). A 10-unit improvement in the HOOS quality-of-life score was associated with a 26% reduction in the hazard of hip replacement (adjusted HR 0.74, 95% CI 0.69–0.80). A 10-unit improvement in the ASES pain score was associated with a 10% reduction in the hazard of hip replacement (adjusted HR 0.90, 95% CI 0.85–0.96). Conversely, improvement in the ASES other symptoms score was associated with an increase in the hazard of hip replacement (Table 3).

For the knee OA cohort, changes in knee pain intensity, joint-related quality of life, ASES pain scores, and functional test results were all associated with the hazard of knee replacement. A 10-unit improvement in knee pain intensity was associated with a 19% reduction in the hazard of knee replacement during the first 200 days of the follow-up period (adjusted HR 0.81, 95% CI 0.76–0.86) and a 10% reduction for the remaining follow-up period (adjusted HR 0.90, 95% CI 0.86–0.95). Adjusted HRs for KOOS quality of life and ASES pain scores, based on 10-unit improvements and observed mean improvements, are reported in Table 4. Improvements in the 40-m walk speed and the number of chair rises were each associated with reductions in the hazard of knee replacement but only during the first 200 days of the

Table 1. Baseline cohort characteristics*

Characteristics	Hip OA (n = 2,304)	Knee OA (n = 7,035)
Age, mean (SD), y	66 (9)	64 (10)
Female, n (%)	1,708 (74)	5,150 (73)
Body mass index, mean (SD)	27 (5)	29 (5)
Educational level, n (%)		
Primary or secondary school	611 (27)	2,037 (29)
Postsecondary education	1,693 (73)	4,998 (71)
Waitlisted for joint replacement, n (%)	47 (2)	134 (2)
Previous joint replacement in another joint, n (%)	217 (9)	585 (8)
Charlson comorbidity index, mean (SD)	0.2 (0.7)	0.2 (0.7)
Dispensed opioids, n (%)	338 (15)	1,003 (14)
Baseline hip/knee pain intensity VAS, mean (SD)	46.0 (21.0)	47.8 (21.6)
Baseline HOOS/KOOS quality-of-life scale score, mean (SD)	48.2 (14.6)	45.9 (14.5)
Baseline ASES pain subscale score, mean (SD)	65.3 (19.5)	67.8 (19.1)
Baseline ASES other symptoms subscale score, mean (SD)	70.3 (17.5)	71.6 (16.9)
Baseline 40-m walk test, mean (SD), m/s	1.5 (0.3)	1.5 (0.3)
Baseline timed chair stand test (number of rises), mean (SD)	12.5 (3.9)	12.0 (3.7)

* ASES, Arthritis Self-Efficacy Scale; HOOS, Hip disability and Osteoarthritis Outcome Score; KOOS, Knee injury and Osteoarthritis Outcome Score; OA, osteoarthritis; VAS, visual analog scale.

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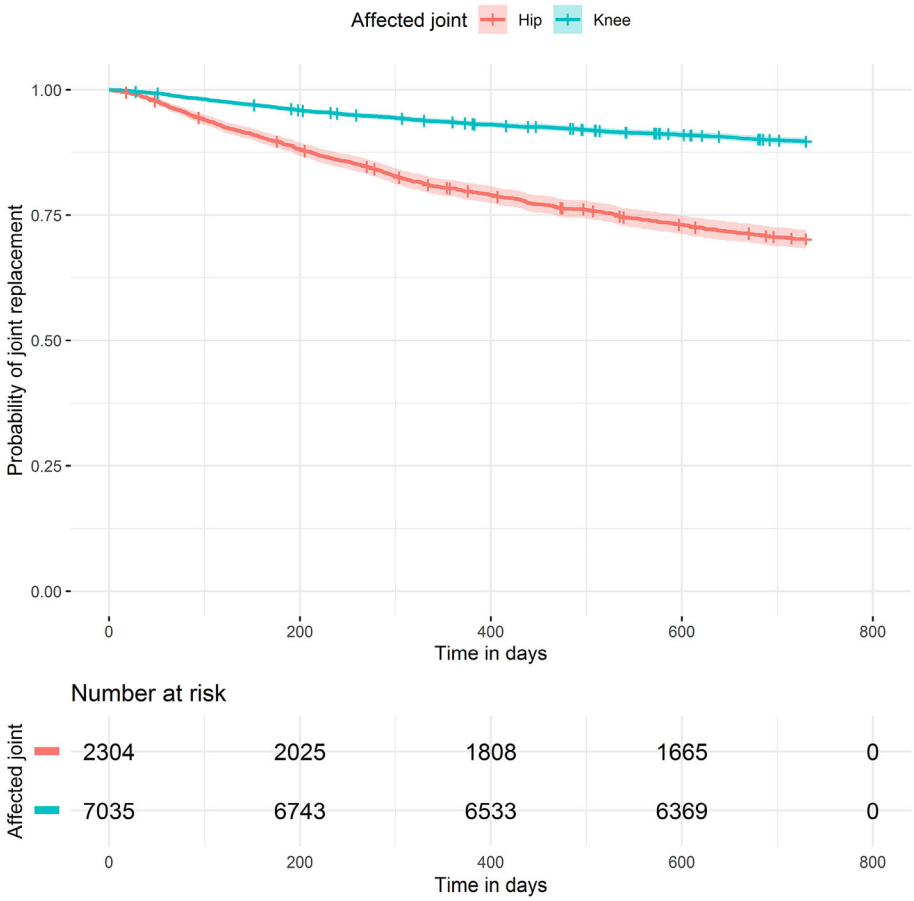

Figure 2. Progression to joint replacement surgery within two years.

follow-up period (Table 4). After adjustment for other factors, patients who were no longer fearful of movement, as well as those who remained fearful of movement, had a reduced hazard of knee replacement (Table 4). HRs for primary total hip or knee replacement according to clinically important improvement in pain intensity, quality of life, ASES scores, 40-m walk speed, and timed chair stands are reported in Tables S3 and S4. These estimates were similar to those reported for a 10-unit improvement and/or the observed mean improvement.

DISCUSSION

Although progression to knee replacement within two years was relatively infrequent (at 10%), almost one-third of GLA:D participants with hip OA progressed to total hip replacement within this time frame. Our data also show that participants who progressed to joint replacement had worse symptoms before the program, and they experienced smaller postprogram improvements in pain intensity and joint-related quality of life plus deterioration in arthritis self-efficacy. The magnitude of improvement in several clinical outcomes was significantly associated with the likelihood of progression to joint replacement in the short-term.

We are not aware of previous studies that have examined associations between the magnitude of improvement in patient outcomes after supervised exercise therapy and education and progression to joint replacement. We recognize that some of the observed improvements were relatively small in relation to published thresholds for clinically important improvement,[25–28] although moderate effect sizes were evident for improvements in pain. In the present study, we found that patients who had larger improvements in joint-related quality of life or arthritis self-efficacy pain scores (plus knee pain and functional tests, for patients with knee OA) were less likely to progress to joint replacement than those with less improvement. Progression to joint replacement is undoubtedly multifactorial,[10,11,29–31] incorporating patient characteristics plus pain and functional status as well as other unmeasured factors (eg, a person's willingness to undergo surgery[29] or a surgeon's recommendation, particularly for hip replacement, for which excellent surgical outcomes are common). Our results can be used by clinicians to consider the short-term likelihood of joint replacement surgery based on the magnitude of postprogram improvement in patient-reported or measured functional outcomes. Such knowledge could guide further intensive nonsurgical care or referral for orthopedic assessment after the exercise therapy and education program. These findings can also be used

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Table 2. Comparison of patients who progressed to joint replacement and those who did not*

Variable	Hip OA cohort		Knee OA cohort	
	Hip replacement (n = 683)	No hip replacement (n = 1,621)	Knee replacement (n = 725)	No knee replacement (n = 6,310)
Age, mean (SD), y	67 (8)	65 (9)	66 (8)	64 (10)
Female, n (%)	478 (70)	1,230 (76)	497 (69)	4,653 (74)
Body mass index, mean (SD)	27 (5)	27 (5)	29 (5)	28 (5)
Attendance at GLA:D supervised exercise sessions, n (%)				
<10 sessions	98 (14)	242 (15)	103 (14)	1,075 (17)
≥10 sessions	585 (86)	1,379 (85)	622 (86)	5,235 (83)
Attendance at specific GLA:D sessions, n (%)				
Two educational sessions	576 (84)	1,356 (84)	584 (81)	5,201 (82)
Instructions for individual exercise program	639 (94)	1,526 (94)	678 (94)	5,920 (94)
Hip/knee pain VAS, mean (SD)				
Baseline	49.6 (21.2)	44.6 (20.8)	56.1 (20.8)	46.8 (21.5)
3 mo	43.0 (22.7)	31.8 (20.7)	49.0 (21.7)	31.5 (20.5)
Baseline to 3-mo change	−6.5 (21.8)	−12.8 (22.4)	−7.1 (22.4)	−15.3 (22.7)
HOOS/KOOS quality-of-life score, mean (SD)				
Baseline	44.4 (14.2)	49.8 (14.4)	39.4 (13.8)	46.6 (14.4)
3 mo	45.5 (15.4)	56.3 (15.8)	41.0 (14.5)	53.5 (15.4)
Baseline to 3-mo change	1.2 (13.4)	6.5 (13.5)	1.6 (13.7)	6.9 (14.2)
ASES pain subscale score, mean (SD)				
Baseline	62.9 (20.3)	66.3 (19.0)	61.9 (19.8)	68.5 (18.9)
3 mo	58.8 (22.9)	69.8 (19.9)	57.7 (21.2)	71.6 (19.9)
Baseline to 3-mo change	−4.1 (21.4)	3.5 (18.9)	−4.2 (20.6)	3.1 (19.0)
ASES other symptoms subscale score, mean (SD)				
Baseline	69.0 (18.3)	70.8 (17.1)	67.9 (17.9)	72.0 (16.7)
3 mo	67.6 (19.4)	74.4 (17.4)	66.8 (19.0)	75.7 (16.9)
Baseline to 3-mo change	−1.4 (16.8)	3.5 (15.2)	−1.1 (16.5)	3.7 (14.8)
40-m walk test, mean (SD), m/s				
Baseline	1.5 (0.3)	1.5 (0.3)	1.4 (0.3)	1.5 (0.3)
3 mo	1.5 (0.4)	1.7 (0.4)	1.5 (0.3)	1.7 (0.3)
Baseline to 3-mo change	0.1 (0.2)	0.1 (0.2)	0.1 (0.2)	0.1 (0.2)
Baseline timed chair stand test (number of rises), mean (SD)				
Baseline	12.2 (3.8)	12.6 (3.9)	11.6 (3.4)	12.1 (3.8)
3 mo	14.0 (4.3)	15.1 (4.5)	13.2 (4.1)	14.4 (4.3)
Baseline to 3-mo change	1.8 (2.9)	2.5 (3.1)	1.7 (2.9)	2.3 (3.2)

* Decrease in hip/knee pain VAS indicates improvement; increases in HOOS/KOOS quality of life, ASES scores, 40-m walk test result, and timed chair stand test result indicate improvement. ASES, Arthritis Self-Efficacy Scale; GLA:D, Good Life with osteoArthritis in Denmark; HOOS, Hip disability and Osteoarthritis Outcome Score; KOOS, Knee injury and Osteoarthritis Outcome Score; OA, osteoarthritis; VAS, visual analog scale.

to discuss possible progression to surgery with program participants. For example, GLA:D participants can be counseled that a 10-point improvement in the HOOS quality-of-life score is associated with a 26% lower likelihood of hip replacement within two years. Although our study focused on postprogram improvements with adjustment for baseline scores, future research could examine patient-perceived thresholds (such as the patient acceptable symptom state,[32] noting that this can vary by population) after exercise therapy and education and its relationship to joint replacement surgery.

We found that a substantially higher proportion of patients progressed to hip replacement compared with knee replacement. However, for those who did receive joint replacement, the average time to surgery was similar for hip and knee replacement (approximately 11 months). Despite different study time frames, the proportion of participants who received hip replacement is

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Table 3. Cox proportional hazards analysis of time to primary total hip replacement surgery*

Variable	Adjusted hazard ratio[a] (95% CI)	
	For a 10-unit increase or defined category change[b]	For the observed mean improvement[c]
Baseline to 3-mo change in hip pain intensity VAS	1.02 (0.97–1.07)	1.02 (0.97–1.08)
Baseline to 3-mo change in HOOS quality-of-life scale score	0.74 (0.69–0.80)	0.87 (0.84–0.90)
Baseline to 3-mo change in ASES pain subscale score	0.90 (0.85–0.96)	0.99 (0.98–0.99)
Baseline to 3-mo change in ASES other symptoms subscale score	1.12 (1.04–1.20)	1.02 (1.01–1.04)
Baseline to 3-mo change in 40-m walk test (m/s)	0.65 (0.41–1.04)	0.95 (0.89–1.00)
Baseline to 3-mo change in timed chair stand test (number of rises)	1.01 (0.98–1.04)	1.02 (0.95–1.09)
Baseline to 3-mo change in fear of movement		
No (baseline) to no (3 mo)	1.00 (reference)	1.00 (reference)
No (baseline) to yes (3 mo)	1.01 (0.70–1.46)	1.01 (0.70–1.46)
Yes (baseline) to no (3 mo)	1.22 (0.93–1.61)	1.22 (0.93–1.61)
Yes (baseline) to yes (3 mo)	0.93 (0.56–1.56)	0.93 (0.56–1.56)

* ASES, Arthritis Self-Efficacy Scale; CI, confidence interval; HOOS, Hip disability and Osteoarthritis Outcome Score; VAS, visual analog scale.
[a] Derived from a multivariable model that was adjusted for baseline values of hip pain intensity, HOOS quality-of-life score, ASES pain score, ASES other symptoms score, 40-m walk speed, and timed chair stand test and sex, body mass index, educational level, Charlson comorbidity index, waitlisted for surgery status, previous joint replacement in another joint, and opioid medication (≥1 dispensed opioid prescription within 3 mo before the first visit). Age was used as a timescale.
[b] Adjusted hazard ratios are estimated for a 1-unit change in the 40-m walk test and the timed chair stand test.
[c] Based on mean improvement for the cohort: 10.9 points for hip pain intensity VAS, 4.89 points for HOOS quality of life, 1.27 points for ASES pain, 2.07 points for ASES other symptoms, 0.13 m/s for 40-m walk test, and 2.29 rises for timed chair stand test.

consistent with an earlier GLA:D Registry analysis.[10] A recent analysis of data from the Better Management of Patients with Osteoarthritis registry in Sweden also reported higher rates of progression to hip replacement compared to knee replacement at one year and five years among people with OA who were referred for an education and exercise therapy program.[11] The authors hypothesized that the results relate to people with hip OA presenting later for care than those with knee OA plus a perceived greater capacity for knee OA to respond to first-line treatment, although this not supported by recent findings.[33] Two randomized controlled trials have found that structured nonsurgical management programs can delay hip and knee replacement surgery. In Norway, Svege et al[7] reported that providing 12 weeks of exercise therapy and patient education resulted in people with hip OA being 44% less likely to receive hip replacement at six years compared to provision of education alone. For those who received hip replacement, the provision of exercise therapy plus education delayed the progression to surgery by almost two years (median 3.5 vs 5.4 years for the education-only group). In Denmark, Skou et al[8] reported that 74% of participants with moderate-severe knee OA who were eligible for knee replacement surgery and were randomized to receive nonsurgical treatments did not have surgery in the following year. At two years' follow-up, 68% of the nonsurgical group had still avoided knee replacement surgery.[9] Notably, these studies involved highly selected patient populations as part of the randomized controlled trial design. Future data linkage of the GLA:D Registry to national health registries will enable longer-term progression to joint replacement surgery (eg, at 5 or 10 years) and surgical outcomes (potentially patient-reported outcomes and revision surgery) to be evaluated in a real-world context.

Our joint replacement data are conservative given the need to exclude patients who received hip or knee replacement before three months and who did not complete the program and follow-up period (Figure 1). We are unable to comment on the treatment course (including progression to joint replacement) for patients who did not take part in the GLA:D program given the cohort design and absence of a matched control group. However, the rate of joint replacement among our study cohort can be examined in the context of other estimates. Anecdotal reports suggest that 25% to 50% of patients referred for orthopedic assessment in Denmark are listed for joint replacement. Although our hip replacement rate aligns with these data, our rate of knee replacement was considerably lower. Our baseline KOOS quality-of-life scores also indicate that, on average, GLA:D participants had less severe symptoms than patients undergoing either patellofemoral or total knee replacement in Denmark.[34] However, when compared to population-level data, the observed rates of joint replacement can be considered high (the incidence in Denmark was 237 hip replacements and 174 knee replacements per 100,000 population in 2021[35]).

An earlier study involving linkage of the GLA:D Registry with the DNPR focused on preprogram predictors of total hip replacement within two years.[10] It identified several demographic and clinical characteristics that were associated with a greater likelihood of surgery, including male sex, self-reported radiographic hip OA, three or more comorbidities, use of pain medication in the previous three months, being waitlisted for surgery, and having had prior joint replacement in another joint. Greater hip pain before the program was also associated with an increased hazard of hip replacement, whereas better HOOS quality-of-life scores and faster walking speed before the program were associated with a reduced hazard of hip replacement. A Norwegian study of exercise therapy and education for hip OA reported that participants who progressed to total hip replacement had worse Western Ontario and McMaster Universities Osteoarthritis Index pain, stiffness, and physical function scores over 29 months compared with participants who did not have hip replacement,[7]

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Table 4. Cox proportional hazards analysis of time to primary knee replacement surgery*

Variable	Adjusted hazard ratio[a] (95% CI)	
	For a 10-unit increase or defined category change[b]	For the observed mean improvement[c]
Baseline to 3-mo change in knee pain intensity VAS		
Day 0–200	0.81 (0.76–0.86)	0.74 (0.67–0.81)
Day 201–730	0.90 (0.86–0.95)	0.86 (0.80–0.93)
Baseline to 3-mo change in KOOS quality-of-life scale score		
Day 0–200	0.70 (0.63–0.78)	0.80 (0.75–0.85)
Day 201–730	0.79 (0.72–0.86)	0.86 (0.82–0.91)
Baseline to 3-mo change in ASES pain subscale score	0.89 (0.83–0.94)	0.97 (0.96–0.99)
Baseline to 3-mo change in ASES other symptoms subscale score	1.04 (0.97–1.12)	1.01 (0.99–1.04)
Baseline to 3-mo change in 40-m walk test, m/s		
Day 0–200	0.51 (0.27–0.96)	0.92 (0.84–0.99)
Day 201–730	1.24 (0.73–2.12)	1.03 (0.96–1.10)
Baseline to 3-mo change in timed chair stand test (number of rises)		
Day 0–200	0.95 (0.91–0.99)	0.89 (0.81–0.97)
Day 201–730	1.01 (0.98–1.05)	1.03 (0.95, 1.11)
Baseline to 3-mo change in fear of movement		
No (baseline) to no (3 mo)	1.00 (reference)	1.00 (reference)
No (baseline) to yes (3 mo)	0.90 (0.63–1.29)	0.90 (0.63–1.29)
Yes (baseline) to no (3 mo)	0.51 (0.38–0.70)	0.51 (0.38–0.70)
Yes (baseline) to yes (3 mo)	0.46 (0.28–0.77)	0.46 (0.28–0.77)

* ASES, Arthritis Self-Efficacy Scale; CI, confidence interval; KOOS, Knee injury and Osteoarthritis Outcome Score; VAS, visual analog scale.
[a] Model adjusted for baseline values of knee pain intensity, KOOS quality-of-life score, ASES pain score, ASES other symptoms score, 40-m walk speed, and timed chair stand test and age, sex, body mass index, educational level, Charlson comorbidity index, waitlisted for surgery status, previous joint replacement in another joint, and opioid medication (≥1 dispensed opioid prescription within 3 mo before the first visit). Because of violations of the proportional hazard assumption, baseline to 3-mo change in pain intensity, KOOS quality of life, 40-m walk test result, and timed chair stand test result was modeled with time-varying coefficients (using the two intervals "day 0–200" and "day 201–730").
[b] Adjusted hazard ratios are estimated for a 1-unit change in the 40-m walk test and the timed chair stand test results.
[c] Based on mean improvement for the cohort: 14.5 points for knee pain intensity VAS, 6.33 points for KOOS quality of life, 2.35 points for ASES pain, 3.24 points for ASES other symptoms, 0.13 m/s for 40-m walk test, and 2.26 rises for timed chair stand test.

although the study was relatively small, and predictors of surgery were not investigated.

We acknowledge the study limitations. Our study focused on patients with clinically diagnosed OA (consistent with clinical practice guideline recommendations[1]), and we do not report any radiographic data. The eligibility criteria for GLA:D are broad to ensure most people with OA are included. Although this could result in the inclusion of patients without OA, the certified GLA:D physiotherapists are specifically trained in the clinical diagnosis of OA and differential diagnosis. A large number of people were excluded from the analysis because of incomplete data. To evaluate potential selection bias, we examined the baseline characteristics of people with incomplete data and those with complete data, similar to the approach used previously by Clausen et al.[10] Both groups were similar with respect to demographics, baseline patient-reported scores, and baseline functional assessments, and imputation methods for missing data were not used. We are unaware of whether participants continued their exercise programs or self-management activities after the GLA:D program. Having access to systematically collected representative data on the use of exercise and other nonpharmacological treatments for OA after GLA:D program completion would enable a more complete understanding of factors potentially associated with progression to surgery. Additionally, we do not have data on radiographic or symptomatic OA progression after the follow-up period. Although the GLA:D program is available internationally, the generalizability of the study findings is not yet known. A key strength of this study was the linkage of clinical registry data with comprehensive national administrative registries. This enabled a robust analysis of joint replacement outcomes based on well-established treatment codes. We included unicompartmental knee replacement outcomes in the knee analysis to ensure all joint replacement interventions for OA were captured. The large linked data set allowed for multivariable modeling, with adjustment for baseline scores and possible confounding factors. We explored changes in patient-reported assessments of pain, quality of life, and arthritis self-efficacy, as well as measured functional outcomes.

In conclusion, 30% of GLA:D participants with clinically diagnosed hip OA and 10% of participants with clinically diagnosed knee OA progressed to joint replacement within two years. After adjustment for other factors, improvements in joint-related quality of life and arthritis self-efficacy (pain subscale) scores after the program were associated with a reduced hazard of hip and knee replacement, and improvements in knee pain and functional tests (in relation to the first 200 days of follow-up for the latter) were also associated with a reduced hazard of knee replacement. These findings can be used to guide clinical conversations with GLA:D

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participants (and potential participants) about short-term progression to joint replacement based on their degree of improvement and to initiate other nonsurgical or surgical care. Future research is needed to evaluate longer-term progression to surgery.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr Johansson and Mr Ernst had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Ackerman, Johansson, Grønne, Clausen, Ernst, Overgaard, Odgaard, Roos, Skou.

Acquisition of data. Johansson, Grønne, Ernst, Roos, Skou.

Analysis and interpretation of data. Ackerman, Johansson, Grønne, Clausen, Ernst, Overgaard, Odgaard, Roos, Skou.

Data availability

Data were stored on a secure server managed by the Danish Health Data Authority. MSJ and MTE had full access to all study data through an institutional authorization and take responsibility for the integrity of the data and the accuracy of the data analysis. The data that support the findings of this study cannot be shared publicly because of potentially identifiable or sensitive information (General Data Protection Regulation, European Union). Data may be accessed upon reasonable request by contacting GLA:D® (https://gladinternational.org/contact/).

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