Does Clinical Presentation Predict Response to a Nonsurgical Chronic Disease Management Program for Endstage Hip and Knee Osteoarthritis?

Jillian P. Eyles, Barbara R. Lucas, Jillian A. Patterson, Matthew J. Williams, Kate Weeks, Marlene Fransen, and David J. Hunter

ABSTRACT. *Objective.* To identify baseline characteristics of participants who will respond favorably following 6 months of participation in a chronic disease management program for hip and knee osteoarthritis (OA).

Methods. This prospective cohort study assessed 559 participants at baseline and following 6 months of participation in the Osteoarthritis Chronic Care Program. Response was defined as the minimal clinically important difference of an 18% and 9-point absolute improvement in the Western Ontario and McMaster Universities Arthritis Index global score. Multivariate logistic regression modeling was used to identify predictors of response.

Results. Complete data were available for 308 participants. Those who withdrew within the study period were imputed as nonresponders. Three variables were independently associated with response: signal joint (knee vs hip), sex, and high level of comorbidity. Index joint and sex were significant in the multivariate model, but the model was not a sensitive predictor of response.

Conclusion. Strong predictors of response to a chronic disease management program for hip and knee OA were not identified. The significant predictors that were found should be considered in future studies. (J Rheumatol First Release Sept 15 2014; doi:10.3899/jrheum.131475)

Key Indexing Terms:
OSTEOARTHRITIS   CHRONIC DISEASE   REHABILITATION
MULTIDISCIPLINARY   PREDICTOR   REGRESSION ANALYSIS

Osteoarthritis (OA) is one of the world's top 10 most disabling conditions[1]. According to global burden of disease estimates, musculoskeletal (MSK) disorders rank second only to mental and behavioral disorders in overall contribution to years lived with a disability (YLD)[2]. A large proportion of YLD attributed to MSK disorders results from hip and knee OA, estimated at over 17 million YLD worldwide[2].

From the Physiotherapy Department and Department of Rheumatology, Royal North Shore Hospital; Northern Clinical School; Kolling Institute of Medical Research; Institute of Bone and Joint Research; University of Sydney, Sydney; Physiotherapy Department, Wollongong Hospital, Wollongong, New South Wales, Australia.

J.P. Eyles, BAppSc(Phty); B.R. Lucas, MPH, FACP, BAppSc(Phty), Physiotherapy Department, Royal North Shore Hospital; J.A. Patterson, BScAdv(Hons), MBiostat, Kolling Institute of Medical Research; M.J. Williams, BAppSc(Phty), Physiotherapy Department, Royal North Shore Hospital; K. Weeks, BAppSc(Phty), Physiotherapy Department, Wollongong Hospital; M. Fransen, PhD, MPH, University of Sydney; D.J. Hunter, MBBS, PhD, FRACP, Department of Rheumatology, Royal North Shore Hospital; Northern Clinical School, Kolling Institute of Medical Research, Institute of Bone and Joint Research, University of Sydney.

Address correspondence to Prof. D.J. Hunter, Department of Rheumatology, Royal North Shore Hospital, Reserve Road, St. Leonards, Sydney, New South Wales, Australia. E-mail: David.Hunter@sydney.edu.au

Accepted for publication July 15, 2014.

Treatments for this disabling, prevalent, and incurable disease focus on symptomatic relief. Numerous international evidence-based guidelines for management of hip and knee OA have become available[3,4,5,6,7,8,9]. There is consistency in most of the recommendations made by the guidelines[10] and agreement that nonsurgical management of hip and knee OA should combine both nonpharmacological and pharmacological treatment modalities[3,4,5,6,7,8,9]. However, the recommendations are numerous and are not arranged systematically to indicate the order of priority in which treatments should be undertaken or which combinations of modalities should be used. Faced with a plethora of choices, it would be helpful for clinicians to be able to base treatment decisions on the identification of specific clinical presentations that foretell greater likelihood of success following implementation of an individual or combination of treatments. In an era when the delivery of quality care is being promoted coupled with finite resources, the ability to predict outcome/s to intervention would allow clinicians to prioritize those who will get the greatest benefit.

There is a growing body of evidence for clinical characteristics that predict response to nonsurgical interventions for participants with hip and knee OA[11]. Four previous studies attempted to identify predictors of response to

programs involving combinations of nonsurgical interventions[12,13,14,15]; however, consistent predictors of response were not found. All 4 treatment protocols involved strategies for self-management of OA including dietary advice; 2 studies provided weight loss advice if indicated[13,14], and all were of relatively short duration, ranging from 3 to 12 weeks[12,13,14,15]. To our knowledge, studies reporting outcomes or predictors of response to longer duration self-management programs do not exist. The aim of our research was to determine participant characteristics predictive of favorable outcomes following participation in a longer-term nonsurgical chronic disease management program for hip and knee OA. We hypothesized that it would be possible to predict participants likely to respond to the program using baseline demographic, psychological, disease-related, and functional performance variables.

MATERIALS AND METHODS

Study design. This observational clinical cohort study followed consecutive participants of the Osteoarthritis Chronic Care Program (OACCP) from 2 teaching hospitals in New South Wales (NSW), Australia, over a period of 6 months. The OACCP was developed by the Agency for Clinical Innovation MSK Network in response to the growing recognition of the need for a nonsurgical care program for people awaiting elective hip or knee joint replacement surgery (JRS). Participants with symptomatic and radiographic hip and knee OA were recruited for the OACCP at Royal North Shore/Ryde and Wollongong Hospitals from JRS waiting lists or referral by rheumatologists, orthopedic surgeons, and general practitioners. This equates to a doctor diagnosis of OA, which provides good face validity[16]. People with a diagnosis of knee or hip OA were eligible for the OACCP at initial assessment if they had pain in the affected knee/hip on most days of the past month[17]. Participants who had completed a reassessment at 26 weeks (within 140-225 days following initial assessment) were included in the analysis (Figure 1). There were no exclusion criteria for the OACCP, but participants who did not return for their 26-week assessment, or who were reassessed outside 140-225 days following initial assessment, were considered for imputation as nonresponders. Participants imputed as nonresponders included those who underwent JRS more than 90 days (and less than 225 days) following initial assessment, those discharged on medical advice, or participants who cited dissatisfaction with the program as their reason for discharge. Those receiving JRS within 90 days of initial assessment were excluded from analysis on the basis that there was insufficient time to determine whether they responded to the OACCP. The remaining participants without a complete 26-week assessment within 140-225 days were excluded from the regression analysis.

Intervention. The OACCP aimed to reduce pain, increase function, and improve the quality of life of participants with hip and knee OA through provision of access to relevant health professionals to support self-management and longterm behavior change. At initial assessment, the MSK Coordinator engaged participants to set goals around the management of their OA and comorbidities[18]. The MSK Coordinator was a specialized MSK physical therapist; all participants were prescribed an individualized exercise program that focused on strengthening muscles around affected joints, increasing physical activity levels, and other exercises depending on clinical presentation. These programs were reviewed at 12 and 26 weeks. All participants were provided with education about their OA and any identified comorbidities.

Following initial assessment, participants were referred to members of the multidisciplinary team (MDT) according to clinical need. If participants required medication review they were referred to a rheumatologist or pain clinical nurse consultant. Intraarticular injections were not part of the treatment provided. A dietitian provided interventions when indicated to assist participants with weight loss and/or comorbidity management. Participants requiring assessment of efficiency and safety of functional tasks were referred to an occupational therapist. Psychosocial interventions and linkage with community support services were provided by a social worker as required. Some participants with tibiofemoral or patellofemoral joint malalignment were referred to an orthotist for application of knee bracing or foot orthoses. Participants were also referred to healthcare providers outside the MDT for other interventions (e.g., hydrotherapy, diabetes education, psychology, etc.) as required.

Outcome measures. During a structured interview at initial assessment, the MSK coordinator recorded demographic and comorbidity data. Demographic data included sex, date of birth, referral source, residential status, language spoken at home, employment, and level of education. Signal joint, the predominant site of OA, was determined by clinical examination, patients' symptoms, and radiographic evidence of disease. All physical measures performed at initial and 26-week assessments were performed using a standardized protocol[17], including height, weight, waist and hip circumferences, and body mass index (BMI). Disease-specific self-report measures administered at 0 and 26 weeks included the Hip Dysfunction and Osteoarthritis Score (HOOS) or Knee Injury and Osteoarthritis Score (KOOS), according to the signal joint. The Depression Anxiety Stress 21 Scale (DASS 21) was used to measure these 3 negative emotional states at initial and 26-week assessments. The Six-minute Walk Test (6MWT) was completed at baseline and 26 weeks.

The validated, disease-specific HOOS[19] and KOOS[20] require participants to use 5-point Likert scales to rate their symptoms, stiffness, pain, physical function, recreational activities, and quality of life. The HOOS and KOOS subsume all of the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questions, enabling conversion into WOMAC scores[21,22]. The WOMAC subscales for pain, stiffness, and function were calculated by summation of the numerical responses provided by the WOMAC questions within the HOOS and KOOS. The WOMAC subscores were combined to calculate a WOMAC global score = 100– (sum of pain + stiffness + function items) × 100/96. Normalized WOMAC global scores were used, reflecting the convention that 100 indicated no problems and 0 indicated severe problems[21,22].

Using a 4-point Likert scale, the DASS 21 asks participants to rate how much 21 separate statements applied to them over the past week. The DASS 21 provides subscores to indicate the presence or absence of symptoms of depression, anxiety, and stress and has previously been shown to predict the diagnostic presence of depression and anxiety in older adults[23]. We were concerned primarily with the depression subscores; with 0-9 indicating no depressive symptoms, 10-13 mild, 14-20 moderate, 21-27 severe, and greater than 28, extremely severe symptoms. The DASS depression subscores were categorized into low depressive (0-13) versus high depressive (≥ 14) groups for the regression analyses.

The Modified Self-Administered Comorbidity Questionnaire asks participants, "Has your doctor told you that you have any of the following problems?" and then lists 21 commonly reported conditions plus an "other" category to indicate comorbidities not included on the list. Response is "yes" or "no". This questionnaire was adapted from The Self-Administered Comorbidity Questionnaire[24] and is scored by counting "yes" responses to indicate the number of comorbidities experienced by the participant. The number of comorbidities variable was categorized into low (0-2), high (3-5), and very high (≥ 6) groups for the analyses.

The 6MWT is recommended by the Osteoarthritis Research Society International to assess long-distance walking and aerobic capacity for participants with hip and knee OA[25]. Participants were asked to walk as quickly as they could for 6 min on a flat 25-m track with no corners[26] and the distance walked was recorded in meters. Baseline measurement of oxygen saturation, heart rate, and perceived exertion (Borg Scale) were taken prior to and at test completion. Participants with respiratory or cardiac concerns had measures taken at 1-min intervals during the test,
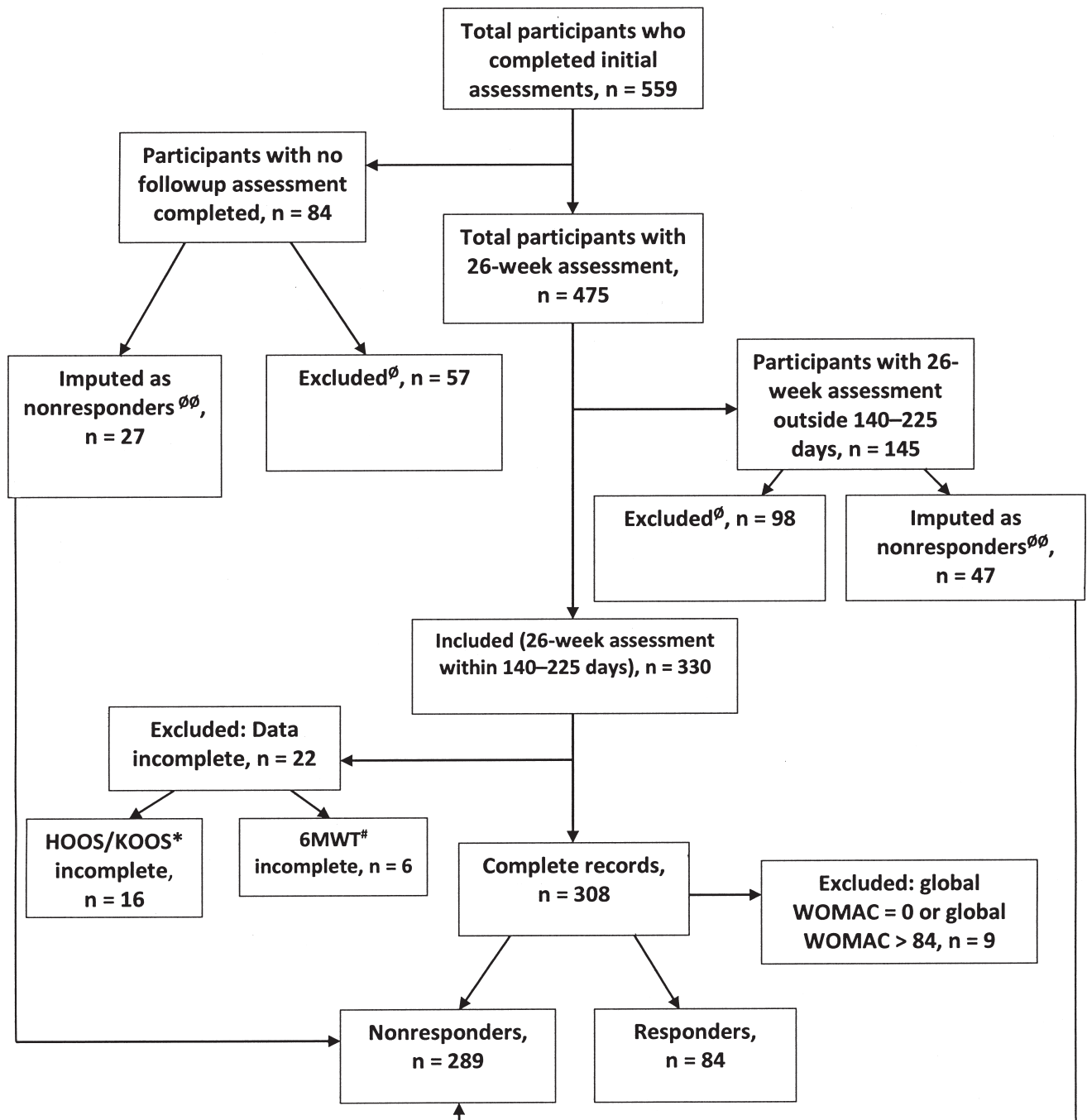
Figure 1. Study flowchart. Ø Participants with incomplete 26-week assessment or 26-week assessment outside 140–225 days or receiving joint replacement surgery (JRS) within 90 days of initial assessment. ØØ Participants who underwent JRS more than 90 days (and less than 225 days) following initial assessment, or were discharged on medical advice or who cited dissatisfaction with the program as the reason for their discharge. *HOOS or KOOS at either 0 or 26 weeks were incomplete so that WOMAC global scores could not be calculated. #6MWT results were unavailable because participants were unable to complete the test: 5 because of high blood pressure and 1 with back pain. HOOS: Hip Dysfunction and Osteoarthritis Score; KOOS: Knee Injury and Osteoarthritis Score; WOMAC: Western Ontario and McMaster Universities Arthritis Index; 6MWT: Six-minute Walk Test.

which was discontinued for the following: chest pain or discomfort, mental confusion, lack of coordination, dizziness, intolerable dyspnea, leg cramps, extreme muscle fatigue, persistent oxygen saturation < 85%, or other clinically warranted reasons.

Participants were asked to rate their average pain on the day of assessment using a visual analog scale (VAS; 0 indicated no pain and 10 the most pain imaginable). The pain VAS was categorized into low pain (VAS 0-5) and high pain (VAS 6-10) for the regression analyses.

Statistical analyses. Participants were dichotomized according to response or non-response at the 26-week assessment according to treatment based on

the notion of minimal clinically important difference (MCID), which can be defined as the smallest difference in scores of the variable concerned that is considered beneficial by participants of the intervention[27]. The MCID used was first developed by Angst, et al[28] to reflect the treatment effect considered to be clinically relevant to a comprehensive rehabilitation intervention for participants with OA of the lower extremities. This MCID required a relative change greater than or equal to 18% (100 × change of score/baseline score) and an absolute change of 9 points improvement of WOMAC global scores at the 26-week assessment compared to baseline. Using an MCID comprising both relative and absolute change standardized the amount of improvement required to achieve response across the spectrum of disease severity. Hence participants with very low global WOMAC scores were not classified as responders for small absolute changes in score compared with those whose baseline scores were higher. Participants who demonstrated improvements in WOMAC global scores at 26 weeks of ≥ 18% with an absolute change in score ≥ 9 were categorized as responders[28]; those who did not were nonresponders.

Participants censored at their 26-week followup because of JRS performed at least 90 days after their initial assessment and within the 26-week assessment window (≤ 225 days) were imputed into the analysis as nonresponders. Participants who withdrew from the OACCP owing to dissatisfaction with the program or following medical advice were also imputed as nonresponders.

The potential predictor variables were chosen following literature review[11] and discussion among this study's authors. The MSK coordinators collecting the data at both study sites were blinded to which variables were to be analyzed as predictors of response. Eight baseline predictor variables were identified *a priori* for consideration in the model: BMI, pain VAS, DASS subscore, signal joint, 6MWT, age, sex, and number of comorbidities. The power calculation was set to include at least 10 "responders" per predictor variable[29,30]. Previous studies have reported 34%-47% of participants with hip or knee OA may be expected to satisfy responder criteria following nonsurgical multimodal interventions[14,15]. A sample of 267 was considered sufficient to accommodate 8 predictor variables.

Univariate logistic regression analyses examined the association between each of the predictor variables and response, and continuous variables were categorized when necessary to meet linearity requirements. All variables were entered into a multivariate binary logistic regression model; the least significant predictor was removed at each step of the modeling until only significant variables remained. To control for confounding, when any variables associated with response in the univariate analyses were removed from the model, the regression coefficients of the remaining variables were checked for a change in 10% or more and if so were retained. Testing for interactions was performed by combining variables of interest. SPSS version 21 was used for all statistical analyses.

Ethics approval was granted by the NSW Population and Health Services Research Ethics Committee (AUREI Reference HREC/12/CIPHS/63); Cancer Institute NSW Reference Number 2012/08/413.

RESULTS

Of 559 patients consecutively referred to the Wollongong and Royal North Shore/Ryde Hospitals OACCP from July 2011 to December 2013, 475 participants had completed their 26-week assessment as shown in Figure 1. There were 145 participants who were excluded because their 26-week assessment occurred outside the assessment range. A further 16 participants were excluded with incomplete HOOS or KOOS, 6 were unable to complete the 6MWT because of high blood pressure or back pain, and 84 did not return for followup assessment. That left 308 participants with complete datasets remaining for the analysis. A further 74 were imputed as nonresponders: 55 discharged from the

OACCP after JRS 90-225 days following initial assessment, 16 withdrew because of dissatisfaction with the program, and 3 stopped as a result of medical advice.

The baseline demographics of included participants, those excluded because of missing assessments or assessments outside the 26-week range (n = 167), and those who did not return for followup assessment (n = 84) are summarized in Table 1. The included and excluded groups were homogeneous in most respects. About 90% were referred from elective JRS waiting lists; the wait time for JRS in NSW Hospitals is around 12 months. The majority of participants were of similar age, lived at home with an able person, spoke English, were retired, and overweight. Participants reported similar baseline pain. The majority had 0-5 comorbidities and did not finish high school.

There were proportionally more males in the excluded group with no followup assessment (p = 0.07) and the included group reported a higher proportion of OA knees to hips than did the excluded groups (p = 0.02). The mean baseline WOMAC global scores were significantly different (p = 0.03); however, the greatest difference in mean scores was 5.2 points, which is not very clinically important.

The referrals to healthcare providers recorded for included and excluded participants are summarized in Table 2. All participants were assessed by a physical therapist and provided with a graded exercise program; around half were referred to a dietitian; 30-40% to a rheumatologist; and 20-30% to an occupational therapist or a social worker. About 20% of participants were referred to providers within and 40% outside the local health district.

Of 308 included participants with complete datasets, 9 were omitted from analysis because their baseline WOMAC was too high (> 84) or 0, and so were unable to achieve response. Of the 299 participants with complete datasets, 84 (28%) were responders according to the MCID. Results of the univariate regression analyses are shown in Table 3. Compared to females, males were less likely to be responders (OR 0.5, 95% CI 0.31, 0.88). There was strong evidence that participants with knee OA were more likely to be responders than those with hip OA (OR 2.1, 95% CI 1.10, 3.88). Compared to those with a low number (≤ 2) there was evidence that participants with a very high number of comorbidities (≥ 6) were more likely to be responders (OR 2.2, 95% CI 0.99, 4.95). The other baseline variables were not independently associated with response.

All potential predictor variables were entered into the base multivariate model. No significant interactions between the variables were found. Following elimination of nonsignificant variables, the final model (Table 4) contained both signal joint (chi square$_{LR}$ = 4.49, p < 0.05) and sex (chi square$_{LR}$ = 4.95, p < 0.05). Participants with the knee as the signal joint were more likely to be responders compared with those with hip as the signal joint (adjusted OR 1.92, 95% CI 1.02, 3.62). Compared to women, men were less

Table 1. Demographics of included and excluded participants at baseline.

Baseline Characteristics	Included, n = 313	Excluded: 26 Weeks Not Within 140–225 Days, or Missing Data, n = 162	Excluded: No Followup Assessment, n = 84	p [v]
Female (%)	62	59	48	0.067
Age, yrs, mean (SD)	68.5 (9.25)	69.0 (9.92)	68.0 (10.85)	0.76
Signal joint knee (%)	77	65	68	**0.022**
Signal joint knee (%) responders	83			
Signal joint knee (%) nonresponders	75			
On elective joint replacement list (%)	88	90	86	0.68
Residence				
At home with able person (%)	64	68	68	0.46
Home alone (%)	28	22	21	
Other[‡] (%)	8	10	11	
Speaks English[*] (%)	90	92	88	0.61
Employment (%)				0.60
Not currently employed[†]	86	82	84	
Currently employed[^]	14	18	16	
Education (%)				0.94
Finished secondary school or higher[¤]	30	29	32	
Did not finish secondary school[°]	60	71	68	
BMI, mean (SD)	31.9 (6.88)	32.0 (6.57)	31.7 (6.36)	0.94
BMI knees, mean (SD)	32.52 (7.12)			
BMI hips, mean (SD)	30.03 (5.84)			
Pain VAS, mean (SD)	5.5 (1.84)	5.7 (1.74)	5.7 (2.20)	0.65
No. comorbidities (%)				
Low (0–2)	54	44	43	
High (3–5)	39	51	42	
Very high (≥ 6)	8	5	10	
Missing (no.)			5	
WOMAC global score[#], mean (SD), range	43.4 (19.39), 0–100	38.4 (17.17), 0–90	41.3 (21.72), 3–98	**0.027**
WOMAC global score, knees, mean (SD)	44.2 (19.66)	40.8 (18.59)	41.5 (21.23)	
WOMAC global score, hips, mean (SD)	40.7 (18.34)	33.6 (12.96)	40.8 (23.23)	
WOMAC global score for responders, mean (SD), range	33.8 (18.06), 1–79			
WOMAC global score for nonresponders, mean (SD), range	47.4 (18.51), 4–100			
6 Minute Walk Test, m, mean (SD)	337.4 (118.52)	324.3 (120.51)	323.5 (114.51)	0.44

Data in bold face are statistically significant. [‡] Other includes residence at hostel or residence with non-able person. [*] Participants who did not speak English (about 10%) required the use of an interpreter. [†] Not currently employed includes participants who reported they were retired, performed home duties, and other. [^] Currently employed includes participants who reported engaging in full/part time/volunteer work. [¤] Includes participants who reported finishing secondary school, tertiary certificate, or university graduate. [°] Includes participants who did not finish secondary school, and those who reported no formal schooling. [#] The WOMAC global scores are a transformed score calculated from the HOOS and KOOS: 100 indicates no problems and 0 indicates extreme problems. [v] Independent ANOVA or chi-squared statistic comparing included participants with the 2 other groups. VAS: visual analog scale; WOMAC: Western Ontario and McMaster Universities Arthritis Index; BMI: body mass index.

likely to be responders (adjusted OR 0.55, 95% CI 0.32, 0.94). The group with a very high number of comorbidities was not significantly associated with response in the multivariate model (p = 0.07) and removal did not have a confounding effect on the remaining variables. The model fit the data well using the Hosmer-Lemeshow goodness-of-fit test (chi square = 3.03, 3 DF, p = 0.21); however, the model was unable to predict any participants as responders (sensitivity 0%, specificity 100%).

DISCUSSION
To our knowledge, this was the first study attempting to identify predictors of response following longer-term (6 mos) participation in a chronic disease management

Table 2. Percentage of OACCP participants referred to health providers within and outside the OACCP.

Healthcare Provider Type	Included Participants, n = 300	Participants Without Followup, Imputed as Nonresponders, n = 74	Excluded Participants, n = 185
OACCP multidisciplinary team			
OACCP physical therapist* (%)	100	100	100
OACCP dietitian* (%)	53.7	55.7	41.3
OACCP rheumatologist# (%)	40.4	46.3	31.1
OACCP occupational therapist* (%)	28.4	36.6	30.5
OACCP social worker# (%)	19.4	28.5	13.8
OACCP orthotist# (%)	23.7	17.8	13.5
Other** (%)	16	12.9	10.7
Other health providers within the local health district± (e.g., hydrotherapy, exercise groups; %)	21	20.3	19.4
Other health providers outside the local health district‡ (e.g., GP, hydrotherapy, diabetes educator, exercise groups; %)	42	39.2	39.2

* Available at both OACCP sites. # Available at Royal North Shore Hospital OACCP (only this rheumatologist saw patients in the OACCP clinic, they did not refer participants to the OACCP). **Other may include pain CNC at Wollongong Hospital and education sessions at both sites. ± Other healthcare providers within the local health district may include hydrotherapy, exercise groups, falls clinic, physiotherapist, pulmonary rehabilitation, smoking cessation, or geriatrician. ‡Other healthcare providers outside the local health district may include general practitioner (GP), hydrotherapy, exercise groups, diabetes clinic, orthopedic surgeon, psychologist, geriatrician, physiotherapist, dietitian, falls clinic, pain clinic, social worker, orthotist, smoking cessation, pulmonary and cardiac rehabilitation. OACCP: Osteoarthritis Chronic Care Program; CNC: clinical nurse consultant.

program for hip and knee OA. The relatively low response rate (28%) was not surprising considering the severity of disease in this sample indicated by the large proportion of participants on JRS waiting lists (around 90%). Assuming that participants on JRS waiting lists would have clinically and radiographically significant disease, it may be expected that given the natural history of the disease, without intervention the majority of participants would stay the same or worsen over a period of 6 months. A similar response rate was reported by Weigl, et al using a less stringent definition of response (≥ 18% improvement in global WOMAC score) 6 months following a 3-4 week rehabilitation program for participants with hip and knee OA[15].

The univariate analysis and the multivariate model adjusting for sex found participants with the knee as signal joint were almost twice as likely to be responders compared to those referred with hip OA (OR 1.92, 95% CI 1.02, 3.62). Although signal joint is not a significant predictor of response in the literature[13,14,15], this finding makes sense in the clinic. A central aim of the OACCP was to increase physical activity. There is evidence that participants with knee OA experience reduced pain and improvement in physical function following land-based therapeutic exercise[31]; however, the evidence for such benefits is weaker in those with hip OA[32]. Perhaps the participants with knee OA derived higher levels of therapeutic benefit from the exercise prescribed by the physical therapist of the OACCP and so were more likely to respond than were those with hip OA. Included participants with knee OA had a

higher mean BMI (32.52 kg/m^2) than those with hip OA (30.03 kg/m^2; Table 1). Given that a common goal for OACCP participants was to lose weight, and that participants with knee OA were more overweight, it was hypothesized that knees would be more likely to respond to interventions that involved weight loss. Interestingly, BMI was not an independent predictor of response, and it was not significant in the multivariate model when adjusted for signal joint. This confirms previous findings that BMI was not predictive of responsiveness to weight loss or multimodal nonpharmacological and pharmacological interventions for participants with hip and knee OA[13,14,33].

Sex was a univariate predictor of response that remained significant in the multivariate model adjusting for signal joint (OR 0.54, 95% CI 0.31, 0.95). Men were half as likely to be responders as women, a result that is difficult to explain. The literature yields conflicting results: being female was predictive of response to a rehabilitation program for hip and knee OA[15], but sex was not significantly associated with response in other previous predictor studies[13,14].

Compared to participants with a low number of comorbidities (0-2), participants with a very high number of comorbidities (> 6) were independently associated with response (OR 2.2, 95% CI 0.99, 4.95). A very high number of comorbidities was not significantly associated with response when adjusting for sex and signal joint, so number of comorbidities was removed from the model.

The absence of depression has been identified previously

Table 3. Univariate analyses of potential predictors of response to the OACCP.

Variable		Unadjusted OR (95% CI)	p
Age		0.9 (0.071, 1.20)	0.539
Sex	Female	Reference	
	Male	0.5 (0.31, 0.88)	0.015
Signal joint	Knee	2.1 (1.10, 3.88)	0.023
	Hip	Reference	
Comorbidity	Low (0–2)	Reference	
	High (3–5)	0.8 (0.47, 1.37)	0.414
	Very high (≥ 6)	2.2 (0.99, 4.95)	0.053
Depression*	≤ 13	Reference	
	≥ 14	1.2 (0.68, 1.98)	0.592
Pain †	0–5	Reference	
	6–10	1.2 (0.72, 1.92)	0.526
BMI		1.0 (0.98, 1.05)	0.329
6MWT**		1.0 (1.0, 1.0)	0.755

*Depression measured using the Depression component of the Depression Anxiety Stress Scales. †Pain measured using visual analog scale (self-rated; 0 no pain, 10 worst pain). **Distance participants are able to walk on flat ground during Six-minute Walk Test. OACCP: Osteoarthritis Chronic Care Program; BMI: body mass index.

Table 4. Final multivariate# prediction model for response to the Osteoarthritis Chronic Care Program.

Variable	β Coefficient	p	Adjusted OR	95% CI
Constant	–1.496			
Sex	–0.594	0.029	0.55	0.32, 0.94
Signal joint knee	0.651	0.045	1.92	1.02, 3.62

The base adjusted or multivariate model included age, sex, index joint, comorbidity, depression, pain, body mass index, and Six-minute Walk Test.

as a predictor of response to a 3-4 week inpatient multimodal rehabilitation intervention[15] and positive outcomes from a weight loss program in overweight veterans with knee OA[33]. The absence of depression was not a significant predictor of response in the present study. Participants reporting depressive symptoms on the DASS depression subscale were referred for treatment as required. The treatment of depression in people with arthritis has been shown to reduce pain and depressive symptoms, and improve function and quality of life[34]. The treatment of depression as an adjunct to the other multidisciplinary interventions in our study may have diminished the negative effect depressive symptoms had on response to treatment.

Age was not a predictor of response to the OACCP. Most studies include age in their list of potential predictor variables to control for the effects of confounding. Previous evidence for age as a predictor of response is conflicting. Higher age was a predictor of response to a multimodal stepped-care model for participants with hip and knee OA[13] and a physical therapy intervention for patients with hip OA[35] but was insignificant in other predictor studies[14,15]. The 6MWT was not predictive of response and while functional performance measures have not been widely used

in previous prediction studies, 1 study found the self-paced 40-m walk test predictive of response to physical therapy interventions for patients with hip OA[35]. A recent systematic review rated the 40-m walk test as the best walk test based on the limited evidence available[36] and perhaps it would have been a more useful predictor of response for our study. This is an interesting area for future research.

Notable strengths of this study design included the large sample size, the clinically meaningful followup period, and that the potential predictor variables were identified *a priori* through literature and peer review, with due consideration to not overfitting the model with excessive degrees of freedom. The potential predictors included a broad mix of disease, psychological, physical, and demographic variables. To minimize bias, the data were collected prospectively by the MSK coordinators, who were blinded to which variables were to be analyzed as predictors.

This clinical cohort study used data from a real-life clinic. The participants required doctor diagnosis of OA, which provides good face validity but may present potential limitations because different symptom labels for OA may exist between independent medical practitioners[16]. Recruited largely from JRS waiting lists, many participants of the OACCP were censored when their date for JRS came up. Excluded participants reported worse global WOMAC scores at baseline compared to included participants. To control for selection bias, participants who had experienced at least 90 days in the OACCP and had surgery within the 26-week window (≤ 225 days) were imputed as nonresponders, in addition to those who discontinued the OACCP citing dissatisfaction with the program or who withdrew under medical advice. The transformed baseline global WOMAC score (100 indicates no problems and 0 indicates extreme problems) was significantly lower in responders

compared to nonresponders (p < 0.05), and although there is marked overlap between groups, the mean difference of 10 points may suggest some regression toward the mean.

A control group was not used in this study, so it could be argued that it is impossible to distinguish between predictors of response to the chronic disease management program and natural progression of the disease. Previous studies concerned with progression of OA indicate a slow evolution and progression of the disease over time[37]. Given that the vast majority of patients were on the waiting list for JRS indicating endstage disease, it would be unlikely that the natural course of OA in these participants would allow improvement in symptoms sufficient to achieve the MCID over a period of 6 months. However, this does limit the generalizability of the results of our study to those with severe OA. A previous study reported that compared to participants not waiting for surgery, patients on the waitlist for knee JRS experienced smaller improvements that were not as lasting in response to participation in a chronic disease management program[12]. It would be interesting in future research to investigate a more heterogeneous sample of participants to enable analysis of referral for JRS as a potential predictor of response.

We can only assume that referral for JRS was a proxy measure of disease severity in this study. Future research should include a standardized measure of structural disease severity. Higher radiographic severity of knee and hip OA measured using the Kellgren-Lawrence (KL) Grading Scale was a predictor of response to acetaminophen as part of a Dutch multimodal stepped-care model[13]. Conversely, an earlier study investigating predictors of response to the same intervention found that KL grade was not associated with a more stringent definition of response[14]. It would be interesting to investigate whether radiographic severity is associated with response to the longer-term chronic disease management program. Another predictor variable in the literature associated with response was history of previous nonsurgical interventions. Two studies reported history of previous nonsurgical therapies as associated with good response to rehabilitation programs for participants with hip or knee OA[12,15]. This should be addressed in future studies concerned with prediction of response to chronic disease management programs for hip and knee OA.

Response to intervention could not be predicted using the variables studied in this sample following 6 months of participation in the OACCP. Although significant predictors of response were identified, the model was not sensitive. The significant predictors of our study should be considered for future research, and alternative variables for investigation have been highlighted. It is possible that an alternative battery of variables could be more useful for prediction of response to this intervention. If response can be predicted, it may enable clinicians to better tailor management of hip and knee OA according to clinical presentation.

REFERENCES

1. World Health Organisation. Chronic diseases and health promotion: chronic rheumatic conditions. [Internet. Accessed Aug 7, 2014.] Available from: www.who.int/chp/topics/rheumatic/en/
2. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2163-96.
3. Zhang W, Moskowitz RW, Nuki G, Abramson S, Altman RD, Arden N, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. Osteoarthritis Cartilage 2008;16:137-62.
4. Zhang W, Doherty M, Arden NK, Bannwarth B, Bijlsma J, Gunther KP, et al. EULAR evidence based recommendations for the management of hip osteoarthritis: report of a task force of the EULAR Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis 2005; 64:669-81.
5. Pendleton A, Arden N, Dougados M, Doherty M, Bannwarth B, Bijlsma JW, et al. EULAR recommendations for the management of knee osteoarthritis: report of a task force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). Ann Rheum Dis 2000;59:936-44.
6. Royal Australian College of General Practitioners. Guideline for the non-surgical management of hip and knee osteoarthritis. July 2009. [Internet. Accessed Aug 7, 2014.] Available from: www.racgp.org.au/your-practice/guidelines/musculoskeletal/ hipandkneeosteoarthritis/
7. Zhang W, Nuki G, Moskowitz RW, Abramson S, Altman RD, Arden NK, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: Changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage 2010;18:476-99.
8. National Institute for Health and Care Excellence (UK). Osteoarthritis: the care and management of osteoarthritis in adults. 2008. [Internet. Accessed Aug 7, 2014.] Available from: http://guidance.nice.org.uk/CG59.
9. Hochberg MC, Altman RD, April KT, Benkhalti M, Guyatt G, McGowan J, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res 2012;64:465-74.
10. Misso M, Pitt V, Jones K, Barnes H, Piterman L, Green S. Quality and consistency of clinical practice guidelines for diagnosis and management of osteoarthritis of the hip and knee: a descriptive overview of published guidelines. Med J Aust 2008;189:394-9.
11. Eyles J, Lucas B, Hunter DJ. Targeting care tailoring nonsurgical management according to clinical presentation. Rheum Dis Clin North Am 2013;39:213-33.
12. Lamb SE, Toye F, Barker KL. Chronic disease management programme in people with severe knee osteoarthritis: efficacy and moderators of response. Clin Rehabil 2008;22:169-78.
13. Snijders GF. Treatment outcomes of a Numeric Rating Scale (NRS)-guided pharmacological pain management strategy in symptomatic knee and hip osteoarthritis in daily clinical practice. Clin Exp Rheumatol 2012;30:164-70.
14. Snijders GF, den Broeder AA, van Riel PL, Straten VH, de Man

FH, van den Hoogen FH, et al; NOAC Study Group. Evidence-based tailored conservative treatment of knee and hip osteoarthritis: between knowing and doing. Scand J Rheumatol 2011;40:225-31.

15. Weigl M, Angst F, Aeschlimann A, Lehmann S, Stucki G. Predictors for response to rehabilitation in patients with hip or knee osteoarthritis: a comparison of logistic regression models with three different definitions of responder. Osteoarthritis Cartilage 2006;14:641-51.

16. Jordan K, Clarke AM, Symmons DP, Fleming D, Porcheret M, Kadam UT, et al. Measuring disease prevalence: a comparison of musculoskeletal disease using four general practice consultation databases. Br J Gen Pract 2007;57:7-14.

17. New South Wales Agency for Clinical Innovation. Osteoarthritis Chronic Care Program Site manual. 2013. [Internet. Accessed Aug 7, 2014.] Available from: www.aci.health.nsw.gov.au/__data/assets/pdf_file/0007/190987/ACI-Musculoskeletal-Network-Osteoarthritis-Chronic-Care-Program-Site-Manual.pdf#zoom=100

18. New South Wales Agency for Clinical Innovation. Musculoskeletal Network — Osteoarthritis Chronic Care Program Model of Care. 2012. Available from: www.aci.health.nsw.gov.au/__data/assets/pdf_file/0020/165305/Osteoarthritis-Chronic-Care-Program-Mode-of-Care.pdf#zoom=100

19. Thorborg K, Roos EM, Bartels EM, Petersen J, Hölmich P. Validity, reliability and responsiveness of patient-reported outcome questionnaires when assessing hip and groin disability: a systematic review. Br J Sports Med 2010;44:1186-96.

20. Collins NJ, Misra D, Felson DT, Crossley KM, Roos EM. Measures of knee function: International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Knee Outcome Survey Activities of Daily Living Scale (KOS-ADL), Lysholm Knee Scoring Scale, Oxford Knee Score (OKS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Activity Rating Scale (ARS), and Tegner Activity Score (TAS). Arthritis Care Res 2011;63 Suppl 11:S208-28.

21. KOOS User's Guide. 2003. [Internet. Accessed Aug 7, 2014.] Available from: www.koos.nu/KOOSGuide2003.pdf.

22. HOOS User's Guide. 2003. [Internet. Accessed Aug 7, 2014.] Available from: www.liv.se/Global/Jobb,%20utbildning%20och%20forskning/Forskning/FoU-enheter/Division%20HHR/Utv%C3%A4rderings instrument/HOOS%20User's%20Guide%202003.pdf

23. Gloster AT, Rhoades HM, Novy D, Klotsche J, Senior A, Kunik M, et al. Psychometric properties of the Depression Anxiety and Stress Scale-21 in older primary care patients. J Affect Disord 2008;110:248-59.

24. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. Arthritis Rheum 2003;49:156-63.

25. Dobson F, Hinman RS, Roos EM, Abbott JH, Stratford P, Davis AM, et al. OARSI recommended performance-based tests to assess physical function in people diagnosed with hip or knee osteoarthritis. Osteoarthritis Cartilage 2013;21:1042-52.

26. Bennell K, Dobson F, Hinman R. Measures of physical performance assessments: Self-Paced Walk Test (SPWT), Stair Climb Test (SCT), Six-Minute Walk Test (6MWT), Chair Stand Test (CST), Timed Up & Go (TUG), Sock Test, Lift and Carry Test (LCT), and Car Task. Arthritis Care Res 2011;63 Suppl 11:S350-70.

27. Jaeschke R, Singer J, Guyatt G. Measurement of health status. Ascertaining the minimal clinically important difference. Control Clin Trials 1989;10:407-15.

28. Angst F, Aeschlimann A, Beat M, Stucki G. Minimal clinically important rehabilitation effects in patients with osteoarthritis of the lower extremities. J Rheumatol 2002;29:131-8.

29. Peduzzi P, Concato J, Holford T, Feinstein A. The importance of events per independent variable in multivariable analysis, II: accuracy and precision of regression estimates. J Clin Epidemiol 1995;48:1503-10.

30. Peduzzi P, Concato J, Kemper E, Holford T, Feinstein A. A simulation study of the number of events per variable in logistic regression analysis. J Clin Epidemiol 1996;49:1373-9.

31. Fransen M, McConnell S. Land-based exercise for osteoarthritis of the knee: a metaanalysis of randomized controlled trials. J Rheumatol 2009;36:1109-17.

32. Fransen M, McConnell S, Hernandez-Molina G, Reichenbach S. Does land-based exercise reduce pain and disability associated with hip osteoarthritis? A meta-analysis of randomized controlled trials. Osteoarthritis Cartilage 2010;18:613-20.

33. Wolf S, Foley S, Budiman-Mak E, Moritz T, O'Connell S, Jelinek C, et al. Predictors of weight loss in overweight veterans with knee osteoarthritis who participated in a clinical trial. J Rehabil Res Dev 2010;47:171.

34. Lin EH, Katon W, Von Korff M, Tang L, Williams JW Jr., Kronke K, et al. Effect of improving depression care on pain and functional outcomes among older adults with arthritis: a randomized controlled trial. JAMA 2003;290:2428-9.

35. Wright AA, Cook CE, Flynn TW, Baxter GD, Abbott JH. Predictors of response to physical therapy intervention in patients with primary hip osteoarthritis. Phys Ther 2011;91:510-24.

36. Dobson F, Hinman RS, Hall M, Terwee CB, Roos EM, Bennell KL. Measurement properties of performance-based measures to assess physical function in hip and knee osteoarthritis: a systematic review. Osteoarthritis Cartilage 2012;20:1548-62.

37. Felson DT, Zhang Y, Hannan MT, Naimark A, Weissman BN, Aliabadi P, et al. The incidence and natural history of knee osteoarthritis in the elderly. The Framingham Osteoarthritis Study. Arthritis Rheum 1995;38:1500-5.