BMJ Open Patient characteristics associated with a poor response to non-surgical multidisciplinary management of knee osteoarthritis: a multisite prospective longitudinal study in an advanced practice physiotherapist-led tertiary service

Shaun O'Leary ^{1,2}, Maree Raymer,² Peter Window,² Patrick Swete Kelly,² Bula Elwell,³ Ian McLoughlin,³ Will O'Sullivan,⁴ Ben Phillips,⁴ Anneke Wake,⁴ Andrew Ralph,⁵ Helen O'Gorman,⁶ Ellen Jang,⁶ Karen Groves,⁶ Andrew Hislop,⁷ Darryl Lee,² Linda Garsden,² Michael Conroy,⁸ Daniel Wickins,⁹ Bill Vicenzino,¹ Tracy Comans,¹⁰ Michelle Cottrell,^{1,2} Asaduzzaman Khan,¹ Steven McPhail^{11,12}

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For numbered affiliations see end of article.

Correspondence to

Dr Shaun O'Leary;
s.oleary@uq.edu.au

ABSTRACT

Objectives To explore patient characteristics recorded at the initial consultation associated with a poor response to non-surgical multidisciplinary management of knee osteoarthritis (KOA) in tertiary care.

Design Prospective multisite longitudinal study.

Setting Advanced practice physiotherapist-led multidisciplinary orthopaedic service within eight tertiary hospitals.

Participants 238 patients with KOA.

Primary and secondary outcome measures Standardised measures were recorded in all patients prior to them receiving non-surgical multidisciplinary management in a tertiary hospital service across multiple sites. These measures were examined for their relationship with a poor response to management 6 months after the initial consultation using a 15-point Global Rating of Change measure (poor response (scores -7 to +1)/positive response (scores +2 to +7)). Generalised linear models with binomial family and logit link were used to examine which patient characteristics yielded the strongest relationship with a poor response to management as estimated by the OR (95% CI).

Results Overall, 114 out of 238 (47.9%) participants recorded a poor response. The odds of a poor response decreased with higher patient expectations of benefit (OR 0.74 (0.63 to 0.87) per 1/10 point score increase) and higher self-reported knee function (OR 0.67 (0.51 to 0.89) per 10/100 point score increase) ($p < 0.01$). The odds of a poor response increased with a greater degree of varus frontal knee alignment (OR 1.35 (1.03 to 1.78) per 5° increase in varus angle) and a severe (compared with mild) radiological rating of medial compartment degenerative change (OR 3.11 (1.04 to 9.3)) ($p < 0.05$).

Conclusions These characteristics may need to be considered in patients presenting for non-surgical

Strengths and limitations of this study

- This study was conducted during routine care within an advanced practice physiotherapist-led orthopaedic service involving 15 clinicians across eight tertiary hospitals, increasing practice representation of findings.
- Multiple accessible clinical measurement domains (patient-reported, physical, radiological) were evaluated but only included measures considered to be consistently available across sites.
- A 17% dropout rate to follow-up potentially impacted the findings.
- Findings are directly relevant to comparable services managing knee osteoarthritis (KOA) in tertiary care settings, with some cautioned relevance to all services providing management for KOA.
- Further study is required to prospectively evaluate the capacity of identified patient characteristics to predict a poor outcome in KOA within this service.

multidisciplinary management of KOA in tertiary care. Measurement of these patient characteristics may potentially better inform patient-centred management and flag the need for judicious monitoring of outcome for some patients to avoid unproductive care.

INTRODUCTION

Knee osteoarthritis (KOA) is a leading cause of disability in the community.¹ Patients with more advanced pain and functional limitations due to KOA may be referred to tertiary hospitals for specialist opinion regarding

management options, but for many of these patients, non-surgical multidisciplinary management is the first line of care.² While evidence supports non-surgical interventions such as exercise and weight loss for the management of KOA,^{3–7} individual patient responses may vary. It would be clinically and economically advantageous to identify patients with KOA at risk of a poor response to non-surgical multidisciplinary management at the initial consultation. Potentially at-risk patients could receive additional care to address identified risk factors, and their treatment response closely monitored to facilitate a timely referral for surgical consultation if not responding. However, it is crucial that studies are specific to patient populations, service settings and intervention types. Potentially interpreting the meaning of risk factors may be misguided when models are applied to different patients in different health settings (eg, primary vs tertiary) where marked variation in patient demographics and interventions may exist.⁸

Our previous retrospective audit of medical records explored patient characteristics associated with a poor response to non-surgical multidisciplinary management of KOA. This audit was conducted within a multisite advanced practice physiotherapist-led multidisciplinary orthopaedic service (herein referred to as the ‘service’) in tertiary hospitals.⁸ The service employs experienced musculoskeletal physiotherapists (service leader) to assess and determine management pathways for non-urgent patients within orthopaedic specialist outpatient departments.² Where non-surgical management is appropriate, care provided by the service is patient centred with an emphasis on progression from supported to non-supported self-management and is multidisciplinary (as required; physiotherapy, occupational therapy, dietetics and/or psychology) to pragmatically address the mix of biopsychosocial factors potentially underlying each patient’s KOA presentation.^{7,9} The retrospective audit showed that patients who reported lower knee function and higher levels of anxiety at their initial appointment within the service were at greater odds of a poor response to non-surgical multidisciplinary management.⁸ There were marked limitations of this prior study due to its retrospective nature and limited patient characteristics recorded. In particular, the literature suggests that many other potentially relevant risk factors should be considered such as patient expectations¹⁰ and physical examination findings of the knee,¹¹ which were previously not examined due to a lack of standardised recording within medical records.⁸

To address limitations of our previous retrospective audit, this study prospectively explored the relationship between a broader selection of patient characteristics and a poor outcome to non-surgical multidisciplinary management of KOA in the service. Based on our previous findings⁸ and others,^{10,11} we hypothesised that a mix of patient-reported, physical and radiological patient characteristics may be associated with a poor outcome.

METHODS

Study design

A prospective longitudinal study was conducted across eight tertiary hospital service sites in Queensland, Australia. Service leader engagement ensured selected measures and equipment (eg, questionnaires, goniometers, radiological findings) were accessible across sites. This manuscript follows the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines.¹²

Patient and public involvement

No patient involved.

Participants

Participants were recruited within the service at participating hospitals between January 2014 and December 2016 (follow-up completed July 2017). Potential participants had been triaged from the specialist orthopaedic outpatient waiting list by the medical consultant and/or service leader to undergo non-surgical management within the service for their knee condition. At the initial service consultation, potential participants were further screened for study eligibility based on an accepted clinical and radiological diagnosis of KOA.¹³ Specifically, participants had to report persistent knee pain (pain on most days for at least a month or longer in the past year), limited morning stiffness (less than 30 min) and functional limitations (self-reported functional impairment, eg, knee muscle weakness), as well as demonstrate radiological evidence of KOA on imaging (determined from a radiological report or medical consultant notes within the medical records). Participants were excluded if they presented with a potentially serious medical condition (red flags), knee pain of lumbar spine or hip origin, an active inflammatory condition (eg, rheumatoid arthritis), severe symptoms likely to be aggravated by therapies, significant or unstable neurovascular involvement, or if the referring medical practitioner or patient requested specialist medical consultation specifically.

Criteria for a poor response to non-surgical multidisciplinary management (dependent variable)

A poor response to management for each patient case was determined with a 15-point Global Rating of Change (GROC).^{14–16} Patients rated their overall perception of change since beginning treatment on a scale ranging from –7 (a very great deal worse) to zero (about the same) to +7 (a very great deal better). Investigators dichotomised (binary outcome) responses between –7 (a very great deal worse) and +1 (almost the same, hardly any better at all) as a poor response, and responses between +2 (a little better) and +7 (a very great deal better) as a positive response. This decision was based on the generally high level of KOA presentation severity seen within this specialty tertiary service, where marginal improvements in baseline function may for some patients be considered a positive response. Therefore, scores between –7 and

+1 representing worsening or negligible change in the disorder were considered a poor response. This outcome was assessed at 6 months after entry to the service as this is a conservative timeframe for decision-making regarding the potential impact of non-surgical management for these patients based on our previous study.⁸

Potential explanatory patient variables assessed for their relationship with outcome (independent variables)

Patient characteristics recorded at the initial consultation with the service leader included routine demographic and clinical information from the patient interview, self-report questionnaires capturing condition specific, as well as general health and psychosocial information (that had been premailed and completed by patients prior to the initial session as is the standard procedure in these clinics), information from standardised physical tests and radiological imaging findings. In cases of a referral for bilateral KOA, participants were asked to nominate the most severe/problematic knee, which, for the purposes of this study, was recorded as the affected knee.

Variables included:

Demographic and social measures: This includes age (years), sex (% male), English first language (% yes), education level (% yes; school incomplete, completed secondary school, completed Technical and Further Education/trade/university), work status (% yes; employed (full or part-time), unemployed, retired), marital status (% yes; married/defacto, single), dependents (% yes).

General and global health measures: This includes body mass index (kg/m^2), disability benefits (% yes), smoking status (% yes), comorbidities (number/18 listed conditions), total body pain areas (number/18 segmented body chart), health-related quality of life (utility score/1) measured with the Assessment of Quality of Life questionnaire (AQoL-6D).¹⁷

Psychological measures: General psychological distress was evaluated with the Depression, Anxiety and Stress Scale (DASS-21) with each of the three dimensions of depression (score/42), anxiety (score/42) and stress (score/42) scored separately.¹⁸ Pain-related psychological measures included the Pain Self-Efficacy Questionnaire (score/60)¹⁹ and the Örebro Musculoskeletal Pain Screening Questionnaire (ÖMPSQ-short) (score/100).²⁰ The patient's expectation of benefit (score/10) from the non-surgical management approach was also recorded using a visual analogue scale anchored by the terms 'No benefit' and 'Extreme benefit'.

Condition-specific symptoms and signs: The Knee Injury and Osteoarthritis Outcome Score (KOOS) including separate scores for symptoms and stiffness (score/100), pain (score/100), function and daily living (score/100) and quality of life (score/100).^{21 22} Participant-nominated functional deficits were evaluated with the Patient Specific Functional Scale (score/10).^{23 24} The potential presence of neuropathic pain was evaluated with the Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) pain scale (% yes, score of ≥ 12 points).²⁵ Other self-reported

information regarding the condition included symptom duration (% yes; >12 months), traumatic onset (% yes), previous surgery (% yes) for the same condition and the presence of associated symptoms such as bilateral knee pain (% yes), instability/giving way (% yes), true locking (% yes), swelling (% yes) and joint noises (% yes).

Physical examination measures conducted by the advanced physiotherapist included knee flexion and extension (lack) range of motion ($^{\circ}$) measured with a goniometer, observed lateral thrust of the affected knee during the examination of gait (% yes)²⁶ and a reliable weight-bearing frontal knee alignment measure in standing using a goniometer.²⁷ In this method, the goniometer axis is positioned over the centre of the patella with arms aligned to the anterior superior iliac spine and the centre of the ankle joint with the resultant knee angle recorded as either a valgus ($-^{\circ}$), neutral (0°) or varus ($+^{\circ}$) angle.²⁸ Findings from four knee ligament stress tests (valgus, varus, anterior, posterior) were judged (normal or altered) and individually recorded (% altered). A measure of symptom modification during the initial examination was also evaluated.²⁹ In this test, patients rated any perceived improvement (%) (taking all things into consideration such as pain, mobility, effort) in the replication of a self-nominated problematic activity (eg, squatting), comparing the overall experience before and then during a modification of the activity guided by the therapist (eg, corrected movement pattern instructions, manual assistance from therapist, use of strapping tape). Up to three modification trials were permitted with improvement needing to be repeatable over at least two repetitions.

Radiological findings (X-ray, MRI, CT) of degenerative change in the medial, lateral and patellofemoral compartments of the knee were recorded based on either a specific radiological report or radiological findings specified in the medical notes by the medical consultant. Degenerative change was recorded as either absent, mild, moderate or severe. This approach was based on consensus by the service leaders that these ratings were consistently used in radiological reporting for imaging across all sites. Relevance of the imaging with regard to how recently it was taken was at the service leader's discretion.

Procedure

All potential explanatory patient characteristics were recorded during the initial consultation with the service leader following screening and consent procedures. Participants then underwent their normal care within the service at the respective sites. Each patient's management (duration of management period, disciplines consulted) was pragmatically based on the initial examination findings of the service leader and the clinical discretion of the involved discipline-specific treatment providers. The study research officer contacted the participant at the 6-month follow-up period and mailed them the clinical outcome measure (GROC) independently of the service at all sites. Participants may or may not have been still

receiving management within the service at this time point, according to their individual treatment plan.

Sample size estimation

It was estimated that 224 cases would be required to identify explanatory variables with a strong relationship to a poor response based on an expected 50% non-responder rate,⁸ the inclusion of up to seven explanatory variables in a final multivariable (logistic family) model and a conservative number of non-responders ($n=16$) per variable based on prior simulations.³⁰ To account for up to 15% dropout, it was estimated that a minimum number of 264 participants were required to be recruited for this study.

Statistical analysis

Analyses were conducted using Stata V.13 (StataCorp, 2013, Stata Statistical Software: Release 13, College Station, Texas, USA: StataCorp LP). Participant characteristics and outcomes were described using conventional descriptive statistics with number (%) for categorical data, mean (SD) for normally distributed data and median (IQR) for non-normally distributed data. Generalised linear models with binomial family and logit link with site as a random effect were used to examine the association between potential explanatory variables with patients being classified as either having a poor response (GROC score ≤ 1) or positive response (GROC score 2–7) to multidisciplinary non-surgical management in this sample. To select the most appropriate explanatory variables to carry forward to a multivariable model, univariate analyses were initially conducted, and an unadjusted OR (95% CI) was calculated for each variable's relationship with

a poor response. Due to the high number of potential explanatory variables and the study's intention to identify a clinically relevant and preferably quantifiable parsimonious selection of explanatory variables associated with a poor response, only explanatory variables that displayed a univariate relationship of $p \leq 0.1$ with the reference score (GROC score ≤ 1) were considered for the multivariable analyses.³¹ Eligible variables were then further screened as to their relative level of potential clinical impact and priority to take to the final model. This was particularly the case if multiple variables from a similar domain (eg, psychological measures, physical measures) were eligible. Potential multicollinearity issues between eligible explanatory variables were then evaluated with a Spearman's rho (r_s) correlational coefficient as it is appropriate for both continuous and discrete ordinal variables.³² If variables were shown to have significant moderate ($r_s=0.4-0.6$) or strong ($r_s=0.7-0.9$) correlations,^{33 34} only one variable was selected (investigators choice based on clinical reasoning) to be carried forward for the final model. After accounting for potential non-independence associated with site by including site as a random effect, and the aforementioned variable selection process to avoid multicollinearity, we did not detect any breaches of model assumptions in the final model. The c-statistic was also calculated for the final model, and in the final model, ORs were expressed per 5° for range of motion variables, per 10 points on the KOOS and per 10% for symptom modification test. In addition, to examine whether findings were robust against this variable selection process which included investigator judgement, any correlated variables that were not selected were substituted into the multivariable analysis in place of the selected variable as sensitivity analyses to determine if findings were impacted by the choice of included variable.

RESULTS

The flow of participants through the study is depicted in figure 1. Of the 375 patients deemed eligible following screening and invited to participate, 286 participants completed written consent forms and baseline measures. At the 6-month follow-up period, GROC measures were received from 238 participants representing a 17% dropout rate; however, exploratory independent t-tests suggest that those who did/did not complete their outcomes were not different in their baseline level of knee disability (KOOS Function—Daily Living, $p=0.43$), suggesting the completers were a representative sample.

For the 238 patients who completed the 6-month follow-up GROC measure, the median (IQR) GROC score was +2 (–2 to +4) with the range of scores from –7 to +7. Overall, 114 (47.9%) patients fitted the criteria as a poor responder. The characteristics of participants classified as poor responders or positive responders are described in table 1.

Twenty potential explanatory variables demonstrated a univariate relationship ($p \leq 0.1$) with a poor response to

Figure 1 Participant flow diagram for patients with knee osteoarthritis (KOA) and Global Rating of Change (GROC) completions.

Table 1 Means ($\pm$ SD) (normally distributed continuous data), medians (IQR) (non-normally distributed continuous data) and row participant percentages (n) (categorical data) for the independent variables grouped for participants dichotomised as a poor response (GROC $\leq +1$) or a positive response (GROC $\geq +2$) to the non-surgical multidisciplinary management of KOA

Variables	Poor response (n=114)	Positive response (n=124)	Unadjusted OR (95% CI)	P value
Demographic and social measures				
Age (years)	63.45 $\pm$ 9	62.27 $\pm$ 12.17	1.01 (0.99 to 1.04)	0.31
Sex: Male (% yes (n))	54% (46)	46% (40)	1.5 (0.87 to 2.6)	0.15
English first language (% yes (n))	49% (110)	51% (116)	2.03 (0.57 to 7.22)	0.28
Education level				
School incomplete (% yes (n))	52% (53)	48% (49)	Referent	
Completed secondary school (% yes (n))	40% (23)	60% (34)	0.64 (0.33 to 1.24)	0.18
Completed TAFE/Trade/ University (% yes (n))	48% (33)	52% (36)	0.88 (0.47 to 1.64)	0.68
Work status				
Employed (% yes (n))	48% (54)	52% (59)	Referent	
Unemployed (% yes (n))	50% (5)	50% (5)	1.04 (0.28 to 3.85)	0.95
Retired (% yes (n))	45% (44)	55% (53)	0.89 (0.51 to 1.56)	0.69
Marital status: Married/de facto (% yes (n))	51% (64)	49% (62)	1.34 (0.79 to 2.26)	0.28
Dependents (% yes (n))	38% (11)	62% (18)	0.62 (0.28 to 1.38)	0.25
General and global health measures				
Body mass index (kg/m ²)	34.84 $\pm$ 7.7	33.68 $\pm$ 8.22	1.02 (0.98 to 1.05)	0.35
Disability benefits (% yes (n))	46% (22)	54% (26)	0.83 (0.43 to 1.61)	0.58
Smoking status (% yes (n))	57% (17)	43% (13)	1.44 (0.65 to 3.17)	0.36
Comorbidities (number)	2 (1–3)	2 (1–3)	1.03 (0.89 to 1.2)	0.65
Total body pain areas (number/18 body regions)	5 (3–8)	4 (2–6)	1.1 (1.01 to 1.19)	0.02*
Quality of Life (utility score/1)	0.63 (0.45–0.74)	0.69 (0.51–0.8)	0.2 (0.05 to 0.82)	0.03*
Psychological measures				
DASS-21				
Depression score (score/42)	6 (2–16)	6 (2–14)	1.02 (0.99 to 1.05)	0.19
Anxiety score (score/42)	6 (2–14)	4 (0–10)	1.04 (1.01 to 1.08)	0.03*
Stress score (score/42)	10 (2–16)	8 (2–14)	1.01 (0.98 to 1.04)	0.56
Pain Self-Efficacy Questionnaire (score/60)	32.09 $\pm$ 13.37	37.91 $\pm$ 13.12	0.97 (0.95 to 0.99)	0.003*
ÖMPSQ (score/100)	59.81 $\pm$ 15.13*	52.52 $\pm$ 13.35	1.04 (1.02 to 1.06)	<0.001*
Patient expectations of benefit (score/10)	4.29 $\pm$ 2.63*	6.2 $\pm$ 2.25	0.74 (0.65 to 0.83)	<0.001*
Condition specific symptoms and signs				
KOOS				
Symptoms and stiffness (score/100)	39.52 $\pm$ 17.24*	51.05 $\pm$ 18.8	0.97 (0.95 to 0.98)	<0.001*
Pain (score/100)	38.02 $\pm$ 16.02*	50.41 $\pm$ 16.21	0.95 (0.94 to 0.97)	<0.001*
Function—Daily Living (score/100)	45.72 $\pm$ 16.13*	55.97 $\pm$ 16.31	0.96 (0.94 to 0.98)	<0.001*
Quality of life (score/100)	22.8 $\pm$ 17.14*	32.31 $\pm$ 16	0.97 (0.95 to 0.98)	<0.001*
Patient Specific Functional Scale (score/10)	3.83 $\pm$ 1.74	4.45 $\pm$ 1.56	0.79 (0.67 to 0.94)	0.01*
S-LANSS pain score (% $\geq$ 12 points (n))	51% (30)	49% (29)	1.24 (0.67 to 2.27)	0.49
Symptom Duration (% $>$ 12 months (n))	53% (94)	47% (85)	2.02 (1.08 to 3.78)	0.03*
Traumatic onset (% yes (n))	44% (40)	56% (51)	0.76 (0.44 to 1.3)	0.32
Previous surgery (% yes (n))	51% (29)	49% (28)	1.19 (0.65 to 2.19)	0.57
Associated symptoms				
Bilateral knee pain (% yes (n))	51% (35)	49% (33)	1.16 (0.63 to 2.14)	0.63
Instability/giving way (% yes (n))	54% (56)	46% (47)	1.54 (0.89 to 2.66)	0.13
True locking (% yes (n))	50% (10)	50% (10)	1.05 (0.41 to 2.67)	0.92
Swelling (% yes (n))	51% (49)	49% (48)	1.15 (0.68 to 1.97)	0.6

Continued

Table 1 Continued

Variables	Poor response (n=114)	Positive response (n=124)	Unadjusted OR (95% CI)	P value
Joint Noises (% yes (n))	54% (80)	46% (69)	1.88 (1.05 to 3.36)	0.03*
Physical findings				
Knee extension lack (-ve value denotes flexion°)	-4.87±6.34	-2.88±6.11	0.95 (0.91 to 0.99)	0.02*
Knee flexion range (°)	111.39±17.89	115.45±18.29	0.98 (0.97 to 1)	0.06*
Gait lateral thrust (% yes (n))	59% (30)	41% (21)	1.71 (0.9 to 3.24)	0.1*
Frontal knee alignment (valgus (-) to varus (+)°)	1.84±7.5*	-2.11±6.86	1.09 (1.05 to 1.14)	<0.001*
Ligament stress tests				
Valgus stress test (% altered (n))	63% (43)	37% (25)	2.63 (1.41 to 4.9)	0.002*
Varus stress test (% altered (n))	51% (22)	49% (21)	1.2 (0.61 to 2.37)	0.6
Anterior stress test (% altered (n))	60% (12)	40% (8)	1.73 (0.67 to 4.49)	0.26
Posterior stress test (% altered (n))	80% (4)	20% (1)	5.74 (0.59 to 55.54)	0.13
Symptom modification test (% improvement)	20 (5–60)	30 (7.5–75)	0.99 (0.98 to 1)	0.1*
Radiological findings				
Medial compartment degenerative change				
Absent (% yes (n))	33% (7)	67% (14)	Referent	
Mild (% yes (n))	24% (10)	76% (32)	0.66 (0.2 to 2.16)	0.49
Moderate (% yes (n))	51% (43)	49% (42)	2.15 (0.77 to 6.05)	0.15
Severe (% yes (n))	65% (52)*	35% (28)	4.36 (1.5 to 12.69)	0.01*
Lateral compartment degenerative change				
Absent (% yes (n))	47% (43)	53% (49)	Referent	
Mild (% yes (n))	54% (34)	46% (29)	1.39 (0.72 to 2.69)	0.33
Moderate (% yes (n))	48% (25)	52% (27)	1.07 (0.53 to 2.15)	0.86
Severe (% yes (n))	48% (10)	52% (11)	1.09 (0.41 to 2.86)	0.87
Patellofemoral joint degenerative change				
Absent (% yes (n))	38% (8)	62% (13)	Referent	
Mild (% yes (n))	41% (28)	59% (41)	1.09 (0.4 to 3.01)	0.86
Moderate (% yes (n))	56% (53)	44% (41)	2.08 (0.78 to 5.55)	0.14
Severe (% yes (n))	52% (23)	48% (21)	1.84 (0.63 to 5.39)	0.27

Each variable's relationship with the dependent variable of a poor response (GROC $\leq +1$) is presented as an unadjusted OR and 95% CI and p value. OR reflects either an increased (OR >1) or a decreased (OR <1) odds of a poor response associated with higher scores (continuous measures expressed as a one unit increase in measure) or presence of patient characteristics (categorical measures).

*Variables with a univariate relationship ($p \leq 0.1$) with a poor response in outcome that were considered for the final analysis.

DASS-21, Depression, Anxiety and Stress Scale; GROC, Global Rating of Change; KOA, knee osteoarthritis; KOOS, Knee Injury and Osteoarthritis Outcome Score; ÖMPSQ-Short, Örebro Musculoskeletal Pain Screening Questionnaire; S-LANSS, Leeds Assessment of Neuropathic Symptoms and Signs; TAFE, Technical and Further Education.

non-surgical management of KOA, as shown in table 1. Of these 20 variables, 9 were retained in the final multivariable model following exclusion of variables based on likely clinical utility/priority and potential multicollinearity (or both). The specific rationale for excluding the following variables was KOOS subscales (symptoms and stiffness; pain; quality of life) were moderate to strongly correlated with the KOOS Function—Daily Living subscale ($r_s=0.6$ – 0.8 , $p<0.001$) which was retained as it was considered most clinically informative based on its measure of pain-related function; PSFS was excluded as it was moderately correlated ($r_s=0.4$, $p<0.001$) with the KOOS Function—Daily Living subscale which already provided a measure of function; the QOL, PSEQ and ÖMPSQ measures were

moderately correlated with the KOOS Function—Daily Living subscale ($r_s=0.4$ – 0.5 , $p<0.001$); the DASS Anxiety subscale was excluded as findings for the poor responder group (median score 6/42 points) was below the lowest end of the mild anxiety category (8–9 points)¹⁸; flexion knee range was excluded on the basis of the very small difference between poor/positive responders and negligible OR (95% CI) (OR 0.97–1); the quantifiable frontal knee alignment measure was maintained instead of the clinician-rated measures of gait lateral thrust and valgus stress test. Additionally, findings of the valgus stress test were considered to reflect pseudolaxity associated with medial compartment degenerative change as supported by their weak but significant correlation ($r_s=0.17$, $p<0.02$).

Table 2 Patient characteristics in final model (c-statistic=0.82) demonstrating a relationship with reporting a poor response (GROC $\leq +1$) to the non-surgical multidisciplinary management of KOA

Variables	Adjusted OR (95% CI)	P value
General and global health measures		
Total body pain areas (per 1/18 additional reported painful body regions)	1.08 (0.97 to 1.21)	0.17
Psychological measures		
Patient expectations of benefit (per 1/10 points increase in score)	0.74 (0.63 to 0.87)	<0.001
Condition-specific symptoms and signs		
KOOS Function—Daily Living (per 10/100 points increase in score)	0.67 (0.51 to 0.89)	<0.01
Frontal knee alignment (per 5° increase in varus angle)	1.35 (1.03 to 1.78)	0.03
Medial compartment degenerative change		
Absent	1.27 (0.29 to 5.64)	0.75
Mild	Referent	
Moderate	2.39 (0.84 to 6.79)	0.1
Severe	3.11 (1.04 to 9.3)	0.04
Symptom duration (%>12 months (n))	1.26 (0.53 to 3.01)	0.6
Associated symptoms—Joint noises (% yes (n))	1.28 (0.59 to 2.75)	0.54
Knee extension lack (per 5° increase in extension range)	0.95 (0.71 to 1.27)	0.71
Symptom modification test (per 10% improvement)	1.06 (0.95 to 1.20)	0.29

ORs reflect either an increased (OR >1) or a decreased (OR <1) odds of a poor response associate higher scores (continuous measures) or presence of patient characteristics (categorical measures). Specifically, higher patient expectations of benefit and reported daily knee function (KOOS) reduced the odds of a poor response (OR <1), while a higher degree of varus frontal knee alignment and radiologically reported severe medial compartment degenerative change increased the odds of a poor response (OR >1).

GROC, Global Rating of Change; KOA, knee osteoarthritis; KOOS, Knee Injury and Osteoarthritis Outcome Score.

In addition, when the variables that were not selected (eg, other subscales of KOOS, ÖMPSQ, PSEQ) were substituted into the multivariable model as sensitivity analyses, findings were consistent regardless of which of the variables were used (not presented).

Of the nine variables retained in the final model, only four were observed to be independently associated with a poor response to the non-surgical management of KOA, as shown in table 2. Patient characteristics associated with a lower odds of a poor response included higher patient expectations of benefit with the OR 0.74 (0.63 to 0.87) per 1/10 point score increase ($p<0.001$), indicating the odds of a poor response reduces with higher patient expectations; higher self-reported knee function (KOOS Function—Daily Living) with the OR 0.67 (0.51 to 0.89) per 10/100 point score increase ($p<0.01$), indicating the odds of a poor response reduced with higher self-reported knee function. Patient characteristics associated with greater odds of a poor response included greater varus frontal knee alignment in standing with the OR 1.35 (1.03 to 1.78) per 5° increase in varus angle ($p=0.03$), suggesting increased odds of a poor response with greater recording of knee varus angle; and reported severe medial compartment degenerative change on imaging with the OR 3.11 (1.04–9.3) ($p=0.04$), suggesting a severe rating on imaging is associated with greater odds of a poor response than a reported mild degenerative

rating. Service site was not a significant factor in the model ($p=0.64$).

DISCUSSION

Study findings support our hypothesis that a mix of patient characteristics including cognitive (expected benefit of management, perceived daily function), physical (frontal knee alignment) and radiological (degenerative severity) characteristics may be associated with a poor response to non-surgical multidisciplinary management of KOA within the tertiary care service under study. Collectively, these findings describe poor responders within a biopsychosocial context as generally being more severely disabled, matched by more severe knee pathology, and more negative outlook regarding their likely capacity to benefit from non-surgical management. These findings provide clinicians within these tertiary settings some scope to identify patients at the initial consultation who may be more unlikely to benefit from this line of care. This knowledge provides opportunity for early management planning that may include more finely tailored non-surgical interventions to specifically address identified risk factors, or earlier referral for specialist medical consultation if not benefitting.

We evaluated the patient's perceived expected benefit from the recommended multidisciplinary management using a simple visual analogue scale. With higher patient

expectation of benefit, the odds of patients reporting a poor response to management is reduced (OR 0.74 (0.63 to 0.87) per 1 point increase). These findings are consistent with previous studies in KOA¹⁰ and other conditions^{35–40} showing negative/positive patient expectations about treatment benefits to influence outcomes. An individual's cognitive actions in response to recommended treatments are thought to reflect his or her beliefs about the potential benefits of recommended management approaches,⁴¹ potentially impacting his or her motivation to engage in interventions.^{42–43} Older adults with KOA have been reported to have low expectations of benefit from non-surgical interventions such as exercise.⁴⁴ Patient expectancy may be shaped by multiple factors including psychological variables such as fear avoidance, disease severity and X-ray findings, confidence in exercise capacity, and pain and disability level.^{44–45} Lower reported knee function at initial consultation was associated with a poorer response in both this current study and our previous study in KOA.⁸ This current study suggests that the odds of a poor response reduced (OR 0.67 (0.51 to 0.89) per 10 point increase) with higher Daily Knee Function (KOOS) score signifying a better level of knee function. While lower perceived knee function may simply reflect a more severe disorder, cognitively it may also reduce the patient's expectations that an activity-based management approach (such as that provided by the multidisciplinary service under study) will be beneficial. While factors influencing patient expectations vary between individuals, findings support recommendations for determining patient expectations in the initial examination as it may impact patient–therapist communication.⁴⁶ Skilled clinicians may communicate management options with patients engaging them on a personal level, collaboratively problem solving personal perceived barriers to recovery and providing reassurance, and ultimately improving the patients' motivation to participate in recommended management approaches.

Patients with a severe radiological rating of medial knee compartment degeneration had, on average, greater than three times the odds (OR 3.11 (1.04 to 9.3)) of reporting a poor response to management compared with those with a mild rating (table 2). Although the wide CIs suggest this relationship may be variable between patients. Traditionally, radiological degenerative severity has not been shown to be strongly associated with knee symptom level^{47–48} and functional impairment.⁴⁹ However, more recent studies, including one incorporating five different racial/ethnic populations, have shown radiographic knee osteoarthritis to be strongly associated with the presence and severity of knee pain.^{50–51} This current study lends support to this more recent literature with a more severe level of medial knee degeneration increasing the odds of a poorer response. However, this was only for the medial compartment, as the severity of degenerative change was not related to response for the lateral or patellofemoral knee compartments. Furthermore, consistent with the wide 95% OR CIs for this measure (1.04–9.3), table 1 shows that 24% of participants

who recorded a positive response to management also had a severe rating of medial degenerative change. This is important in the interpretation of findings as a severe rating of medial knee degeneration should not exclude a patient from a trial of non-surgical multidisciplinary management.

The radiological findings also complement the observed relationship between greater varus knee angle and poorer outcome. Degenerative changes and varus malalignment are thought to affect knee biomechanics, load distribution and quadriceps muscle strength, although the relationship between these variables and their impact on knee function is not entirely clear.^{52–56} We included the frontal knee alignment measure because of literature suggesting local knee mechanics may impact the therapeutic effect of interventions such as exercise.^{57–58} Our findings support this proposition. For every 5° increase in varus knee angle measured at the initial examination, the odds of later reporting a poor response increased notably (OR 1.35 (1.03 to 1.78)) (table 2). This rudimentary clinical measure of frontal plane knee alignment (recorded using a goniometer in standing) has been previously shown to be significantly related to radiological measures of alignment ($r=0.67$, $p<0.0001$).²⁸ Although this clinical measure of frontal knee alignment is obviously influenced by other factors than just radiological knee alignment, it provides an accessible method of evaluating a potentially valuable aspect of frontal knee mechanics associated with a patient's response to management, which does not rely on costly and probably clinically inaccessible motion analysis or radiological measures.

Limitations

This study has limitations. The 17% dropout rate from baseline may have affected results, although baseline levels of knee disability were similar between completers/non-completers. Findings are also specific to patients within the service studied, patient characteristics recorded and outcome used (ie, GROG). Patients referred to this tertiary care service may represent those at the more severe end of the clinical spectrum and findings may be different in patients managed in other settings (eg, primary care). The large number of service leaders collecting measures across sites potentially increased the likelihood of measurement error, but we attempted to minimise this by providing a training manual and training session before the commencement of the study. Radiological findings were limited to clinical descriptors (absent, mild, moderate, severe, degenerative change) to ensure measurement consistency across imaging types and service sites. Other radiological variables (eg, meniscus tear) requiring imaging techniques other than X-ray were not included as they were inconsistently available (ie, X-ray findings noted in 83% of participants, compared with MRI (21%) and CT (2%)). Other patient characteristics (eg, medication use) may have been relevant but were beyond the scope of this study to record in enough detail to not be potentially misleading.

CONCLUSIONS

This study identified four patient characteristics assessed at the initial consultation associated with a poor response to non-surgical multidisciplinary management of KOA in a tertiary care service. While low patient expectations, low self-reported knee function, a greater knee varus angle and severe radiological knee degeneration do not nullify a trial of non-surgical multidisciplinary management, their presence may signal to clinicians the need to further individualise care and judiciously monitor outcomes to avoid unproductive use of health resources and burden to the patient.

Author affiliations

¹School of Health and Rehabilitation Sciences, University of Queensland, Brisbane, Queensland, Australia

²Physiotherapy Department, Royal Brisbane and Women's Hospital, Brisbane, Queensland, Australia

³Physiotherapy Department, Ipswich Hospital, Ipswich, Queensland, Australia

⁴Physiotherapy Department, Townsville Hospital, Townsville, Queensland, Australia

⁵Physiotherapy Department, Mackay Hospital, Mackay, Queensland, Australia

⁶Physiotherapy Department, Mater Hospital, Brisbane, Queensland, Australia

⁷Physiotherapy Department, The Prince Charles Hospital, Brisbane, Queensland, Australia

⁸Physiotherapy Department, Toowoomba Hospital, Toowoomba, Queensland, Australia

⁹Physiotherapy Department, Redcliffe Hospital, Redcliffe, Queensland, Australia

¹⁰Centre for Health Services Research, University of Queensland, Brisbane, Queensland, Australia

¹¹Clinical Informatics Directorate, Metro South Hospital and Health Service, Brisbane, Queensland, Australia

¹²Australian Centre for Health Services Innovation & Centre for Healthcare Transformation, School of Public Health & Social Work, Queensland University of Technology, Brisbane, Queensland, Australia

Twitter Bill Vicenzino @Bill_Vicenzino, Asaduzzaman Khan @khan2_asad and Steven McPhail @StevenMMcPhail

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ORCID iD

Shaun O'Leary <http://orcid.org/0000-0002-2574-129X>

REFERENCES

- Vos T, Flaxman AD, Naghavi 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.
- Standfield L, Comans T, Raymer M, et al. The efficiency of increasing the capacity of physiotherapy screening clinics or traditional medical services to address unmet demand in orthopaedic outpatients: a practical application of discrete event simulation with dynamic queuing. *Appl Health Econ Health Policy* 2016;14:479-91.
- Fransen M, McConnell S, Harmer AR, et al. Exercise for osteoarthritis of the knee. *Cochrane Database Syst Rev* 2015;1:CD004376.
- Fernandes L, Hagen KB, Bijlsma JWW, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. *Ann Rheum Dis* 2013;72:1125-35.
- Hochberg MC, Altman RD, April KT, 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.
- Nelson AE, Allen KD, Golightly YM, et al. A systematic review of recommendations and guidelines for the management of osteoarthritis: the chronic osteoarthritis management initiative of the U.S. bone and joint initiative. *Semin Arthritis Rheum* 2014;43:701-12.
- Hurley M, Dickson K, Hallett R, et al. Exercise interventions and patient beliefs for people with hip, knee or hip and knee osteoarthritis: a mixed methods review. *Cochrane Database Syst Rev* 2018;4:CD010842.
- O'Leary S, Cottrell M, Raymer M, et al. General health factors may be a barrier to effective non-surgical multidisciplinary rehabilitation of common orthopaedic conditions in tertiary care settings. *BMC Musculoskelet Disord* 2018;19:348.
- Scopaz KA, Piva SR, Wisniewski S, et al. Relationships of fear, anxiety, and depression with physical function in patients with knee osteoarthritis. *Arch Phys Med Rehabil* 2009;90:1866-73.
- Damush TM, Perkins SM, Mikesky AE, et al. Motivational factors influencing older adults diagnosed with knee osteoarthritis to join and maintain an exercise program. *J Aging Phys Act* 2005;13:45-60.
- Deyle GD, Gill NW, Allison SC, et al. Knee oa: which patients are unlikely to benefit from manual Pt and exercise? *J Fam Pract* 2012;61:E1-8.
- von Elm E, Altman DG, Egger M, et al. The strengthening of reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Int J Surg* 2014;12:1495-9.
- Zhang W, Doherty M, Peat G, et al. EULAR evidence-based recommendations for the diagnosis of knee osteoarthritis. *Ann Rheum Dis* 2010;69:483-9.
- Bolton JE. Sensitivity and specificity of outcome measures in patients with neck pain: detecting clinically significant improvement. *Spine* 2004;29:2410-7.
- Farrar JT, Young JP, LaMoreaux L, et al. Clinical importance of changes in chronic pain intensity measured on an 11-point numerical pain rating scale. *Pain* 2001;94:149-58.
- Hurst H, Bolton J. Assessing the clinical significance of change scores recorded on subjective outcome measures. *J Manipulative Physiol Ther* 2004;27:26-35.
- Richardson JRJ, Peacock SJ, Hawthorne G, et al. Construction of the descriptive system for the assessment of quality of life AQL-6D utility instrument. *Health Qual Life Outcomes* 2012;10:38.
- Henry JD, Crawford JR. The short-form version of the depression anxiety stress scales (DASS-21): construct validity and normative data in a large non-clinical sample. *Br J Clin Psychol* 2005;44:227-39.
- Nicholas MK. The pain self-efficacy questionnaire: taking pain into account. *Eur J Pain* 2007;11:153-63.
- Linton SJ, Nicholas M, MacDonald S. Development of a short form of the Örebro musculoskeletal pain screening questionnaire. *Spine* 2011;36:1891-5.
- Roos EM, Roos HP, Lohmander LS, et al. Knee Injury and Osteoarthritis Outcome Score (KOOS)-development of a self-administered outcome measure. *J Orthop Sports Phys Ther* 1998;28:88-96.

- 22 Roos EM, Lohmander LS. The knee injury and osteoarthritis outcome score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Outcomes* 2003;1:64.
- 23 Stratford P *et al.* Assessing disability and change on individual patients: a report of a patient specific measure. *Physiotherapy Canada* 1995;47:258–63.
- 24 Cleland JA, Fritz JM, Whitman JM, *et al.* The reliability and construct validity of the neck disability index and patient specific functional scale in patients with cervical radiculopathy. *Spine* 2006;31:598–602.
- 25 Bennett MI, Smith BH, Torrance N, *et al.* The S-LANSS score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. *J Pain* 2005;6:149–58.
- 26 Chang AH, Chmiel JS, Moio KC, *et al.* Varus thrust and knee frontal plane dynamic motion in persons with knee osteoarthritis. *Osteoarthritis Cartilage* 2013;21:1668–73.
- 27 Cibere J, Bellamy N, Thorne A, *et al.* Reliability of the knee examination in osteoarthritis: effect of standardization. *Arthritis Rheum* 2004;50:458–68.
- 28 Navali AM, Bahari LAS, Nazari B. A comparative assessment of alternatives to the full-leg radiograph for determining knee joint alignment. *Sports Med Arthrosc Rehabil Ther Technol* 2012;4:40.
- 29 Tuttle N. Do changes within a manual therapy treatment session predict between-session changes for patients with cervical spine pain? *Aust J Physiother* 2005;51:43–8.
- 30 Vittinghoff E, McCulloch CE. Relaxing the rule of ten events per variable in logistic and COX regression. *Am J Epidemiol* 2007;165:710–8.
- 31 Freedman DA. A note on screening regression equations. *Am Stat* 1983;37:152–5.
- 32 Liu Q, Li C, Wanga V, *et al.* Covariate-adjusted Spearman's RANK correlation with probability-scale residuals. *Biometrics* 2018;74:595–605.
- 33 Akoglu H. User's guide to correlation coefficients. *Turk J Emerg Med* 2018;18:91–3.
- 34 Dancey CP, Reidy J. *Statistics without maths for psychology: Pearson education*, 2007.
- 35 Bishop MD, Mintken PE, Bialosky JE, *et al.* Patient expectations of benefit from interventions for neck pain and resulting influence on outcomes. *J Orthop Sports Phys Ther* 2013;43:457–65.
- 36 Oka H, Matsudaira K, Fujii T, *et al.* Risk factors for prolonged treatment of Whiplash-Associated disorders. *PLoS One* 2015;10:e0132191.
- 37 Palmlöf L, Holm LW, Alfredsson L, *et al.* Expectations of recovery: a prognostic factor in patients with neck pain undergoing manual therapy treatment. *Eur J Pain* 2016;20:1384–91.
- 38 Goossens MEJB, Vlaeyen JWS, Hidding A, *et al.* Treatment expectancy affects the outcome of cognitive-behavioral interventions in chronic pain. *Clin J Pain* 2005;21:18–26.
- 39 Liddle SD, Baxter GD, Gracey JH. Chronic low back pain: patients' experiences, opinions and expectations for clinical management. *Disabil Rehabil* 2007;29:1899–909.
- 40 Hammer NM, Bieler T, Beyer N, *et al.* The impact of self-efficacy on physical activity maintenance in patients with hip osteoarthritis - a mixed methods study. *Disabil Rehabil* 2016;38:1691–704.
- 41 Bandura A. *Self-Efficacy: the exercise of control*. New York: Freeman, 1997.
- 42 Anderson ES, Wojcik JR, Winett RA, *et al.* Social-cognitive determinants of physical activity: the influence of social support, self-efficacy, outcome expectations, and self-regulation among participants in a church-based health promotion study. *Health Psychol* 2006;25:510–20.
- 43 Sallis JF, Johnson MF, Calfas KJ, *et al.* Assessing perceived physical environmental variables that may influence physical activity. *Res Q Exerc Sport* 1997;68:345–51.
- 44 Holden MA, Nicholls EE, Young J, *et al.* Role of exercise for knee pain: what do older adults in the community think? *Arthritis Care Res* 2012;64:1554–64.
- 45 Wilcox S, Der Ananian C, Abbott J, *et al.* Perceived exercise barriers, enablers, and benefits among exercising and nonexercising adults with arthritis: results from a qualitative study. *Arthritis Rheum* 2006;55:616–27.
- 46 Stenneberg MS, Rood M, de Bie R, *et al.* To What Degree Does Active Cervical Range of Motion Differ Between Patients With Neck Pain, Patients With Whiplash, and Those Without Neck Pain? A Systematic Review and Meta-Analysis. *Arch Phys Med Rehabil* 2017;98:1407–34.
- 47 Felson DT, Lawrence RC, Dieppe PA, *et al.* Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Ann Intern Med* 2000;133:635–46.
- 48 Felson DT, Zhang Y. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. *Arthritis Rheum* 1998;41:1343–55.
- 49 McAlindon TE, Cooper C, Kirwan JR, *et al.* Determinants of disability in osteoarthritis of the knee. *Ann Rheum Dis* 1993;52:258–62.
- 50 Neogi T, Felson D, Niu J, *et al.* Association between radiographic features of knee osteoarthritis and pain: results from two cohort studies. *BMJ* 2009;339:b2844.
- 51 Wang K, Kim HA, Felson DT, *et al.* Radiographic knee osteoarthritis and knee pain: cross-sectional study from five different racial/ethnic populations. *Sci Rep* 2018;8:1364.
- 52 Sosdian L, Hinman RS, Wrigley TV, *et al.* Quantifying varus and valgus thrust in individuals with severe knee osteoarthritis. *Clin Biomech* 2016;39:44–51.
- 53 Lim B-W, Hinman RS, Wrigley TV, *et al.* Varus malalignment and its association with impairments and functional limitations in medial knee osteoarthritis. *Arthritis Rheum* 2008;59:935–42.
- 54 Sharma L, Dunlop DD, Cahue S, *et al.* Quadriceps strength and osteoarthritis progression in malaligned and LAX knees. *Ann Intern Med* 2003;138:613–9.
- 55 Lim B-W, Kemp G, Metcalf B, *et al.* The association of quadriceps strength with the knee adduction moment in medial knee osteoarthritis. *Arthritis Rheum* 2009;61:451–8.
- 56 Sharma L, Song J, Felson DT, *et al.* The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *JAMA* 2001;286:188–95.
- 57 Sharma L. Examination of exercise effects on knee osteoarthritis outcomes: why should the local mechanical environment be considered? *Arthritis Rheum* 2003;49:255–60.
- 58 Lim B-W, Hinman RS, Wrigley TV, *et al.* Does knee malalignment mediate the effects of quadriceps strengthening on knee adduction moment, pain, and function in medial knee osteoarthritis? A randomized controlled trial. *Arthritis Rheum* 2008;59:943–51.