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The relationship between radiological OA severity or body weight and outcomes following a structured education and exercise therapy program (GLA:D®) for people with knee osteoarthritis

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ABSTRACT

Background: Clinicians may presume people with higher bodyweight or greater OA severity do not respond to exercise therapy for knee osteoarthritis (OA), but few studies have examined this.
Objective: To examine the relationship between radiographical OA severity or bodyweight and pain and functional outcomes following a structured education and exercise therapy program (Good Life with OsteoArthritis from Denmark: GLA:D®).
Methods: 33 participants with knee OA were assessed at baseline and week 8 following GLA:D®. Outcomes were pain (Visual analogue scale (VAS) 0–100), Knee Injury and Osteoarthritis Outcome Score-12 (KOOS-12 total), 40 m-fast-paced walk and 30-s chair stand. Multilevel models were used to define the severity of OA in medial, lateral and patellofemoral compartments using the Kellgren-Lawrence (KL) system and to examine the relationship between compartment severity, bodyweight and outcomes.
Results: No meaningful relationships between bodyweight and response to GLA:D® were found for any outcome measures. Greater medial OA compartment severity was related to less improvement in pain, KOOS-12 and chair stand repetitions. However, all levels of lateral compartment severity had similar improvements, and greater patellofemoral compartment severity was related to more improvement for KOOS-12 and pain.
Conclusion: Bodyweight may have little influence on a person's response to a structured education and exercise therapy program. While people with greater medial compartment severity were less likely to improve following the program, OA severity in the PF and lateral compartments was not a barrier to improvement.

1. Background

Evidence from more than 100 randomised controlled trials shows that exercise therapy provides moderate benefits on pain and function for individuals with knee osteoarthritis (Fransen et al., 2015; Uthman et al., 2013; Goh et al., 2019; Holden et al., 2023). Several authors have suggested that further clinical trials will not alter these findings and should not be funded (Verhagen et al., 2019; Bricca et al., 2019). More recently, the effectiveness of exercise therapy for knee OA has been scrutinised, with claims that the magnitude of benefit may have been over-emphasised (Bandak et al., 2022; Englund and Turkiewicz, 2023). A key argument is that exercise therapy has not been subject to stringent placebo-controlled trials, with previous clinical trials mostly using a non-exercise control group (Englund and Turkiewicz, 2023). Whilst the effectiveness of exercise has been challenged, it remains important to consider people's different responses. Randomised controlled trials report an average effect size and do not represent individual patient responses (Kent et al., 2020; Rothwell, 1995). Given this current debate, it is timely that we try to understand which patient characteristics influence whether a person will or will not benefit from exercise therapy. This may allow for targeted exercise therapy or assist with decision-making and the appropriateness of knee joint replacement

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surgery (Hawker, 2023).

Many patient characteristics such as obesity and other comorbidities, psychological factors including depression or anxiety, fear of movement or reduced self-efficacy and OA severity have been proposed as potential factors influencing an individual's response to exercise therapy. However, evidence from systematic reviews has identified only a few relevant factors (Holden et al., 2023; Quicke et al., 2020; Couldrick et al., 2023; Clausen et al., 2023). An individual participant data meta-analysis evidence reported that people with higher self-reported pain and lower function benefited more from exercise therapy (Holden et al., 2023). Our recent systematic review could not conclude whether BMI, imaging severity or comorbidities were related to pain and functional outcomes following exercise therapy, OA education, and weight loss programs for knee OA (Couldrick et al., 2023). Drawing conclusions from quantitative studies is difficult as most are exploratory (e.g., subgroup analysis from an RCT), use different statistical methods, and use different variables and outcomes, which prevent synthesis (Quicke et al., 2020).

Clinicians and patients may believe that people with higher body weight or greater OA severity may not respond to exercise therapy, but few studies have specifically examined these factors (Holden et al., 2023; Clausen et al., 2023; Lawford et al., 2022; Hinman et al., 2023; Nissen et al., 2022). Qualitative studies have found that nonresponders to exercise therapy felt their body weight contributed to their lack of improvement in knee pain and function (Hinman et al., 2023) and some clinicians may presume that OA is always progressive, land-based exercise is harmful, and joint replacement surgery is inevitable for knee or hip OA (Nissen et al., 2022). We wanted to explore the relationship between radiological OA severity, body weight, and a person's response to exercise therapy. Specifically, this study aimed to determine the extent to which radiographical OA severity and body weight were related to short-term outcomes following a structured education and exercise therapy program (Good Life with osteoArthritis from Denmark: GLA:D®) for knee OA (Barton et al., 2021).

2. Methods

2.1. Study design

This pre-post-test study reports clinical outcomes from a study that also recorded participants' joint loads during walking and chair rise at week 0 (baseline) and week 8 following the GLA:D® intervention. The study is reported according to the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) (Des Jarlais et al., 2004), the Template for Intervention Description and Replication (TIDieR) and the Bayesian Reporting Guidelines (BARG) (Kruschke, 2021) for the statistical analysis (supplementary data S8 and S9) (Hoffmann et al., 2014). Ethical approval was obtained from the ACT Human Research Ethics Committee (2021.ETH.00061) and the University of Canberra Human Ethics Committee (project no. 9355). The study was prospectively registered in the Australian New Zealand Clinical Trials Register (ACTRN12622000569707).

2.2. Participants

A convenience sample of 33 participants was recruited from the Canberra community in Australia between May 2022 and April 2023 via advertising through local organisations, general practitioners, physiotherapy clinics and social media. Participants were referred from three private practices, mostly from one clinic (29/33). Interested participants completed a brief web-based screening questionnaire via REDcap (Research Electronic Data Capture https://www.project-redcap.org/). Eligible participants were contacted by the primary researcher (JC) for further screening, written informed consent, and for study enrolment. The REDcap e-Consent Framework was used to obtain written consent, store documentation with a certification screen, and store a PDF signed form.

The inclusion criteria was a clinical diagnosis of knee OA (age >45, movement-related knee pain, and morning stiffness lasting less than 30 min) (NICE Guidelines, 2022). The clinical diagnosis of knee OA was confirmed radiologically. Exclusion criteria included a history of joint replacement on the study knee, systemic inflammatory joint diseases such as rheumatoid arthritis, currently undertaking a formal exercise program, or inability to meet all study requirements (compliance with GLA:D® intervention and attending all assessment time points).

2.3. Intervention

The exercise and education intervention was the Good Life with Osteoarthritis in Denmark (GLA:D®) programme. GLA:D® is an 8-week structured program consisting of 2 patient education sessions (60–90-min duration) and 12 supervised neuromuscular exercise sessions (twice weekly for 60 min) (Skou and Roos, 2017). GLA:D® was originally developed and implemented in Denmark (Skou et al., 2014), and has been subsequently adapted for implementation in multiple countries internationally, including Australia (Barton et al., 2021). Further details related to its adaptation and implementation into the Australian healthcare system, including clinician training and evaluation, can be read elsewhere (Barton et al., 2021).

The intervention was delivered by three GLA:D® certified physiotherapists from three private multidisciplinary clinics. Participants completed the exercise sessions in small groups of four to six participants. Participants filled out the GLA:D® specific exercise diaries with the assistance of the physiotherapist and recorded their pain scale before and after each exercise session. The exercise level of difficulty was progressed individually based on the participant's 24-hour response to each session. The intervention details have been well documented in the literature (Skou and Roos, 2017; Ageberg et al., 2013) and further described in supplementary data (S7 and S8).

2.4. Outcomes

Assessments were performed at baseline and immediately following the intervention (i.e. 8 weeks post-baseline). Patient-reported outcomes were completed electronically using the REDcap system, and the primary researcher (JC) was present to help where needed. The outcome variables were usual pain in the last month (VAS 0–100) (Alghadir et al., 2018), 12-item short-form Knee Injury and Osteoarthritis Outcome Score (KOOS-12) (Gandek et al., 2019) and functional performance-based tests (30-s chair stand and 40 m-fast-paced walk) (Dobson et al., 2013). These outcomes are reliable, valid, and responsive measures in people with knee osteoarthritis and were chosen to align with the GLA:D® registry outcomes (Alghadir et al., 2018; Gandek et al., 2019; Dobson et al., 2013; Roos et al., 2021).

Body weight (kg) and height (m) were measured on calibrated scales at week 0 and week 8 at the University of Canberra biomechanics lab. Radiographical disease severity was assessed using the Kellgren-Lawrence grading system (KL 0, I, II, III, IV) (Kellgren and Lawrence, 1957). Radiographs (AP and intercondylar view in weight-bearing and skyline view for the PF joint were obtained for the study knee, taken in the past 12 months (Heng et al., 2015; Hill et al., 2022). Three different raters assessed the KL grade for each compartment (medial, lateral and PF) using the original KL description (Kellgren and Lawrence, 1957). The KL grading system is a semi-quantitative radiological assessment tool that grades the severity of osteoarthritis on a scale of 0 (no radiographic features of OA) to IV (severe radiographical features of OA) (Kellgren and Lawrence, 1957). The raters (study authors JC, JS, and JL) were experienced clinical research physiotherapists and clinical researchers, each with over ten years of experience in orthopaedics. A PhD-qualified orthopaedic surgeon provided training, which was evaluated by reliability testing.

2.5. Statistical analysis

Multilevel models were run for each outcome variable (KOOS-12 total and sub-scores, pain (VAS 0–100), walking speed, chair stand repetitions). Stage (week 0 and week 8), compartment severity (medial, lateral and PF), and body weight were added as predictors with interaction terms for all predictors. Subject-level variation in each outcome was estimated using a between-subject variation in intercepts. The predictor variables (OA severity and body weight) were decided *a priori* based on the findings from our previous systematic review (Couldrick et al., 2023) and were of direct clinical interest (see supplementary data S1 for the directed acyclic graph depicting the pathway between the predictors and the outcome variables).

A Bayesian approach was chosen for the statistical analysis because it is more suited for smaller sample sizes and has an intuitive interpretation of uncertainty (Kruschke, 2021). Models were fitted with the Markov Chain Monte Carlo (MCMC) method implemented in Stan (Carpenter et al., 2017) using the "brms" package (Bürkner, 2017) in R studio (R Core Team., 2021). Four chains of 4000 iterations and a warmup of 2000 resulted in a total of 8000 posterior samples. Normal priors were intended to be weakly informative, incorporating some prior knowledge without being overly restrictive. We considered the plausible ranges in the outcome variable and the effect of the predictors, rescaling for a one-unit increase in the predictor (refer to Bayesian reporting guidelines in supplementary material). Convergence and stability of the Bayesian sampling were assessed using R-hat (below 1.01) and the Effective Sample Size (ESS) (>1000) (Bürkner, 2017; Vehtari et al., 2021). Divergences were resolved by increasing the adapt delta closer to 1 (Stan Development Team, 2023). The model fit was assessed visually using posterior predictive check and residual plotting (Gabry et al., 2019).

The specification of the model in brms syntax (Bürkner, 2017) was:

```
y ~ 1 + weight*stage + PF*stage + medial*stage + lateral*stage + (1|subjects)
```

The '*' indicates the interaction term, which includes OA severity (medial, lateral and PF compartments), body weight and the intervention (stage). Between subject variation in the intercept was applied to each outcome (y) and is represented by (`1|subject`). The outcome variable '`y`' represents each outcome of interest (KOOS-12 total and sub-scores, pain (VAS 0–100), walking speed, chair stand repetitions). The beta distribution (logit link function) was used for KOOS-12 outcomes and pain (VAS 0–100) (bounded continuous variables). The Poisson distribution (log link) was used for chair stand repetitions (count data) and a log transformation for walking speed (positive values). The median and 90% CrI of the posterior distributions were reported for all outcome variables at week 0 and week 8 and for the differences (week 8 minus week 0). For body weight and compartment severity, the estimated values and the 90% CrI were presented, with the remaining predictors held constant (based on the mean values). See supplementary data for the complete code and data analysis with descriptions of all models.

For KL grading, an ordinal regression model (the cumulative link model (CLM)) was fitted using a Bayesian approach (Bürkner and Vuorre, 2019). The model used the observed KL grades (integer-based values 0, I, II, III, IV) from the three raters to estimate the continuous latent severity (an unobserved value) for all three compartments for each participant. We chose this approach because using a CLM reflects the ordinal nature of the KL system that explains the structure and order of the data (Liddell and Kruschke, 2018; Kottner et al., 2011). The CLM assumes the thresholds are portioned into the ordered categories of the response variable (Bürkner and Vuorre, 2019). The thresholds represent cut-off points of the latent variable where transitions occur between the categories, in this case, the KL grades. Each joint compartment is assigned an estimated latent severity (and uncertainty as defined by 90% CrI) or a probability that a certain KL grade will occur.

The specification of the CLM model in brms syntax (Bürkner, 2017) was:

```
y ~ 1 + joint + compartment + (1|reviewer) + (1|participant) + (1|compartment) + (1|compartment:participant)
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The probit link function was used with random intercepts for raters, participants, and compartments. Population-level effects for joints (left or right) and compartments (medial, lateral, and patellofemoral) were added. Normal priors were intended to be weakly informative as we did not know anything about the parameters in advance. We used a standard deviation of two for both the coefficients and grouping variances (for further description of the CLM and R code see Couldrick et al., 2024).

3. Results

3.1. Participant characteristics

All 33 participants enrolled in the study completed the week 8 assessment. The median age of the participants was 70 (range 50–87), 26 (79%) were female, and the median BMI was 28 kg m^{-2} (range 19–56). Twenty-five (76%) participants had moderate to severe knee OA (KL III and IV) (Table 1). Compliance was excellent, with 33 (100%) completing both education sessions and 30 (91%) completing nine or more of the 12 possible exercise sessions (see S2 for flow chart of participants). No adverse effects were reported, but one participant

Table 1
Characteristics of participants.

Characteristic	(n = 33)
Age (yr.); median (range)	70 (50, 87)
Sex; number female (%)	26 (79)
Symptom duration (yr.); median (range)	4 (0.25, 37)
Desire for surgery; number "no" (%)	32 (97%)
BFOMSO (6–24); median (range)	11 (6, 19)
PCS (0–52); median (range)	3 (0, 29)
Weight (kg); median (range)	78.6 (51.8, 150)
Height (m); median (range)	1.66 (1.52, 1.84)
KL grade; number (%)	
I	1 (3)
II	7 (21)
III	14 (42)
IV	11 (33)
Joint compartment severity (KL ≥ II)	
Medial; number (%)	28 (85)
Lateral; number (%)	16 (48)
PF; number (%)	29 (87)

Desire for surgery (yes/no question). Participants were asked, "Do you have so much trouble and pain from your affected knee joint that you want to have surgery?". Brief fear of movement scale for osteoarthritis scores (BFOMSO) range from six to 24 (higher scores indicate greater fear of movement) (Shelby et al., 2012). Pain catastrophising scale scores (PCS) range from 0 to 52, with higher scores indicating higher levels of pain catastrophising (Sullivan et al., 1995). KL grade represents the highest KL grade for each participant from the three raters. Joint compartment severity is the total KL ≥ II for each participant's compartment (total of 33 values for each compartment).

completed six exercise sessions and discontinued the exercise sessions after sustaining an injury from a fall unrelated to the intervention or assessments, but was still assessed at week 8.

3.2. Changes in outcomes (week 0 - week 8)

On average, KOOS-12 total scores increased from 53 to 68 (+28%), usual pain (VAS 0–100) decreased from 43 mm to 21 mm (−24%), 30s chair stand repetitions increased by 2.3 repetitions (+21%) and walking speed by 0.24 m/s (+16%) (Table S2). Table 2 shows the point estimates for week 0 and week 8 and the difference (week 8 minus week 0) for all outcome measures. These estimates represent the expected value of a hypothetical average patient with the sample mean of all the predictors (body weight and OA compartment severity). The minimally clinically important change (MCIC) is shown in Table 2, however, many studies have calculated the MCIC following a total knee replacement (Soh et al., 2022; Eckhard et al., 2021) or from the 42-item KOOS (Mostafaee et al., 2022, 2024; Silva et al., 2023). Participants did not lose weight following the intervention at week 8; the average body weight at week 0 was 82.6 kg (SE = 3.7), and at week 8 was 82.5 kg (SE = 3.7). Refer to S3 and S4 for further descriptive statistics and individual participant changes for all outcomes.

Table 2
Estimated values for all outcome variables at week 0 and week 8.

Outcome	Week 0	Week 8	Difference (week 8 minus week 0)	Minimally clinically important change (MCIC)
	Point estimate (posterior median) (90%CrI)	Point estimate (posterior median) (90% CrI)	Point estimate (posterior median) (90% CrI)	
KOOS-12 total (0-100)	53.5 (49.0, 57.8)	68.3 (64.2, 72.3)	14.9 (10.9, 18.7)	15.5–22.5 (Soh et al., 2022) 14.9 (Eckhard et al., 2021) 11.1 (Eckhard et al., 2021)
KOOS-12 pain (0-100)	51.4 (45.8, 57.1)	68.4 (63.2,73.4)	17.0 (11.0, 21.0)	15 (Mostafaee et al., 2022) 14.5–22.1 (Soh et al., 2022) 11.5 (Eckhard et al., 2021)
KOOS-12 QOL (0-100)	46.3 (42.2, 50.4)	58.9 (54.8,62.9)	12.6 (8.0, 17.1)	12.5 (Mostafaee et al., 2022) 16.5–24.4 (Soh et al., 2022) 5.5 (Eckhard et al., 2021)
KOOS-12 function (0-100)	62.8 (56.6, 68.7)	79.7 (75.2,84.1)	17.0 (11.4, 22.7)	15.5 (Mostafaee et al., 2022) 14.2–21.3 (Soh et al., 2022) 15.2 (Eckhard et al., 2021)
Usual pain last month (0-100)	43.0 (37.3, 48.8)	21.6 (17.3,26.3)	−21.5 (−27.7, −15.0)	−19.9 (Tubach et al., 2005)
30sec chair stand test (reps)	11.0 (10.0, 12.0)	13.3 (12.2,14.4)	2.3 (0.9, 3.7)	2.5 (Mostafaee et al., 2024)
40m-fast-paced walk (ms^{-1})	1.50 (1.4, 1.6)	1.73 (1.6, 1.8)	0.24 (0.2, 0.3)	0.21 (Mostafaee et al., 2024)

Point estimates represent the expected value for a hypothetical average with the sample mean of all the predictors (body weight, OA compartment severity). The posterior median is a statistical measure used in Bayesian inference, representing the posterior distribution's middle value (van de Schoot et al., 2021). The credible interval (CrI) represents the uncertainty of our estimates and can be directly interpreted as the probability our estimate lies between these values (Kruschke et al., 2018). The minimally clinically important change (MCIC) is defined as the minimal change in a score that patients perceive to be important and meaningful (Terwee et al., 2021).

3.3. Relationship between body weight and outcomes

For pain, our data showed that the relationship between a person's body weight and their pain response following GLA:D® was small and not clinically meaningful (β: −0.001, 95% CrI: −0.016, 0.014) (Fig. 1A). Heavier people had a similar reduction in pain to lighter people, although the response was more variable for heavier people. For the 30-second chair stand test, our data suggest a small relationship between body weight and estimated chair stand repetitions, people with higher body weight had larger improvements in their chair stand repetitions at week 8 but started from a lower number of repetitions (β: 0.002, 95% CrI: −0.04, 0.008) (Fig. 1C).

For walking speed, our data showed that the relationship between a person's body weight and their walking speed response following GLA:D® was small and not clinically meaningful (β: 0.0, 95% CrI: −0.001, 0.002). Heavier people had a similar improvement in walking speed at week 8 (Fig. 1D). There was a negative relationship between body weight and walking speed at both week 0 and week 8; heavier people, despite similar improvements, started and finished with lower walking speeds.

Heavier body weight was related to a slightly smaller response for KOOS-12 total, as defined by a reduced improvement in KOOS-12 score (0–100) (β: −0.003, 95% CrI: -0.011, 0.005) (Fig. 1B). This is unlikely to be clinically meaningful and was very uncertain due to the limited number of participants with a body weight greater than 110 kg. Body weight was negatively related to KOOS-12 total at both week 0 and week 8 (see S5 for KOOS-12 subscores and S6 for the linear model tables).

3.4. Relationship between radiological OA severity and outcomes

3.4.1. Pain

Greater medial compartment severity was related to a smaller response (β: 0.28, 95% CrI: 0.05, 0.50). People with very severe medial compartment severity had increased pain at week 8 following GLA:D® (Fig. 2A). Greater lateral compartment severity was related to a slightly larger response (improvement in pain) but this is unlikely to be clinically meaningful (β: −0.03, 95% CrI: −0.24, 0.19). Greater PF compartment severity was related to a larger improvement in pain at week 8 following GLA:D®. There was a negative relationship between PF compartment severity and pain at week 0 and week 8; those with greater severity started and finished with lower pain levels.

3.4.2. KOOS-12 total

Greater medial compartment severity was related to a smaller improvement in KOOS-12 total scores (β: −0.17, 95% CrI: −0.31, −0.03). People with severe medial compartment osteoarthritis had worse KOOS-12 total scores at week 8 following GLA:D® (Fig. 3A). Greater lateral (β: 0.03, 95% CrI: −0.11, 0.17) and PF compartment severity (β: 0.01, 95% CrI: −0.07, 0.17) was related to a slightly larger improvement in KOOS-12 total, but this was very uncertain and unlikely to be clinically meaningful. There was a negative relationship between lateral and PF compartment severity and KOOS12-total at week 0, and those with greater compartment severity started from a lower baseline (or greater total pain, symptoms, and reduced function).

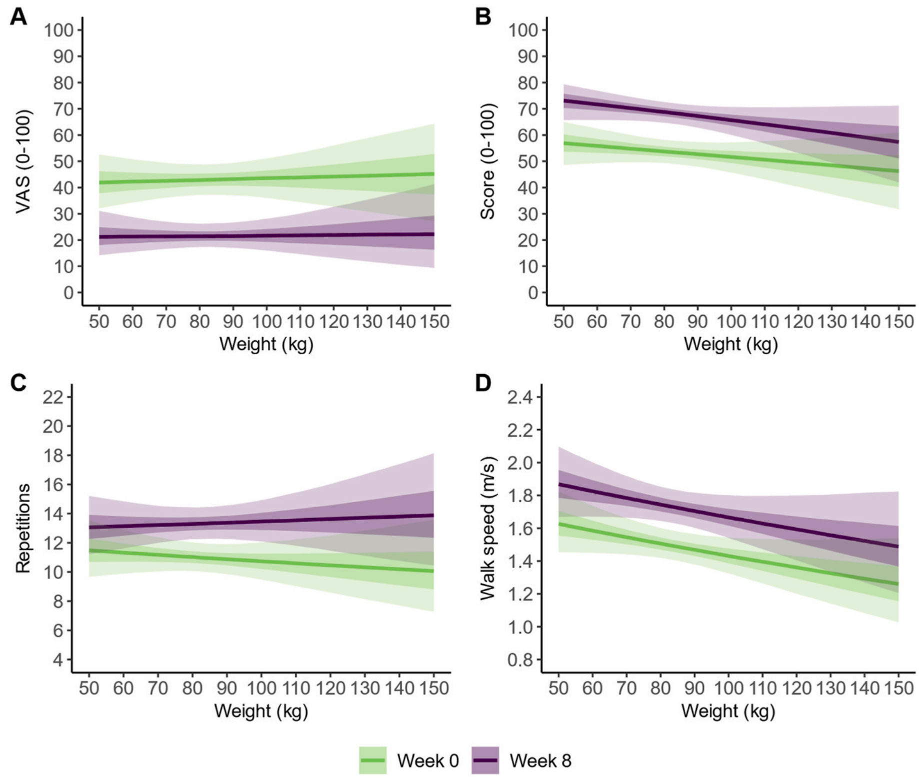

Fig. 1. Pain (VAS 0–100) (A), KOOS-12 total score (B), 30-second chair stand repetitions (C) and walking speed (m/s) (D) and relationship with body weight at baseline (week 0) and immediately following GLA:D® (week 8). The solid line represents the posterior median estimate of the expected response, obtained from the statistical model of the relationship between body weight and the outcome for a hypothetical average subject where the other predictors are held to their sample mean. The shaded area represents the approximate 90% (light areas) and the 50% (dark area) credible region, which indicates the uncertainty in the estimated relationships.

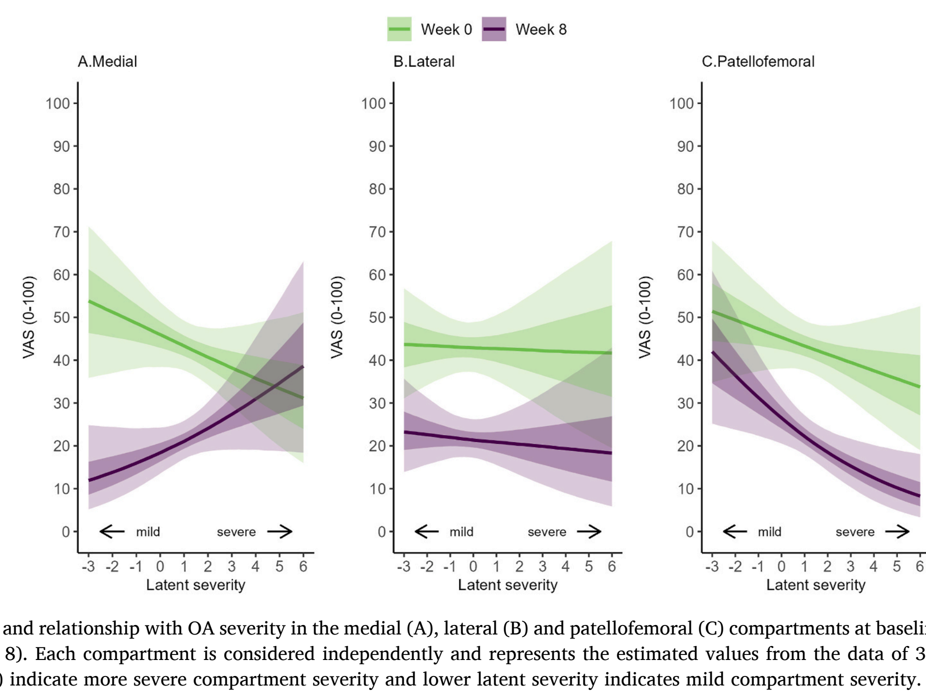

Fig. 2. Pain (VAS 0–100) and relationship with OA severity in the medial (A), lateral (B) and patellofemoral (C) compartments at baseline (week 0) and immediately following GLA:D® (week 8). Each compartment is considered independently and represents the estimated values from the data of 33 participants. Higher latent severity estimates (x-axis) indicate more severe compartment severity and lower latent severity indicates mild compartment severity. The solid line represents the posterior median estimate obtained from the statistical model of the relationship between compartment severity and pain for a hypothetical average subject where the other predictors are held to their sample mean. The shaded area represents the approximate 90% (light areas) and the 50% (dark area) credible region, which indicates the uncertainty in the estimated relationships.

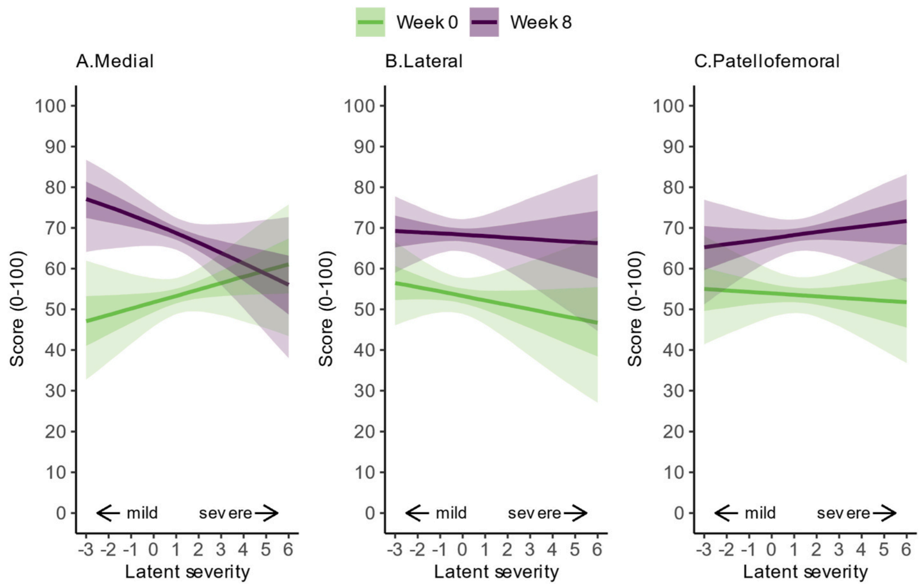

Fig. 3. KOOS-12 total score and relationship with OA severity in the medial (A), lateral (B) and patellofemoral (C) compartments at baseline (week 0) and immediately following GLA:D® (week 8). Higher latent severity estimates (x-axis) indicate more severe compartment severity, and lower latent severity indicates mild compartment severity. Lower KOOS-12 total scores indicate greater total pain, reduced function and quality of life and higher scores less total pain, better function and quality of life. The solid line represents the posterior median estimate obtained from the statistical model of the relationship between compartment severity and KOOS-12 total for a hypothetical average subject where the other predictors are held to their sample mean. The shaded area represents the approximate 90% (light areas) and the 50% (dark area) credible region, which indicates the uncertainty in the estimated relationships.

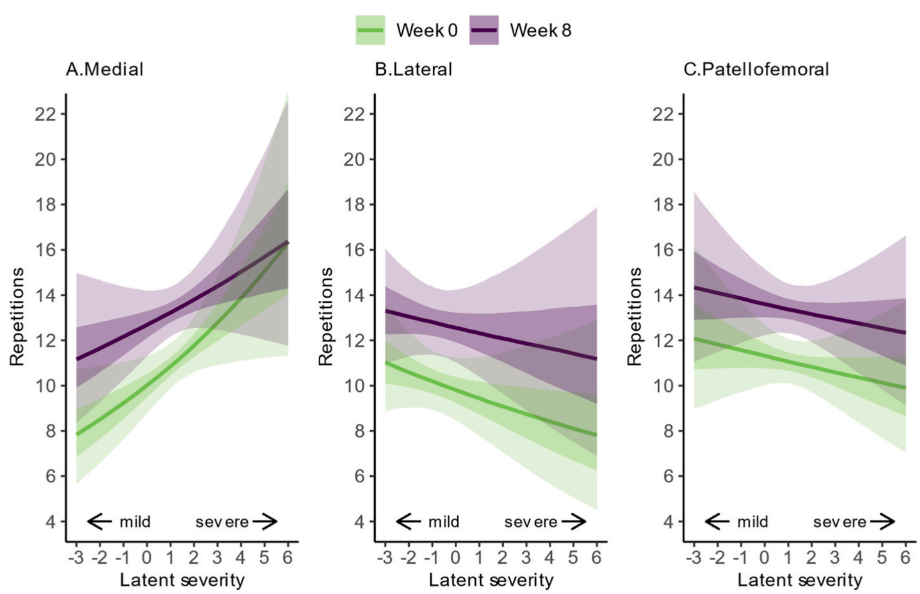

Fig. 4. 30-second chair stand repetitions and relationship with OA severity in the medial (A), lateral (B) and patellofemoral compartments (C) at baseline (week 0) and immediately following GLA:D® (week 8). Higher latent severity estimates (x-axis) indicate more severe compartment severity, and lower latent severity indicates mild compartment severity. The solid line represents the posterior median estimate obtained from the statistical model of the relationship between compartment severity and chair stand repetitions for a hypothetical average subject where the other predictors are held to their sample mean. The shaded area represents the approximate 90% (light areas) and the 50% (dark area) credible region, which indicates the uncertainty in the estimated relationships.

3.4.3. 30-second chair stand

Greater medial compartment severity was related to a reduced response as defined by less improvement in the number of chair stand repetitions (β: −0.04, 95% CrI: −0.13, 0.06) (Fig. 4A). This finding was difficult to interpret as greater medial OA severity was positively related to the number of chair stand repetitions at week 0. Less improvement could relate to the ceiling effect of this test, with less improvement seen in those with a high number of chair stand repetitions. Any level of OA severity in the lateral and PF compartments was related to similar improvements in chair stand repetitions at week 8 following GLA:D®. There was a negative relationship between lateral or PF compartment severity at week 0 and week 8; despite the similar improvements, those with greater severity started at week 0 and finished at week 8 with fewer chair stand repetitions (Fig. 4B and C).

3.4.4. Walking speed

For all medial compartment OA severity levels, similar improvements were found for walking speed at week 8 following GLA:D® (β:

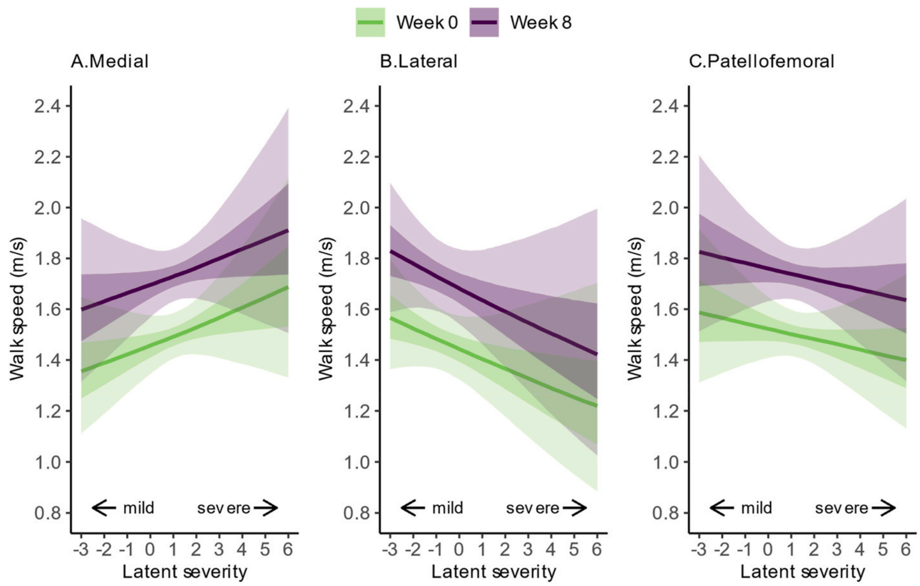

Fig. 5. Walking speed (m/s) and relationship with OA severity in the medial (A), lateral (B) and patellofemoral (C) compartments at baseline (week 0) and immediately following GLA:D® (week 8). Higher latent severity estimates (x-axis) indicate more severe compartment severity, and lower latent severity indicates lesser compartment severity. The solid line represents the posterior median estimate obtained from the statistical model of the relationship between compartment severity and walking speed for a hypothetical average subject where the other predictors are held to their sample mean. The shaded area represents the approximate 90% (light areas) and the 50% (dark area) credible region, which indicates the uncertainty in the estimated relationships.

−0.005, 95% CrI: −0.026, 0.016). There was a positive relationship between walking speed and medial compartment severity at both week 0 and week 8; despite the similar improvements, those with greater compartment severity started and finished with a faster walking speed (Fig. 5A). The reverse was true for the lateral and PF compartments. There was a negative relationship between walking speed and lateral or PF compartment severity at week 0 and week 8; despite the similar improvements, those with greater compartment severity started and finished with a slower walking speed (Fig. 5B and C).

4. Discussion

This study aimed to evaluate the relationship between radiological compartment severity, body weight, and an individual's response following a structured education and exercise therapy intervention (GLA:D®). No meaningful relationship was found between a person's body weight and their response to GLA:D® for any outcome measures but greater medial compartment severity was related to a poorer response at week 8 for pain (VAS 0–100), 30-s chair stands, and KOOS-12 total. All levels of body weight (50–150 kg) had similar improvements at week 8, and it is reasonable to expect the average improvements following GLA:D® for pain (−21 mm), KOOS-12 total (+15 points) and walking speed (+0.24 m/s). Heavier people, despite similar improvements, had slower walking speeds at both week 0 and week 8. This pattern was also observed for the lateral and PF compartments. For example, at week 0 and week 8, individuals with increased lateral or PF compartment severity performed fewer chair stand repetitions and had slower walking speeds, despite similar improvements.

The finding that heavier people had similar improvements to lighter people suggests that clinicians can reasonably expect improvements in pain and function following a structured education and exercise therapy program, regardless of a person's body weight. All levels of body weight showed similar improvements following GLA:D®, which were consistent with the MCIC reported in previous studies (see Table 2). Our findings align with studies that have examined the relationship between an individual's body weight or BMI and their response to exercise therapy (Holden et al., 2023; Quicke et al., 2020; Couldrick et al., 2023; Del-l'Isola et al., 2020). Holden et al. (2023) conducted an individual participant data meta-analysis (Holden et al., 2023) and found that baseline BMI did not moderate the effects of exercise therapy on pain (κ = 28 RCT, n = 3681) and function (κ = 28 RCT, n = 3636) in the short term in people with hip and knee OA.

The clinical implications of our findings for body weight are important due to the stigma often faced by individuals with obesity and the inherent bias of clinical practitioners, which may discourage participation in programs such as GLA:D® (Rubino et al., 2020; Godziuk and Hawker, 2024). It is important that clinicians communicate a positive message, emphasising that a person's body weight is not likely to influence their short-term response to exercise therapy programs like GLA:D®. Where appropriate, clinicians should support weight management strategies alongside exercise therapy as studies demonstrate a dose-dependent relationship between weight loss and reductions in pain reduction and improvements in function for individuals with knee OA (Messier et al., 2018; Panunzi et al., 2021). However, we note that our study participants did not lose weight following GLA:D®, and their outcomes were not attributed to weight loss.

In our study, heavier people had slower walking speeds and lower KOOS-12 values at both week 0 and week 8, despite similar absolute improvement. Similar study findings have been found for other patient characteristics (Pihl et al., 2022). A large cohort study of 24 513 individuals (Pihl et al., 2021) with hip or knee OA found that the number of comorbidities was not related to a worse or better outcome following a structured education and exercise therapy intervention, but those with comorbidities (compared to those without) had worse pain, function, and quality of life measures at baseline.

In our cohort, greater medial OA compartment OA severity was related to a poorer response for all outcomes except walking speed, where similar improvements (0.24 ms^{-1}, 90% CrI 0.19, 0.28) were observed across all severity levels (Fig. 5). This finding is interesting, considering previous studies have reported little relationship between radiological severity and outcomes following exercise therapy for knee OA (Holden et al., 2023; Couldrick et al., 2023; Clausen et al., 2023; Kudo et al., 2013; Tuna et al., 2022; Henriksen et al., 2023; Dissanayaka et al., 2023). However, these studies did not examine the severity of individual compartments and were mostly secondary data analyses from clinical trials. Studies have typically stratified the population based on

KL grade, for example, severe OA (KL IV) compared to mild to moderate (KL II and III) and then reported the difference in treatment effects between the two groups (Kent et al., 2020; Quicke et al., 2020; Kudo et al., 2013; Henriksen et al., 2023). We used a similar method to Holden et al. (2023), including an interaction term in our model between the predictor variable (OA compartment severity) and the intervention (week 0 and week 8). Holden et al. (2023) found that radiological OA severity, measured with the KL grading system, did not moderate the effect of exercise therapy on pain and function. Only four studies were included in this individual participant data meta-analysis, and two groups (KL > II and KL < II) were compared. No studies have examined individual compartment severity, a gap that our study addressed. We demonstrated a range of responses following the intervention, which were related to the compartment location and severity and the measured outcome.

A limitation of our study was the small sample size, which prevented us from examining relationships between combinations of joint compartments, such as the patellofemoral and medial compartments. However, a strength was the flexibility of our model because it allowed us to retain the information from each participant's joint compartment and prevented the costly loss of information that occurs with the practice of dichotomising KL grades (Senn, 2003) or excluding participants with PF or lateral compartment OA. Our two-stage modelling approach may introduce bias. The latent severity estimates from the cumulative link model were subject to measurement error, which will introduce attenuation bias when used as predictors. BMI and body weight have limitations as obesity measures, often overestimating or underestimating adiposity, providing little information about an individual's health status (Rubino et al., 2025). Further studies should include additional metrics like waist-to-hip ratio to better examine the relationship between weight, BMI, and treatment outcomes (Rubino et al., 2025).

A study strength was the high participant compliance with the GLA:D® program. GLA:D® is well documented in the literature and easily replicated (Ageberg et al., 2013). Bias may have been introduced as we recruited a narrow sample of participants, primarily from one private clinic (Burchett et al., 2020). Additionally, our study population were predominantly female (79%), motivated not to have surgery and had low pain catastrophising and brief fear of movement scores at baseline which may influence the generalisability of our results. Due to our study design and lack of a control group, causation cannot be established, and improvements might relate to regression to the mean (Barnett et al., 2005). However, the interpretation is strengthened as the observed changes in pain and functional outcomes immediately following GLA:D® were consistent with effect sizes observed in previous studies (Barton et al., 2021; Roos et al., 2021). Future studies could alleviate some of this problem by measuring at multiple time points or including a randomly allocated control group if conducting an RCT.

5. Conclusion

Our findings suggest body weight may have little influence on a person's response to a structured education and exercise therapy program for knee OA. People with more severe medial compartment OA had a reduced improvement in pain (VAS 0–100), 30-second chair stands, and KOOS-12. There were small differences in responses for the lateral and PF compartment severity for pain (VAS 0–100) and KOOS-12 total. Clinicians can be encouraged that body weight or OA severity in all compartments may not always influence the person's response. Given the challenges of engaging individuals with knee OA in first-line interventions, all people should be encouraged to participate in exercise therapy, OA education, and weight management where appropriate before considering joint replacement surgery.

CRediT authorship contribution statement

Jacqui M. Couldrick: Writing – review & editing, Writing – original draft, Visualization, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Andrew P. Woodward:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Software, Methodology, Formal analysis, Data curation, Conceptualization. **Joseph T. Lynch:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization. **Nicholas A.T. Brown:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. **Christian J. Barton:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. **Jennie M. Scarvell:** Writing – review & editing, Writing – original draft, Supervision, Resources, Project administration, Methodology, Formal analysis, Conceptualization.

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Declaration of competing interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.msksp.2025.103307.

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