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Moderators and Mediators of Pain and Function Outcomes in a New Service Delivery Model for Management of Knee Osteoarthritis in Primary Care: Secondary Exploratory Analysis of a Randomized Controlled Trial

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Objective. Our objective was to explore moderators and mediators influenced changes in pain and function in people with knee osteoarthritis (OA) receiving a new model of primary care service delivery (Optimizing Primary Care Management of Knee Osteoarthritis [PARTNER]), at 12 months (ACTRN: 12617001595303).

Methods. This was a secondary analyses of a cluster randomized controlled trial comparing PARTNER to the usual general practitioner–delivered care (n = 217 patients: 112 PARTNER patients and 105 usual care patients) on knee pain and function. Pain was measured using a numerical rating scale (range 0–10, with a higher score indicating more severe pain), and function was measured using the function subscale of the Knee Injury and Osteoarthritis Outcome Score (range 0–100, with a higher score indicating better outcome). Baseline variables selected as potential moderators included age, sex, body mass index, pain duration, residential state, living arrangements, education, employment status, back pain, and other joint issues. Mediation variables included physical activity, fear of movement, pain catastrophizing, OA self-management, self-efficacy, sleep, fatigue, quality of life, depression, and satisfaction.

Results. For change in pain, no moderators influenced the intervention effect. However, age moderated change in function, with intervention participants <50 years demonstrating greater functional improvement than their older counterparts, compared to the control group (50–69 years: coefficient −32.88, 95% confidence interval [CI] −45.02 to −20.74; ≥70 years: coefficient −24.28, 95% CI −36.53 to −12.02). Mediation analysis revealed significant indirect effects of overall, treatment-related, and symptom-related satisfaction on mean change in pain (−0.10, −0.06, and −0.08, respectively) and function (0.09, 0.05, and 0.07, respectively).

Conclusion. Younger PARTNER participants showed greater functional improvement compared to older age groups (moderating effect). Additionally, indirect mediation effects suggest increased satisfaction across the three satisfaction domains led to reduced knee pain and enhanced function.

INTRODUCTION

Osteoarthritis (OA), a common disabling joint disease, significantly impacts individuals and societies worldwide.[1] It is the most prevalent form of arthritis, affecting millions globally and placing a substantial burden on health care systems. The prevalence of OA, particularly knee OA, is universally increasing, likely due to escalating global obesity rates, aging populations, and physical inactivity.[1–4] Knee OA accounts for approximately 60% of the worldwide burden of OA.[2,4] The core recommended approaches to OA management are lifestyle and behavioral treatments, including patient education for self-management, therapeutic

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SIGNIFICANCE & INNOVATIONS

- This study explored factors influencing knee pain and function in people with knee osteoarthritis (OA) following the new Optimizing Primary Care Management of Knee Osteoarthritis (PARTNER) model of service delivery.
- Participant demographic variables did not exhibit any moderating effect on the PARTNER intervention's ability to change pain in people with knee OA.
- Age was a moderator of change in function following the PARTNER intervention, with younger people in the PARTNER group demonstrating greater functional improvements than older people, when compared to usual general practitioner–delivered care.
- The majority of the impacts of the PARTNER model of service delivery on pain and function were mediated through participants' overall, treatment-related, and symptom-related satisfaction levels, highlighting the importance of ensuring responsive, person-centered, and acceptable care in people with knee OA.

exercise and physical activity, and weight loss (if required).[5–7] These treatments can be supported by the judicious use of pharmacologic interventions for additional pain management, as necessary. However, the effective delivery of these interventions in real-world care has encountered challenges in implementation because of a lack of knowledge and confidence by health professionals to deliver this type of care, a lack of services in the community to support the lifestyle and behavioral changes needed, and health system structures such as financing models.[8–10]

The new Optimizing Primary Care Management of Knee Osteoarthritis (PARTNER) model of service delivery was developed to bridge this gap between the recommended evidence-based OA care and its actual delivery in Australian primary care, using a telehealth approach.[11] The PARTNER model aimed to enhance outcomes in people with OA by improving general practitioner (GP) knowledge on current evidence-based OA care, and then providing eligible participants with knee OA access to a centralized multidisciplinary "care support team" (CST). The role of the CST was to remotely support participants in their OA self-management for 12 months. The PARTNER model was tested against usual GP care in a cluster randomized controlled trial (cRCT)[11,12] to compare changes in the two primary outcomes of self-reported knee pain and knee function at 12 months. The primary results showed that although the PARTNER model showed significant improvements in knee pain and function compared to the usual GP care, the magnitude of improvement was not clinically meaningful for pain and was uncertain for function.[13]

To understand the cRCT outcomes and their consequences and implications for research and practice more comprehensively, it is important to examine what other factors may have affected the primary outcomes. Identifying potential moderators of the PARTNER primary outcomes, for example, would enable us to concentrate and allocate resources more effectively to the subset of people with knee OA most likely to benefit from the model, particularly when resources are constrained. Moderators describe the participants' baseline characteristics that interact with the treatment to influence clinical outcomes, thus revealing the populations or situations in which the treatment may be most effective, particularly when an unexpectedly weak or inconsistent relationship exists between an intervention and an outcome.[14,15] On the other hand, mediators are variables through which the intervention affects the outcome (Supplementary Figure 1). Considering potential mediators of the intervention can provide insights into why and how an intervention operates[14] and provide a basis to refine the PARTNER model to enhance effectiveness. Therefore, this study sought to identify the moderators and mediators of the effect of the PARTNER model of service delivery on changes in knee pain and function at 12 months, compared to usual GP care.

PATIENTS AND METHODS

Study design. This is a secondary analysis of data from the PARTNER study, a pragmatic, two-arm cRCT conducted within general practices in New South Wales (NSW) and Victoria, Australia (September 2018 to December 2020). Participant recruitment was finalized in December 2019 before the onset of COVID-19, and there was no impact of the pandemic on recruitment, randomization, or baseline data collection. Written informed consent was obtained from the general practices, GPs, and patient participants. The study protocol was approved by The

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University of Sydney Human Research Ethics Committee (2016/959), prospectively registered (ACTRN: 12617001595303) and published.[11] The primary results were published[13] in 2023. This article is reported in accordance with the A Guideline for Reporting Mediation Analyses statement.[16]

Study participants. A total of 38 general practices, 71 GPs, and 217 people with knee OA (112 people in the PARTNER group and 105 people in the usual care group) were enrolled in the study,[13] although the intended sample size was 44 general practices and 572 people with OA. Recruitment was stopped early due to a delayed start, slow initial recruitment, and our funder's time frame. Eligibility criteria for participant inclusion were age 45 years or older, experiencing activity-related knee pain for a duration exceeding three months, and reporting moderate to very severe pain of 4 or more on an 11-point numerical rating scale (NRS) (higher scores indicated more severe pain). Exclusion criteria were an inability to consent in English, limited mobility requiring the use of a wheelchair or scooter, a history of (or had been booked for) knee replacement surgery targeting the specified knee, or the presence of a significant health condition affecting participation.

Randomization was performed at the level of the general practice. Participating practices were assigned to either the PARTNER group or usual care group, using a 1:1 allocation ratio in random permuted blocks and stratified by geographic location (metropolitan or regional and rural) and practice size (<4 GPs and ≥4 GPs).

The PARTNER intervention and the usual care group. Full details of the PARTNER model and its development were published elsewhere.[11,12,17] The PARTNER model intervention had a dual focus on the person with OA and their GPs. Intervention group GPs were given the opportunity to update their knowledge regarding the management of OA through a suite of online professional development activities. After visiting their GP for a knee pain–specific consultation, participants in the PARTNER arm were referred to the multidisciplinary CST. The primary role of the CST team was to offer guidance on OA management and behavior change support and to empower people to effectively self-manage their knee OA. The CST consultations were delivered remotely (eg, phone, email, mail, short message service) according to the preferences of the participants. The primary focus of the PARTNER intervention was to encourage greater uptake of therapeutic exercise (leg strengthening), physical activity, and weight loss (if required). Participants had the option of undertaking additional secondary interventions according to clinical need, including online cognitive behavioral therapy courses on pain coping,[18] sleep,[19] and depression[20] if the participant met the predetermined criteria for stepping up care,[11] and the topic areas were identified as a priority action by the person. In contrast, GPs in the usual care group did not receive any specific OA training, and their patients solely received the GP's usual care.[11]

Data collection and primary outcome variables. Data were collected online via the REDCap software or through hardcopy surveys at baseline, 6 months, and 12 months. For this analysis, data were extracted from the baseline and 12-month assessments.[13] The primary cRCT outcome variables were change at 12 months in self-reported knee pain (over last week, 11-point NRS, range from 0 to 10, higher score = worse pain) and knee function (previous week, activities of daily living [ADL] subscale of the Knee Injury and Osteoarthritis Outcome Score [KOOS], range from 0 to 100, higher score = better function).[11,17]

Primary outcomes of the cRCT. At 12 months, the PARTNER model demonstrated statistically significant reductions in pain (0.8 of 10 points, 95% confidence interval [CI] 0.2–1.4) and improvements in knee function (6.5 of 100 points, 95% CI 2.3–10.7) compared to usual care.[13] Despite the reported improvements, this change did not reach our threshold for a minimal clinically important difference, which was set at ≥1.8 NRS points for pain and ≥8 of 100 KOOS for ADL function.[13]

Potential moderators and mediators. Potential moderators were identified a priori,[11] based on clinical or theoretical rationale[21] and previous evidence associated with individual outcomes of complex OA interventions that existed at the time.[8] An additional moderator, state of residence, was added post hoc to examine if the difference in COVID-19 lockdowns in each state influenced the results.[22] Eleven baseline variables were ultimately selected (Supplementary Table 1). Categorization of the baseline variables for the moderating effect analysis was undertaken on a pragmatic approach based on the existing literature and the relative frequency of responses. Body mass index (BMI) was analyzed as both a categorical and continuous variable to enable a more detailed analysis of the results. The final variables and categories were age (<50 years, 50–69 years, and ≥70 years), sex (male or female), BMI (healthy [18.5–24.9], overweight [25–29.9], or obese [≥30]), pain duration (≤10 years or >10 years), state of residence (NSW or Victoria), living arrangements (alone or with others), educational status (with or without tertiary education), employment status (part-time job or other), inability to work due to knee problems or other health issues (yes or no), coexisting back pain (yes or no), and other coexisting joint issues (yes or no) (Supplementary Table 1).

Candidate mediators were variables measured at baseline and 12 months. Similar to the moderator selection, these variables were identified a priori,[11] and based on existing evidence at the time,[8] and their clinical and theoretical potential to influence the primary outcomes in a complex intervention.[23] The included candidate mediators, their measurement tools, and parameters are detailed in Supplementary Table 1. These included

12-month changes in self-reported physical activity, fear of movement, pain catastrophizing, ability to manage their condition, arthritis self-efficacy, sleep quality, fatigue, health-related quality of life, and depression as well as satisfaction in three domains (global, with treatment, and with change in symptoms).

Statistical analysis. All statistical analyses were conducted using Stata version 17.0 (StataCorp). The data were summarized as means, SDs (symmetric normal data), medians, ranges (skewed or ordinal data), and proportions with 95% CIs. The sample size calculations for the main trial have been reported in the main results article.[13] We did not conduct power analyses specifically for the mediation analyses. However, the sample size was comparable or slightly lower than similar studies conducted moderation and mediation analyses.[24,25]

The moderation analysis was undertaken using a general linear model to test the effect of treatment on the change in knee pain and function. The model specification included the main effects of treatment allocation (PARTNER vs usual care group), moderator variables, and their interaction effect. The model effects were adjusted for baseline pain and function scores. A univariate analysis was performed on individual candidate moderators, with a multivariable analysis undertaken if more than one candidate. The coefficient presented indicates the mean difference in the outcome (knee pain or function) between two categories of a variable after interaction with the PARTNER intervention. When the moderator was demonstrated as having a significant coefficient, it was presented as being in the 95% CI.

The mediation analysis was based on the approach done by Zhao et al[26] and involved decomposition of the total effect into the indirect effect (ie, the average causal mediation effect of treatment allocation on change in pain or function score being mediated by the variable being tested) and average direct effect (ie, the effect of treatment allocation on change in pain or function that is not passed through the mediator) (Supplementary Figure 1). Complete case data were used for the mediation analysis and performed using "mediate" and "sem" packages in Stata. The test for the significance of the mediation effect was based on a sampling distribution derived from 1,000 bootstrapping replications. Models were adjusted for baseline pain and function scores. The standardized direct, indirect, and total effects are reported along with 95% CIs and associated *P* values. Data and the analytical code are available from the authors on request.

RESULTS

Sample characteristics. Two hundred and seventeen participants had baseline data available for the moderator analysis, including 112 PARTNER participants and 105 usual care participants (Figure 1 and Supplementary Table 2). For the mediation analysis, data were available for 173 to 183 participants at 12 months, depending on the outcome measured (Supplementary Table 1). Baseline participant characteristics were similar between groups, with the exception of the number of participants reporting a BMI of ≥27 (usual care 66% vs PARTNER 47%) and those reporting back pain (usual care 30% vs

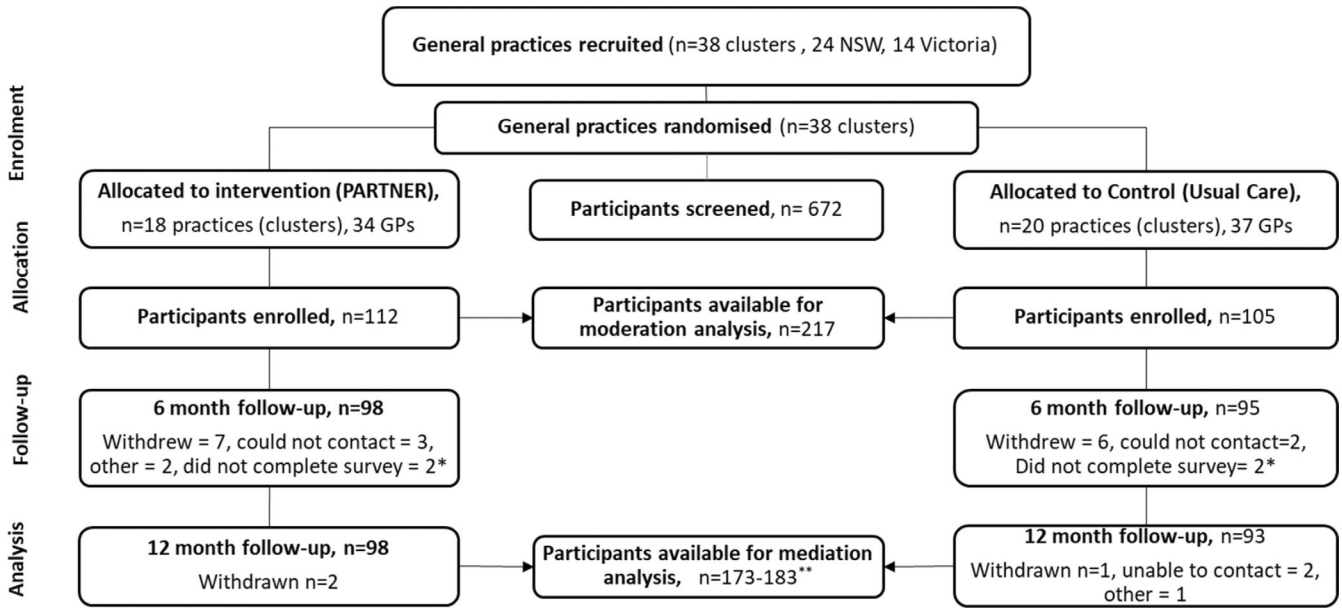

Figure 1. Consolidated Standards of Reporting Trials diagram of the PARTNER study. Participant flow through the cluster randomized controlled trial. Online screening was considered incomplete if patients did not include their contact details in the online screening tool. *Did not complete the 6-month survey but did complete the 12-month survey. **Vary depending on the outcome variable between the range. GP, general practitioner; NSW, New South Wales; PARTNER, Optimizing Primary Care Management of Knee Osteoarthritis.

PARTNER 46%). Most participants identified as female (63% PARTNER vs 57% usual care) and were aged between 50 and 69 years (both groups).

Moderation analysis. *Knee pain.* The univariate main effects and interaction effects with treatment allocation for each candidate moderator are shown in Tables 1 and 2. There was no evidence that any baseline characteristic moderated change in knee pain at 12 months (Table 1).

Knee function. Age emerged as the only moderator of change in knee function (Table 2 and Supplementary Figure 2). There was a significant interaction found between age band and knee function. It was found that the treatment effect as measured by the mean difference in KOOS ADL score between PARTNER and usual care groups for participants aged <50 years was significantly higher as compared with older age groups (Supplementary Figure 2 and Table 2). In detail, the improvement in knee function for participants aged 50 to 69 years was 32.88 points lower (95% CI 20.74–45.02) than for those under 50 years. Similarly, for participants aged 70 years and older, the improvement was 24.28 points lower (95% CI 12.02–36.53) compared to the <50 years group.

Mediation analysis. *Knee pain.* We only observed a mediating effect for variables linked to the three satisfaction measures (Tables 3 and 4). The results showed significant indirect effects of global satisfaction (–0.10, 95% CI –0.15 to –0.07), satisfaction with treatment (–0.06, 95% CI –0.10 to –0.02), and satisfaction with knee symptoms (–0.08, 95% CI –0.12 to –0.05), compared to usual care. The corresponding direct effects are shown in Table 3.

Knee function. When considering change in knee function, the three satisfaction measures showed a more pronounced influence through indirect effects on the PARTNER scores compared to the usual care group. Specifically, the effects were global satisfaction (0.09, 95% CI 0.06–0.14), satisfaction with treatment

Table 1. Univariate regression model for moderators of change in pain scores (range 0–10, higher = worse pain) from baseline to 12 months*

Characteristic	Main effect coefficient	*P* value	Interaction effect coefficient	*P* value
Age groups, y				
<50	0[a]		0[a]	
50–69	0.00 (−1.14 to 1.14)	1.000	1.95 (−0.02 to 3.92)	0.053
≥70	0.02 (−1.20 to 1.24)	0.970	1.55 (−0.43 to 3.52)	0.125
Sex				
Female	0[a]		0[a]	
Male	0.03 (−0.53 to 0.59)	0.924	−0.33 (−1.15 to 0.50)	0.440
BMI[b]	0.08 (0.02 to 0.13)	0.008	0.01 (−0.07 to 0.09)	0.833
18.5–24.9	0[a]		0[a]	
25–29.9	0.22 (−0.47 to 0.91)	0.527	0.05 (−0.94 to 1.03)	0.929
≥30	0.93 (0.19 to 1.68)	0.014	0.01 (−1.07 to 1.09)	0.987
Pain duration, y				
≤10	0[a]		0[a]	
>10	0.68 (−0.02 to 1.37)	0.057	−0.28 (−1.24 to 0.68)	0.569
State of residence				
NSW	0[a]		0[a]	
Victoria	−0.35 (−1.10 to 0.40)	0.363	0.25 (−0.73 to 1.23)	0.620
Living arrangements				
Living with others	0[a]		0[a]	
Living alone	0.76 (0.10 to 1.41)	0.024	−0.54 (−1.51 to 0.44)	0.281
Tertiary education				
No	0[a]		0[a]	
Yes	−0.66 (−1.24 to −0.09)	0.024	−0.16 (−0.99 to 0.67)	0.712
Employment as a part-time job				
No	0[a]		0[a]	
Yes	0.26 (−0.67 to 1.19)	0.586	−0.50 (−1.68 to 0.68)	0.409
Inability to work				
No	0[a]		0[a]	
Yes	1.33 (0.53 to 2.14)	0.001	−0.92 (−2.37 to 0.53)	0.215
Other joint issues				
No	0[a]		0[a]	
Yes	−0.08 (−0.68 to 0.51)	0.784	−0.06 (−1.19 to 1.07)	0.916
Back pain				
No	0[a]		0[a]	
Yes	−0.24 (−0.82 to 0.33)	0.407	0.07 (−0.74 to 0.88)	0.860

* BMI, body mass index; NSW, New South Wales.
[a] Reference group.
[b] BMI was calculated as both a continuous and a categorical variable.

Table 2. Univariate regression model for moderators of change in function scores (range 0–100, higher = better outcome) from baseline to 12 months*

Characteristic	Main effect coefficient	*P* value	Interaction effect coefficient	*P* value
Age groups, y				
<50	0[a]		0[a]	
50–69	12.30 (4.28 to 20.32)	0.003	−32.88 (−45.02 to −20.74)	<0.001
≥70	6.84 (−1.85 to 15.53)	0.123	−24.28 (−36.53 to −12.02)	<0.001
Sex				
Female	0[a]		0[a]	
Male	0.03 (−0.53 to 0.59)	0.924	−0.33 (−1.15 to 0.50)	0.440
BMI[b]	−0.76 (−1.30 to −0.21)	0.007	−0.32 (−0.98 to 0.34)	0.346
18.5–24.9	0[a]		0[a]	
25–29.9	−3.49 (−9.89 to 2.92)	0.286	4.33 (−3.93 to 12.59)	0.304
≥30	−7.96 (−15.95 to 0.04)	0.051	−4.17 (−14.08 to 5.74)	0.410
Pain duration, y				
≤10	0[a]		0[a]	
>10	−1.02 (−7.97 to 5.94)	0.774	1.87 (−7.28 to 11.01)	0.689
State of residence				
NSW	0[a]		0[a]	
Victoria	2.35 (−3.85 to 8.55)	0.458	−1.967 (−9.90 to 5.96)	0.627
Living arrangements				
Living with others	0[a]		0[a]	
Living alone	−2.98 (−8.90 to 2.93)	0.323	−3.00 (−11.29 to 5.29)	0.478
Tertiary education				
No	0[a]		0[a]	
Yes	7.01 (1.44 to 12.58)	0.014	−0.20 (−7.62 to 7.22)	0.958
Employment as a part-time job				
No	0[a]		0[a]	
Yes	5.24 (−1.57 to 12.06)	0.131	−2.00 (−10.96 to 6.95)	0.661
Inability to work				
No	0[a]		0[a]	
Yes	−20.29 (−26.02 to −14.57)	<0.001	−1.54 (−12.50 to 9.43)	0.784
Other joint issues				
No	0[a]		0[a]	
Yes	5.72 (0.34 to 11.10)	0.037	−3.18 (−11.97 to 5.61)	0.478
Back pain				
No	0[a]		0[a]	
Yes	−0.98 (−7.02 to 5.06)	0.750	−0.65 (−8.36 to 7.06)	0.868

* BMI, body mass index; NSW, New South Wales.
[a] Reference group.
[b] BMI was calculated as both a continuous and a categorical variable.

Table 3. Standardized estimates of the total, direct, and indirect effects of treatment allocation on change in pain scores at 12 months for each potential mediator considered for full mediation analysis*

Variables and measurement tools	Total effect	Direct effect	Indirect effect (95% CI)	*P* value
Physical activity levels (PASE)	−0.03	−0.04	0.00 (−0.01 to 0.01)	0.800
Fear of movement (BFMS)	−0.04	−0.05	0.01 (−0.03 to 0.04)	0.713
Pain catastrophizing (PCS)	−0.04	−0.03	−0.01 (−0.05 to 0.03)	0.592
Ability to manage their condition (EC-17)	0.03	0.03	−0.00 (−0.02 to 0.00)	0.274
Arthritis self-efficacy (ASES)	0.03	0.02	−0.01 (−0.04 to 0.01)	0.239
Sleep quality (PROMIS adult Sleep-Related Impairment SF 8a)	0.04	0.04	0.00 (−0.02 to 0.03)	0.777
Health-related quality of life (AQoL-8D)	0.03	0.02	−0.01 (−0.04 to 0.02)	0.410
Fatigue (PROMIS Fatigue SF 8a)	0.04	0.04	0.01 (−0.02 to 0.03)	0.588
Depression (PHQ-9)	0.03	0.03	−0.00 (−0.03 to 0.02)	0.873
Satisfaction, global (7-point rating scale)	−0.05	0.05	−0.10 (−0.15 to −0.01)	<0.001
Satisfaction with treatment (7-point rating scale)	−0.06	0.00	−0.06 (−0.10 to −0.02)	0.003
Satisfaction with change in symptoms (7-point rating scale)	−0.06	0.02	−0.08 (−0.12 to −0.05)	<0.001

* AQoL-8D, Assessment of Quality of Life 8 dimensions; ASES, Arthritis Self-Efficacy Scale; BFMS, Brief Fear of Movement Scale for Osteoarthritis; CI, confidence interval; EC-17, Effective Consumer Scale; PASE, Physical Activity Scale for the Elderly; PCS, Pain Catastrophizing Scale; PHQ-9, Patient Health Questionnaire 9; PROMIS, Patient-Reported Outcomes Measurement Information System; SF, Short Form.

Table 4. Standardized estimates of the total, direct, and indirect effects of treatment allocation on change in function scores at 12 months for each potential mediator considered for full mediation analysis*

Variables and measurement tools	Total effect	Direct effect	Indirect effect(95% CI)	*P* value
Physical activity levels (PASE)	0.01	0.01	−0.00 (−0.02 to 0.01)	0.736
Fear of movement (BFMS)	0.00	0.01	−0.00 (−0.05 to 0.03)	0.715
Pain catastrophizing (PCS)	0.00	−0.01	0.01 (−0.03 to 0.06)	0.619
Ability to manage their condition (EC-17)	0.00	−0.02	0.02 (−0.00 to 0.04)	0.087
Arthritis self-efficacy (ASES)	0.00	−0.03	0.03 (−0.02 to 0.07)	0.215
Sleep quality (PROMIS adult Sleep-Related Impairment SF 8a)	0.00	0.01	−0.00 (−0.04 to 0.03)	0.788
Health-related quality of life (AQoL-8D)	0.01	−0.01	0.02 (−0.03 to 0.07)	0.394
Fatigue (PROMIS Fatigue SF 8a)	0.00	0.02	−0.01 (−0.05 to 0.03)	0.579
Depression (PHQ-9)	0.00	0.00	0.00 (−0.03 to 0.04)	0.847
Satisfaction, global (7-point rating scale)	0.03	−0.06	0.09 (0.06 to 0.14)	<0.001
Satisfaction with treatment (7-point rating scale)	0.03	−0.01	0.05 (0.01 to 0.09)	0.011
Satisfaction with change in symptoms (7-point rating scale)	0.03	−0.04	0.07 (0.04 to 0.11)	<0.001

* AQoL-8D, Assessment of Quality of Life 8 dimensions; ASES, Arthritis Self-Efficacy Scale; BFMS, Brief Fear of Movement Scale for Osteoarthritis; CI, confidence interval; EC-17, Effective Consumer Scale; PASE, Physical Activity Scale for the Elderly; PCS, Pain Catastrophizing Scale; PHQ-9, Patient Health Questionnaire 9; PROMIS, Patient-Reported Outcomes Measurement Information System; SF, Short Form.

(0.05, 95% CI 0.01–0.09), and satisfaction with change in knee symptoms (0.07, 95% CI 0.04–0.11). The corresponding direct effects are shown in Table 4.

The proportion of indirect effects to direct effects and total effects are shown in Supplementary Table 3. The proportion of indirect effects to direct effects of these three satisfaction variables was always greater than one and at least 96% of the total effects of the PARTNER intervention were mediated by these satisfaction variables (Supplementary Table 3).

DISCUSSION

This study explored the potential moderators and mediators of the effects of the PARTNER model of service delivery, a telehealth service for people with knee OA, on changes in knee pain and knee function at 12 months. We found some evidence that age may moderate the effects of physical function, particularly for younger individuals, and that satisfaction may mediate changes in both knee pain and function.

In our analysis, only age emerged as a moderator of change in knee function, highlighting that adults aged less than 50 years were more likely to experience improvement in knee function with the PARTNER model than older individuals compared to the usual care group. Our results were in contrary to previous studies, in which age has not been shown to moderate OA interventions in similar populations.[25,27,28] However, our observation concerning improved responses in younger people may reflect their willingness to engage more with telehealth, either due to greater familiarity with the technology or ease of convenience of access. This is supported by an Australian cross-sectional study, which showed younger participants with hip or knee OA preferred to use mailed information packs, online education programs, and telephone helplines more than other methods due to perceived usefulness and accessibility.[29] Moreover, a UK-based study on people with psychosis showed that the younger age group had greater uptake of remotely delivered therapy, whereas older people preferred to be seen in person.[30] The use of e-consultations in primary care has also been observed to be less frequent among older people,[31] although it appears that the COVID-19 pandemic has shifted attitudes toward remotely delivered services in health, including in musculoskeletal conditions, with great satisfaction in all age groups.[32,33]

Our observation may underscore the potential utility of specifically targeting the telehealth model to younger adults, or by improving the accessibility and usability of the telehealth model to better suit older individuals. For example, this intervention was delivered only by phone. Provision of video conferencing capacity and real-time feedback of exercise in particular may improve older participants' engagement with the program, given that a recent trial in knee OA showed that video consultations with a physiotherapist for exercise, education, and physical activity were noninferior to in-person care.[34] An alternative hypothesis is that our intervention could not comprehensively address all six critical domains of intrinsic capacity (ie, locomotor capacity, psychologic capacity, cognitive capacity, hearing capacity, visual capacity, and vitality) as defined by the World Health Organization, which would be more likely to decline in older participants.[35,36] In this context, the older participants may, on average, have presented with more complex health states manifesting across intrinsic capacity domains and may be less likely to experience benefit from an intervention that targeted only OA. However, because the number of participants in the younger age group was limited (4% of all participants and 4.5% of the PARTNER group were aged <50 years), the clinical significance of our finding remains inconclusive and needs to be confirmed by further research.

Our exploration yielded no significant moderating effects of other examined parameters including sex, BMI, pain duration, state of residence, living arrangements, education or employment status, and the presence of back pain or issues in other joints. These findings are supported by two systematic reviews that found no moderating effect of age, BMI, education, pain duration, pain elsewhere, or comorbidities on changes in pain or function with exercise.[25,28] Recent registry-based data also identified that individuals with knee OA and lumbar spinal stenosis did not experience poorer outcomes of a meaningful clinical magnitude from an exercise and education intervention, compared to people with knee OA and no lumbar spinal stenosis.[37] The PARTNER model, however, is a complex multilayered approach to care, with a focus on more than just exercise, but our results are also in agreement with a secondary analysis of an RCT that evaluated a multifaceted, internet-delivered program for people with knee OA and similarly did not find any moderators at nine months.[27,38] An alternative reason for the failure to uncover more moderators could be due to having fewer than expected participants, which led to the study being underpowered. As such, the possible moderating effects of some variables may be unrecognizable.

When we examined potential mediators of the PARTNER intervention, our results showed that participant satisfaction measures (satisfaction with treatment, satisfaction with change in symptoms, and global satisfaction) demonstrated a significant mediation effect on both knee pain and knee function, and there was no other evidence of mediating effects. In other words, the pain reduction and function improvement seen with the PARTNER model mainly resulted from a higher level of satisfaction in the PARTNER participants or vice versa. The direction of causality remains unknown until proven by another clinical trial. Although participants were more satisfied with the PARTNER model than the usual care group, the overall number of participants reporting moderate to extreme satisfaction with the model (ie, score of 6 or 7 on a 7-point scale with terminal descriptors of 1 = extremely dissatisfied to 7 = extremely satisfied) was only[13] 30%. Participant satisfaction results may have been influenced by COVID-19, and the general well-being of participants during this time. Unfortunately, COVID-19 also impacted on our ability to undertake qualitative interviews to explore participant experiences with the new model, and we rely solely on our survey scores to address this question. This observation underscores the substantial influence of psychologic factors and context, particularly participant satisfaction, and emphasizes the importance of evaluation and addressing these factors in OA management strategies.

Contrary to our initial hypotheses, we did not find any mediation effect by changes in physical activity levels, fear of movement, pain catastrophizing, ability to manage their condition, arthritis self-efficacy, sleep quality, fatigue, health-related quality of life, or depression. Our findings were consistent with a secondary analysis of an RCT in which there was no association between physical activity levels and future pain or physical function during an exercise intervention for older adults with knee pain.[39] A 2023 systematic review aimed at finding potential mediators of the effects of diet and exercise on improvement of pain and function in people with OA, found some evidence of mediation effect with changes in body weight and self-efficacy.[24] In addition, a secondary analysis of an RCT identified changes in pain beliefs as a potential mediator of improvements in OA clinical outcome with exercise and manual therapy in people with hip and knee OA.[40] However, our results are not consistent with these studies. Similar to the moderators, it is feasible the mediating effects may be unrecognized because of the power of the study.

Alternatively, the results may have been influenced by low sensitivity of the measurement tools and inability to detect a significant mediation effect, or that the intervention was not powerful enough for a mediation effect. Fidelity to the intervention may also have impacted the results. Although participants in the PARTNER arm self-reported good adherence in undertaking physical activity and exercise (both 79% at 12 months) and lower adherence to weight loss (48% at 12 months),[13] we did not have any objective measures to confirm these data. The participants recruited also had a mean BMI of 28.8, which is at the lower end of what we typically report in our clinical trials in Australia (eg, >30).[34,41,42] Many of those who were overweight or obese potentially did not achieve the weight-loss gains needed to derive benefit (ie, >7% body weight).[13] Similarly, we did not specifically recruit people with poor self-efficacy or high fear of movement, and thus the intervention was not impacted by these factors.

The notable strengths of this study were its design as a secondary analysis of a robust RCT. We included a comprehensive list of potential moderators and mediators, derived from the evidence at the time, which were mostly determined a priori. However, certain limitations warrant consideration. It is plausible that some nonsignificant interactions could be attributed to statistical power constraints rather than an actual absence of effect. The main PARTNER study was underpowered, and these analyses were all exploratory; hence, prudence dictates that further research be undertaken to validate our findings. Furthermore, the multifaceted nature of the PARTNER model complicates the identification of specific treatment components interacting with each moderator or mediator variable, thus engendering a challenge in establishing causal relationships. There is also the risk of violation by unidentified confounding variables. Finally, as the recruited PARTNER participants had limited cultural and ethnic diversity, these findings cannot be applied universally.

In conclusion, our study revealed that the PARTNER model's impact on people with knee OA may be moderated by age, particularly with individuals younger than 50 years old showing greater functional improvement than older individuals. Moreover, heightened patient satisfaction, including global satisfaction, satisfaction with treatment, and satisfaction with symptoms, mediated changes in pain and function in patients with knee OA in the PARTNER group compared to participants undertaking usual GP care.

AUTHOR CONTRIBUTIONS

All authors contributed to at least one of the following manuscript preparation roles: conceptualization AND/OR methodology, software, investigation, formal analysis, data curation, visualization, and validation AND drafting or reviewing/editing the final draft. As corresponding author, Dr Hunter confirms that all authors have provided the final approval of the version to be published and takes responsibility for the affirmations regarding article submission (eg, not under consideration by another journal), the integrity of the data presented, and the statements regarding compliance with institutional review board/Declaration of Helsinki requirements.

ROLE OF THE STUDY SPONSOR

Medibank Better Health Foundation, Bupa Australia, and Medibank Private had no role in the study design or in the collection, analysis, or interpretation of the data, the writing of the manuscript, or the decision to submit the manuscript for publication. Publication of this article was not contingent upon approval by Medibank Better Health Foundation, Bupa Australia, or Medibank Private.

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