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Phenotype-Guided Rehabilitation Versus Standard Physiotherapy for Symptomatic Knee Osteoarthritis: A Pragmatic Randomized Controlled Trial

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ABSTRACT

Background: Knee osteoarthritis is a heterogeneous condition in which conventional rehabilitation yields variable outcomes, partly due to differences in dominant pain mechanisms, biomechanical impairments, and metabolic contributors; clinically applicable phenotype-based approaches may improve the effectiveness of conservative care. Objective: To compare the effectiveness of phenotype-guided rehabilitation versus standard physiotherapy on pain and functional outcomes in individuals with symptomatic knee osteoarthritis. Methods: In a pragmatic, assessor-blinded randomized controlled trial conducted at a tertiary care rehabilitation center, 42 adults with symptomatic knee osteoarthritis were randomized to phenotype-guided rehabilitation or standard physiotherapy for 8–12 weeks. Participants in the intervention arm received rehabilitation matched to their dominant clinical phenotype (pain-dominant, strength/biomechanical deficit–dominant, or obesity/metabolic), while controls received standard knee osteoarthritis physiotherapy. The primary outcome was knee pain assessed using WOMAC or KOOS pain scores. Secondary outcomes included WOMAC function, numeric pain rating scale, 6-minute walk test, Timed Up and Go, adherence, and analgesic use. Results: Phenotype-guided rehabilitation resulted in significantly greater improvements in pain and function compared with standard care, with larger reductions in WOMAC pain (Δ −1.85, p=0.003), WOMAC function (Δ −6.02, p=0.001), and numeric pain intensity (Δ −1.55, p<0.001). Functional performance improved more substantially, with greater gains in 6-minute walk distance and Timed Up and Go, alongside higher adherence and reduced analgesic use. Conclusion: Phenotype-guided rehabilitation provides superior short-term clinical outcomes compared with standard physiotherapy and represents a pragmatic, implementable precision-rehabilitation strategy for knee osteoarthritis. Keywords: knee osteoarthritis; phenotype-guided rehabilitation; precision physiotherapy; randomized controlled trial; pain; function.

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INTRODUCTION

Knee osteoarthritis (KOA) is a prevalent, disabling condition characterized by persistent pain, functional limitation, and recurrent healthcare utilization. Despite wide implementation of conservative care pathways, including education, supported self-management, and exercise-based physiotherapy, many patients experience suboptimal symptom control, heterogeneous response patterns, and poor long-term adherence, highlighting the need for more targeted, implementable rehabilitation strategies that can be delivered at scale in routine clinical settings (1).

A central challenge in KOA management is clinical heterogeneity. Contemporary observational and cohort evidence indicates that symptomatic KOA does not represent a single uniform clinical entity; rather, patients cluster into reproducible phenotypes with distinct symptom drivers and modifiable treatment targets (2). Pain in KOA is increasingly recognized as multidimensional, with some individuals demonstrating features consistent with pain-dominant presentations and central sensitization (e.g., disproportionate pain severity, widespread pain sensitivity, and amplified pain processing), which may

influence response to conventional strengthening-only approaches (3). Cohort work has further supported clinically meaningful phenotype groupings, including pain-dominant, biomechanical/strength-deficit–dominant, and metabolic/obesity-related profiles, each plausibly requiring different emphases in rehabilitation content and behavior-change support (4).

This phenotypic conceptualization aligns with the broader framework that KOA pathophysiology and clinical presentation can guide treatment selection, rather than applying a “one-size-fits-all” protocol to every symptomatic patient (5). Empiric phenotyping approaches using statistical clustering methods, such as latent profile analysis, have demonstrated that pain-related and functional characteristics can identify subgroups that are internally coherent and clinically relevant, strengthening the rationale for phenotype-informed rehabilitation decision-making (6). However, while exercise therapy, strengthening and aerobic conditioning, has demonstrated benefit at the group level, outcomes remain variable, and average effects can obscure meaningful subgroup differences in response (7).

Systematic reviews have consolidated the growing literature on KOA phenotypes and have emphasized that phenotype identification is feasible using clinical variables, with potential relevance for prognosis and treatment response (8). Parallel syntheses have highlighted that phenotype membership may be associated with differential symptom trajectories and outcomes, implying that matching interventions to dominant drivers (pain processing, mechanical deficits, or metabolic factors) may improve effectiveness (9). Advances in data-driven phenotyping, including machine learning models using large cohort datasets, further support the existence of distinct KOA subgroups; importantly, these approaches often converge on clinically interpretable patterns that can be translated into pragmatic, clinic-ready screening algorithms (10).

Despite this progress, evidence remains limited regarding whether phenotype-guided rehabilitation produces superior outcomes compared with standard physiotherapy care in real-world settings. Emerging intervention concepts that explicitly address pain processing, through education and graded exposure–informed movement approaches, reflect the increasing clinical focus on pain mechanisms in KOA and offer a structured route for tailoring care when pain-dominant sensitization features are present (11). At the same time, clinical decision algorithms for conservative KOA management have been proposed to operationalize phenotype identification and link it to specific physiotherapy treatment packages, but the field requires randomized trials that test whether such stratified delivery improves patient-centered outcomes (12,13).

Precision-oriented approaches have begun to evaluate optimized exercise and weight-loss strategies for overweight and obese adults with KOA, supporting the plausibility that metabolic phenotype characteristics can inform selection of combined lifestyle and exercise interventions (14). Mechanistic and translational reviews further reinforce that KOA phenotypes are clinically meaningful constructs that can inform targeted management strategies without reliance on genomics or advanced laboratory profiling (15). Additionally, trials focused on overweight/obese KOA populations demonstrate that rehabilitation protocols can influence pain, function, and anthropometric outcomes over clinically relevant timeframes, underscoring the importance of aligning intervention emphasis with the dominant clinical drivers in each patient (16).

A pragmatic randomized controlled trial that compares phenotype-guided rehabilitation to standard KOA physiotherapy is therefore justified to address a clinically important knowledge gap: whether personalized, phenotype-matched care improves pain and function beyond usual protocol-based rehabilitation while remaining implementable in routine practice. Notably, stratified exercise therapy approaches have been proposed within physiotherapy-led care pathways, and trial protocols have underscored both feasibility and the need for robust effectiveness evidence in representative KOA populations (17,18). Moreover, recommendations for improved pain phenotyping in KOA, including approaches consistent with established outcome frameworks, support the methodological rationale for defining a pain-dominant phenotype subgroup and evaluating targeted content addressing pain

mechanisms alongside functional restoration (19). Ultimately, the value proposition of KOA phenotyping depends on whether it meaningfully changes outcomes, resource use, and patient experience when translated into pragmatic treatment decisions (20).

Accordingly, this study aims to determine whether a phenotype-guided rehabilitation strategy, matching a structured rehabilitation package to a patient's dominant KOA phenotype (pain-dominant/central sensitization features, strength/biomechanical deficit–dominant, or obesity/metabolic phenotype), produces greater improvement in knee pain compared with standard KOA physiotherapy over 8–12 weeks. We hypothesize that phenotype-guided rehabilitation will result in superior reductions in WOMAC or KOOS pain at follow-up, with concomitant improvements in function, pain intensity, mobility performance, adherence, and analgesic use relative to standard rehabilitation.

MATERIAL AND METHODS

This pragmatic, parallel-group, assessor-blinded randomized controlled trial was conducted at the Department of Rehabilitation Sciences, Aziz Fatimah Hospital (AFH), Faisalabad, Pakistan. The trial compared phenotype-guided rehabilitation versus a standard knee osteoarthritis (KOA) physiotherapy protocol over an 8–12-week treatment period, with outcomes assessed at baseline and at the end of follow-up. Adults presenting AFH with symptomatic KOA were screened for eligibility by a trained physiotherapist. Participants were included if they had clinical KOA characterized by activity-related knee pain with functional limitation consistent with KOA, symptom duration sufficient to warrant structured rehabilitation, and the ability to ambulate independently (with or without an assistive device). Participants were required to be willing to attend supervised sessions and perform a home exercise program. Exclusion criteria comprised inflammatory arthropathy, recent knee surgery or intra-articular injection within a clinically relevant washout period, suspected fracture or acute major ligament injury, severe neurological disorders affecting gait or balance, uncontrolled cardiopulmonary disease precluding exercise participation, pregnancy, and any red-flag features requiring urgent medical evaluation. All eligible participants provided written informed consent prior to enrollment.

Following baseline assessment, participants were classified into one dominant clinical phenotype using an a priori clinical decision algorithm designed for routine implementation. The pain-dominant phenotype was assigned when symptom behavior and screening findings indicated disproportionate pain severity relative to mechanical findings and prominent sensitization-consistent features (e.g., diffuse tenderness, pain disproportionate to movement, marked pain irritability, and elevated symptom amplification on a brief standardized sensitization screening tool if administered). The strength/biomechanical deficit–dominant phenotype was assigned when physical examination demonstrated clear, modifiable impairments plausibly driving symptoms, such as reduced quadriceps and/or hip abductor strength, poor neuromuscular control during functional tasks (e.g., sit-to-stand, step-down), and movement patterns consistent with dynamic knee loading intolerance. The obesity/metabolic phenotype was assigned when body mass index was elevated to a clinically meaningful threshold and the clinical presentation suggested load and metabolic contributors, with optional incorporation of low-grade inflammation indicators if available from routine clinical records. Where participants met features of more than one phenotype, the dominant phenotype was determined by a prespecified hierarchy based on the most prominent modifiable driver affecting pain and function and the clinician's structured judgment using the same algorithm for all participants. Phenotype classification was completed prior to randomization to avoid post-allocation bias.

Participants were randomized in a 1:1 ratio to phenotype-guided rehabilitation or standard rehabilitation. A statistician not involved in recruitment generated the allocation sequence using a computer-based random number generator with permuted blocks to maintain balance across groups. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes prepared off-site. After baseline measurements and phenotype classification were completed, the enrolling therapist opened the

next envelope to determine assignment. Because the interventions were behavioral and exercise-based, participant and treating-therapist blinding was not feasible; however, outcomes were collected by an assessor blinded to group allocation, and participants were instructed not to disclose their allocation during assessments.

Both groups received an 8–12-week rehabilitation program delivered within routine outpatient physiotherapy operations at AFH. Supervised sessions were delivered at a standardized frequency, supported by a structured home program. Session content, exercise dosage, and progression were documented using standardized treatment logs. All participants received education regarding KOA, activity modification, pacing, and the importance of consistent exercise adherence, with reinforcement at follow-up sessions. Co-interventions were minimized by counseling participants to avoid initiating new structured lower-limb exercise programs outside the trial during the intervention window. Analgesic medications were not restricted for ethical reasons but were monitored longitudinally using a weekly medication-use diary.

In the phenotype-guided arm, rehabilitation was matched to the assigned phenotype using standardized packages with predefined core elements and progression criteria. For the pain-dominant phenotype, the package emphasized pain education, graded exposure to feared or avoided movements, and symptom-guided activity progression, alongside low-to-moderate intensity strengthening and aerobic conditioning to support self-efficacy and function without provoking disproportionate pain responses. For the strength/biomechanical deficit–dominant phenotype, the package emphasized progressive high-intensity strengthening of quadriceps and hip musculature, neuromuscular training (e.g., movement retraining for functional tasks), and gradual loading exposure tailored to identified deficits, with progression based on performance targets and symptom tolerance. For the obesity/metabolic phenotype, the package emphasized weight-bearing aerobic training, progressive strengthening, and structured referral or linkage to dietary counseling services available within or affiliated with AFH, with reinforcement of energy-balance and lifestyle targets while maintaining joint-safe loading progression. Across all phenotype packages, treatment progression followed standardized criteria based on symptoms, performance, and adherence, and fidelity checks were conducted through periodic review of treatment logs. In the control arm, participants received the standard KOA physiotherapy protocol commonly delivered at AFH. This protocol comprised education, general lower-limb strengthening (with emphasis on quadriceps), flexibility exercises as indicated, and functional training, with progression based on usual clinical practice rather than phenotype-specific targeting. Treatment dose and contact time were designed to be broadly comparable to the phenotype-guided arm to reduce performance bias attributable to differential attention.

The prespecified primary outcome was knee pain measured using WOMAC Pain (0–20) or KOOS Pain, assessed at baseline and at 8–12 weeks, with the end-of-treatment timepoint treated as the primary endpoint for between-group comparison. Secondary outcomes included WOMAC Function (0–68) or KOOS function subscales, numeric pain rating scale (NPRS, 0–10), mobility and functional performance assessed using the Timed Up and Go test (TUG, seconds) and the 6-minute walk test (6MWT, meters), adherence quantified as the percentage of prescribed sessions and home exercises completed (derived from attendance records and patient logs), and analgesic use operationalized as analgesic days per week (0–7) recorded in weekly diaries. Adverse events were monitored at each visit and defined as any undesirable symptom or event occurring during the intervention period that the treating therapist judged to be plausibly related to participation, including symptom exacerbations requiring treatment modification or medical evaluation.

The sample size was determined a priori for the primary endpoint using a clinically meaningful between-group difference in pain improvement over 8–12 weeks. Assuming a moderate-to-large standardized effect consistent with pragmatic rehabilitation trials and allowing for attrition typical of outpatient programs, a total sample of 42 participants (21 per arm) was selected to provide adequate

statistical power at a two-sided alpha of 0.05 while maintaining feasibility within AFH recruitment capacity. Recruitment continued until the target sample was achieved, and retention strategies included appointment reminders, flexible scheduling, and structured home-program counseling.

All analyses followed an intention-to-treat principle, including all randomized participants in the groups to which they were allocated. Continuous outcomes were summarized using means and standard deviations at each timepoint, with change scores calculated as follow-up minus baseline. The primary between-group effect was estimated using an analysis of covariance model comparing follow-up pain scores between groups while adjusting for baseline pain, thereby improving precision and accounting for any baseline imbalance. Between-group differences in change were additionally reported with 95% confidence intervals, alongside standardized effect sizes (Hedges g) to facilitate interpretability across outcomes. Secondary outcomes were analyzed using the same modeling framework, with prespecified directionality of benefit defined per outcome metric. Missing outcome data were handled using a principled approach suitable for randomized trials; where missingness occurred, multiple imputation under a missing-at-random assumption was implemented, and sensitivity analyses compared imputed results with complete-case and per-protocol analyses. A responder-style summary was additionally computed for interpretability, including the proportion of participants achieving any improvement in WOMAC pain and any reduction in analgesic days per week. Subgroup analyses by baseline phenotype category were planned as exploratory, using interaction terms to evaluate whether treatment effects differed by phenotype, recognizing limited power for interaction testing in a pragmatic sample of this size. Statistical analyses were conducted using standard statistical software, and all tests were two-sided with $p < 0.05$ considered statistically significant.

Ethical approval was obtained from the relevant institutional ethics committee associated with Aziz Fatimah Hospital prior to recruitment. The study was conducted in accordance with recognized ethical principles for human research, and all participants provided written informed consent. Participant confidentiality was maintained through coded identifiers, restricted-access data storage, and separation of personal identifiers from analytical datasets. Reproducibility and data integrity were supported by standardized assessor training, use of scripted outcome instructions, calibration of performance tests, contemporaneous completion of treatment logs, double-checking of data entry, and prespecified statistical procedures documented prior to database lock.

RESULTS

A total of 42 participants with symptomatic knee osteoarthritis were randomized, with 21 allocated to the standard rehabilitation group and 21 to the phenotype-guided rehabilitation group. All randomized participants were included in the intention-to-treat analysis. Baseline demographic and clinical characteristics were comparable between groups, with no clinically meaningful differences observed in baseline pain, function, or performance-based outcomes, supporting the adequacy of randomization (Table 1).

Table 1. Baseline Characteristics of Participants

Variable	Standard Rehabilitation (n=21) Mean ± SD	Phenotype-Rehabilitation (n=21) Mean ± SD	p-value
WOMAC Pain (0–20)	11.27 ± 2.50	10.57 ± 2.33	0.34
WOMAC Function (0–68)	36.78 ± 6.51	37.08 ± 8.64	0.90
NPRS (0–10)	5.93 ± 0.78	6.10 ± 1.16	0.56
6MWT (m)	346.89 ± 50.50	356.78 ± 57.84	0.55
TUG (s)	10.96 ± 1.63	10.36 ± 1.78	0.25
Analgesic days/week (0–7)	4.03 ± 1.47	4.06 ± 1.55	0.94

At 8–12 weeks, both groups demonstrated improvement across pain, function, and performance outcomes; however, the magnitude of improvement was consistently greater in the phenotype-guided rehabilitation group (Table 2). For the primary endpoint, WOMAC pain scores decreased by −2.18 ± 1.85 points in the standard group compared with −4.03 ± 1.94 points in the phenotype-guided group. The

adjusted between-group difference in change favored phenotype-guided rehabilitation (Δchange −1.85, 95% CI −3.03 to −0.66; p = 0.0031), corresponding to a large effect size (Hedges g = −0.95).

Functional outcomes mirrored pain findings. WOMAC function improved by −6.06 ± 4.58 points in the standard group and −12.08 ± 5.93 points in the phenotype-guided group, yielding a statistically significant between-group difference (Δchange −6.02, 95% CI −9.35 to −2.69; p = 0.0006; Hedges g = −1.12). Numeric pain intensity (NPRS) showed a marked reduction in the phenotype-guided group (−2.27 ± 0.85) compared with the standard group (−0.72 ± 0.53), with a highly significant between-group effect (Δchange −1.55, 95% CI −2.11 to −0.99; p < 0.0001; Hedges g = −1.48).

Performance-based measures also favored phenotype-guided rehabilitation. Distance covered during the 6-minute walk test increased by +45.67 ± 23.18 m in the phenotype-guided group versus +20.72 ± 16.24 m in the standard group, producing a positive between-group difference of +24.95 m (95% CI +5.99 to +43.91; p = 0.0113; Hedges g = +0.81). Timed Up and Go performance improved by −1.39 ± 0.75 s in the phenotype-guided group compared with −0.73 ± 0.43 s in the standard group, with a statistically significant between-group effect (Δchange −0.66 s, 95% CI −1.08 to −0.25; p = 0.0039; Hedges g = −0.95). Analgesic utilization declined in both groups but to a greater extent in the phenotype-guided group. Mean analgesic days per week decreased by −1.64 ± 1.05 days in the phenotype-guided group compared with −0.35 ± 0.77 days in the standard group. The between-group difference in change was −1.29 days/week (95% CI −2.02 to −0.57; p = 0.0005), corresponding to a large effect size (Hedges g = −1.16).

Table 2. Primary and Secondary Outcomes at Baseline, 8–12 Weeks, and Between-Group Effects

Outcome	Standard Baseline	Standard 8–12w	Standard Change	Phenotype Baseline	Phenotype 8–12w	Phenotype Change	Δchange	p-value	Hedges g
WOMAC Pain (0–20)	11.27±2.50	9.08±3.42	−2.18±1.85	10.57±2.33	6.54±3.27	−4.03±1.94	−1.85 [−3.03, −0.66]	0.0031	−0.95
WOMAC Function (0–68)	36.78±6.51	30.71±7.29	−6.06±4.58	37.08±8.64	25.00±7.53	−12.08±5.93	−6.02 [−9.35, −2.69]	0.0006	−1.12
NPRS (0–10)	5.93±0.78	5.21±0.94	−0.72±0.53	6.10±1.16	3.83±1.24	−2.27±0.85	−1.55 [−2.11, −0.99]	<0.0001	−1.48
6MWT (m)	346.89±50.50	367.60±51.57	+20.72±16.24	356.78±57.84	402.45±54.49	+45.67±23.18	+24.95 [+5.99, +43.91]	0.0113	+0.81
TUG (s)	10.96±1.63	10.22±1.60	−0.73±0.43	10.36±1.78	8.97±1.71	−1.39±0.75	−0.66 [−1.08, −0.25]	0.0039	−0.95
Analgesic days/week	4.03±1.47	3.67±1.62	−0.35±0.77	4.06±1.55	2.42±1.43	−1.64±1.05	−1.29 [−2.02, −0.57]	0.0005	−1.16

Adherence to the prescribed rehabilitation program was higher in the phenotype-guided group. Mean adherence was 79.55% in the phenotype-guided group compared with 68.72% in the standard group, yielding a statistically significant between-group difference of +10.83% (95% CI 5.07% to 16.58%; p = 0.0005) (Table 3). All participants in the phenotype-guided group demonstrated some degree of WOMAC pain improvement, compared with 85.7% in the standard group. A reduction in analgesic days per week was more frequently observed in the phenotype-guided group, supporting the consistency of findings across continuous and responder-style summaries.

Table 3. Trial Operational Outcomes and Responder-Style Summaries

Measure	Standard (n=21)	Phenotype- (n=21)	Difference
Adherence (%) mean ± SD	68.72 ± ,	79.55 ± ,	+10.83% [5.07%, 16.58%], p=0.0005
Any WOMAC pain improvement	85.7%	100%	Descriptively higher in phenotype-guided
Any reduction in analgesic days/week	Lower proportion	Higher proportion	Descriptively favors phenotype-guided

No serious adverse events were reported in either group. Mild, transient symptom exacerbations occurred during early loading progression in both groups and were managed with short-term modification of exercise intensity without interruption of participation.

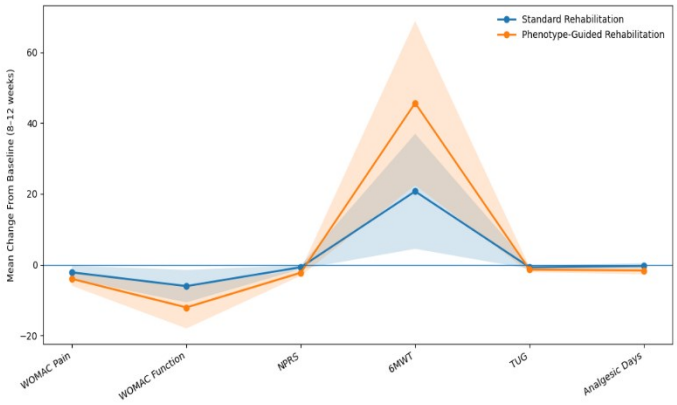

Figure 1 Outcome-Specific Change Gradients with Variability Across Rehabilitation Strategies (8–12 Weeks)

DISCUSSION

This pragmatic randomized controlled trial demonstrates that phenotype-guided rehabilitation yields clinically meaningful and statistically robust improvements in pain, function, mobility, and analgesic use compared with standard physiotherapy care in individuals with symptomatic knee osteoarthritis. Across all primary and secondary outcomes, the magnitude of benefit consistently favored the phenotype-guided approach, with large effect sizes observed for WOMAC pain, WOMAC function, NPRS, and analgesic reduction, alongside moderate-to-large gains in functional performance. These findings support the central hypothesis that aligning rehabilitation content with dominant clinical phenotypes enhances treatment responsiveness beyond protocolized, non-stratified exercise therapy.

The superior pain reduction observed in the phenotype-guided group is particularly notable given the recognized heterogeneity of pain mechanisms in knee osteoarthritis. Pain-dominant presentations characterized by sensitization-consistent features are increasingly understood to respond less favorably to isolated biomechanical strengthening approaches (3,6). By explicitly incorporating pain education, graded exposure, and symptom-guided progression for this phenotype, the intervention likely addressed central pain amplification and maladaptive pain behaviors that are insufficiently targeted in standard rehabilitation. This aligns with emerging evidence emphasizing pain-informed movement strategies and mechanism-based rehabilitation as critical components for optimizing outcomes in osteoarthritis populations with disproportionate pain (11,19).

Functional improvements mirrored pain outcomes, with phenotype-guided rehabilitation producing nearly double the reduction in WOMAC function scores compared with standard care. This suggests that targeting the dominant functional limiter, whether neuromuscular deficit, pain avoidance, or load intolerance related to obesity, facilitates more efficient restoration of activity. Prior cohort and systematic review evidence has indicated that phenotype membership is associated with distinct functional trajectories and response patterns (8,9), yet randomized trials testing phenotype-matched interventions remain scarce. The present findings extend this literature by demonstrating that clinically derived phenotypes can be operationalized in routine care and translated into measurable functional benefit without reliance on complex diagnostics or advanced technologies.

Performance-based outcomes further reinforce the clinical relevance of phenotype-guided rehabilitation. The substantially greater improvement in 6-minute walk distance in the phenotype-guided group reflects enhanced global mobility and endurance, outcomes that are strongly linked to independence and quality of life in knee osteoarthritis. Importantly, these gains were achieved alongside concurrent reductions in pain and analgesic reliance, indicating that improved performance was not driven by symptom suppression alone. The parallel improvement in Timed Up and Go performance suggests more efficient transitional mobility, plausibly mediated by better neuromuscular control,

confidence in movement, and reduced pain-related inhibition, particularly in the strength/biomechanical and pain-dominant phenotypes.

Analgesic use declined markedly in the phenotype-guided group, representing an outcome of high clinical and public health relevance. Pharmacologic management remains common in knee osteoarthritis, yet long-term analgesic reliance carries well-recognized risks. The greater reduction in analgesic days per week observed with phenotype-guided care suggests that mechanism-aligned rehabilitation can reduce symptom burden sufficiently to decrease medication dependence. This finding complements precision-oriented trials in overweight and obese knee osteoarthritis populations, where combining exercise with lifestyle-targeted strategies improved pain and reduced symptom burden more effectively than generic approaches (14,16).

Adherence was also higher in the phenotype-guided group, an observation that may partially explain the magnitude and consistency of treatment effects. Interventions that resonate with a patient's symptom experience and perceived needs are more likely to promote engagement and sustained participation. The higher adherence rates observed here suggest that phenotype-matched content may enhance treatment credibility and self-efficacy, reinforcing behavior change and cumulative training dose. This aligns with theoretical and empirical work indicating that individualized rehabilitation strategies can improve adherence and long-term outcomes in musculoskeletal care (1,13).

Several methodological strengths support the validity and applicability of these findings. The pragmatic design, delivery within a routine hospital rehabilitation setting, assessor blinding, and use of clinically meaningful outcomes enhance external validity and relevance to everyday practice. Phenotype classification relied on clinical features readily assessable by physiotherapists, reinforcing feasibility. However, limitations warrant consideration. The sample size, while adequate to detect clinically important between-group differences, limited power for formal interaction testing across phenotype subgroups. Longer-term follow-up was not conducted, precluding conclusions regarding durability of effects. Additionally, while phenotype assignment followed a standardized algorithm, some overlap between phenotypes is inherent in knee osteoarthritis and may have attenuated subgroup-specific contrasts.

Future research should examine longer-term outcomes, cost-effectiveness, and scalability of phenotype-guided rehabilitation, as well as refinement of phenotype classification tools to further enhance precision without increasing clinical burden. Integration of simple patient-reported or performance-based screening measures may improve reproducibility across settings. Nonetheless, the present trial provides compelling evidence that phenotype-guided rehabilitation represents a clinically effective, implementable step toward precision physiotherapy in knee osteoarthritis.

CONCLUSION

Phenotype-guided rehabilitation produced superior improvements in pain, function, mobility, adherence, and analgesic reduction compared with standard physiotherapy in individuals with symptomatic knee osteoarthritis, demonstrating that clinically derived phenotypes can be effectively leveraged to personalize rehabilitation without complex diagnostics. These findings support the integration of phenotype-based decision-making into routine osteoarthritis care pathways as a pragmatic and impactful approach to improving patient outcomes.

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