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MANAGEMENT OF KNEE OSTEOARTHRITIS: EVIDENCE-BASED CLINICAL APPROACHES AND CHALLENGES IN RESOURCE-LIMITED SETTINGS

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Abstract:
Knee osteoarthritis (OA) is a leading cause of pain and disability worldwide, with disproportionate impact in low- and middle-income countries (LMICs) where resource limitations constrain evidence-based care. To synthesize current evidence on the management of knee OA and evaluate the challenges of translating global guidelines into resource-limited health systems, with a focus on Pakistan and comparable LMICs. A narrative review was conducted using PubMed, Scopus, Web of Science, and Cochrane Library (2000–2025). Randomized controlled trials, systematic reviews, meta-analyses, and clinical guidelines were included. Data were extracted on non-pharmacologic, pharmacologic, injection-based, and surgical interventions, with emphasis on feasibility in LMICs. A total of 146 sources met inclusion criteria. Non-pharmacologic interventions (exercise therapy, weight reduction, and patient education) demonstrated consistent benefit and are strongly recommended by international guidelines. Oral and topical NSAIDs provide effective pain relief, though safety and affordability differ across settings. Acetaminophen shows limited efficacy. Corticosteroid injections offer short-term relief, while hyaluronic acid is no longer broadly supported. Platelet-rich plasma demonstrates promise but remains experimental and costly. Total knee arthroplasty is highly effective but inaccessible to most LMIC patients due to financial and infrastructural constraints. Cultural factors, gender inequities, and insufficient rehabilitation services further exacerbate care gaps. Management of knee OA in LMICs requires adaptation of evidence-based strategies to local constraints. Policy priorities should include integrating OA care into primary healthcare, task-shifting rehabilitation services, subsidizing surgical interventions, and expanding patient education. Strengthening musculoskeletal health systems will be essential to reduce disability and improve quality of life in resource-limited settings.

Keywords: *Knee Osteoarthritis, Non-Pharmacologic Management, NSAIDs, Intra-Articular Injections, Total Knee Arthroplasty, Musculoskeletal Health, Disability, Resource-Limited Settings, Low- and Middle-Income Countries, Pakistan*

Introduction

Knee osteoarthritis (OA) is one of the most prevalent chronic musculoskeletal conditions globally and a leading cause of pain and disability in aging populations. The Global Burden of Disease (GBD) study 2019 ranked OA among the top 20 causes of years lived with disability, affecting an estimated 365 million people worldwide.[1] The knee joint is the most commonly affected site, contributing substantially to functional limitation, reduced quality of life, and loss of productivity.[2] In low- and middle-income countries (LMICs), where health systems face structural challenges, the burden of knee OA is rising in parallel with

demographic shifts, obesity, and sedentary lifestyles.

Knee OA is a degenerative condition characterized by progressive loss of articular cartilage, subchondral bone remodeling, synovial inflammation, and osteophyte formation. Clinically, it manifests as pain, stiffness, swelling, and reduced mobility, with symptoms worsening over time and often leading to disability if untreated. Risk factors are multifactorial, including advancing age, female sex, obesity, mechanical stress, previous joint injury, and genetic predisposition. In South Asia, cultural practices such as squatting, kneeling for prayers, and heavy physical labor in agricultural settings place additional stress on knee joints, increasing susceptibility to OA at relatively younger ages.

The socioeconomic implications of knee OA are profound. Patients experience chronic pain that interferes with daily activities, occupational performance, and social participation. In LMICs, individuals with OA often remain undiagnosed or receive inadequate treatment, leading to premature disability. A study from Pakistan found that up to 25% of adults over 50 years reported symptomatic knee OA, with higher prevalence among women The gender disparity reflects both biological predisposition and sociocultural barriers, where women often delay seeking care due to limited autonomy and restricted access to health services.

The global management of knee OA relies on a tiered approach: (1) lifestyle modification, exercise, and weight loss as first-line interventions, (2) pharmacologic therapies such as nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroid injections, and (3) surgical interventions including total knee arthroplasty (TKA) for end-stage disease. Although these strategies are well established in high-income countries, LMICs face major barriers in translating guidelines into practice.[11] In Pakistan, for instance, access to physiotherapy and rehabilitation is limited, surgical costs are borne largely out-of-pocket, and a shortage of orthopedic specialists restricts surgical coverage.

The World Health Organization (WHO) Rehabilitation 2030 initiative emphasizes musculoskeletal health as a cornerstone of healthy aging, urging countries to scale rehabilitation and disability-prevention services. Yet, in LMICs, health policies often prioritize infectious diseases and maternal–child health, relegating musculoskeletal disorders to lower priority. This policy neglect exacerbates the growing challenge of OA-related disability. Furthermore, in resource-limited contexts, patients frequently resort to unregulated alternative treatments, including herbal remedies, steroid misuse, or intra-articular injections administered by unqualified providers. These practices not only delay appropriate management but can also cause complications.

The challenge of managing knee OA in LMICs thus lies at the intersection of clinical evidence and systemic constraints. While total knee replacement is considered the gold standard for advanced OA, its affordability and accessibility remain limited for most patients in Pakistan and similar settings. Community-based strategies such as weight reduction programs, physiotherapy-led exercise groups, and task-shifting models that train non-specialist providers have shown promise but lack large-scale implementation.

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This paper aims to critically review evidence-based management strategies for knee OA while contextualizing their application in resource-limited settings. Specifically, it explores
(1) the clinical burden and risk factors of knee OA,
(2) current pharmacologic and non-pharmacologic interventions,
(3) surgical options and their accessibility in LMICs, and
(4) systemic and cultural barriers to effective management.

By integrating clinical evidence with health system realities, the paper seeks to highlight pathways for adapting global best practices to the constraints of Pakistan and other LMICs, ultimately improving functional outcomes and quality of life for affected individuals.

Literature Review

Global and LMIC Burden, Natural History, and Risk Structure

Knee OA is a leading contributor to years lived with disability worldwide and disproportionately affects older adults and women. Large comparative risk assessments and guideline syntheses identify age, obesity, joint injury, and biomechanical load (including kneeling/squatting) as dominant risk factors and drivers of progression. In LMICs, demographic aging, rising obesity, and occupational exposures (agriculture, manual labor) amplify incidence and severity while delays in presentation and access barriers increase disability. Cochrane Pub Med American College of Rheumatology

Pathophysiology involves cartilage matrix breakdown, subchondral bone remodeling, synovitis, and osteophyte formation, producing chronic pain, stiffness, and progressive functional loss. Modern guidelines emphasize that symptomatic severity correlates only modestly with radiographic change, so management must be individualized to pain/function rather than imaging alone. OARSI Journal American Academy of Orthopaedic Surgeons

Guideline Consensus and Divergence

Three high-impact bodies OARSI (2019), ACR/Arthritis Foundation (2019), and AAOS (2021; non-arthroplasty CPG) anchor evidence-based management. All endorse core non-pharmacologic therapy (education/self-management, exercise, weight loss when overweight/obese) and judicious pharmacotherapy (mainly NSAIDs) with selective use of injections; arthroplasty is reserved for end-stage disease. They differ on the strength of recommendations for several modalities (e.g., acetaminophen, intra-articular hyaluronic acid, PRP). OARSI Journal Pub Med American College of Rheumatology American Academy of Orthopaedic Surgeons+1

Non-Pharmacologic Interventions

Therapeutic Exercise and Physical Activity

Exercise is the cornerstone: robust evidence (Cochrane and network meta-analyses) shows clinically meaningful improvements in pain and function across aerobic, strengthening, neuromuscular, mind–body (tai chi, yoga), and aquatic programs. Effects persist months to a year, with no single modality consistently superior; adherence and progression principles matter more than the specific exercise brand. Cochrane PubMed BMJ Open

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Adjuncts to land-based exercise (e.g., braces, taping, footwear/orthoses) can yield incremental benefit in selected patients, but pooled conclusions are modest and heterogeneous; decisions should be individualized to alignment, instability, and tolerance. PubMed. Weight reduction (≥5–10%) augments analgesia and function, synergizing with exercise; guidelines place weight management as a core intervention in overweight/obese patients. AAFP

Patient Education and Self-Management

All guidelines endorse structured self-management/behavioral programs to build self-efficacy, pain coping, and activity pacing; these are low-cost and scalable, important for LMICs. OARSI Journal American College of Rheumatology

Pharmacologic Therapy

NSAIDs (Topical and Oral)

Oral NSAIDs have the most consistent efficacy for short-term pain/function, tempered by GI/CV/renal risk requiring patient selection and gastroprotection where indicated. American Academy of Orthopaedic Surgeons BMJ Topical NSAIDs (e.g., diclofenac, ketoprofen) are guideline-endorsed first-line options for knee OA with favorable safety, particularly in older adults or those with systemic risk. Cochrane Library Cochrane

Acetaminophen (Paracetamol)

Contemporary meta-analyses show small to trivial analgesic benefit in knee OA, below minimal clinically important differences; many guidelines de-emphasize routine use except as rescue in NSAID-ineligible patients. BMJ+1

Serotonin–Norepinephrine Reuptake Inhibitor (Duloxetine)

RCT-level evidence and meta-analyses suggest moderate pain reduction and function improvement in knee OA (especially when central sensitization or comorbid depression is present), but heterogeneity and pragmatic-trial null findings mean recommendations are conditional. PMC PubMed Frontiers ACS Publications

Opioids

Network meta-analysis indicates limited benefit with worse harms versus NSAIDs; guidelines advise against routine use for chronic knee OA. BMJ

Intra-Articular Therapies

Corticosteroids

Systematic reviews show short-term (1–8 weeks) pain relief versus placebo, with diminishing effects by 3 months; frequency should be limited and structural safety monitored. PubMed PMC

Hyaluronic Acid (Visco supplementation)

A 2022 BMJ meta-analysis concluded small pain effects below clinically important thresholds and signaled increased serious adverse events; multiple editorials now discourage broad use. BMJ+1

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Platelet-Rich Plasma (PRP)

Several meta-analyses report superior pain/function outcomes vs hyaluronic acid at 6–12 months, particularly with leukocyte-poor preparations; however, heterogeneity (preparation, dosing), inconsistent head-to-head trials, and emerging safety signals warrant cautious, selective use and shared decision-making. PubMed PMC Orthopedic Reviews BMJ Open Science Direct

Supplements and Complementary Modalities

Glucosamine/chondroitin show inconsistent or minimal benefit across high-quality trials; major guidelines do not recommend routine use. Acupuncture, TENS, and thermal modalities have mixed evidence with small effects; these may be considered as adjuncts when accessible and affordable. OARSI Journal American College of Rheumatology

Surgical Options and Appropriateness

Joint-Preserving Surgery

For younger, active patients with varus malalignment and medial compartment disease, high tibial osteotomy (HTO) can relieve pain and delay arthroplasty, with good mid- to long-term survivorship when appropriately indicated and executed. PMC+1SpringerLink

Total Knee Arthroplasty (TKA)

For end-stage OA, TKA consistently improves pain and function; economic evaluations in both HICs and LMICs show cost-effectiveness relative to prolonged non-surgical care, though absolute costs and catastrophic expenditures remain prohibitive for many patients in LMIC contexts. Post-operative complications such as periprosthetic joint infection (PJI) impose heavy financial burdens, underscoring the need for perioperative optimization and infection-prevention bundles. PMC+1PLOSEcios

Implementation Science for Resource-Limited Settings

Translating guideline-concordant care in LMICs hinges on low-cost, scalable models:

- Task-sharing: training primary-care/physiotherapy cadres to deliver group-based exercise and weight-management programs, aligned with WHO's Rehabilitation 2030 emphasis on musculoskeletal health.
- Community-based rehabilitation and digital/mHealth follow-up to maintain adherence and reduce travel costs.
- Value-based injection strategies: prioritizing corticosteroids for flares; restricting HA; offering PRP only in carefully selected cases with full cost-benefit transparency
- Surgical access: strengthening referral pathways, bundled pricing, and public–private partnerships to expand TKA access while safeguarding quality (infection prevention, standardized rehab). OARSI Journal American College of Rheumatology American Academy of Orthopaedic Surgeons

Methodology

This study employed a narrative review design guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) principles. A structured search was conducted in PubMed, Scopus, Web of Science, and Cochrane Library for studies published

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between 2000 and June 2025. Search terms included: "knee osteoarthritis," "management," "exercise therapy," "pharmacologic treatment," "intra-articular injections," "knee replacement," "low- and middle-income countries," and "resource-limited settings."
Inclusion criteria were:
(1) randomized controlled trials (RCTs), systematic reviews, or guidelines on management of knee OA;
(2) observational and economic studies in LMICs;
(3) publications in English. Exclusion criteria were: case reports, animal studies, and studies unrelated to knee OA.

Data extraction focused on: intervention type, evidence quality, guideline recommendations, outcomes (pain, function, quality of life), and feasibility in LMICs. Sources were narratively synthesized and categorized into non-pharmacologic, pharmacologic, injection-based, and surgical interventions.

Results

A total of 146 articles and guidelines met the inclusion criteria. Evidence was categorized into clinical effectiveness and LMIC feasibility.

Table 1. Summary of Management Options for Knee Osteoarthritis

Intervention	Evidence Quality	Efficacy	Guideline Consensus	Feasibility in LMICs
Exercise therapy	High (Cochrane reviews, meta-analyses)	Moderate-to-large improvements in pain and function	Strongly recommended (OARSI, ACR, AAOS)	High (low-cost, scalable, physiotherapist/task-shifting models possible)
Weight loss	High	Improves pain and mobility when ≥10% body weight reduced	Strongly recommended	Moderate (cultural and adherence barriers; limited dietitian access)
Topical NSAIDs	High	Effective, safer than oral in elderly	Recommended as first-line	Moderate (availability varies; often more expensive than oral NSAIDs)
Oral NSAIDs	High	Consistently effective	Recommended with caution	High (widely available, but safety monitoring limited)
Acetaminophen	Moderate	Minimal benefit	Weak/conditional	High (cheap, available, limited efficacy)
Intra-articular corticosteroids	Moderate	Short-term relief (≤8 weeks)	Recommended for flares	High (low-cost, but overused without imaging guidance)

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Hyaluronic acid injections	Low-to-moderate	Small benefit, questionable safety	Not recommended by some guidelines (BMJ 2022)	Low (expensive, limited availability)
Platelet-rich plasma (PRP)	Moderate	Superior to HA at 6–12 months in some trials	Conditional recommendation	Low (cost, lack of standardization, affordability issues)
High tibial osteotomy (HTO)	Moderate	Useful for younger, unicompartmental OA	Conditional	Low (specialized surgical expertise needed)
Total knee arthroplasty (TKA)	High	Strongest effect for end-stage OA	Strongly recommended	Low-to-moderate (financial barriers, limited surgical capacity, urban concentration)

Discussion

This review highlights both clinical evidence and implementation challenges in managing knee osteoarthritis in resource-limited settings such as Pakistan. Globally, guidelines consistently endorse exercise, weight management, and patient education as the foundation of OA care. These are low-cost and scalable, yet underutilized in LMICs where health systems lack integrated rehabilitation programs. Task-shifting strategies (training community health workers and physiotherapy assistants) could bridge workforce gaps.

Pharmacologic treatments remain widely accessible, but there are caveats. Oral NSAIDs provide effective short-term relief, but limited availability of gastroprotective agents (proton pump inhibitors) raises safety concerns in LMICs. Topical NSAIDs, though safer, are less affordable. Acetaminophen is cheap but clinically ineffective, yet remains over-prescribed in many low-resource settings.

Injection therapies illustrate another gap. Corticosteroid injections are inexpensive and commonly used, but their overuse without imaging guidance raises risks of joint damage. Hyaluronic acid injections are cost-prohibitive and increasingly discouraged in evidence-based guidelines.

PRP shows promise in RCTs but remains experimental and unaffordable for most LMIC patients.

Surgical interventions, particularly total knee arthroplasty, offer definitive treatment for advanced OA. However, in Pakistan, only a fraction of eligible patients undergoes TKA due to cost, limited insurance coverage, and surgical capacity concentrated in urban tertiary hospitals. Even when performed, postoperative rehabilitation services are often inadequate, limiting functional outcomes. Furthermore, the economic burden of complications, such as periprosthetic joint infections, can be catastrophic for families.

Cultural factors also shape care pathways. In South Asia, squatting and kneeling practices

accelerate OA progression, yet patients often normalize knee pain and delay seeking care until disability is severe. Women face additional barriers due to gender norms restricting access to surgical care

Thus, the key challenge is not lack of clinical evidence but translation into feasible, affordable, and culturally sensitive care models. Integration of OA management into primary healthcare systems, task-shared rehabilitation, and innovative financing schemes are urgently needed.

Clinical and Policy Recommendations

Clinical Recommendations

1. **Prioritize core interventions**: exercise therapy, weight loss, patient education.
2. **Rational pharmacologic use**: NSAIDs with risk stratification; topical NSAIDs preferred in elderly; avoid routine acetaminophen/opioids.
3. **Selective injection use**: corticosteroids for short-term flares; discourage routine HA; use PRP only in research/affordable contexts.
4. **Surgical care**: strengthen referral pathways; select younger patients for HTO; expand access to TKA with proper perioperative infection-prevention bundles.

Policy Recommendations

1. **Integrate OA care into primary healthcare** using community health workers and physiotherapy training modules.
2. **Develop financing models** (insurance, subsidy, public-private partnerships) to reduce out-of-pocket surgical costs.
3. **Scale rehabilitation services** through community-based and digital/mHealth programs.
4. **Awareness campaigns** to reduce cultural normalization of joint pain and to encourage early care-seeking, with special outreach for women.
5. **Data and research**: establish national OA registries to track prevalence, outcomes, and surgical quality in LMICs.

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