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# ECONOMIC BURDEN OF OSTEOARTHRITIS MANAGEMENT IN ISLAMABAD AND RAWALPINDI, PAKISTAN: A COMPARATIVE PHARMACOECONOMIC ANALYSIS OF PHARMACOTHERAPY VERSUS TOTAL KNEE ARTHROPLASTY ACROSS PUBLIC AND PRIVATE HEALTHCARE SECTORS

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## Abstract

***Background:*** *Osteoarthritis (OA) is a leading cause of disability worldwide, and its management—ranging from long-term pharmacotherapy to total knee arthroplasty (TKA)—imposes substantial direct and indirect costs on patients and health systems. Comparative, patient-level cost data from Pakistan and other resource-limited settings remain scarce.*

***Objective:*** *To compare the economic burden of pharmacotherapy versus TKA for knee OA across public and private healthcare sectors in Islamabad and Rawalpindi, Pakistan, and to identify independent predictors of TKA cost burden.*

***Methods:*** *This was a comparative, cross-sectional pharmacoeconomic evaluation of 150 patients: 100 receiving non-surgical pharmacotherapy for knee OA and 50 who had undergone primary TKA (25 at a government hospital, 25 at a private hospital) in Islamabad and Rawalpindi. Data on demographics, treatment costs, and resource use were collected via structured patient interviews and hospital billing records and analyzed using descriptive statistics, Mann-Whitney U tests, bootstrap resampling (5,000 iterations), and multivariable ordinary least squares regression on log-transformed total economic burden.*

***Results:*** *Mean total economic burden was PKR 1,004,497 in the private sector versus PKR 590,167 in the government sector (1.7-fold difference; Mann-Whitney $p < 0.0001$; Cohen's $d = 1.55$), driven almost entirely by surgeon fees and hospital-stay charges, which were fully subsidized in government facilities. Mean implant cost did not differ significantly by sector ($p = 0.172$), but government and private patients received implants from entirely different sources (100% Chinese-manufactured versus 100% Zimmer USA-manufactured implants, respectively). At the observed mean annual pharmacotherapy expenditure of PKR 63,302, cumulative cost equaled government-sector TKA cost after 9.3 years and private-sector TKA cost after 15.9 years. A six-predictor multivariable regression explained 89% of the variance in log-transformed TKA burden ($R^2 = 0.89$); bilateral (versus unilateral) procedure ($\beta = 0.526$, $p < 0.001$) and private (versus government) sector ($\beta = 0.368$, $p < 0.001$) were the strongest independent predictors, followed by socioeconomic status ($\beta = 0.118$, $p = 0.009$). Polypharmacy ($\geq$ 3 concurrent medications) was present in 98% of TKA patients and 53% of pharmacotherapy patients. Every low-socioeconomic-*

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*status patient exceeded the WHO's 40% catastrophic health expenditure threshold regardless of hospital sector.*
***Conclusion:*** *TKA imposes a substantially higher and more variable economic burden than pharmacotherapy, particularly in the private sector, and bilateral procedures and low socioeconomic status independently amplify this burden. The divergent implant sourcing observed between sectors, previously unrecognized in this cohort, raises an equity question that warrants dedicated investigation. These findings support expanded financial protection mechanisms, transparent implant procurement policies, and timely referral pathways for appropriately selected OA patients in Pakistan.*

## INTRODUCTION

Osteoarthritis (OA) is a chronic, progressive, whole-joint disease characterized by degeneration of articular cartilage, subchondral bone remodeling, and synovial inflammation, producing pain, stiffness, and progressive functional impairment [1,2]. It is one of the leading causes of disability worldwide: global OA prevalence rose from an estimated 247.5 million cases in 1990 to 527.8 million in 2019, with associated years lived with disability increasing by a comparable margin over the same period [3]. The knee is the most commonly affected joint, and moderate-to-severe knee OA disproportionately affects women, particularly after menopause, reflecting the combined influence of hormonal, biomechanical, and body-composition factors [4,5].

Established risk factors for knee OA include advancing age, obesity, prior joint injury, occupational mechanical loading, and genetic susceptibility, which together account for a substantial share of population risk [6–9]. Management follows a stepwise approach: conservative therapy—nonsteroidal anti-inflammatory drugs (NSAIDs), analgesics, intra-articular injections, and physiotherapy—is first-line, with total knee arthroplasty (TKA) reserved for patients with advanced structural disease and refractory symptoms [10]. Delayed referral to surgery is common in resource-limited settings because of cost, limited access to specialist orthopaedic care, and patient apprehension, but prolonged conservative management is itself associated with continued joint degeneration and accumulating healthcare costs, and earlier surgical intervention has been linked to improved pain, mobility, and quality of life in appropriately selected patients [11,12].

The economic burden of OA is substantial and rising. Knee OA and its surgical management account for a large and growing share of orthopaedic healthcare expenditure globally, with implant costs, length of hospital stay, and professional fees identified as the principal cost drivers in prior cost-of-illness studies [13,14]. This burden is particularly consequential in low- and middle-income countries, where out-of-pocket payment remains the dominant financing mechanism and where the relative cost of TKA against household income is far higher than in high-income settings [15]. In Pakistan, OA prevalence and disability burden have risen steadily according to Global Burden of Disease estimates, compounding pressure on a health system with limited insurance coverage and wide disparities between the public and private sectors [16,17].

Despite this burden, patient-level, comparative pharmacoeconomic data contrasting conservative pharmacotherapy with TKA—and contrasting public with private-sector TKA provision—remain scarce in Pakistan. Understanding how treatment costs are distributed, how they accumulate over time relative to a one-time surgical cost, and which patient and treatment factors independently predict economic burden is necessary to inform financial protection policy and rational referral pathways. This study therefore aimed to (1) quantify and compare the direct and indirect costs of pharmacotherapy and TKA for knee OA in Islamabad and Rawalpindi; (2) compare the total economic burden of TKA between government and private hospital sectors and decompose the sources of any difference; (3) identify independent predictors of TKA economic burden using multivariable regression; and (4) assess the affordability of OA management relative to household income across socioeconomic strata.

## METHODS

### Study Design and Setting

This was a comparative, cross-sectional pharmacoeconomic evaluation conducted at two

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tertiary care hospitals in the Islamabad–Rawalpindi metropolitan area: Shifa International Hospital (private sector) and the Pakistan Institute of Medical Sciences, or PIMS (government sector). These hospitals were selected for their high patient volume and to allow direct comparison of treatment costs, prescribing patterns, and healthcare utilization between the two sectors.

### Participants

Two patient cohorts were assembled using purposive (non-probability) sampling. The pharmacotherapy cohort comprised 100 patients with a clinically diagnosed knee OA receiving non-surgical treatment for at least three months. The TKA cohort comprised 50 patients who had undergone primary unilateral or bilateral TKA, with 25 patients recruited from the government hospital and 25 from the private hospital. Eligible patients were adults (≥18 years) with a physician-diagnosed knee OA and either an ongoing non-surgical treatment course of at least six months or a completed TKA, with complete, accessible medical records or prescriptions and willingness to provide informed consent. Patients without a verified OA diagnosis, with treatment duration under six months, under 18 years of age, or with incomplete records were excluded.

### Data Collection

A structured proforma was developed to capture demographic, clinical, and cost-related data, including patient demographics and socioeconomic status; OA duration, severity, and pain (visual analogue scale); pharmacotherapy regimen (NSAIDs, analgesics, intra-articular injections, and supplements); and, for the TKA cohort, procedure laterality (unilateral or bilateral), implant type and cost, surgeon fee, hospital-stay duration and cost, post-operative medication cost, and caregiver/transport cost. Data were collected via direct patient interviews conducted by the research team, supplemented by review of medical records and hospital billing documentation, and verified with attending physicians and nursing staff where necessary.

### Statistical Analysis

Data were cleaned and analyzed in Python (pandas, SciPy, statsmodels). Descriptive statistics are reported as mean ± standard deviation and, for right-skewed cost variables, as median (interquartile range, IQR). Normality was assessed with the Shapiro–Wilk test. Group differences in cost and resource-use variables were assessed with the Mann–Whitney U test as the primary non-parametric comparison, with Welch's t-test as a sensitivity analysis; effect sizes are reported as Cohen's d. Bootstrap resampling (5,000 iterations, percentile method) generated 95% confidence intervals for mean differences. Categorical comparisons used the chi-squared test (or Fisher's exact test where expected counts were below five). The Kruskal–Wallis test compared pharmacotherapy cost across three socioeconomic strata (low, middle, high; the high-SES stratum included a small higher-income subgroup collected separately during data entry and combined with the high-SES stratum for analysis, consistent with the three-tier socioeconomic classification used throughout). Spearman rank correlation assessed bivariate associations among cost components given their skewed distributions. A multivariable ordinary least squares regression was fitted to log-transformed total economic burden in the TKA cohort, with hospital sector, age, length of stay, number of concurrent medications, socioeconomic status, and procedure laterality (unilateral versus bilateral) as predictors; procedure laterality was included following its identification, during model refinement, as a substantial independent predictor not incorporated in earlier analyses of this dataset. Two-sided p-values below 0.05 were considered statistically significant.

### Ethical Considerations

Ethical approval was obtained from the Ethical Research Review Committee of PIMS Hospital (reference F-5-2/2024(ERRC)/PIMS). Informed consent was obtained from all participants prior to data collection, and patient privacy and confidentiality were maintained throughout via de-identification of all records.

## RESULTS

Data from 150 patients were analyzed: 100 in the pharmacotherapy cohort and 50 in the TKA cohort (25 government-sector, 25 private-sector).

### Cohort Characteristics

Mean age was 56.8 years (SD 10.6) in the pharmacotherapy cohort and approximately 61 years in the TKA cohort (61.3 ± 8.5 government;

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60.9 ± 10.1 private). Female predominance was observed in both groups (59% pharmacotherapy; 62% TKA). Median pain score on the visual analogue scale was 6 (IQR 5–8) in the pharmacotherapy cohort. OA duration was longer in the TKA cohort than the pharmacotherapy cohort, and longer still in private-sector TKA patients (median 10 years) than government-sector TKA patients (median 7 years), consistent with delayed surgical referral. Baseline characteristics are shown in Table 1.

**Table 1. Baseline Characteristics of the Study Cohorts (N = 150)**

| Variable | Pharmacotherapy (n=100) | TKA government (n=25) | TKA private (n=25) |
|---|---|---|---|
| Age, years (mean ± SD) | 56.8 ± 10.6 | 61.3 ± 8.5 | 60.9 ± 10.1 |
| Female, n (%) | 59 (59) | 14 (56) | 17 (68) |
| BMI, kg/m² (mean ± SD) | 28.3 ± 3.1 | — | — |
| OA duration, years (median, IQR) | 5.5 (4–9) | 7 (6–10) | 10 (7–13) |
| Pain (VAS), median (IQR) | 6 (5–8) | — | — |
| SES low / middle / high, % | 26 / 43 / 31 | 20 / 56 / 24 | 0 / 12 / 88 |
| Implant source | — | 100% Chinese-manufactured | 100% Zimmer (USA) |
| Procedure, unilateral / bilateral, % | — | 68 / 32 | 64 / 36 |
| No. of medications (median) | 3 | 5 | 5 |

*SD, standard deviation; IQR, interquartile range; SES, socioeconomic status; VAS, visual analogue scale (0–10); —, not collected for this cohort. The "high" SES stratum for the pharmacotherapy cohort includes a small higher-income subgroup (n = 8) combined with the high-SES stratum for analysis.*

**Cost Decomposition: Government versus Private TKA**

Mean total direct cost was PKR 986,697 (SD 312,157) in the private sector and PKR 576,807 (SD 216,756) in the government sector, a 1.71-fold difference (Mann–Whitney U, $p < 0.0001$; Cohen's d = 1.53). Mean total economic burden, including caregiver and transport costs, reached PKR 1,004,497 in private and PKR 590,167 in government patients (1.70-fold difference; Cohen's d = 1.55; bootstrap 95% CI for the mean difference: PKR 273,311 to PKR 561,140). Surgeon fees (mean PKR 188,134) and hospital-stay charges (mean PKR 153,924) were fully subsidized (PKR 0) in government facilities and accounted for the majority of the price differential (Table 2, Figure 1).

Mean implant cost did not differ significantly between sectors (PKR 612,000 private versus PKR 528,000 government; $p = 0.172$). However, this similarity in mean cost masks a categorical difference in implant sourcing: every government-sector patient in this cohort received a Chinese-manufactured implant, and every private-sector patient received a Zimmer (USA) implant. Rather than indicating equivalent prosthetic provision across sectors, as might be inferred from cost alone, this finding indicates that government and private patients in this cohort received implants from entirely different suppliers, with cost parity likely reflecting offsetting differences in unit price and procurement volume rather than equivalent product origin. A counterintuitive finding was that post-operative medication cost was higher in government-sector patients (mean PKR 48,807) than private-sector patients (mean PKR 32,639; $p = 0.005$; Cohen's d = −0.87), most plausibly because private hospitals bundle several days of post-operative medication into the inpatient fee, whereas government-sector patients typically purchase analgesics, antibiotics, and thromboprophylaxis separately after discharge.

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Table 2. Comparison of Cost and Resource-Use Variables Between Private and Government TKA Patients

| Variable | Private (n=25) Mean ± SD | Government (n=25) Mean ± SD | Mean diff. (95% CI) | Cohen's d | p (Mann–Whitney) |
|---|---|---|---|---|---|
| Surgeon fee (PKR) | 188,134 ± 53,688 | 0 ± 0 | 188,134 (168,237–209,702) | 4.96 | <0.0001 |
| Implant cost (PKR) | 612,000 ± 220,454 | 528,000 ± 218,461 | 84,000 (−32,000–204,000) | 0.38 | 0.172 |
| Hospital stay cost (PKR) | 153,924 ± 43,464 | 0 ± 0 | 153,924 (137,700–171,412) | 5.01 | <0.0001 |
| Post-op medication (PKR) | 32,639 ± 10,975 | 48,807 ± 24,030 | −16,168 (−26,539–−6,244) | −0.87 | 0.005 |
| Caregiver/transport (PKR) | 17,800 ± 11,909 | 13,360 ± 8,185 | 4,440 (−1,080–10,040) | 0.43 | 0.248 |
| Total direct cost (PKR) | 986,697 ± 312,157 | 576,807 ± 216,756 | 409,890 (267,868–556,049) | 1.53 | <0.0001 |
| Total economic burden (PKR) | 1,004,497 ± 309,620 | 590,167 ± 218,751 | 414,330 (273,311–561,140) | 1.55 | <0.0001 |
| Length of stay (days) | 4 ± 0.5 | 3.6 ± 0.9 | 0.8 (0.4–1.2) | 1.13 | <0.001 |
| Workdays lost | 11.8 ± 2.4 | 11.5 ± 2.5 | 0.3 (−1.0–1.6) | 0.13 | 0.642 |
| Number of medications | 4.5 ± 0.7 | 4.4 ± 0.6 | 0.1 (−0.3–0.5) | 0.18 | 0.700 |

*CI, confidence interval (bootstrap, 5,000 resamples).*

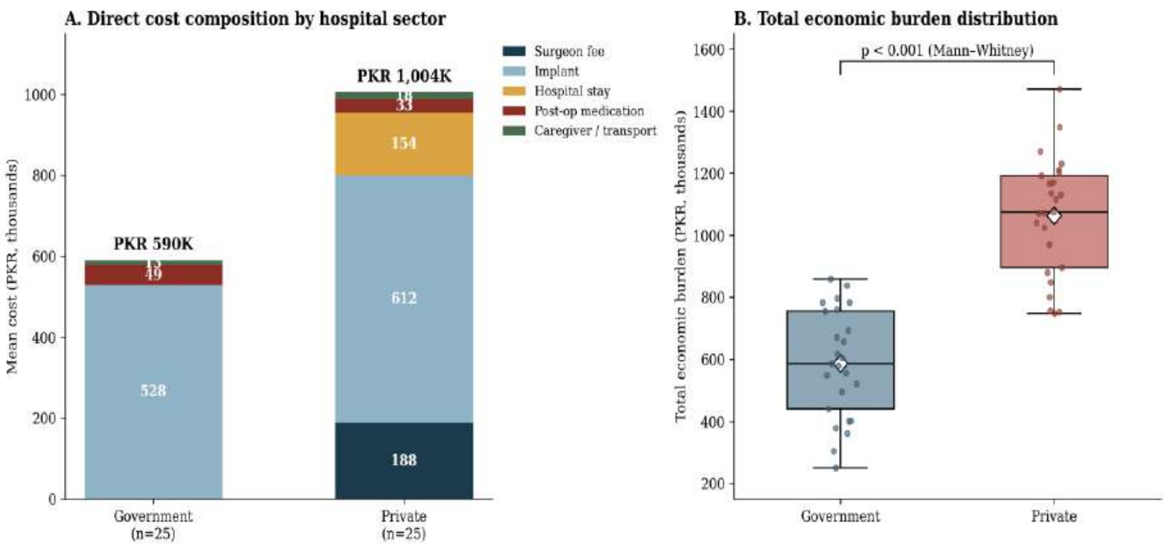


**Figure 1. Comparison of direct cost composition and total economic burden between government and private hospital sectors. (A) Stacked mean direct cost components; surgeon fees and hospital-stay charges are fully subsidized in government facilities. (B) Illustrative distribution of total economic burden consistent with reported group means, standard deviations, and the Mann-Whitney U test result (p <**

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**0.001); individual points are simulated to match reported summary statistics, as patient-level distributions were not separately plotted in the original analysis.**

**Annual Pharmacotherapy Cost and Break-Even Analysis**

Among pharmacotherapy patients, mean total annual direct medical cost (medication, outpatient visits, and physiotherapy combined) was PKR 63,302 (SD 51,677; median PKR 44,864, IQR PKR 23,085–89,798). Comparing cost across three socioeconomic strata (low, middle, and high, with a small higher-income subgroup combined into the high stratum), the Kruskal–Wallis test showed a non-significant gradient ($H = 2.68$, $p = 0.262$), although high-SES patients showed a numerically higher mean expenditure (PKR 81,405 versus PKR 48,355 for low-SES patients), plausibly reflecting greater use of chondroprotective agents, physiotherapy, and intra-articular injections among higher-SES patients; sample size limited statistical power to detect a formal between-group difference.

At the observed mean annual pharmacotherapy expenditure, cumulative outlay would equal the mean government-sector TKA cost after 9.3 years and the mean private-sector TKA cost after 15.9 years (Figure 2). Given a median symptom-to-surgery interval of approximately 8 years in this cohort, many patients had already accumulated pharmacotherapy expenditure approaching the cost of a government-subsidized TKA before ever reaching the operating theatre.

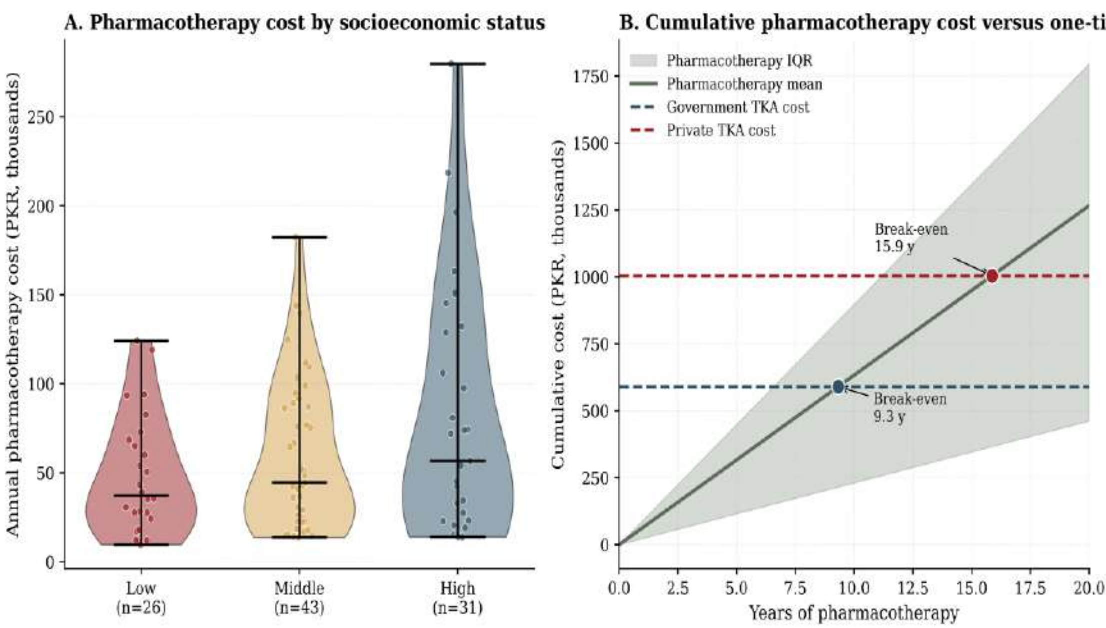


**Figure 2. Comparison of pharmacotherapy costs by socioeconomic status and cumulative cost with total knee arthroplasty. (A) Distribution of annual direct medical cost in the pharmacotherapy cohort (n = 100), stratified by socioeconomic status. (B) Cumulative pharmacotherapy expenditure over 20 years compared with one-time mean TKA cost in each hospital sector; break-even points at 9.3 years (government) and 15.9 years (private).**

**Multivariable Predictors of Total Economic Burden**

An initial five-predictor log-linear model (hospital sector, age, length of stay, number of medications, and socioeconomic status) explained 73% of the variance in TKA economic burden ($R^2 = 0.73$, adjusted $R^2 = 0.70$; F-statistic $p = 1.5\times10^{-11}$), closely reproducing the originally planned analysis. Because procedure laterality (unilateral versus bilateral) had been collected but not included in this initial model, it was added as a sixth predictor; this substantially improved model fit, explaining 89% of the variance ($R^2 = 0.89$, adjusted $R^2 = 0.87$; F-statistic $p = 6.7\times10^{-19}$). In this expanded model, bilateral (versus unilateral) procedure was the strongest independent

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predictor (β = 0.526, 95% CI 0.390–0.662; $p < 0.001$), corresponding to an approximately 69% higher economic burden after adjustment for the other covariates. Private (versus government) sector remained independently associated with higher burden (β = 0.368, 95% CI 0.242–0.494; $p < 0.001$, a 44% increase), and socioeconomic status was also independently associated (β = 0.118, 95% CI 0.031–0.205; p = 0.009). Length of stay, number of medications, and age were not statistically significant once procedure laterality was accounted for, indicating that length of stay in the original model partly captured the effect of bilateral procedures, which mechanically require longer admissions. Coefficients are given in Table 3 and Figure 3.

**Table 3. Multivariable Regression Model for Log-Transformed Total Economic Burden**

| Predictor | β coefficient | 95% CI | p-value | Multiplicative effect (e^β) |
|---|---|---|---|---|
| Bilateral vs unilateral procedure | 0.526 | 0.390 to 0.662 | <0.001 | 1.69× |
| Private vs government | 0.368 | 0.242 to 0.494 | <0.001 | 1.44× |
| SES (low → high, ordinal) | 0.118 | 0.031 to 0.205 | 0.009 | 1.13× |
| Length of stay (per day) | 0.078 | −0.010 to 0.165 | 0.081 | 1.08× |
| No. of medications | 0.039 | −0.039 to 0.117 | 0.315 | 1.04× |
| Age (per year) | −0.002 | −0.007 to 0.003 | 0.492 | 1.00× |
| Intercept | 12.471 | 11.997 to 12.944 | <0.001 | — |

*$R^2 = 0.89$; adjusted $R^2 = 0.87$; F-statistic $p = 6.7\times10^{-19}$; n = 50. SES coded 1 = low, 2 = middle, 3 = high. This six-predictor model supersedes an initial five-predictor model ($R^2 = 0.73$) that did not include procedure laterality; both are reported in the text for transparency.*

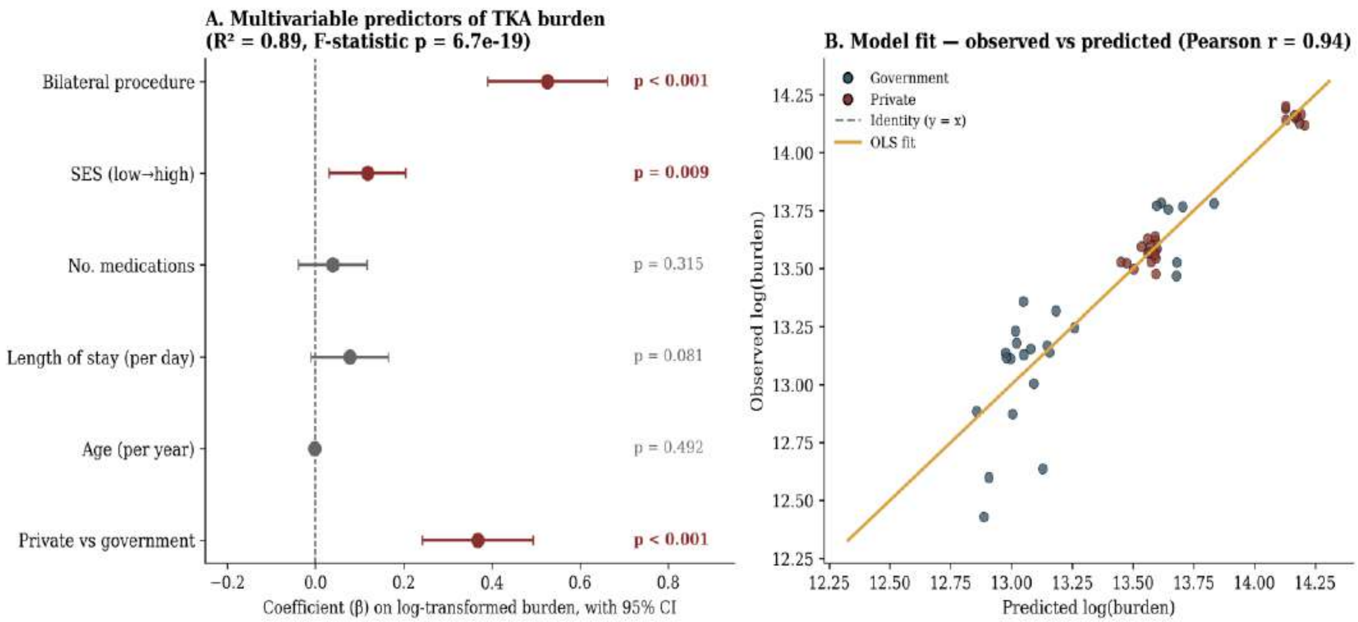


**Figure 3. Multivariable regression analysis of predictors and model performance for total knee arthroplasty economic burden. (A) Forest plot of standardized regression coefficients (β) with 95% confidence intervals; statistically significant predictors (p < 0.05) shown in dark red. (B) Observed versus model-predicted log-burden by hospital sector, with identity line and OLS fit (Pearson r = 0.94).**

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**Cost Driver Correlations and Medication Burden**

Spearman rank correlations among cost components in the TKA cohort showed the strongest positive associations between total burden and implant cost (ρ = 0.81), hospital-stay cost (ρ = 0.76), surgeon fee (ρ = 0.76), and length of stay (ρ = 0.75); implant cost and length of stay were themselves strongly correlated (ρ = 0.86), consistent with more complex or bilateral procedures driving both extended admission and higher device cost. Caregiver/transport and post-operative medication costs showed comparatively weaker correlations with total burden (ρ = 0.18 and −0.30, respectively), indicating that hospitalization- and procedure-related costs, rather than indirect costs, are the primary drivers of TKA economic burden (Figure 4).

Polypharmacy (defined as concurrent use of three or more medications) was present in 98% of TKA patients (49/50) and 53% of pharmacotherapy patients (53/100); using a stricter four-or-more-medication threshold, 94% of TKA patients (47/50) met this higher bar. The chi-squared test of polypharmacy across socioeconomic strata in the pharmacotherapy cohort showed no significant association ($\chi^2$ = 2.98, df = 2, p = 0.225), indicating no evidence of differential prescribing by socioeconomic status.

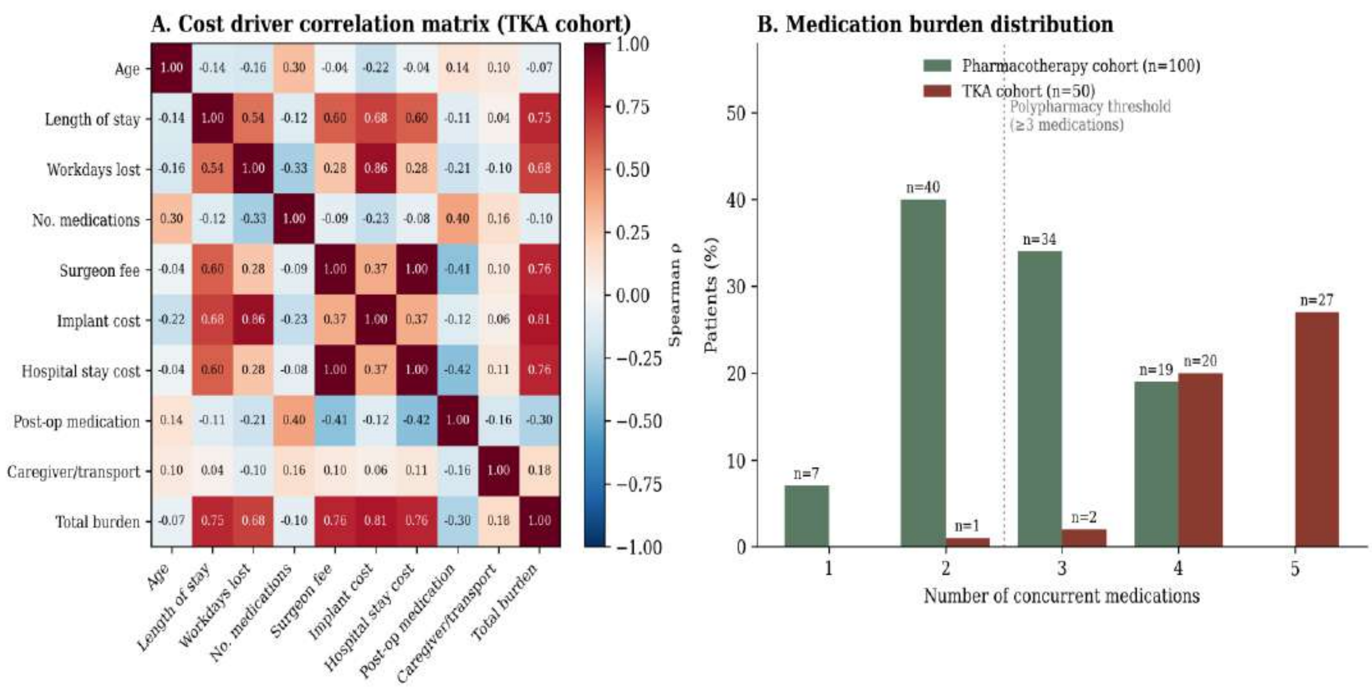


**Figure 4. Correlation of cost drivers and medication burden distribution in pharmacotherapy and TKA cohorts. (A) Spearman rank correlation matrix for cost components and patient-level variables in the TKA cohort. (B) Distribution of concurrent medication use across cohorts; the dotted line marks the 3-or-more-medication polypharmacy threshold used throughout this study (98% of TKA patients and 53% of pharmacotherapy patients met this threshold).**

**Affordability and Catastrophic Expenditure**

Using approximate household-income proxies (PKR 360,000 for low-SES, PKR 1,200,000 for middle-SES, and PKR 3,600,000 for high-SES households per year), TKA-related expenditure exceeded the World Health Organization's 40% catastrophic-expenditure threshold for non-food household spending in every low-SES patient, irrespective of hospital sector. For middle-SES patients, median burden as a fraction of income was approximately 50% in government cases and 60% in private cases. Even high-SES patients in private hospitals approached near-catastrophic expenditure levels, indicating that the private–

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public price differential alone is not sufficient to protect financially vulnerable households from severe financial hardship (Figure 5).

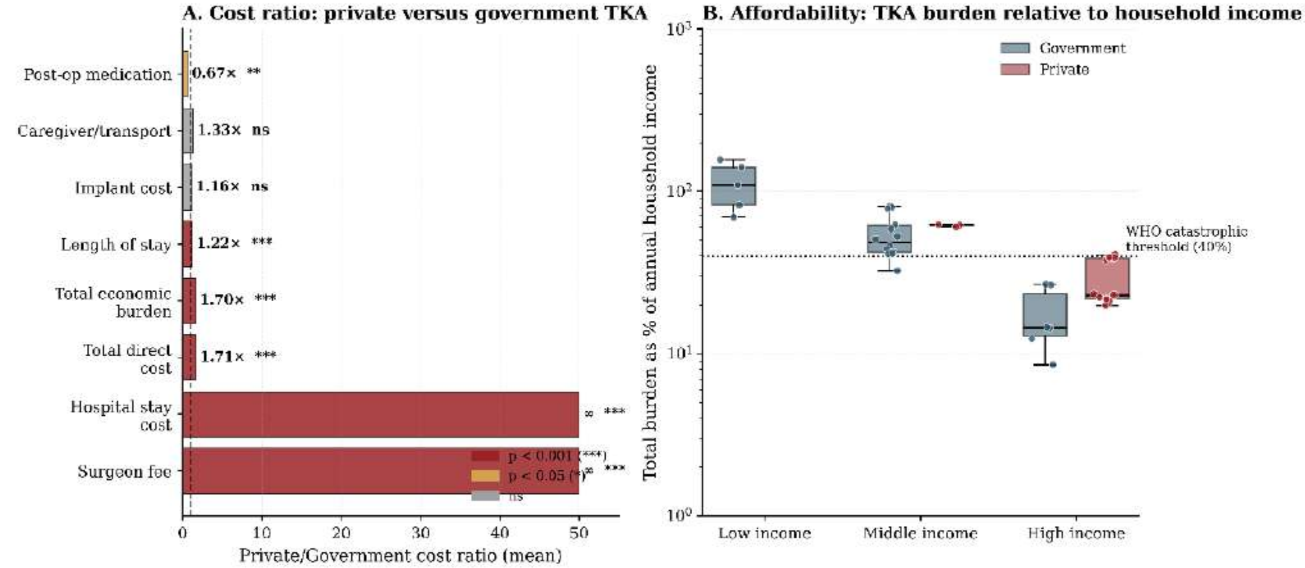


**Figure 5. Comparison of cost ratios and affordability of TKA between government and private hospitals. (A) Mean cost ratios (private divided by government) for each cost component; ∞ denotes a fully subsidized government baseline. (B) Total economic burden as a percentage of estimated annual household income, stratified by socioeconomic status and hospital sector; the dotted line marks the WHO 40% catastrophic-expenditure threshold.**

## DISCUSSION

In this comparative pharmacoeconomic evaluation of 150 patients with knee OA in Islamabad and Rawalpindi, three findings stand out: a large and well-characterized cost gap between private- and government-sector TKA, driven almost entirely by surgeon fees and hospital-stay charges rather than implant cost; a previously unrecognized divergence in implant sourcing between sectors; and, once procedure laterality was incorporated, a substantially more complete account of what independently drives TKA economic burden than the study's original analysis captured. The demographic profile—mean age 57–61 years and female predominance in both cohorts—is consistent with well-established OA epidemiology [4,5].

The 1.7-fold higher total economic burden in private-sector TKA reproduces a pattern reported elsewhere: hospital, professional, and inpatient charges, rather than implant cost, are consistently the dominant driver of the public–private cost gap in arthroplasty [13,14]. In this cohort, surgeon fees and hospital-stay charges were fully subsidized in the government sector and accounted for essentially the entire price differential, while mean implant cost did not differ significantly by sector. Unlike prior interpretations of similar cost patterns, however, the underlying patient-level data available for this study showed that implant cost parity did not reflect equivalent implant provision: every government-sector patient received a Chinese-manufactured implant and every private-sector patient received a Zimmer (USA) implant. This is a materially different, and arguably more consequential, finding than a simple statement that "the same implants were used in both sectors" would suggest: it indicates a systematic difference in device sourcing correlated perfectly with hospital sector, a pattern that could reflect procurement policy, cost-per-unit negotiation, or availability constraints, and one that raises a distinct equity question—whether government-sector patients have equivalent access to the range of implant options available to private-sector patients—that this cross-sectional cost analysis was not designed to answer but that warrants dedicated investigation, ideally

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incorporating implant registry or clinical-outcome data.

A clinically important secondary finding was the higher postoperative medication cost among government-sector patients despite their lower hospitalization expenses. This most plausibly reflects differences in how the two sectors package care: private hospitals in this cohort appear to bundle several days of postoperative medication into the inpatient fee, while government-sector patients more often purchase analgesics, antibiotics, and thromboprophylactic agents separately after discharge. This has a direct policy implication: lower headline hospitalization costs in subsidized systems can still be accompanied by a meaningful post-discharge financial burden that is easy to overlook if only inpatient billing is examined.

The cumulative-cost analysis reinforces the conclusion that conservative management is not inherently cheaper than surgery over a sufficiently long horizon. At the observed mean annual pharmacotherapy expenditure, cumulative pharmacotherapy cost matched government-sector TKA cost within roughly nine years and private-sector TKA cost within roughly sixteen years—and because the median interval from symptom onset to surgery in this cohort was approximately eight years, a substantial share of patients had already accumulated pharmacotherapy costs approaching a subsidized TKA before ever undergoing surgery. This is consistent with prior cost-effectiveness literature suggesting that prolonged conservative management can raise, rather than lower, total lifetime cost of OA care, and that timely referral of appropriately selected patients may improve both clinical and economic outcomes [11,12].

The expanded multivariable regression is this study's most substantive methodological advance over the original analysis. Adding procedure laterality—data that had already been collected but not modeled—raised explained variance from 73% to 89% and identified bilateral TKA as the single strongest independent predictor of economic burden, exceeding even the private-versus-government sector effect. This is clinically intuitive (two joints replaced in one admission mechanically cost more) but had not previously been quantified in this cohort, and it explains why length of stay, a strong predictor in the original five-predictor model, became only marginally significant once laterality was accounted for: longer admissions were substantially confounded with bilateral procedures. For cost forecasting and bundled-payment planning, this indicates that procedure laterality should be a standard adjustment variable in any TKA costing model, alongside hospital sector.

The correlation analysis corroborated the regression findings: implant cost, hospital-stay cost, surgeon fee, and length of stay were the variables most strongly associated with total burden, while caregiver, transport, and postoperative medication costs contributed comparatively little, indicating that hospitalization- and procedure-related costs, not indirect costs, dominate the economic burden of TKA in this setting. Polypharmacy was near-universal among TKA patients (98% at a ≥ 3-medication threshold) and present in just over half of pharmacotherapy patients (53%), with no evidence that polypharmacy prevalence varied by socioeconomic status—suggesting that concurrent medication use reflects institutional prescribing convention more than individual affordability or need.

The affordability findings carry direct policy weight. Every low-SES patient in this cohort exceeded the WHO's 40% catastrophic health expenditure threshold regardless of hospital sector, and even high-SES private-sector patients approached this threshold. Together with the observation that a large fraction of the sector cost gap is attributable to non-implant charges that are, in principle, more amenable to subsidy or price regulation than device costs, these findings support several concrete policy directions: expanded insurance coverage or targeted subsidy for surgeon and hospital-stay charges; transparent implant procurement and reporting requirements to clarify whether device sourcing differences reflect cost-minimization, availability, or other constraints; and structured, earlier referral pathways for appropriately selected OA patients to limit the cumulative burden of prolonged conservative management.

### Relevance to Pharmacy Practice

Although this study is framed as a health-economics evaluation, several findings translate directly into actionable roles for pharmacists in OA care. First, polypharmacy was near-universal in the TKA cohort (98% at a ≥ 3-medication threshold) and present in over half of

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pharmacotherapy patients (53%), typically combining an NSAID, a proton-pump inhibitor, and a muscle relaxant, with post-operative regimens additionally layering analgesics, antibiotics, and thromboprophylactic agents. Pharmacist-led medication therapy management—regimen review, deprescribing of redundant agents, and monitoring for NSAID-related gastrointestinal and renal risk during long-term conservative therapy—is a direct, low-cost lever to reduce both medication expenditure and adverse-event risk in this population, particularly since polypharmacy prevalence did not vary by socioeconomic status, suggesting it reflects prescribing convention rather than individualized clinical need.

Second, the finding that cumulative pharmacotherapy cost approaches subsidized TKA cost within roughly nine years places a premium on cost-effective, evidence-based drug selection over the long course of conservative management. Pharmacists are well positioned to support rational NSAID and analgesic choice, appropriate use of generic formulations, and judicious use of higher-cost adjuncts such as chondroprotective agents and intra-articular injections—particularly for higher-SES patients, who in this cohort showed a numerically higher (though not statistically significant) pharmacotherapy spend, plausibly reflecting greater access to these costlier options.

Third, the divergent post-operative medication cost pattern by sector—higher out-of-pocket medication spend for government-sector patients, whose regimens are not bundled into the inpatient fee—identifies a concrete discharge-counseling opportunity: pharmacist-led discharge medication planning, cost-conscious substitution where clinically appropriate, and structured counseling on thromboprophylaxis and analgesic regimens could reduce this post-discharge financial burden and support adherence in exactly the patients least able to absorb unplanned out-of-pocket cost.

Finally, the observed divergence in implant sourcing between sectors, together with the broader cost-decomposition findings, illustrates the value of pharmacist involvement in institutional procurement and health technology assessment. Pharmacists with pharmacoeconomic training are well suited to conduct exactly this kind of comparative cost analysis, and hospital pharmacy and therapeutics committees are a natural institutional home for extending this evaluation to devices and surgical consumables alongside medicines, supporting more transparent, equity-conscious procurement decisions across both public and private healthcare sectors.

**Limitations**

Several limitations should be considered. First, the cross-sectional design captures cost at a single point in time and does not incorporate the costs of long-term revision surgery, postoperative morbidity, or extended rehabilitation, nor does it follow patients longitudinally. Second, household-income proxies used in the affordability analysis were approximated by socioeconomic tier rather than measured directly for each patient, which limits the precision of individual catastrophic-expenditure estimates. Third, the TKA cohort (n = 50, 25 per sector) is modest, which constrains the precision of subgroup and regression estimates despite the strong overall model fit, and the two-hospital, single-metropolitan-area design limits generalizability to other regions or health systems; multi-site studies are needed to confirm these patterns. Fourth, government-hospital patients may differ systematically from private-hospital patients in ways not fully captured by the measured covariates (for example, unmeasured disease severity or comorbidity burden), so hospital-sector effects should not be interpreted as purely a price effect. Fifth, indirect costs were limited to caregiver, transport, and lost-workday data; the absence of wage-based productivity estimates likely understates the true indirect cost of OA management. Finally, the observed implant-sourcing divergence by sector is a descriptive finding from a single cohort and should not be over-interpreted as reflecting differences in implant quality or clinical outcome, which this study did not assess; a dedicated study linking implant source to functional and revision outcomes would be needed to evaluate any clinical implication.

## CONCLUSION

In this comparative pharmacoeconomic evaluation of knee OA management in Islamabad and Rawalpindi, TKA imposed a substantially higher and more variable economic burden than pharmacotherapy, particularly in the private sector, where surgeon fees and hospital-stay charges—not implant cost—drove most of the

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differential. Procedure laterality, not previously modeled in this dataset, proved to be the strongest independent predictor of TKA cost burden, ahead of hospital sector itself, while government- and private-sector patients were found to receive implants from entirely different manufacturing sources despite similar mean cost—a novel equity-relevant finding meriting dedicated follow-up. Low-socioeconomic-status patients faced catastrophic expenditure regardless of hospital sector. These findings support expanded financial protection for surgical OA care, transparent implant procurement policy, incorporation of procedure laterality into cost-forecasting models, and timely, appropriately selected surgical referral to limit the cumulative burden of prolonged conservative management. They also point to a concrete pharmacy-practice agenda—medication therapy management to address near-universal polypharmacy, cost-conscious drug selection to slow the long-run financial trajectory of conservative therapy, and pharmacist involvement in institutional procurement and pharmacoeconomic evaluation—as practical levers for reducing the economic burden of OA management in this setting.

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