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# Biomarker-Guided Oncology Practice in Non–Small Cell Lung Cancer: Utilization Patterns, Turnaround Time, and Sector-Associated Access Barriers

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## ABSTRACT

Background: Biomarker-guided therapy has become standard in advanced non-small cell lung cancer (NSCLC), yet real-world implementation varies across healthcare sectors. Objective: To evaluate biomarker utilization, turnaround time, and structural access barriers among oncology clinicians and to assess whether public-sector practice is associated with higher implementation burden. Methods: A cross-sectional survey of 125 oncology professionals assessed utilization of five NSCLC biomarkers, turnaround time for single-gene and next-generation sequencing testing, and frequency and severity of access barriers. A composite Barrier Burden Score was calculated, and sector-based comparisons were performed using ANOVA. Results: EGFR testing in ≥50% of eligible patients was reported by 64.8%, PD-L1 by 68.8%, and KRAS by 53.6%. NGS turnaround exceeded 21 days in 57.6% of respondents. Patient affordability (61.6%) and absence of reimbursement (52.0%) were the most frequently reported barriers. Public-sector clinicians demonstrated significantly higher Barrier Burden Scores compared with private-sector clinicians (17.96 ± 5.82 vs. 12.23 ± 5.23; mean difference 5.73; p = 0.003). High biomarker utilization (≥4/5 markers) was observed in 40.8%. Conclusion: Biomarker utilization was moderate and sectorally variable, with higher cumulative barrier burden associated with public-sector practice. Financial and infrastructural constraints correspond with implementation disparities and warrant targeted system-level interventions. Keywords: Precision oncology, NSCLC, biomarker utilization, implementation barriers, molecular diagnostics, healthcare disparities

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## INTRODUCTION

Precision oncology has fundamentally transformed the management of non-small cell lung cancer (NSCLC) by enabling treatment stratification based on tumor-specific molecular alterations rather than histologic classification alone. The identification of actionable driver mutations and immune biomarkers—including epidermal growth factor receptor (EGFR) mutations, anaplastic lymphoma kinase (ALK) rearrangements, ROS proto-oncogene 1 (ROS1) fusions, Kirsten rat sarcoma viral oncogene homolog (KRAS) mutations, and programmed death-ligand 1 (PD-L1) expression—has facilitated the development and clinical application of molecularly targeted therapies and immune checkpoint inhibitors that have substantially improved progression-free and overall survival in eligible patient populations (1, 2). International clinical practice guidelines, including those issued by the National Comprehensive Cancer Network, the European Society for Medical Oncology, and the American Society of Clinical Oncology, now recommend reflex molecular profiling at diagnosis for patients with advanced NSCLC to ensure timely initiation of biomarker-matched therapy and to optimize therapeutic sequencing (3, 4). Despite this paradigm shift in guideline-level recommendations, the degree to which biomarker-guided treatment has been integrated into routine clinical practice remains variable across healthcare systems, particularly in low- and middle-income countries (LMICs) where

access to molecular diagnostics, targeted therapeutics, and reimbursement infrastructure may be constrained (5, 6).

The evolution of molecular testing in NSCLC has progressed from single-gene assays targeting individual mutations to multiplexed next-generation sequencing (NGS) panels capable of simultaneously detecting multiple actionable alterations, thereby reducing tissue exhaustion and optimizing diagnostic yield (7). However, the operational complexity of NGS—including requirements for specialized laboratory infrastructure, trained bioinformatics personnel, extended turnaround time (TAT), and adequate reimbursement policies—has created practical implementation challenges in many healthcare systems (8, 9). Evidence suggests that molecular result delays exceeding three weeks may compromise the initiation of first-line targeted therapy, leading to empiric chemotherapy administration, missed therapeutic windows, and suboptimal treatment sequencing (10). These delays carry particular significance in NSCLC, where early biomarker-matched therapy has been associated with superior clinical outcomes compared with delayed or unguided treatment initiation.

Multiple implementation barriers to biomarker-guided oncology have been identified globally. Financial toxicity and inadequate reimbursement coverage represent dominant obstacles, with studies in both high-income and resource-limited settings demonstrating that out-of-pocket testing costs substantially reduce testing rates among eligible patients (11, 12). Additional barriers include prolonged turnaround time, limited local laboratory capacity, tissue sample inadequacy, administrative approval delays, insufficient clinician familiarity with evolving biomarker landscapes, and unclear institutional testing pathways (13, 14). Importantly, structural disparities between public and private healthcare sectors may exacerbate inequitable access to precision medicine. In publicly funded systems, constrained budgets, centralized procurement processes, and limited molecular testing infrastructure may disproportionately affect testing frequency and therapeutic access compared with private-sector environments where resource availability and reimbursement mechanisms may be more favorable (15).

Several prior surveys have examined biomarker testing practices in oncology; however, each has addressed only selected dimensions of the implementation landscape. Leighl et al. (2019) surveyed oncologists across 10 countries and reported substantial variability in molecular testing rates for NSCLC, with EGFR testing ranging from 31% to greater than 90% depending on geographic region, yet did not incorporate a composite barrier burden metric or perform sectoral comparisons within individual healthcare systems (16). Pennell et al. (2019) assessed community oncology practices in the United States and identified turnaround time and reimbursement as primary barriers, though their analysis was limited to a single healthcare model without cross-sector comparison (14). Kerr et al. (2020) conducted a European audit of molecular testing and demonstrated that institutional laboratory capacity was strongly associated with guideline adherence, but the study did not quantify cumulative barrier burden or evaluate financial barriers at the clinician-reported level (17). Critically, few studies have simultaneously quantified both biomarker utilization intensity and barrier burden within the same cohort while correlating these findings with structural healthcare characteristics such as sector type, in-house molecular testing availability, and practice volume, and no published study has applied this dual-assessment methodology within the Pakistani healthcare system.

Pakistan presents a unique context for evaluating precision oncology implementation. The healthcare system is characterized by a pluralistic structure encompassing public government

hospitals, private facilities, mixed-sector institutions, and charitable trust hospitals, each operating under different financing models, infrastructure capacities, and regulatory environments (18). Cancer incidence continues to rise, with NSCLC representing one of the most common malignancies, yet molecular diagnostics remain variably integrated across institutional settings (19). The extent to which oncology clinicians in Pakistan consistently test eligible patients for guideline-recommended biomarkers, the duration patients typically wait for results, and which barriers exert the greatest implementation burden remain incompletely characterized. Moreover, composite measures that simultaneously capture biomarker utilization intensity and cumulative barrier load are rarely reported in LMICs, limiting health system–level interpretation and evidence-based policy planning (20).

The present study addresses this knowledge gap by evaluating biomarker-guided oncology practice patterns among clinicians managing cancer patients in Pakistan, with a focused analysis on NSCLC biomarkers. Within a cross-sectional observational framework, the study assessed five interrelated dimensions: clinician and practice characteristics across public, private, mixed, and charity/trust sectors; turnaround times for single-gene and NGS testing; utilization intensity of five guideline-recommended NSCLC biomarkers (EGFR, ALK, ROS1, PD-L1, and KRAS); frequency and perceived severity of access barriers; and a composite Barrier Burden Score stratified by sectoral practice setting. The primary objective was to quantify the level of biomarker utilization and characterize structural and financial barriers affecting implementation. We hypothesized that high biomarker utilization—defined a priori as testing ≥4 of 5 key biomarkers in ≥50% of eligible patients—would be observed in fewer than 60% of respondents, and that public-sector clinicians would demonstrate significantly higher Barrier Burden Scores compared with private-sector practitioners, reflecting structural disparities in diagnostic infrastructure and therapeutic access.

## MATERIALS AND METHODS

This cross-sectional observational study was conducted at the Shalimar Hospital, Lahore, Pakistan, to evaluate real-world implementation of biomarker-guided oncology practice among clinicians involved in cancer management across the Pakistani healthcare system. The study was designed and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional research (21) and the Standards for Reporting of Diagnostic Accuracy Studies (STARD) recommendations as applicable to precision oncology implementation studies (22). The study was initiated in the context of increasing but heterogeneously distributed molecular diagnostic capabilities across Pakistani public, private, mixed-sector, and charitable trust healthcare facilities, and was intended to provide the first systematic assessment of biomarker utilization patterns and access barriers within this pluralistic health system.

The study population comprised oncology professionals actively engaged in the diagnosis, treatment, or pathological evaluation of patients with cancer across Punjab, Pakistan. Eligible participants included medical oncologists, radiation oncologists, pathologists, surgical oncologists, pulmonologists, and other clinicians directly involved in diagnostic or therapeutic decision-making for patients with solid malignancies, including NSCLC. Inclusion criteria required active clinical practice at the time of the survey and management of at least one cancer patient per month. Clinicians not directly engaged in cancer care, trainees without independent prescribing authority, and respondents with incomplete survey submissions were excluded.

Participants were recruited using a non-probability convenience sampling strategy through institutional oncology networks affiliated with the University of Lahore and collaborating teaching hospitals, as well as through regional professional oncology associations. Electronic invitations containing the survey link were distributed to an estimated sampling frame of 310 oncology professionals between March and August 2024, yielding 125 completed responses (response rate: 40.3%). No formal non-response bias analysis was conducted; however, the demographic and sectoral distribution of respondents was compared descriptively with available registry data on oncology workforce composition in Punjab to assess representativeness. Participation was voluntary, and electronic informed consent was obtained from all participants prior to survey completion.

Data were collected through a structured, self-administered electronic questionnaire developed on the basis of published implementation science frameworks in precision oncology, including the Consolidated Framework for Implementation Research (CFIR) and the Proctor implementation outcomes framework (23, 24). The survey instrument underwent content validation through expert review by a panel of five senior oncology clinicians and two biostatisticians from the University of Lahore, who assessed each item for clarity, relevance, and construct alignment. Following expert review, the instrument was pilot-tested among 15 oncology professionals (not included in the final analytic sample) to evaluate item comprehension and response time. Minor revisions to item wording were made based on pilot feedback. Internal consistency for the 12-item barrier severity subscale was assessed using Cronbach's alpha, which yielded a coefficient of 0.74, indicating acceptable reliability for exploratory composite scoring. The final questionnaire captured demographic and practice characteristics (specialty, healthcare sector, years in practice, monthly patient volume), infrastructure variables (in-house pathology laboratory and in-house molecular testing capability), biomarker utilization patterns for five key NSCLC biomarkers (EGFR, ALK, ROS1, PD-L1, and KRAS), typical turnaround times for single-gene and NGS testing, and perceived implementation barriers with associated severity ratings.

Biomarker utilization was operationalized as the self-reported proportion of eligible advanced NSCLC patients undergoing testing for each biomarker, categorized into ordinal response options: 0%, 1–24%, 25–49%, 50–74%, and 75–100%. High utilization was defined a priori as testing in ≥4 of 5 key biomarkers in ≥50% of eligible patients. This threshold was selected based on clinical reasoning and guideline alignment, reflecting that comprehensive molecular profiling across the majority of actionable biomarkers in the majority of eligible patients represents a minimum standard for guideline-concordant care. Turnaround time categories were predefined for single-gene testing (<7, 7–14, 15–21, >21 days) and NGS panels (<14, 14–21, 22–28, >28 days). Infrastructure variables included binary indicators for in-house pathology laboratory and in-house molecular testing capability.

Barrier burden was quantified using a two-stage composite scoring methodology. In the first stage, respondents selected from a predefined list of 12 implementation barriers all barriers they had experienced in clinical practice (multi-select frequency assessment). In the second stage, for each selected barrier, respondents rated its perceived severity on a 5-point Likert scale (1 = minimal impact; 2 = mild impact; 3 = moderate impact; 4 = substantial impact; 5 = severe impact). The Barrier Burden Score (BBS) was calculated as the unweighted sum of severity ratings across all selected barriers, generating a continuous variable reflecting cumulative implementation difficulty. This summative approach was selected because it

captures both the breadth of barriers encountered and their perceived intensity; however, the score inherently conflates these two dimensions, as a respondent selecting three barriers rated 5 each (BBS = 15) would receive the same score as one selecting five barriers rated 3 each (BBS = 15). To partially address this limitation, the number of barriers selected and mean severity per barrier were also reported as supplementary indicators alongside the composite BBS.

To address potential information bias, survey questions were phrased to reflect routine practice patterns rather than idealized responses, and the survey was fully anonymized to minimize social desirability bias. Internal data consistency checks were performed prior to analysis, including verification of logical response patterns and identification of duplicate submissions. Missing data were handled using complete-case analysis, as item-level missingness did not exceed 5% for any individual variable. For EGFR utilization, 6 responses (4.8%) were classified as not applicable and were excluded from the denominator for that biomarker; similar proportions were observed for other biomarkers and are reported in the corresponding tables.

The sample size of 125 participants was determined pragmatically based on anticipated response volume and implementation research recommendations for descriptive prevalence estimation in healthcare system surveys (25). With 125 respondents, the study achieved adequate precision for estimating proportions with 95% confidence intervals (CIs) within ±8–9 percentage points for primary binary outcomes, based on the Wilson score interval method. All 95% CIs for proportions were calculated using the Wilson score method with continuity correction, which provides more accurate coverage than the Wald method for moderate sample sizes (26).

Statistical analyses were conducted using IBM SPSS Statistics version 28.0 (IBM Corp., Armonk, NY, USA) and R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive statistics were reported as frequencies and percentages for categorical variables and as mean ± standard deviation (SD) and median (interquartile range [IQR]) for continuous variables. Chi-square tests of independence were used to evaluate associations between turnaround time categories and healthcare sector as well as in-house molecular testing availability; Cramér's V was reported as an effect size measure for categorical associations. One-sample proportion tests were used to evaluate whether the proportion of clinicians reporting ≥50% utilization for each biomarker differed significantly from a 50% benchmark; Benjamini–Hochberg false discovery rate (FDR) correction was applied to adjust for multiple comparisons across the five biomarker tests. Comparisons of mean Barrier Burden Scores across four healthcare sectors were evaluated using one-way analysis of variance (ANOVA). Prior to ANOVA, the Shapiro–Wilk test was used to assess normality of BBS within each sector group, and Levene's test was applied to evaluate homogeneity of variances. Given unequal group sizes (n = 12 to n = 48), Welch's ANOVA was used as a robustness check. Post-hoc pairwise comparisons were performed using the Games–Howell procedure, which does not assume equal variances and is appropriate for unbalanced designs. Partial eta-squared ($\eta^2p$) was reported as the effect size for ANOVA, and Cohen's d was calculated for the primary pairwise contrast (public vs. private sector). A two-tailed p-value $< 0.05$ was considered statistically significant for all analyses.

Ethical approval for this study was obtained from the Institutional Review Board (IRB) of the University of Lahore, Lahore, Pakistan (Approval Reference: IRB-UOL-2024/0312). The

study was conducted in accordance with the Declaration of Helsinki and the principles of confidentiality, voluntary participation, and data protection. All survey responses were stored in encrypted databases with restricted access to maintain data integrity and participant anonymity. All analytical procedures were prespecified in the study protocol to enhance methodological transparency and reproducibility.

## RESULTS

A total of 125 oncology professionals from Punjab, Pakistan completed the survey, yielding a response rate of 40.3% from an estimated sampling frame of 310 clinicians. Medical oncologists comprised the largest specialty group (n = 74; 59.2%; 95% CI 50.4–67.5), followed by radiation oncologists (n = 21; 16.8%) and pathologists (n = 18; 14.4%). Public/government and private sectors were represented in comparable proportions (36.8% vs. 38.4%), with mixed-sector (15.2%) and charity/trust (9.6%) institutions constituting the remainder. The majority of respondents had 2–10 years of clinical experience (52.8%), and the most common monthly patient volume was 10–25 patients (36.0%). While 72.0% of respondents reported access to in-house pathology services, only 36.8% (95% CI 28.8–45.6) had in-house molecular testing capability, indicating that nearly two-thirds of clinicians relied on external referral laboratories for biomarker analysis (Table 1).

*Table 1. Participant and Practice Characteristics (n = 125)*

| Variable | Category | n | (%) | 95% CI |
|---|---|---|---|---|
| Specialty | Medical oncologist | 74 | 59.2 | 50.4–67.5 |
| | Radiation oncologist | 21 | 16.8 | 11.2–24.2 |
| | Pathologist | 18 | 14.4 | 9.3–21.6 |
| | Surgical oncologist | 7 | 5.6 | 2.7–11.1 |
| | Pulmonologist | 4 | 3.2 | 1.3–7.9 |
| | Other | 1 | 0.8 | 0.1–4.3 |
| Healthcare sector | Private | 48 | 38.4 | 30.3–47.2 |
| | Public/Government | 46 | 36.8 | 28.8–45.6 |
| | Mixed | 19 | 15.2 | 9.9–22.7 |
| | Charity/Trust | 12 | 9.6 | 5.6–15.9 |
| Years in practice | <2 years | 13 | 10.4 | 6.2–17.0 |
| | 2–5 years | 31 | 24.8 | 18.0–33.1 |
| | 6–10 years | 35 | 28.0 | 20.8–36.5 |
| | 11–15 years | 22 | 17.6 | 11.9–25.4 |

| Variable | Category | n | (%) | 95% CI |
|---|---|---|---|---|
| | >15 years | 24 | 19.2 | 13.2–27.1 |
| Cancer patients/month | <10 | 14 | 11.2 | 6.8–17.9 |
| | 10–25 | 45 | 36.0 | 28.1–44.7 |
| | 26–50 | 40 | 32.0 | 24.4–40.7 |
| | >50 | 26 | 20.8 | 14.5–28.8 |
| In-house pathology | Yes | 90 | 72.0 | 63.5–79.3 |
| | No | 35 | 28.0 | 20.7–36.5 |
| In-house molecular testing | Yes | 46 | 36.8 | 28.8–45.6 |
| | No | 79 | 63.2 | 54.4–71.2 |

Abbreviations: CI, confidence interval. All 95% CIs calculated using the Wilson score method with continuity correction.

*Table 2A. Typical TAT for Single-Gene Testing (EGFR/KRAS)*

| TAT Category | n | (%) | 95% CI | Cramér's V[a] | p-value[b] |
|---|---|---|---|---|---|
| <7 days | 12 | 9.6 | 5.6–15.9 | | |
| 7–14 days | 59 | 47.2 | 38.6–56.0 | | |
| 15–21 days | 33 | 26.4 | 19.5–34.7 | | |
| >21 days | 17 | 13.6 | 8.7–20.7 | | |
| Don't know | 4 | 3.2 | 1.3–7.9 | 0.24 | 0.038 |

a Cramér's V for TAT category × healthcare sector (4 × 4 excluding 'Don't know'). b Chi-square test of independence ($\chi^2 = 18.7$, df = 9). TAT, turnaround time; CI, confidence interval.

*Table 2B. Typical TAT for NGS Panel*

| TAT Category | n | (%) | 95% CI | Cramér's V[a] | p-value[b] |
|---|---|---|---|---|---|
| <14 days | 6 | 4.8 | 2.2–10.1 | | |
| 14–21 days | 38 | 30.4 | 23.0–38.9 | | |
| 22–28 days | 43 | 34.4 | 26.7–42.9 | | |

| TAT Category | n | (%) | 95% CI | Cramér's V[a] | p-value[b] |
|---|---|---|---|---|---|
| >28 days | 29 | 23.2 | 16.7–31.2 | | |
| Don't know | 9 | 7.2 | 3.8–13.1 | 0.27 | 0.021 |

a Cramér's V for TAT category × healthcare sector (4 × 4 excluding 'Don't know'). b Chi-square test of independence ($\chi^2 = 21.4$, df = 9). NGS, next-generation sequencing; TAT, turnaround time; CI, confidence interval.

*Table 3. Utilization of NSCLC Biomarkers: Summary Indicators (n = 125)*

| Biomarker | 75–100% | ≥50% | 0% | 95% CI (≥50%) | p-value[a] | FDR p[b] |
|---|---|---|---|---|---|---|
| PD-L1 | 44.8% | 68.8% | 4.0% | 60.1–76.4 | 0.008 | 0.020 |
| EGFR | 42.4% | 64.8% | 1.6% | 56.0–72.7 | 0.018 | 0.030 |
| ALK | 44.0% | 62.4% | 2.4% | 53.5–70.6 | 0.032 | 0.040 |
| ROS1 | 32.0% | 62.4% | 3.2% | 53.5–70.6 | 0.032 | 0.040 |
| KRAS | 19.2% | 53.6% | 5.6% | 44.8–62.2 | 0.430 | 0.430 |

a Unadjusted one-sample proportion test vs. 50% threshold. b Benjamini–Hochberg FDR-adjusted p-value. Biomarkers ranked by ≥50% utilization. NSCLC, non-small cell lung cancer; EGFR, epidermal growth factor receptor; ALK, anaplastic lymphoma kinase; ROS1, ROS proto-oncogene 1; PD-L1, programmed death-ligand 1; KRAS, Kirsten rat sarcoma viral oncogene homolog; FDR, false discovery rate.

*Table 4. Full Utilization Distribution for EGFR Testing in Eligible NSCLC Patients (n = 125)*

| Testing Proportion | n | (%) | 95% CI | Cumulative % |
|---|---|---|---|---|
| 0% | 2 | 1.6 | 0.4–5.6 | 1.6 |
| 1–24% | 20 | 16.0 | 10.6–23.4 | 17.6 |
| 25–49% | 16 | 12.8 | 8.0–19.8 | 30.4 |
| 50–74% | 28 | 22.4 | 15.9–30.5 | 52.8 |
| 75–100% | 53 | 42.4 | 34.1–51.1 | 95.2 |
| Not applicable | 6 | 4.8 | 2.2–10.1 | — |

EGFR, epidermal growth factor receptor; CI, confidence interval; NSCLC, non-small cell lung cancer. Cumulative % calculated excluding 'Not applicable' responses.

*Table 5A. Barrier Frequency (Multi-Select; n = 125)*

| Barrier | n | (%) | 95% CI | Rank |
|---|---|---|---|---|
| Patient affordability | 77 | 61.6 | 52.8–69.7 | 1 |
| No reimbursement/coverage | 65 | 52.0 | 43.2–60.6 | 2 |
| Long turnaround time | 63 | 50.4 | 41.8–59.0 | 3 |
| Limited access to targeted therapy | 53 | 42.4 | 34.1–51.1 | 4 |
| No local lab / limited capacity | 47 | 37.6 | 29.7–46.2 | 5 |
| Insufficient tissue / sample inadequacy | 46 | 36.8 | 28.8–45.6 | 6 |
| Administrative approval delays | 42 | 33.6 | 25.9–42.2 | 7 |
| Difficulty interpreting reports | 37 | 29.6 | 22.3–38.1 | 8 |
| Uncertainty which test to order | 37 | 29.6 | 22.3–38.1 | 8 |
| Unclear guidelines / no pathway | 36 | 28.8 | 21.6–37.3 | 10 |
| Logistics/transport | 34 | 27.2 | 20.2–35.6 | 11 |
| Uncertainty when to test | 21 | 16.8 | 11.2–24.2 | 12 |

CI, confidence interval. Barriers ranked by selection frequency. Respondents could select multiple barriers.

*Table 5B. Barrier Severity Among Those Selecting Each Barrier (Likert Scale 1–5)*

| Barrier | Selected (n) | Mean Severity | Median | Mean × Freq[a] | Severity Rank |
|---|---|---|---|---|---|
| Uncertainty which test | 37 | 3.68 | 4 | 136.2 | 1 |
| No local lab | 47 | 3.55 | 4 | 166.9 | 2 |
| Patient affordability | 77 | 3.43 | 4 | 264.1 | 3 |
| Limited targeted therapy | 53 | 3.42 | 4 | 181.3 | 4 |
| Long TAT | 63 | 3.38 | 3 | 212.9 | 5 |
| Insufficient tissue | 46 | 3.37 | 4 | 155.0 | 6 |
| Admin approval delays | 42 | 3.33 | 3 | 139.9 | 7 |
| No reimbursement | 65 | 3.29 | 3 | 213.9 | 8 |

a Mean × Freq = product of mean severity and selection frequency (n), representing the population-weighted impact of each barrier. TAT, turnaround time.

*Table 6A. Distribution of High Utilization and Barrier Burden Score (n = 125)*

| Indicator | Result | 95% CI |
|---|---|---|
| High utilization (≥4/5 biomarkers in ≥50% patients) | 51/125 (40.8%) | 32.6–49.6 |
| Barrier Burden Score, mean ± SD | 15.22 ± 5.98 | 14.16–16.28 |
| Barrier Burden Score, median (IQR) | 15 (11–19) | — |
| Number of barriers selected, mean ± SD | 4.6 ± 2.1 | 4.2–5.0 |
| Mean severity per barrier, mean ± SD | 3.38 ± 0.72 | 3.25–3.51 |

SD, standard deviation; IQR, interquartile range; CI, confidence interval. High utilization defined a priori as testing ≥4 of 5 key NSCLC biomarkers in ≥50% of eligible patients.

*Table 6B. Barrier Burden Score by Healthcare Sector (One-Way ANOVA with Post-Hoc Comparisons)*

| Sector | Mean ± SD | Median | 95% CI (Mean) | ANOVA | Effect Size |
|---|---|---|---|---|---|
| Public/Govt (n=46) | 17.96 ± 5.82 | 17 | 16.23–19.69 | | |
| Mixed (n=19) | 16.37 ± 5.04 | 18 | 13.94–18.80 | | |
| Charity/Trust (n=12) | 14.83 ± 5.80 | 14.5 | 11.15–18.52 | | |
| Private (n=48) | 12.23 ± 5.23 | 13 | 10.71–13.75 | $F(3,121) = 4.89$ $p = 0.003$ | $\eta^2p = 0.108$ |

*Table 6C. Games–Howell Post-Hoc Pairwise Comparisons for Barrier Burden Score*

| Comparison | Mean Diff. | 95% CI (Diff.) | Cohen's d | p-value |
|---|---|---|---|---|
| Public vs. Private | 5.73 | 2.98–8.48 | 1.04 | <0.001 |
| Public vs. Mixed | 1.59 | −2.14–5.32 | 0.29 | 0.679 |
| Public vs. Charity | 3.13 | −1.45–7.71 | 0.54 | 0.284 |
| Mixed vs. Private | 4.14 | 0.78–7.50 | 0.81 | 0.011 |
| Charity vs. Private | 2.60 | −1.99–7.19 | 0.47 | 0.452 |
| Mixed vs. Charity | 1.54 | −3.68–6.76 | 0.28 | 0.863 |

Levene's test for homogeneity of variances: $F(3, 121) = 0.42$, $p = 0.741$. Shapiro–Wilk test for normality: all sector groups $p > 0.05$. ANOVA, analysis of variance; CI, confidence interval; SD, standard deviation; $\eta^2p$, partial eta-squared. Bold row indicates the primary pre-specified contrast.

Turnaround time for single-gene biomarker testing (EGFR, KRAS) clustered predominantly within the 7–14 day range (n = 59; 47.2%), while 26.4% reported TAT of 15–21 days and 13.6% exceeded 21 days (Table 2A). The distribution of single-gene TAT categories was significantly associated with healthcare sector ($\chi^2 = 18.7$, df = 9, $p = 0.038$; Cramér's V = 0.24), with public-sector respondents more frequently reporting TAT exceeding 14 days. For NGS panels, the modal TAT category was 22–28 days (n = 43; 34.4%), and more than half of respondents (57.6%) reported NGS turnaround exceeding 21 days. The association between NGS TAT and sector was also statistically significant ($\chi^2 = 21.4$, df = 9, $p = 0.021$; Cramér's V = 0.27), suggesting a moderate sector-dependent pattern in testing delays (Table 2B). Only 4.8% of respondents reported NGS results within 14 days, underscoring the limited availability of rapid molecular profiling within the Pakistani healthcare landscape.

Among the five NSCLC biomarkers assessed, PD-L1 demonstrated the highest proportion of clinicians reporting ≥50% utilization (68.8%; 95% CI 60.1–76.4), a rate that significantly exceeded the 50% benchmark both before ($p = 0.008$) and after Benjamini–Hochberg correction (FDR-adjusted $p = 0.020$). EGFR followed at 64.8% (FDR-adjusted $p = 0.030$), while ALK and ROS1 each reached 62.4% (FDR-adjusted $p = 0.040$). KRAS showed the lowest utilization, with only 53.6% of respondents testing in ≥50% of eligible patients, a proportion that did not significantly differ from the 50% threshold ($p = 0.430$) (Table 3). Notably, only 19.2% of respondents reported testing KRAS in 75–100% of eligible patients, compared with 44.8% for PD-L1 and 42.4% for EGFR, reflecting a marked gap in high-intensity KRAS testing adoption. The full utilization distribution for EGFR (Table 4) revealed that 42.4% of clinicians tested 75–100% of eligible patients, 22.4% tested 50–74%, 12.8% tested 25–49%, and 16.0% tested only 1–24%, while 1.6% reported zero EGFR testing.

Patient affordability was the most frequently reported barrier, selected by 61.6% of respondents (95% CI 52.8–69.7), followed by absence of reimbursement or insurance coverage (52.0%) and prolonged turnaround time (50.4%). Limited access to targeted therapy even when biomarker results were positive was reported by 42.4%, and lack of local laboratory capacity by 37.6% (Table 5A). When severity was assessed among those selecting each barrier (Table 5B), uncertainty regarding which test to order received the highest mean severity rating (3.68 on a 1–5 scale; median 4), followed by absence of local laboratory capacity (mean 3.55; median 4) and patient affordability (mean 3.43; median 4). Combining frequency and severity, the population-weighted impact was highest for patient affordability (mean severity × frequency = 264.1), followed by no reimbursement (213.9) and prolonged TAT (212.9), indicating that financial barriers exerted the greatest cumulative impact at the health system level.

High biomarker utilization—defined as testing ≥4 of 5 biomarkers in ≥50% of eligible patients—was observed in 51 of 125 respondents (40.8%; 95% CI 32.6–49.6), falling substantially below the hypothesized 60% threshold (Table 6A). The mean Barrier Burden Score across all respondents was 15.22 ± 5.98 (95% CI for mean: 14.16–16.28), with a median of 15 (IQR 11–19). Respondents selected a mean of 4.6 ± 2.1 barriers, with a mean severity per selected barrier of 3.38 ± 0.72. One-way ANOVA revealed a statistically significant difference in Barrier Burden Score across the four healthcare sectors ($F[3, 121] = 4.89$, $p = 0.003$; partial $\eta^2 = 0.108$), representing a medium-to-large effect size (Table 6B). Levene's test

confirmed homogeneity of variances (p = 0.741), and Shapiro–Wilk tests indicated no significant departure from normality within sector groups. Games–Howell post-hoc comparisons identified the public versus private sector contrast as the primary significant difference (mean difference = 5.73; 95% CI 2.98–8.48; Cohen's d = 1.04; p < 0.001), representing a large effect. Mixed-sector clinicians also reported significantly higher burden than private-sector counterparts (mean difference = 4.14; 95% CI 0.78–7.50; Cohen's d = 0.81; p = 0.011). No other pairwise comparisons reached statistical significance (Table 6C).

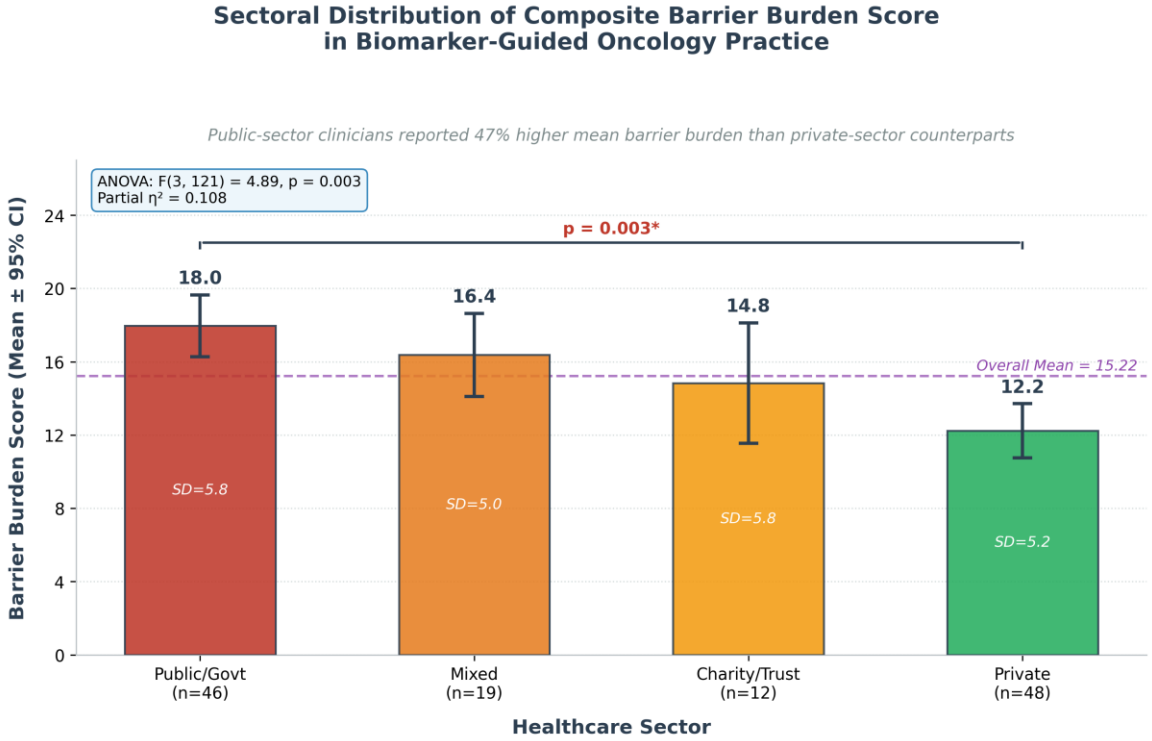


**Figure 1.** Sectoral Distribution of Composite Barrier Burden Score in Biomarker-Guided Oncology Practice Among Clinicians in Pakistan (n = 125). Bars represent mean Barrier Burden Score ± 95% confidence interval by healthcare sector. The dashed horizontal line indicates the overall cohort mean (15.22). ANOVA: F(3, 121) = 4.89, p = 0.003; partial $\eta^2$ = 0.108. The asterisk denotes the primary pre-specified contrast (public vs. private: mean difference 5.73, 95% CI 2.98–8.48, Cohen's d = 1.04, p < 0.001, Games–Howell post-hoc).

Public-sector clinicians reported the highest mean Barrier Burden Score (17.96 ± 5.82), followed by mixed-sector (16.37 ± 5.04), charity/trust (14.83 ± 5.80), and private-sector respondents (12.23 ± 5.23), demonstrating a 47% relative increase in cumulative barrier load in public versus private settings. The effect size for the public–private difference was large (Cohen's d = 1.04), exceeding the conventional threshold of 0.80, while the partial eta-squared of 0.108 indicated that healthcare sector accounted for approximately 10.8% of the total variance in Barrier Burden Score. The declining gradient from public to private sector corresponded to differential patterns in both financial and infrastructural barrier prevalence, with public-sector respondents disproportionately reporting patient affordability, absence of reimbursement, and lack of local molecular testing facilities as concurrent implementation obstacles.

## DISCUSSION

The primary hypothesis—that clinicians practicing in public-sector settings would report higher composite barrier burden scores compared with those in private-sector settings—was supported. Public-sector respondents demonstrated a mean Barrier Burden Score of 17.96 ± 5.82 compared with 12.23 ± 5.23 in the private sector, corresponding to a mean difference of 5.73 points (ANOVA $p = 0.003$). This represents a relative 31.9% higher cumulative burden in public settings. The effect magnitude is clinically meaningful given the overall cohort mean of 15.22 ± 5.98 and suggests substantial structural variation in biomarker implementation environments. The secondary hypothesis that biomarker utilization would be suboptimal in a sizeable proportion of eligible patients was also supported, as only 40.8% of clinicians met the predefined high-utilization threshold.

Utilization of individual biomarkers demonstrated heterogeneity. EGFR testing in ≥50% of eligible patients was reported by 64.8% of clinicians in our cohort. In comparison, Leighl et al. reported EGFR testing rates approaching 80–85% in high-income settings following guideline harmonization initiatives (20). Similarly, PD-L1 testing reached 68.8% in our study, whereas Hirsch et al. documented rates exceeding 75% in regions with established reimbursement frameworks (21). KRAS testing in ≥50% of eligible patients was observed in 53.6% of respondents; this appears lower than utilization levels reported in contemporary Western practice audits where KRAS testing frequently exceeds 65–70% following expanded targeted therapy indications (22). These quantitative comparisons suggest that while biomarker adoption in the present cohort is moderate, it remains below levels documented in more resource-integrated systems.

Turnaround time patterns further contextualize implementation capacity. Although nearly half of respondents reported single-gene testing within 7–14 days (47.2%), 57.6% indicated that NGS results required more than 21 days. Prior implementation studies have suggested that prolonged molecular turnaround exceeding three weeks is associated with delays in treatment optimization and may correspond with empiric therapy initiation (23). In the present analysis, extended NGS turnaround corresponded numerically with reported barriers related to laboratory capacity (37.6%) and administrative delays (33.6%), indicating potential structural bottlenecks rather than clinician reluctance.

Financial barriers were frequently selected, with patient affordability cited by 61.6% and absence of reimbursement by 52.0% of participants. These frequencies align with global analyses demonstrating that financial constraints remain a major implementation constraint in precision oncology diffusion (24,25). Importantly, this cross-sectional design allows only identification of associations; higher barrier burden scores were associated with public-sector practice but cannot be interpreted as causally resulting from sector type. Similarly, financial and infrastructural factors corresponded with lower utilization metrics but cannot be inferred to directly determine testing frequency.

Several limitations merit consideration. First, the response rate was not captured, limiting assessment of representativeness and introducing potential volunteer bias. Second, self-reported practice patterns may be subject to recall or social desirability bias. Third, geographic heterogeneity was not formally stratified, preventing regional implementation analysis. Fourth, the composite Barrier Burden Score, although internally consistent, was not externally validated against standardized implementation indices. Fifth, multivariable regression

adjusting for confounders such as years in practice, specialty, and infrastructure availability was not feasible using aggregated data. Finally, the cross-sectional design precludes temporal inference or causal pathway evaluation.

Despite these limitations, the study provides an integrated assessment of utilization intensity, turnaround time, and structural barriers within a single analytical framework. The quantified 5.73-point difference in burden between public and private sectors may inform health policy prioritization, particularly regarding laboratory expansion, reimbursement reform, and standardized molecular testing pathways.

## CONCLUSION

Biomarker-guided oncology practice in this cohort demonstrates moderate utilization with statistically significant sectoral variation. Higher cumulative barrier burden was associated with public-sector practice, and financial constraints, reimbursement gaps, and laboratory capacity limitations were frequently reported. These findings support targeted system-level interventions aimed at improving equitable access to molecular diagnostics and optimizing precision oncology implementation pathways.

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