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Liquid biopsy in oncology practice: A global survey by the Young Committee of the International Society of Liquid Biopsy (ISLB)

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ABSTRACT

Background: Liquid biopsy is a transformative tool for precision oncology, yet its clinical use remains variable across healthcare systems, and barriers to its implementation are poorly characterized. This survey aims to assess perceptions and practices related to liquid biopsy in oncology practice worldwide.
Methods: A cross sectional, web-based survey was distributed to oncology providers worldwide from November 2024 to December 2025. The survey captured clinical practice characteristics, liquid biopsy uses and workflows, interpretation practices, reimbursement patterns, molecular tumor board (MTB) access, and perceived clinical- and system-level barriers. Descriptive statistics and subgroup comparisons were performed across geographic region, country income level, work setting, years in independent practice, and practice type.
Results: Responses from 393 participants across 59 countries were analyzed, with 53% practicing in Europe. Most were medical oncologists (90%) self-identified as specialists (68%), practicing in academic centers (78%), and in

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high-income countries (70%). Liquid biopsy use was variable: 83% of respondents used it in ≤50% of patients, with pronounced differences across all subgroups (all $p < 0.01$). Circulating tumor DNA (ctDNA) testing predominated (77%), while circulating tumor cell (CTC) use was uncommon (4% alone; 18% in combination with ctDNA). Clinicians in high-income countries, academic settings, and specialists were more likely to have structured workflows and institutional support for test-ordering. Interpretation practices varied, with most respondents relying on self-interpretation (36%) or vendor reports (30%); MTB-based primary interpretation was rare overall (4%), except in Northwestern Europe (23%). MTB availability and use varied substantially across regions and settings. Payment mechanisms differed markedly: government coverage predominated in Europe, private insurance in North America, and patient self-pay in Africa, Asia, and South/Central America–Caribbean. Cost (67%), test availability (55%), difficulty interpreting results (48%), and turnaround time (47%) were the most frequently cited barriers, with cost demonstrating the greatest regional variability ($p < 0.001$). Most clinicians rated liquid biopsy as important (88%) and felt confident applying results (80%), though both varied significantly by region.

Conclusions: These results highlight the high perceived value of liquid biopsy testing, while informing region- and setting-specific differences and challenges, which could be used to guide strategies to implement liquid biopsy in cancer care worldwide.

1. Introduction

Liquid biopsy is transforming the landscape of cancer care [1]. It encompasses the analysis of various circulating analytes, including circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs), and offers a minimally invasive approach for real-time cancer profiling and monitoring [2,3]. Over the past decades, liquid biopsy has emerged as a valuable complement or alternative to tissue biopsy, that comprehensively captures spatial and temporal tumor heterogeneity. Owing to the clinically relevant information it provides for prognosis, treatment selection, and disease monitoring, liquid biopsy has been progressively incorporated into routine practice for several solid tumors and is now included in multiple international clinical guidelines and trial design for prospective studies [4].

Despite this progress, real-world implementation of liquid biopsy remains highly inconsistent across geographic regions and healthcare settings. While limited resources and infrastructure have been reported as important barriers in low- and middle-income countries, the broader determinants influencing liquid biopsy use worldwide remain insufficiently defined [5]. Several factors, such as the cost of testing and availability, differences in healthcare payer systems, clinician familiarity with liquid biopsy technologies, and perceptions regarding test utility, may influence utilization [6]. Moreover, existing surveys assessing clinical implementation of liquid biopsy are often restricted to specific geographic regions or focused on particular tumor types [7–12], preventing a comprehensive understanding of global practices and unmet gaps.

To address these gaps, the present study aims to characterize global patterns of liquid biopsy use and to identify key barriers that limit its implementation across diverse healthcare settings. By examining real-world adoption trends and evaluating obstacles encountered in different regions and practice environments, this international survey seeks to generate evidence that can guide strategies to promote more equitable, consistent, and effective integration of liquid biopsy into cancer care worldwide.

2. Materials and methods

2.1. Survey development and distribution

A preliminary draft of the survey questions was prepared by EN, SS, and CR, after review of published evidence and professional society guidelines. With support from the International Society of Liquid Biopsy (ISLB) Young Committee, the draft was refined and subsequently reviewed by the ISLB Executive Committee which includes experts in the field of liquid biopsy, and feedback was incorporated into the final version. The research team developed a structured online survey using Google Forms that included multiple-choice, Likert-scale, and free-text questions, organized into thematic sections covering: (1) demographic and professional characteristics (*e.g.*, specialty, practice setting, geographic location, years in independent practice); clinical use of liquid biopsy in terms of (2) testing frequency at both the individual practice and system level (country/state), and (3) assay type (ctDNA and/or CTCs), test ordering workflows, processing, results interpretation, and payment methods; (4) perceived importance of liquid biopsy and self-reported confidence in using results in clinical care; and (5) perceived barriers to implementation at both the individual practice and system level. An initial screening question verified eligibility by asking whether respondents currently provided clinical care for patients with cancer; those who did not were automatically exited from the survey. Additional modules focused on disease-specific practices in stage IV breast, colorectal, lung, and prostate cancers, including clinical scenarios for ordering liquid biopsy and specific genomic alterations typically requested. Respondents were instructed to complete only the disease-specific sections relevant to the tumor types they routinely manage. Results derived from these modules will be analyzed and reported separately. All survey questions are provided in **Supplementary File 1**. The study was determined to be exempt under 45 CFR § 46.104 (d) (2) after review by WCG IRB, as the research involved anonymous survey procedures without collection of identifiers. Members of ISLB were invited to participate via email containing a direct link to the online survey. In addition, the survey was disseminated globally through multiple channels, including but not limited to institutional and society email lists, advertised quick-response code, and social media platforms. The online survey was open from November 2024 to December 2025; participation was voluntary and anonymous and not associated with compensation of any kind.

2.2. Statistical analysis

The primary endpoint was the reported percentage of patients who undergo liquid biopsy in respondents' clinical practice. The prespecified hypothesis was that most oncologists (≥50%) would report that ≤50% of their patients receive liquid biopsy testing. This threshold was selected a priori as a pragmatic cutoff to distinguish between minority and majority adoption of liquid biopsy testing in routine clinical practice and was informed by prior published survey data on biomarker testing practices [13]. Secondary endpoints included estimating the proportion of patients undergoing liquid biopsy at the country/state level, evaluating clinical implementation practices, perceptions of utility and provider confidence, and barriers to adoption. A target sample size of 200 respondents was determined to provide greater than 80% power to detect a 0.10 difference in the primary endpoint using a two-sided exact test with a significance level of 0.05, assuming a null proportion of 0.50. The achieved significance level for this design is 0.047, and this sample size ensures that the two-sided 95% confidence interval for the primary

endpoint has a total width of less than 0.15.

All responses were analyzed both in the overall cohort and across predefined subgroups based on: (1) geographic region of practice, classified according to the United Nations Statistics Division (UNSD) geoscheme, with analyses performed across Africa, Asia, Europe (subdivided into South-Eastern and North-Western Europe), and the Americas (further categorized into North America and South/Central America–Caribbean) [14]; (2) country income level, defined according to the World Bank classification (High-Income Countries [HICs], Upper-Middle-Income Countries [UMICs], Lower-Middle-Income Countries [LMICs], and Low-Income Countries [LICs]) [15]; (3) work setting (academic medical center/university vs community or private practice); (4) type of practice (generalist vs specialist), as self-identified by respondents, defined by the routine management of multiple cancer types versus a focus on one or a limited number of cancer types; and (5) years in independent clinical practice (≥10 years vs < 10 years).

All statistical analyses were conducted using descriptive statistics to summarize survey responses. Comparisons between subgroups were performed using Chi-squared tests, with statistical significance defined as $p < 0.05$. To identify factors associated with higher liquid biopsy utilization, a multivariable logistic regression analysis was performed using clinic-level liquid biopsy use (>50% vs ≤ 50%) as the dependent variable. Prespecified covariates included geographic region, country income level, work setting, type of practice, and years in practice. Because complete separation was observed in some geographic categories, Firth's bias-reduced penalized logistic regression was used for parameter estimation. A parsimonious final model was selected using backward elimination based on the Akaike Information Criterion (AIC). Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). Data were analyzed using R software version 4.5.3.

3. Results

3.1. Respondent characteristics

A total of 436 individuals accessed the survey, of whom 43 were excluded because they did not meet the eligibility criterion of providing clinical care for patients with cancer, resulting in 393 respondents included in the final cohort for analysis (Table 1). Most participants held a medical degree or equivalent and primarily practiced medical oncology (354, 90%), with a smaller proportion of surgical and radiation oncologists (4% and 3%, respectively). The cohort represented a wide geographic distribution (Supplementary Figure 1), with the largest proportion practicing in Europe (206, 53%), followed by the Americas (95, 24%) and Asia (69, 18%). Respondents were predominantly from HICs (272, 70%). Regarding the work setting, most respondents were based in academic medical centers or universities (307, 78%), while 21% practiced in community or private settings. Over half of the cohort (242, 62%) had ≥10 years of independent practice, and most self-identified as specialists (269, 68%) rather than generalists. Across the cohort, most frequently managed solid tumors in routine practice included breast, lung, gastrointestinal, and genitourinary malignancies.

3.2. Patterns of liquid biopsy utilization

Across the overall cohort, the majority of respondents (83%) reported using liquid biopsy in ≤50% of their patients. Notably, within this group, 23% reported minimal use, defined as liquid biopsy use in fewer than 1% of cases. Only 16% of respondents reported using liquid biopsy in more than 50% of their patient population (Fig. 1A). Significant differences were observed by geographic region ($p < 0.001$) (Fig. 1B), with a higher proportion of respondents reporting using liquid biopsy in >50% of patients in North America (45%) and Northwestern Europe (39%). In contrast, the lowest utilization was reported in South/Central America–Caribbean and Africa, where no respondent indicated using liquid biopsy in more than half of their patients. Liquid biopsy use was significantly associated with country income classification ($p < 0.001$), with a twofold higher proportion of clinicians in HICs reporting liquid biopsy use in >10% of patients compared with those practicing in middle- and low-income countries (Fig. 1C). Significant differences were also observed by work setting ($p < 0.001$), with oncologists working in academic centers more likely to use liquid biopsy than those in community or private practice (Fig. 1D). Liquid biopsy utilization also differed by years in independent practice ($p = 0.004$) and type of practice ($p = 0.002$), with providers with fewer years in practice and those who self-identified as specialists reporting greater uptake (Fig. 1E and F). To assess independent predictors of liquid biopsy utilization, a multivariable Firth penalized logistic regression analysis was performed. The full model including all prespecified covariates is shown in Supplementary Table 1, and the final AIC-selected model is presented in Table 2. Geographic region and work setting were independently associated with reporting liquid biopsy use in more than 50% of patients. Compared with North America, respondents from Southeastern Europe, Asia, South/Central America-Caribbean, and Africa had significantly lower odds of high liquid biopsy utilization. Clinicians practicing

Table 1
Survey respondent characteristics.

	N = 393 (%)
Terminal degree or primary professional degree	
MD/DO	253 (64.38)
MD, PhD	107 (27.23)
PhD (with a clinical role)	24 (6.11)
Other[a]	9 (2.29)
Primary area of clinical practice	
Medical Oncology	354 (90.08)
Surgical Oncology	15 (3.82)
Radiation Oncology	12 (3.05)
Other	11 (2.80)
Geographic area	
Europe – Northwest	31 (7.93)
Europe – Southeast	175 (44.76)
North America	62 (15.86)
South/Central America - Caribbean	33 (8.44)
Asia	69 (17.65)
Africa	17 (4.35)
Oceania	4 (1.02)
Not available	2 (0.51)
Country income level	
High-income countries (HIC)	272 (70.10)
Upper-middle-income countries (UMIC)	57 (14.69)
Lower-middle-income countries (LMIC)	58 (14.76)
Low-income countries (LIC)	1 (0.25)
Not available	5 (1.27)
Work setting	
Academic Medical Center/University	307 (78.12)
Community or Private Practice	84 (21.37)
Do not know/Prefer not to answer	1 (0.25)
Other	1 (0.25)
Years in practice	
< 10 years	242 (61.58)
≥ 10 years	146 (37.15)
Prefer not to answer	5 (1.27)
Type of practice	
Specialist	269 (68.45)
Generalist	117 (29.77)
Do not know/Prefer not to answer	7 (1.78)
Disease sites treated[b]	
Breast Cancer	211
Lung Cancer	172
Gastrointestinal Cancers (GI)	151
Genitourinary Cancers (GU)	66
Gynecological Cancers	46
Head and Neck Cancers	33

[a] Other includes PA – Physician Assistant, NP – Nurse Practitioner, APN – Advanced Practice Nurse, and DNP - Doctor of Nursing Practice.
[b] The total exceeds 100% because respondents were allowed to select up to three disease sites. Only disease sites reported by more than 30 respondents are included.

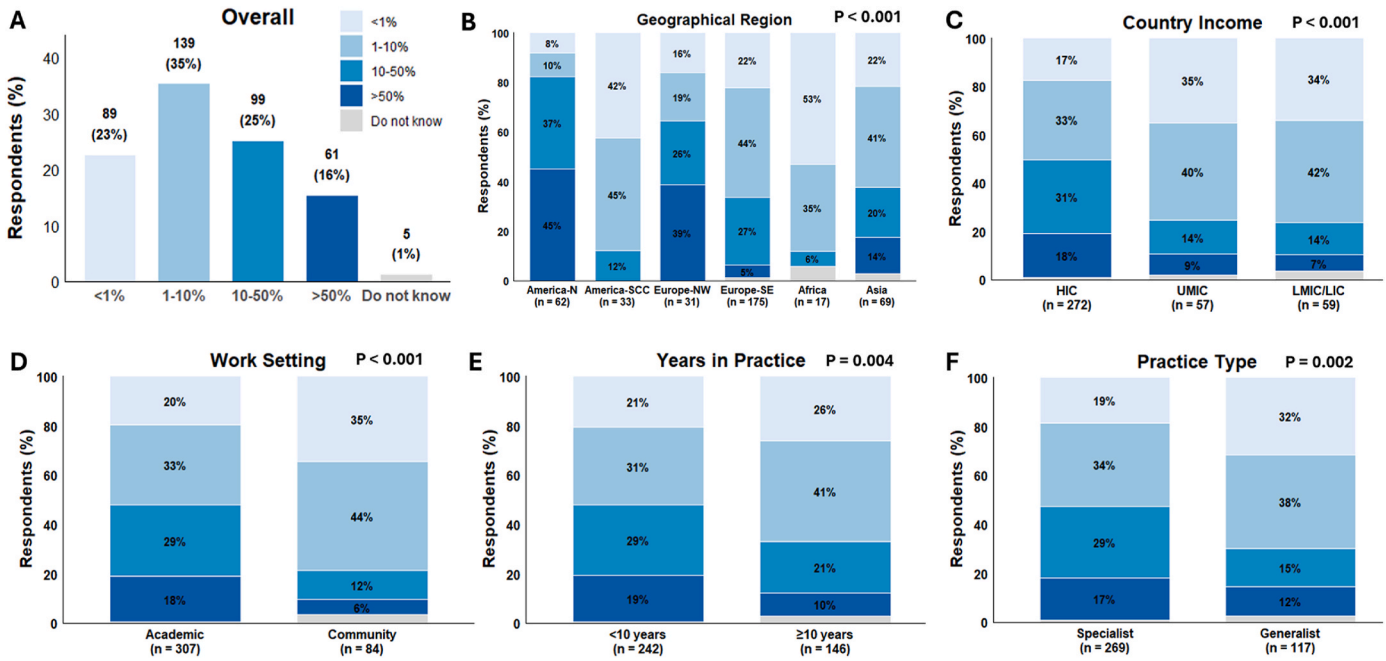

Fig. 1. Liquid biopsy utilization in respondents' clinical practice

Overall distribution and subgroup analyses of the percentage of patients undergoing liquid biopsy in clinical practice. (A) Overall responses. (B) Stratification by geographical region. (C) Stratification by country income level. (D) Stratification by work setting. (E) Stratification by years in practice. (F) Stratification by practice type. P-values refer to χ^2 tests comparing distributions across all groups. Abbreviations: America-N, North America; America-SCC, South/Central America–Caribbean; Europe-NW, North-Western Europe; Europe-SE, South-Eastern Europe; HIC, high-income country; UMIC, upper-middle-income country; LMIC/LIC, lower-middle-income country/low-income country.

Table 2
Multivariable Firth penalized logistic regression analysis of factors associated with clinic-level liquid biopsy utilization in >50% of patients.

Variable	Odds ratio	95% CI	P value
Geographic region			
America-North	—	—	
Europe-NW	0.80	0.33, 1.93	0.6
Europe-SE	0.08	0.03, 0.18	**<0.001**
Asia	0.30	0.12, 0.68	**0.004**
America-SCC	0.03	0.00, 0.23	**<0.001**
Africa	0.04	0.00, 0.31	**<0.001**
Work settings			
Academic Medical Center/University	—	—	
Community or Private Practice	0.30	0.08, 0.86	**0.024**

Odds ratios and 95% CIs are shown for variables retained in the final model following AIC-based backward selection. High liquid biopsy utilization was defined as reported use in >50% of patients. Odds ratios <1 indicate lower odds of reporting liquid biopsy use in >50% of patients compared with the reference category. North America and Academic Medical Center/University were used as reference categories. Abbreviations: America-SCC, South/Central America–Caribbean; Europe-NW, Northwestern Europe; Europe-SE, Southeastern Europe; CI, Confidence Interval.

in community/private settings also had lower odds of reporting >50% liquid biopsy use than those in academic centers (OR 0.30, 95% CI 0.08-0.86, $p = 0.024$).

When asked about the perceived utilization of liquid biopsy in their country or state, respondents reported even lower use (Supplementary Figure 2), only 7% indicated that more than half of patients receive liquid biopsy testing at the system level, with significant differences observed based on geographic area, income, and work setting.

3.3. Clinical implementation practices

Among respondents who reported requesting liquid biopsy in their clinical practice, the modalities of ordering were assessed. The majority of providers (270, 77%) relied on ctDNA-only testing, whereas a smaller proportion requested CTCs (14, 4%) or a combination of ctDNA and CTCs (62, 18%) (Fig. 2A). While use of CTCs was relatively uncommon, we observed significant differences depending on geographic region, income level, and practice characteristics ($p < 0.05$ for all) (Fig. 2B–F) with higher use of CTCs, either alone or in combination with ctDNA, in Asia (47%), in LMICs (42%), and among generalists (35%).

Regarding test-ordering workflows, self-ordering by the clinician was the most common approach (166, 49%), followed by support from nurses/advanced practice providers (80, 24%), vendor support (51, 15%), and administrative support (41, 12%) (Fig. 3A). Statistically significant differences were observed when comparing ordering procedures among geographic regions, country income level, work setting, and practice type ($p < 0.05$ for all), with clinicians in HICs, academic settings, and specialists more likely to have structured workflows and institutional support (Fig. 3B–F).

Differences also emerged in the interpretation of liquid biopsy results (Fig. 4A–F). Most respondents either interpreted the results themselves (128, 36%) or relied on the vendor-generated report (108, 30%), whereas 102 respondents (28%) reported discussing results with colleagues or pathology services. Only 15 respondents (4%) indicated that they routinely discuss liquid biopsy results in a molecular tumor board (MTB). Interpretation practices were largely consistent across most subgroups. The only comparison showing statistically significant variation was geographic region ($p < 0.001$), primarily driven by differences in the proportion of respondents relying on their own interpretation (higher in the Americas), as well as by region-specific extremes such as the higher use of vendor reports in Africa and the elevated reliance on clinician colleagues in Southeastern Europe. A higher use of MTBs was observed in Northwestern Europe, where 23% of respondents reported reviewing liquid biopsy results in this setting, substantially higher than in all other regions, where MTB discussion was reported by ≤ 4% of respondents.

In terms of sample processing, external processing was the most

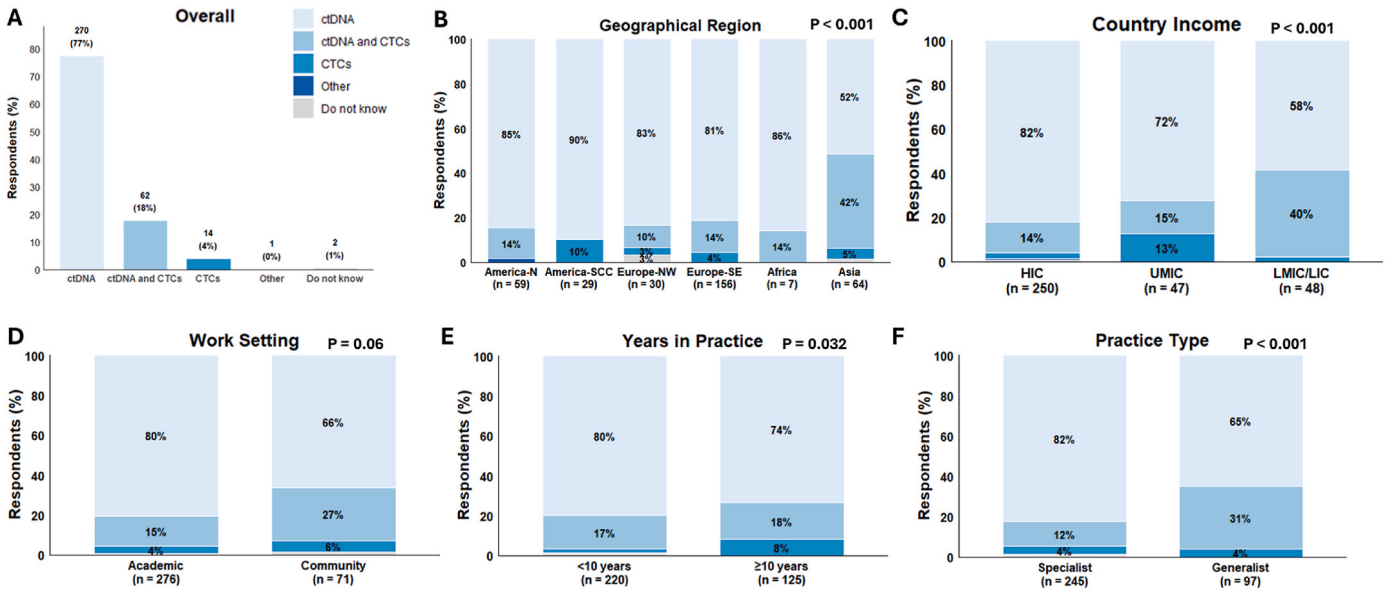

Fig. 2. Types of liquid biopsy tests requested in clinical practice

Overall distribution and subgroup analyses of the types of liquid biopsy tests requested in clinical practice. A total of 44 of 393 respondents reported not requesting liquid biopsy and were excluded from proportional analyses. (A) Overall responses. (B) Stratification by geographical region. (C) Stratification by country income level. (D) Stratification by work setting. (E) Stratification by years in practice. (F) Stratification by practice type. P-values refer to χ^2 tests comparing distributions across all groups. Abbreviations: ctDNA, circulating tumor DNA; CTCs, circulating tumor cells; America-N, North America; America-SCC, South/Central America–Caribbean; Europe-NW, North-Western Europe; Europe-SE, South-Eastern Europe; HIC, high-income country; UMIC, upper-middle-income country; LMIC/LIC, lower-middle-income country/low-income country.

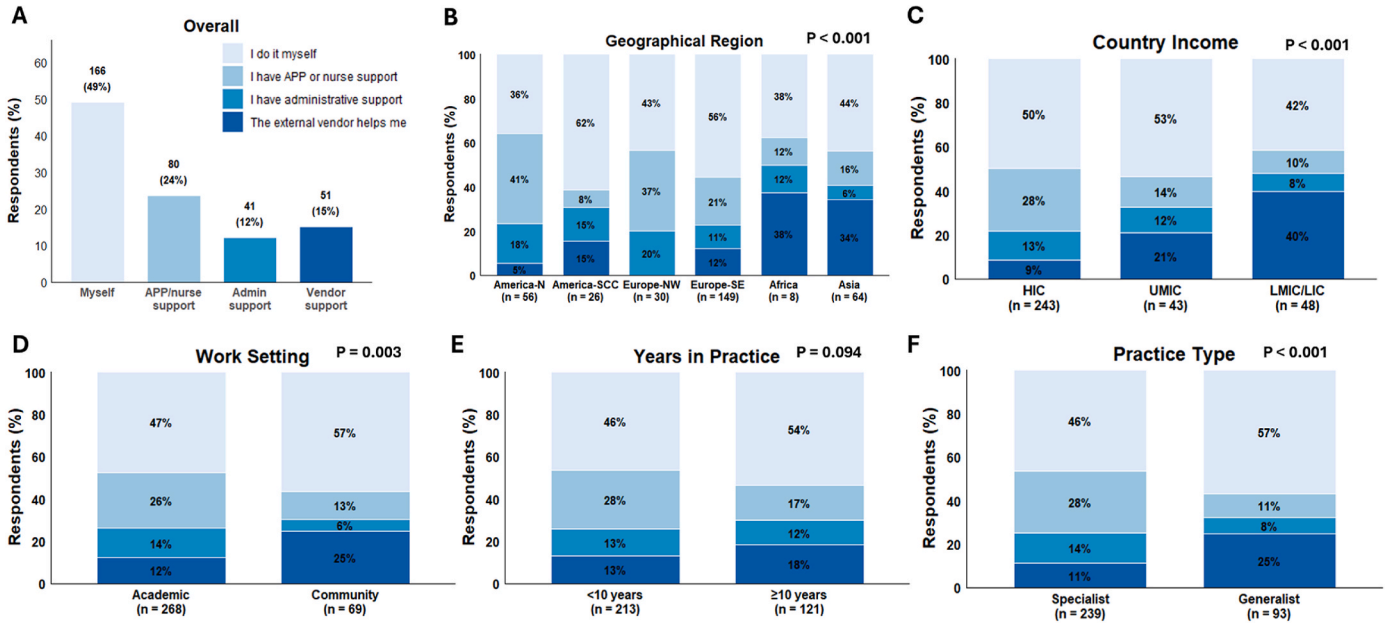

Fig. 3. Liquid biopsy ordering in clinical practice

Overall distribution and subgroup analyses of how liquid biopsy is ordered in clinical practice. A total of 55 of 393 respondents reported not requesting liquid biopsy and were excluded from proportional analyses. (A) Overall responses. (B) Stratification by geographical region. (C) Stratification by country income level. (D) Stratification by work setting. (E) Stratification by years in practice. (F) Stratification by practice type. P-values refer to χ^2 tests comparing distributions across all groups. Abbreviations: APP, advanced practice provider; America-N, North America; America-SCC, South/Central America–Caribbean; Europe-NW, North-Western Europe; Europe-SE, South-Eastern Europe; HIC, high-income country; UMIC, upper-middle-income country; LMIC/LIC, lower-middle-income country/low-income country.

frequently reported modality (186, 47%), followed by in-house laboratory analysis (112, 28%), and a combination of both approaches (66, 17%) (Fig. 5A). Processing mode differed significantly across all measured subgroups (all $p < 0.05$) (Fig. 5B–F). More than three-quarters of respondents in the Americas (83%) and Asia (67%) reported relying primarily on external processing, whereas this proportion was substantially lower in Europe (28%), where a higher use of in-house laboratories was observed (45%). Respondents practicing in HICs, as well as those working in academic centers, specialists, and clinicians with fewer years in practice, were more likely to report access to and use of in-house

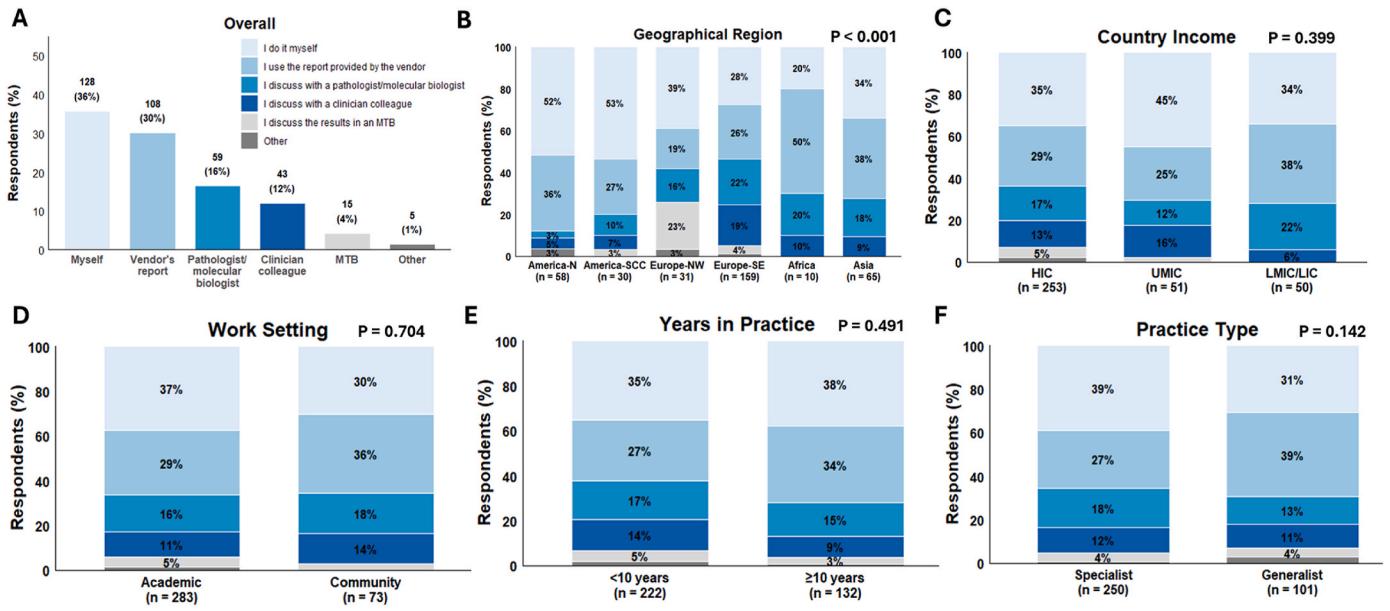

Fig. 4. Liquid biopsy result interpretation practices

Overall distribution and subgroup analyses of how liquid biopsy results are interpreted in clinical practice. A total of 35 of 393 respondents reported not requesting liquid biopsy and were excluded from proportional analyses. (A) Overall responses. (B) Stratification by geographical region. (C) Stratification by country income level. (D) Stratification by work setting. (E) Stratification by years in practice. (F) Stratification by practice type. P-values refer to χ^2 tests comparing distributions across all groups. Abbreviations: MTB, molecular tumor board; America-N, North America; America-SCC, South/Central America–Caribbean; Europe-NW, North-Western Europe; Europe-SE, South-Eastern Europe; HIC, high-income country; UMIC, upper-middle-income country; LMIC/LIC, lower-middle-income country/low-income country.

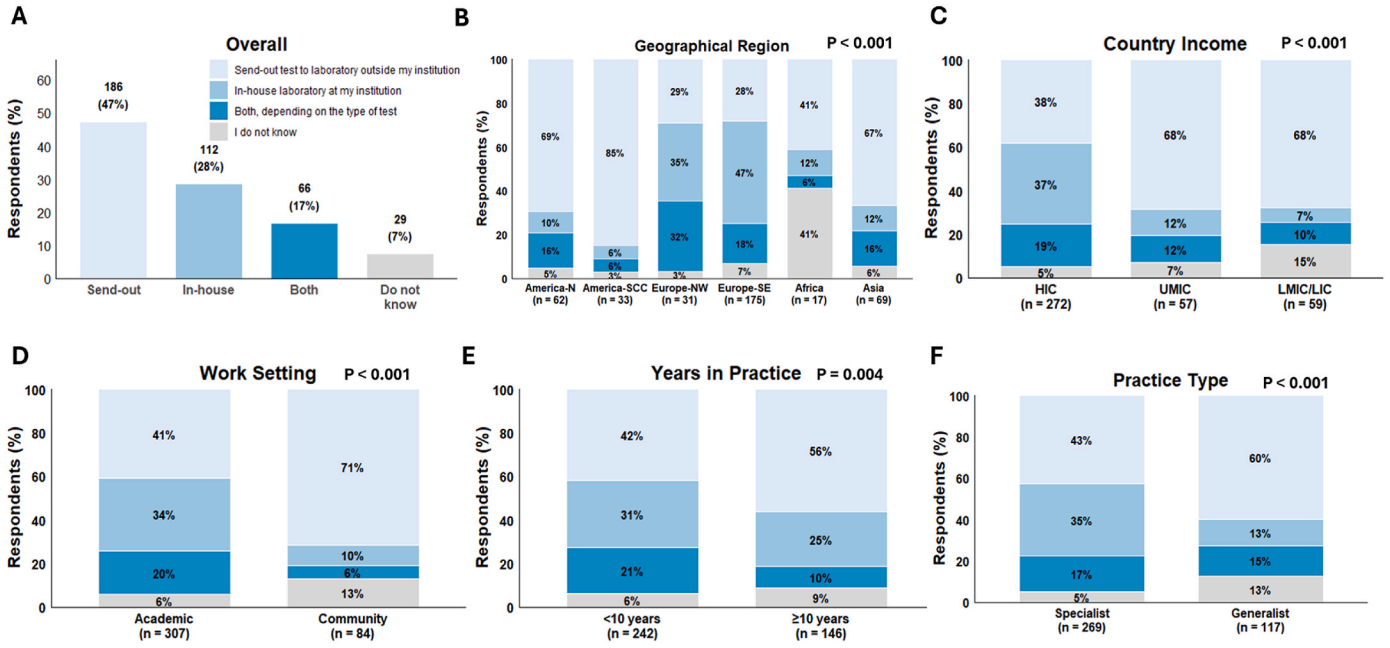

Fig. 5. Liquid biopsy processing modalities

Overall distribution and subgroup analyses of how liquid biopsy tests are processed in clinical practice. (A) Overall responses. (B) Stratification by geographical region. (C) Stratification by country income level. (D) Stratification by work setting. (E) Stratification by years in practice. (F) Stratification by practice type. P-values refer to χ^2 tests comparing distributions across all groups. Abbreviations: America-N, North America; America-SCC, South/Central America–Caribbean; Europe-NW, North-Western Europe; Europe-SE, South-Eastern Europe; HIC, high-income country; UMIC, upper-middle-income country; LMIC/LIC, lower-middle-income country/low-income country.

processing laboratories.

Overall, the most frequently reported source of coverage for liquid biopsy testing was government support (128, 33%), followed by patient self-pay (100, 25%) and industry or company support (73, 19%) (Fig. 6A). However, payment mechanisms (Fig. 6B–F) varied markedly across regions and settings. Although private insurance represented a minority of payment sources overall, it constituted the primary method of coverage in North America (60%), whereas government support

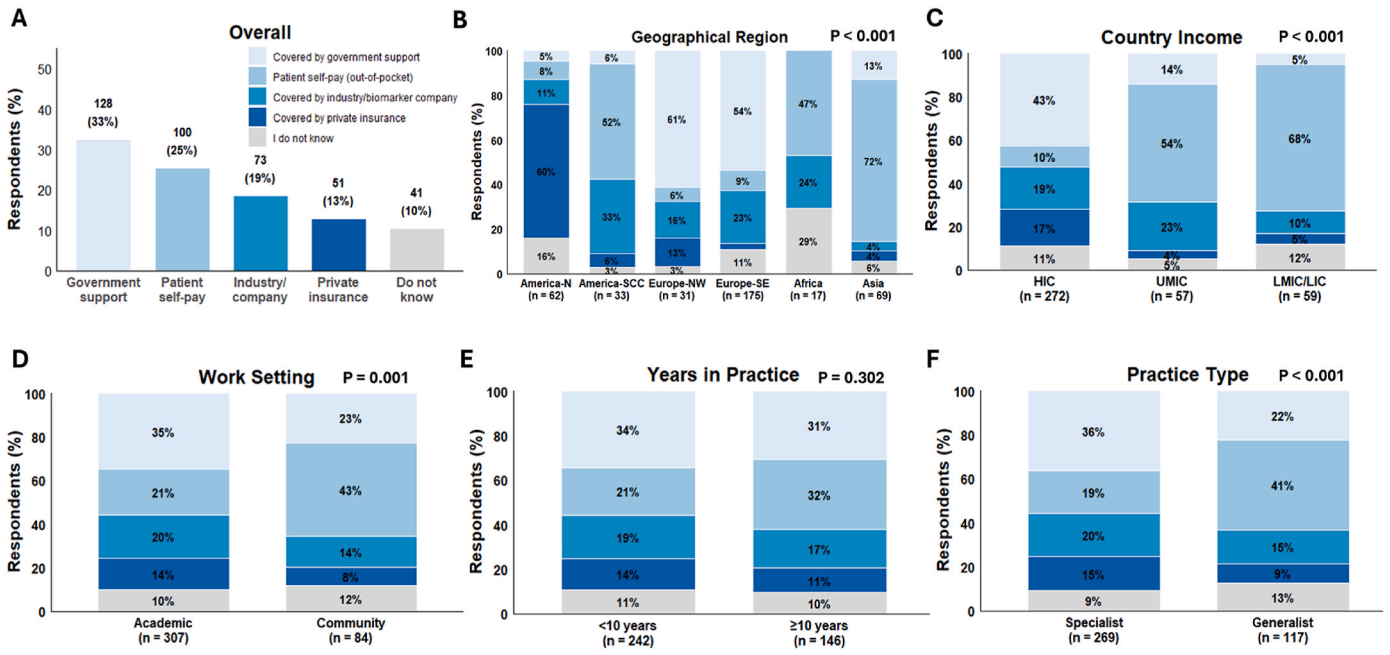

Fig. 6. Source of coverage for liquid biopsy testing

Overall distribution and subgroup analyses of primary method of payment for liquid biopsy tests in clinical practice. (A) Overall responses. (B) Stratification by geographical region. (C) Stratification by country income level. (D) Stratification by work setting. (E) Stratification by years in practice. (F) Stratification by practice type. P-values refer to χ^2 tests comparing distributions across all groups. Abbreviations: America-N, North America; America-SCC, South/Central America–Caribbean; Europe-NW, North-Western Europe; Europe-SE, South-Eastern Europe; HIC, high-income country; UMIC, upper-middle-income country; LMIC/LIC, lower-middle-income country/low-income country.

emerged as the leading mechanism in Europe, where more than half of respondents reported this form of coverage. In contrast, a substantially higher financial burden on patients was reported in Asia, South/Central America–Caribbean, and Africa, where self-pay represented a major source of coverage (72%, 52%, and 47%, respectively). Differences by income level were also evident. In HICs, liquid biopsy was most frequently covered through private insurance or government payors, whereas in lower-income settings, clinicians more commonly reported reliance on patient self-pay. Similarly, a higher patient financial burden was observed among respondents working in community settings (43% vs 21% in academic setting) and those identifying as generalists (41% vs 19% among specialists).

3.4. Perceptions of utility and provider confidence

Overall, most respondents (88%) considered liquid biopsy to be important or very important in their clinical practice, with only 3% reporting it as not important (Fig. 7A). This perception was largely consistent across subgroups, although a significant difference emerged by geographical region ($p < 0.001$), with respondents practicing in the Americas or Northwestern Europe reporting higher perceived importance than others geographic areas. Perceptions did not differ significantly by country income level, work setting, type of practice, or years in practice.

Confidence in applying liquid biopsy results showed a similar pattern (Fig. 7B). Most clinicians reported feeling confident or very confident (80%), while a smaller proportion expressed uncertainty. As with perceived importance, confidence levels differed significantly by geographical region ($p = 0.002$). Differences by type of practice were also observed, with specialists reporting higher confidence compared with generalists ($p = 0.009$). No significant differences were noted by country income level, work setting, or years in practice.

To evaluate whether respondents' confidence in interpreting liquid biopsy results might be influenced by access to an MTB, we examined the availability and use of MTBs across practice settings (Fig. 8). Overall, 166 respondents (42%) reported having an MTB at their institution and using it to discuss liquid biopsy results. An additional 64 respondents (16%) indicated that an MTB was available institutionally but was not routinely used for liquid biopsy interpretation. A further 44 (11%) and 26 (7%) respondents indicated access to an external MTB, either with or without discussing liquid biopsy results, respectively. In contrast, 92 respondents (24%) reported having no access to an MTB. This pattern varied significantly by geographical region ($p < 0.001$). Nearly half of respondents in South/Central America–Caribbean and Africa reported no MTB access. In other regions, MTB availability was substantially higher, with the highest overall presence and use observed in Northwestern Europe. Differences were also linked to country income level, work setting, and type of practice (all $p < 0.05$). Lower availability and lower use of MTBs were observed in lower-income countries, community practices, and among generalists, whereas clinicians in academic centers, high-income settings, and specialist roles more frequently reported access to and engagement with MTBs.

3.5. Barriers to adoption and integration

Respondents were asked to rate the impact of potential barriers to liquid biopsy implementation in their clinical practice and in their country/state (system level) (Fig. 9 and Supplementary Figs. 3 and 4). Overall, the barriers most frequently rated as "very relevant" or "relevant" for clinical practice were cost (67%), limited test availability (55%), difficulty interpreting or applying results (48%), and long turnaround time (47%) (Fig. 9 and Supplementary Fig. 3). In contrast, 30% of respondents indicated that liquid biopsy "does not add value". All perceived barriers varied significantly across geographic regions (Fig. 9, Supplementary Table 2). Cost showed the greatest variability, being rated as relevant by >90% of respondents in South/Central America–Caribbean, followed by Asia (78%), and Africa (75%), compared with 50% in North America ($p < 0.001$). Test availability was also a major barrier in Africa (76%), South/Central America–Caribbean (78%), and Southeastern Europe (61%), whereas turnaround time and

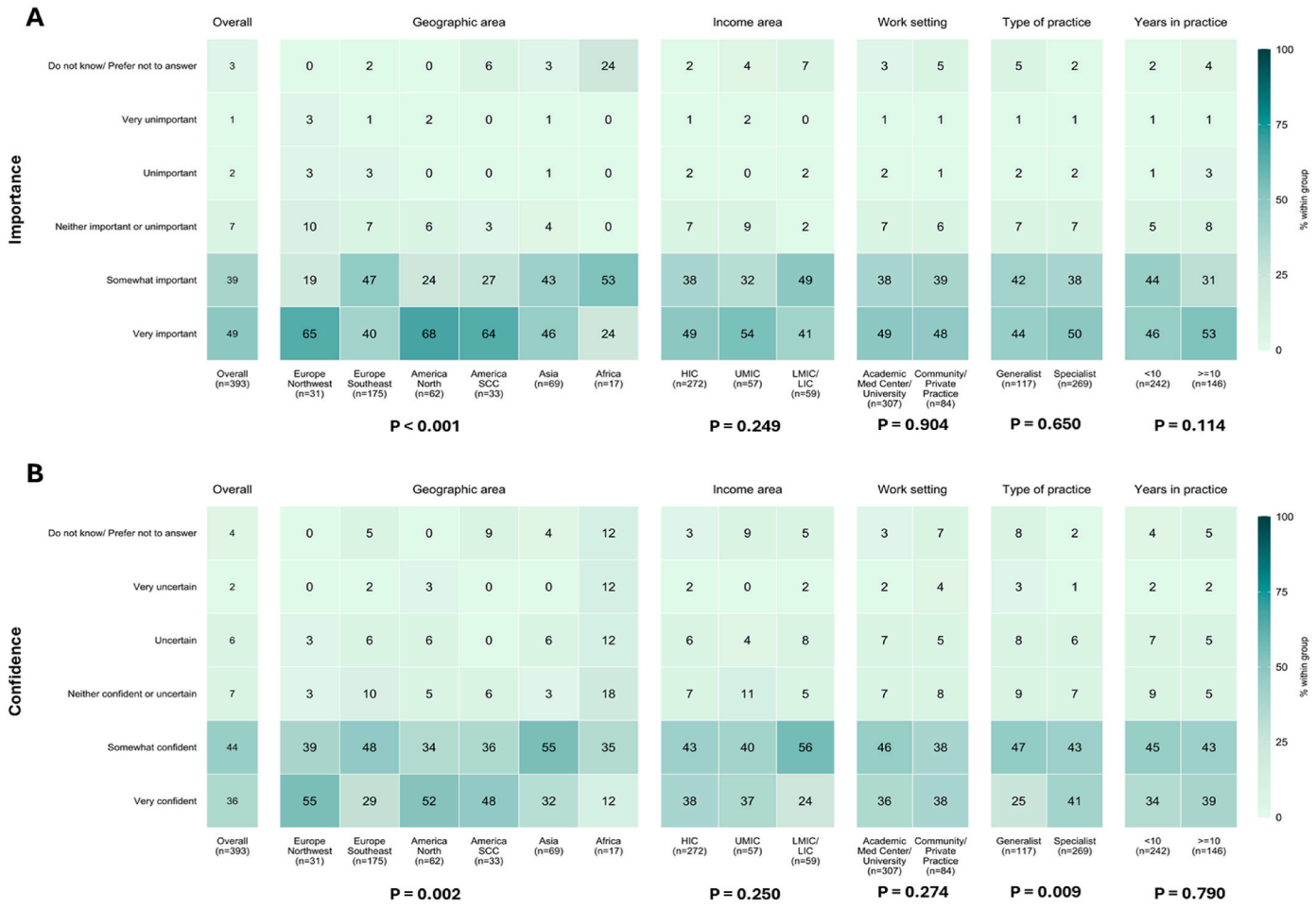

Fig. 7. Perceived importance and confidence in using liquid biopsy

Perceptions of the importance of liquid biopsy in clinical practice (**A**) and confidence in applying liquid biopsy results (**B**). Each panel includes overall responses and subgroup heatmaps stratified by geographical region, country income level, work setting, type of practice, and years in practice. Percentages represent within-group distributions. P-values refer to χ^2 tests comparing distributions across all groups within each stratification variable. Abbreviations: America-N, North America; America-SCC, South/Central America–Caribbean; Europe-NW, North-Western Europe; Europe-SE, South-Eastern Europe; HIC, high-income country; UMIC, upper-middle-income country; LMIC/LIC, lower-middle-income country/low-income country.

difficulty interpreting results were reported as relevant barriers by ≥ 40% of respondents in all regions except North America. When comparing barriers across country income levels (Fig. 9, Supplementary Table 3), significant differences emerged for the perceived clinical value of liquid biopsy, which was rated as less relevant among UMICs compared with HICs and LMIC/LIC ($p = 0.035$). Cost was reported as a relevant barrier more frequently in UMICs (82%) and LMIC/LIC (84%) than in HICs (60%) ($p < 0.001$), and turnaround time was also more frequently cited as relevant in UMICs and LMIC/LIC than in HICs ($p < 0.001$). In contrast, test availability and difficulty interpreting results did not differ significantly across income groups at the clinical practice level, although both varied significantly at the system level (Fig. 9 and Supplementary Fig. 4). No significant differences were observed across work setting, years in practice, or type of practice (Fig. 9, Supplementary Figure 4 and Tables 4–6), with two exceptions: respondents with ≥10 years of independent practice were more likely to report difficulty interpreting results as a relevant barrier at the system level ($p = 0.034$), and generalists more frequently than specialists identified turnaround time as a relevant barrier in clinical practice ($p = 0.037$).

Free-text responses, provided by 84 survey participants, further emphasized the central role of cost and lack of reimbursement as primary barriers to liquid biopsy implementation. Many respondents also highlighted the insufficient clinical evidence supporting ctDNA testing in some tumor types, together with its limited inclusion in national guidelines. A recurrent theme was the lack of standardization, with no universally accepted protocols for sample collection, processing, or analysis, leading to concerns about result consistency. Several participants reported the presence of too many laboratories or commercial providers, making it difficult for clinicians to assess which assays are reliable and adequately validated. The need for greater clinician education and genomic literacy was repeatedly mentioned. Finally, some respondents noted that even when liquid biopsy identifies an actionable alteration, access to targeted or experimental therapies remains limited in some countries, reducing the practical utility of testing.

4. Discussion

This global survey provides one of the most comprehensive characterizations to date of real-world liquid biopsy implementation across diverse healthcare systems and jurisdictions, revealing a discordance between its recognized clinical value and its adoption. Despite being regarded as an important clinical tool by most respondents (88%), liquid biopsy was used in more than half of patients by only a minority (16%). This discrepancy underscores that the primary constraints are structural rather than attitudinal: financial coverage, limited access, workflow fragmentation, and insufficient interpretative support continue to impede routine implementation.

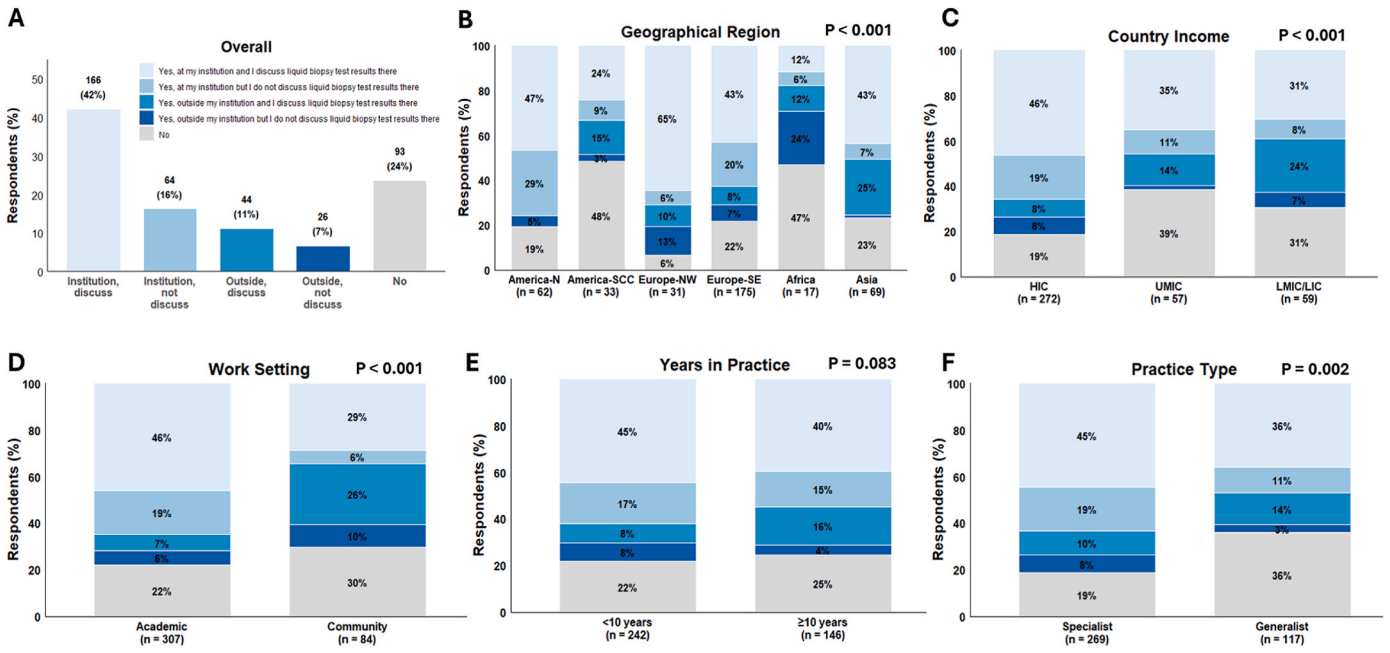

Fig. 8. Access to molecular tumor boards and discussion of liquid biopsy results

Overall distribution and subgroup analyses of access to a molecular tumor board and discussion of liquid biopsy results within it. (A) Overall responses. (B) Stratification by geographical region. (C) Stratification by country income level. (D) Stratification by work setting. (E) Stratification by years in practice. (F) Stratification by practice type. P-values refer to χ^2 tests comparing distributions across all groups. Abbreviations: America-N, North America; America-SCC, South/Central America–Caribbean; Europe-NW, North-Western Europe; Europe-SE, South-Eastern Europe; HIC, high-income country; UMIC, upper-middle-income country; LMIC/LIC, lower-middle-income country/low-income country.

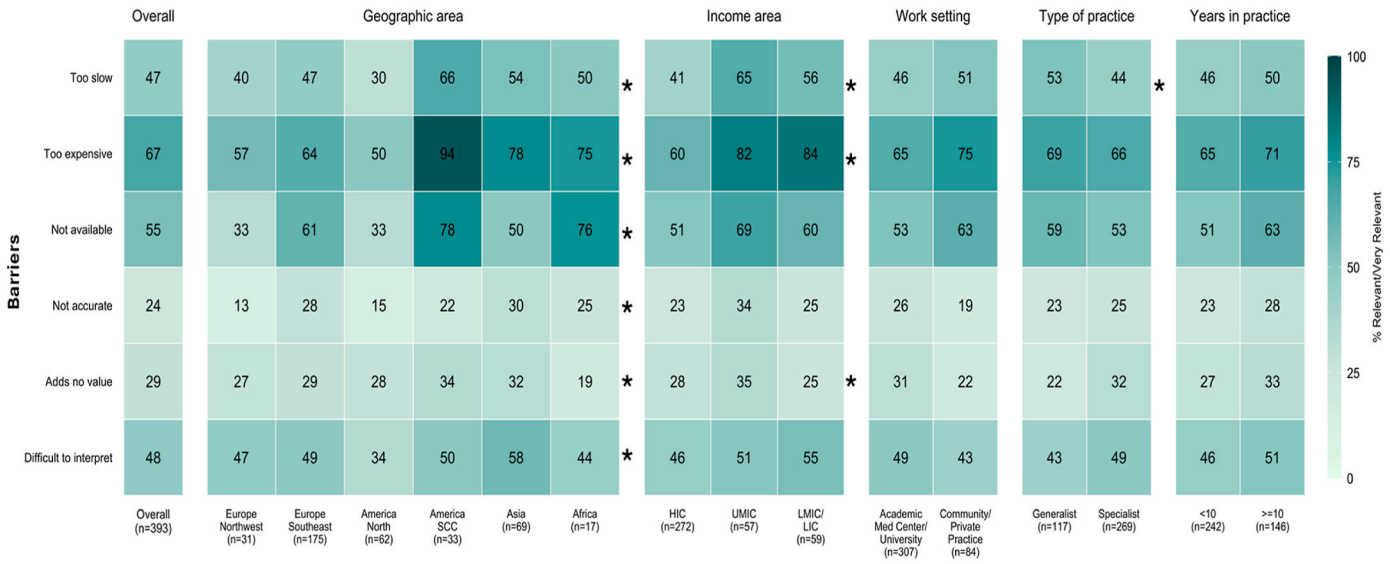

Fig. 9. Perceived barriers to liquid biopsy implementation in respondents' clinical practice

Heatmap of perceived barriers to the use of liquid biopsy in respondents' clinical practice, shown overall and stratified by geographic region, country income level, work setting, type of practice, and years in practice. Values represent the percentage of respondents who rated each barrier as "relevant" or "very relevant." An asterisk (*) denotes statistically significant differences ($p \leq 0.05$), based on comparisons across the full distribution of responses (very relevant, relevant, marginally relevant, not relevant, and "I do not know") for each barrier, reported in Supplementary Tables 2-6. Abbreviations: America-N, North America; America-SCC, South/Central America–Caribbean; Europe-NW, North-Western Europe; Europe-SE, South-Eastern Europe; HIC, high-income country; UMIC, upper-middle-income country; LMIC/LIC, lower-middle-income country/low-income country.

A dominant theme emerging from the survey is the profound influence of healthcare resources, captured both through geographic region and country income level analyses, on the real-world adoption of liquid biopsy. These two dimensions, although partially overlapping, consistently pointed to the same pattern: regions and countries with stronger infrastructures (particularly North America, Northwestern Europe, and high-income economies) reported highest utilization, broader assay availability, structured test-ordering pathways, and institutional support systems. However, in multivariable analysis, geographic region and work setting, but not country income level, remained independently associated with higher liquid biopsy utilization. While the overlap between geographic region and country income level should be

considered, these findings suggest that regional and institutional factors may be more important determinants of liquid biopsy adoption than country income level alone. This pattern may also reflect the geographic concentration of clinical validation studies and prospective trials supporting liquid biopsy use in these regions, potentially fostering greater clinician familiarity and confidence and, consequently, higher use. Aligned payment structures, primarily government or private insurance coverage, further reduced out-of-pocket costs and facilitated broader adoption. In contrast, clinicians working in South/Central America–Caribbean, Africa, and in many middle- and low-income settings described environments shaped by scarce institutional resources and support, reliance on external laboratories, and substantial patient out-of-pocket costs. These observations mirror broader disparities previously documented for precision oncology tools, including access to tissue genomic testing, MTBs, and innovative therapies [16,17]. Nevertheless, even in high-income settings, access is not uniform. Although our sample size did not allow for country-level granular analyses, the United States is a notable example where reimbursement for commercially available liquid biopsy tests remains inconsistent and fragmented across private insurers, Medicare policies, and variable state-level regulations [18]. This highlights that financial barriers to widespread implementation persist even in well-resourced health systems, albeit in different forms (lack of resources versus allocation of existing resources), and represent the leading obstacle to liquid biopsy implementation worldwide.

Beyond geographical and economic determinants, our findings also show meaningful differences in liquid biopsy adoption related to practice environment and provider characteristics, underscoring how institutional infrastructure, clinical specialization, and exposure to precision oncology directly influence real-world utilization. Clinicians in academic medical centers reported substantially higher use of liquid biopsy than those in community hospitals or private practice, a finding that remained significant in multivariable analysis. This reflects the advantages typically associated with academic settings, including greater diagnostic resources, more standardized and coordinated workflows, and routine access to MTBs [11], all of which support more frequent and consistent integration of liquid biopsy into practice. Provider characteristics also played an important role: clinicians with fewer years in independent practice (<10 years) and specialists demonstrated higher adoption. The former may reflect more recent training that increasingly incorporates molecular profiling as a core competency [19], alongside greater familiarity with digital ordering platforms, variant interpretation tools, and biomarker-driven treatment paradigms. Clinicians with greater years in practice more frequently cited difficulty interpreting results as a system-level barrier, although overall confidence in applying liquid biopsy findings did not differ substantially between groups. Specialists reported higher testing rates and greater interpretive confidence than generalists, which may reflect deeper disease-specific expertise, more frequent engagement with precision oncology workflows, and greater system support such as access to MTBs. In contrast, generalists, often managing a broader variety of pathologies and higher patient volumes, in settings with fewer precision oncology resources, reported lower use and more frequent operational barriers, particularly turnaround time. These suggest that both expertise and the surrounding support infrastructure meaningfully shape the degree to which liquid biopsy is incorporated into routine practice.

As expected, ctDNA represented the predominant liquid biopsy test, consistent with its stronger evidence base and broader availability [4,20]. Consequently, this survey predominantly captures real-world practice related to ctDNA testing. The limited use of CTCs aligns with previous surveys [7], and likely reflects variable levels of supporting evidence across tumor types, a lack of straightforward clinical utility in some settings, insufficient clinician training, and more limited reimbursement pathways [20,21]. Nonetheless, the relatively higher use of CTCs in Asia and LMICs suggests regional research interests and differences in assay accessibility that warrant further exploration.

MTBs represent a critical component of precision oncology, yet availability and use varied substantially across regions and settings in our survey. Northwestern Europe reported the highest integration (only 6% with no access; 65% on-site MTBs), while nearly half of respondents in Africa and South/Central America–Caribbean reported no access at all, highlighting a substantial structural gap in precision oncology resources. Across Europe overall, 54% reported using MTBs for liquid biopsy interpretation, consistent with prior European surveys showing ~50% MTB availability, particularly in centers with access to multigene testing [11,16]. North America showed a different pattern: although ~80% reported MTB access, only about half routinely used them for liquid biopsy interpretation, suggesting variability in integration rather than availability. This difference may be related to distinct liquid biopsy processing models observed in our survey, with testing predominantly performed in-house in Europe and more commonly outsourced to commercial vendors in North America. In-house testing is often associated with greater variability in report format and content, which may be challenging for clinicians to interpret and underscores the importance of ongoing efforts to standardize ctDNA test reporting to facilitate consistent clinical decision-making, an area in which the ISLB is actively engaged [22,23]. As previously mentioned, lower MTB use was also observed in community settings and among generalists. This may further limit testing uptake, particularly when complex genomic results require multidisciplinary interpretation [24]. Interestingly, across all groups, many respondents indicated high confidence in interpreting results despite infrequent use of MTBs, suggesting a possible overestimation of individual interpretative ability. This is further supported by an internal inconsistency observed in our data: despite 80% of respondents reporting confidence in interpreting liquid biopsy results, nearly half simultaneously identified difficulty interpreting or applying these tests as a relevant barrier to implementation. While automated vendor reports—utilized by 30% of respondents—might mask underlying interpretive complexities and contribute to an overestimation of confidence in some cases, this discrepancy broadly suggests that challenges relate less to understanding test outputs *per se* and more to their integration into complex clinical decision-making. This underscores the need for expanded education and harmonized interpretative frameworks, an important priority for the ISLB.

Despite differences in implementation, oncologists across regions and settings consistently rated liquid biopsy as clinically important. This disconnect between high perceived value and limited real-world use, also noted in prior studies [9,11,13], suggests that suboptimal adoption is not primarily driven by skepticism regarding test accuracy or clinical value, although these factors were still cited as relevant barriers by 24% and 29% of respondents, respectively. Instead, structural constraints such as cost, access, turnaround time, and difficult interpretation emerged as the primary obstacles – finding aligned with prior surveys [7,9,10,12,13]. Cost emerged as the most impactful barrier, exceeding 80% in the lowest resource regions. Limited test availability, especially in UMICs/LMICs, further restricted equitable access and underscored the demand for improved access and affordability in liquid biopsy testing. Difficulty interpreting results was also a frequently reported challenge. Accurate interpretation requires a nuanced understanding of tumor biology, assay limitations (including detection thresholds, pre-analytical variability, and risks of false positives or negatives), and the clinical context in which the test is being used. These complexities underscore the need for improved educational initiatives and for broader access to MTBs or centralized interpretation support [24]. The reliance on vendor-generated reports, used as the primary interpretative tool for complex genomic profiles by approximately one-third of respondents may have limitations. Indeed, automated therapy matching included in reports, which often include all approved drugs relevant to a detected alteration rather than preferred therapies, should be interpreted with caution. This is especially relevant in cases in which there are multiple somatic mutations and/or several potential therapeutic options. In this scenario, discussion in the context of an MTB would be

valuable to guide treatment selection [25]. Operational barriers further shape implementation. Turnaround time was consistently reported among the top barriers, with delays particularly evident in settings that rely heavily on external laboratories rather than in-house processing, which can create bottlenecks in time-sensitive treatment decisions. This complex interplay of factors influencing implementation of liquid biopsy in clinical practice is also highlighted by a recent scoping review, that similarly identified four main themes limiting liquid biopsy implementation: pre-analytical factors, disease-specific considerations, biomarker reliability, and regulatory contrains [5]. Overcoming pre-analytical and analytical barriers requires investment in local laboratory capacity and trained personnel, particularly in settings where workflow relies on in-house testing [23].

Collectively, these results show that liquid biopsy is widely valued but unevenly implemented and its adoption is shaped far more by healthcare system architecture than by clinician perceptions or motivation. Efforts to close these gaps must therefore operate at multiple levels. Addressing financial barriers is a first-order priority: more consistent reimbursement and reduced reliance on patient self-pay are essential. To help catalyze these policy changes strategies may include generating stronger evidence of cost-effectiveness of liquid biopsy [26–30] and fostering collaboration among clinicians, advocacy groups, payers, policymakers, regulators, and industry stakeholders to streamline coverage pathways [31,32]. Equally important is the need to strengthen infrastructure and establish more standardized workflows, including clearer ordering pathways and institutional support for sample processing and reporting, particularly in low- and middle-income settings and non-academic centers. Improving access to expert interpretation represents another critical step: wider implementation of MTBs could help ensure consistent and accurate interpretation and application of test results, with direct impact on patient outcomes [33]. Finally, targeted educational initiatives, especially for generalists and community oncologists, must be prioritized to reduce disparities in interpretative expertise and promote broader, more consistent integration of liquid biopsy across practice environments. The ISLB is positioned to play a key role in these efforts through guideline development, training, and global advocacy [34].

Despite the valuable insights offered by this survey, supported by the large international sample size and broad representation across settings, there are several limitations to be acknowledged. Recruitment through professional societies, email lists, and social media may have introduced sampling and self-selection bias, enriching the survey population for clinicians already engaged with liquid biopsy while under-representing those with limited internet access or those less connected to professional networks. Because the survey was disseminated through multiple open channels, a response rate could not be calculated. Consistent with this potential recruitment bias, the cohort was skewed toward specialists and clinicians working in academic centers, which could overestimate real-world adoption; however, subgroup analyses were performed to partially mitigate this concern. The English-only administration of the survey may have further constrained participation and introduced language bias. Geographic representation was uneven, with over-representation of respondents from Southeastern Europe (45%) and limited participation from South/Central America–Caribbean (8%), Northwestern Europe (8%), and Africa (4%). Therefore, findings from these regions may not be generalizable to national practice patterns. Only four responses were received from Oceania, limiting any subgroup analysis. Additionally, responses were self-reported and not validated against institutional policies or actual utilization data. This leaves open the possibility of social desirability bias leading to responses overestimating the utilization of or positive attitudes towards liquid biopsy in this ISLB sponsored survey. Finally, while this survey provides a cross-sectional overview across multiple cancer types, it reflects a snapshot of current practices in a rapidly evolving landscape. Longitudinal follow-up will be essential to track how implementation strategies evolve, identify persistent barriers, and refine future interventions across diverse settings and jurisdictions.

5. Conclusions

This international survey reveals that, while liquid biopsy is widely regarded as an essential component of precision oncology, its integration into routine care remains uneven and dependent on system level capacity. Gaps in reimbursement pathways, assay availability, and organizational infrastructure continue to restrict its reach, particularly in lower-resource settings. Ensuring increased coverage, expanding accessibility, and harmonizing operational pathways are essential to achieving more consistent incorporation of liquid biopsy into cancer care worldwide. Strengthening interpretive frameworks through wider adoption of MTBs and targeted education will help reduce variability in use and improve complex clinical decision-making. Sustained collaboration across clinical, advocacy, industry, and policy stakeholders is essential to translate liquid biopsy advances into cancer care. The ISLB is committed to playing a central role in advancing these efforts on a global scale to support the equitable and effective implementation of liquid biopsy.

Author contributions

Conceptualization: EN, SS, ES, RB, CR. Data curation: EN, SS, CR, XJ, XKZ. Formal analysis: EN, XJ, XKZ. Investigation: EN, SS, ES, RB, CR. Methodology: EN, SS, ES, XJ, XKZ, RB, CR. Project administration: EN, RB, CR. Resources: EN, RB, CR. Visualization: EN, XJ, XKZ, CR. Interpretation: all authors. Writing - original draft: EN. Writing - review & editing: all authors.

Ethics declaration

The authors have NOT obtained informed consent from participants or their legal representatives. The study was determined to be exempt under 45 CFR § 46.104(d) (2) after review by WCG IRB, as the research involved anonymous survey procedures without collection of identifiers.

This study was performed in compliance with relevant laws, regulatory frameworks and guidelines where the research took place.

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Conflict of interest disclosures

EN Uncompensated member of Precision Medicine Action for Cancer (PMAC) Board of Directors. Speaker: Guardant Health. **KV** Has received honoraria for speaker bureau from Merck Sharp & Dohme (MSD), Roche, AstraZeneca, Veracyte, and Johnson & Johnson. **LP** Travel grant from Pfizer, Eli Lilly, Gilead; speakers' fees from Daiichi Sankyo and Novartis and personal grants from the Università Cattolica del Sacro Cuore-Italy (study award for international mobility, 2024). **MG** reports advisory board participation for Foundation Medicine, Caris Life Sciences, and Immunocore; and other support from MD Education. **RB** reports a travel grant from Eli Lilly and research funding to his institution from Sanofi. **CR** Uncompensated member of Precision Medicine Action for Cancer (PMAC) Board of Directors. Research support: Menarini Silicon Biosystems, Angle plc, Tethis SpA, Qiagen. **EN, SS, ES, KV, LP, SM, DdMP, AD, NG, PP, AOF, MG, BB, CM, PS, OM, EE, RB, and CR** are part of the Young Committee of the International Society of Liquid Biopsy. All the competing interests were outside the submitted work. All the other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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