JA PCM
Joint Action Personalised Cancer Medicine

Mapping the Adoption of Liquid Biopsy and Minimal Residual Disease Monitoring Across Europe

Work Package 10 – Tertiary Prevention

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Executive summary

This report, produced under JA PCM WP10 (Tertiary prevention), maps the implementation of Liquid Biopsy (LB) and Minimal Residual Disease (MRD) monitoring for tertiary cancer prevention across 49 institutes in 24 European countries. Targeted at healthcare policymakers, clinical directors, and oncology professionals, it identifies the structural and economic challenges hindering the integration of these methodologies into routine European cancer care.

Key findings reveal a significant "implementation gap": while 73.5% of participating centres have established the foundational infrastructure for LB, only 41.7% currently apply it to tertiary prevention, such as early relapse detection. The analysis identifies systemic bottlenecks rather than technical failures as the primary hurdles, specifically a lack of clinical validation and high operational costs. A major economic disconnect exists, with current costs (often 600–1000€ per sample) far exceeding the sustainable target of 100–300€ identified by the majority of centres.

Despite these barriers, there is a unanimous (100%) expectation of growth by 2030, with MRD monitoring emerging as the definitive clinical priority across all European macro-regions. To bridge this gap, the report recommends: standardization of pre-analytical workflows to ensure data reproducibility; evidence generation to support the clinical guidelines and reimbursement models requested by healthcare providers; economic sustainability initiatives to align molecular surveillance costs with hospital feasibility.

Ultimately, this report provides the evidence-based foundation required to transition LB into a cornerstone of standard clinical practice, ensuring equitable access to advanced post-treatment surveillance across the European Union.

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Abbreviation List

cfDNA	Cell-free DNA
ctDNA	Circulating tumour DNA
dPCR	Digital polymerase chain reaction
JA PCM	Joint Action Personalised Cancer Medicine
LB	Liquid Biopsy
MRD	Minimal Residual Disease
NGS	Next Generation Sequencing
PCM	Personalised Cancer Medicine
WP	Work Package

1. Introduction

Liquid Biopsy (LB) is revolutionizing the landscape of precision oncology. Rather than waiting for a relapse to become visible on traditional imaging, clinicians can now detect microscopic traces of tumour DNA directly from body biofluids, such as blood. This capability may transform tertiary cancer prevention from a phase of passive waiting into an active, molecular surveillance strategy, allowing for the detection of minimal (or molecular) residual disease (MRD) immediately after curative surgery and the continuous monitoring for early signs of recurrence. However, transition from clinical research into routine practice is a complex challenge. To understand the state-of-art for tertiary prevention, our WP10 (Tertiary prevention) has conducted a comprehensive survey among centres participating to the JA PCM initiative. The objective was to address real world data, understanding how LB technologies are being implemented, which patient populations are benefiting, and what structural or economic barriers are slowing down broader adoption. Results are presented hereafter in this report.

2. Results

Responses have been collected from 49 Institutes belonging to 24 different countries. While the majority of respondents were from Spain, Belgium, Italy, and Denmark, the final dataset is representative of the entire Europe (Fig.1). For convenience, data have been aggregated into five European macro-regions[1,2,3,4,5] used here as analytical categories, to allow for a comparative analysis. The Mediterranean (n=15 centres), Continental (11), Nordic (10), and Central-Eastern (10) macro-regions are comparably represented. The Anglo-Saxon region, represented by Ireland, accounts for the remaining 3 centres. While regional aggregation provides a preliminary comparative framework, the results should be interpreted with caution due to the limited sample size.

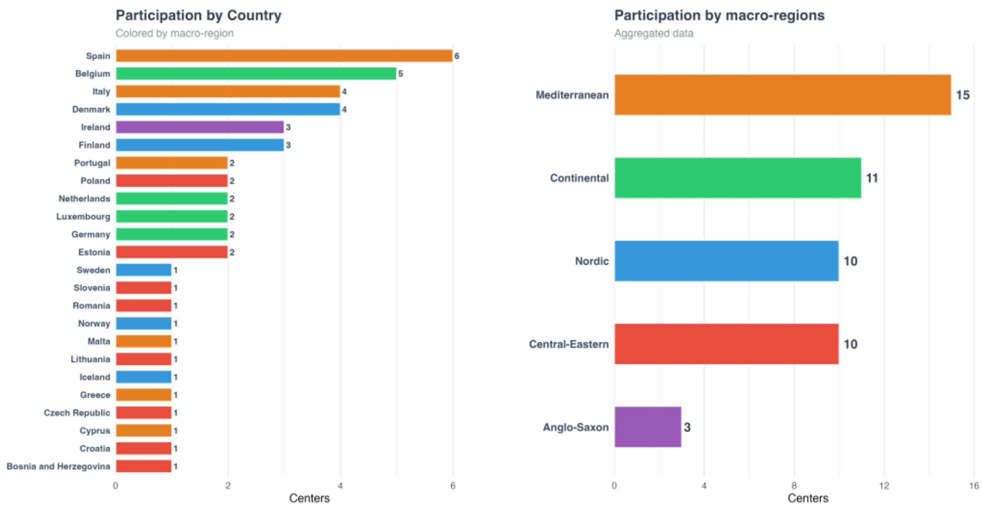

Figure 1. European participation to the survey by country (left) or macro-regions (right).

2.1 LB implementation

LB is largely adopted within the participating centres (73.5% of respondents) (Fig.2), demonstrating that the foundational infrastructure, equipment, and general know-how for LB are established. Most of the institutes use it for both research and diagnostics (66.7%). Remarkably, while technical capacity is high, only 41.7% of the centres currently apply LB to tertiary prevention (e.g., detecting relapse as early as possible or monitoring recurrence). Therefore, participating centres have been categorized into two distinct groups: (a) not active in tertiary prevention, including those not performing LB or utilizing the technology for other clinical/research purposes, and (b) already active in monitoring patients through LB for tertiary prevention. This classification should be interpreted cautiously, as some centres may be transitioning between categories or applying LB in pilot settings not fully captured by the survey.

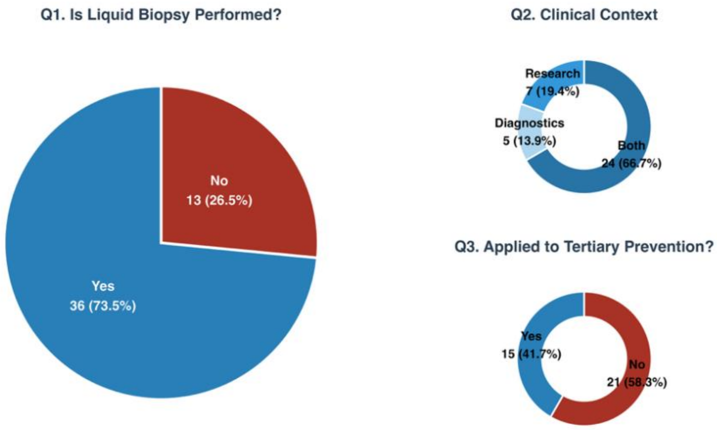

Figure 2. LB implementation in JA PCM centres. Survey question numbers are indicated (Q1, Q2 and Q3).

Among the survey respondents, the Mediterranean region leads in technical adoption (Fig.3), with 13 out of 15 centres (87%) performing LB, and with the highest percentage for application on tertiary prevention (7 out 13, 54%). Nordic regions report a slightly lower implementation: 6 out of 10 perform LB, and 3 of them use LB for tertiary prevention. Only a single Central-Eastern institute out of 7 use LB for both research and diagnostic, while 100% of the Continental responders performs both.

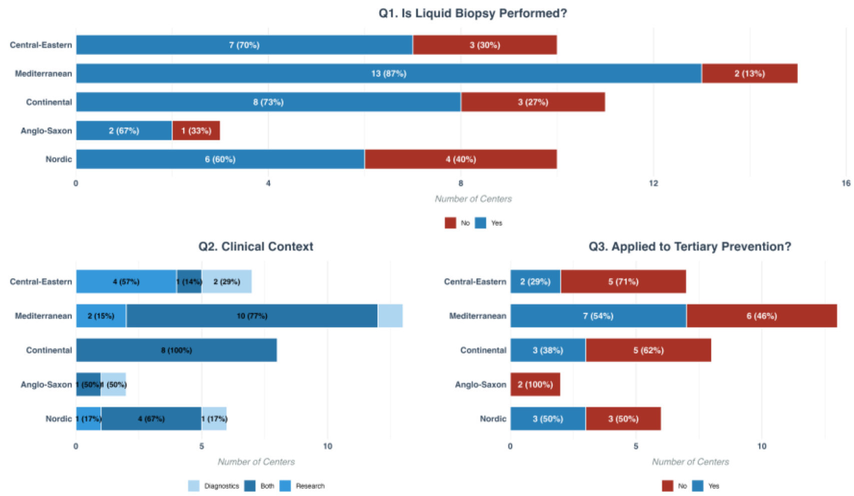

Figure 3. LB implementation by macro region. Analysis of absolute volumes and relative penetration within each model.

2.2 Analysis of barriers

2.2.1 Barriers for centres not actively using LB for tertiary prevention

To investigate the small adoption of LB for tertiary prevention, we compared responses from two distinct groups: institutes that do not use LB at all, and those applying LB but not for tertiary prevention (Fig.4). Comparative data analysis reveals similarities in perceived barriers. Regardless of the available technological ecosystem, the main barriers preventing the integration of LB into tertiary prevention appear systemic rather than strictly operational. The most frequently cited barriers were economic constraints (e.g., lack of reimbursement models, high operational costs) and lack of clinical validation (e.g., absence of robust guidelines demonstrating clinical utility in early recurrence surveillance). Even centres fully equipped for LB cannot justify its use as preventive tool without stronger evidence-based frameworks and sustainable funding mechanisms. Smaller but still critical hurdles include the lack of specialized personnel and insufficient infrastructure(s). Even when LB for tertiary prevention is indicated, the majority of the institutes do not perform the test at all, while other institutes ship the samples outside.

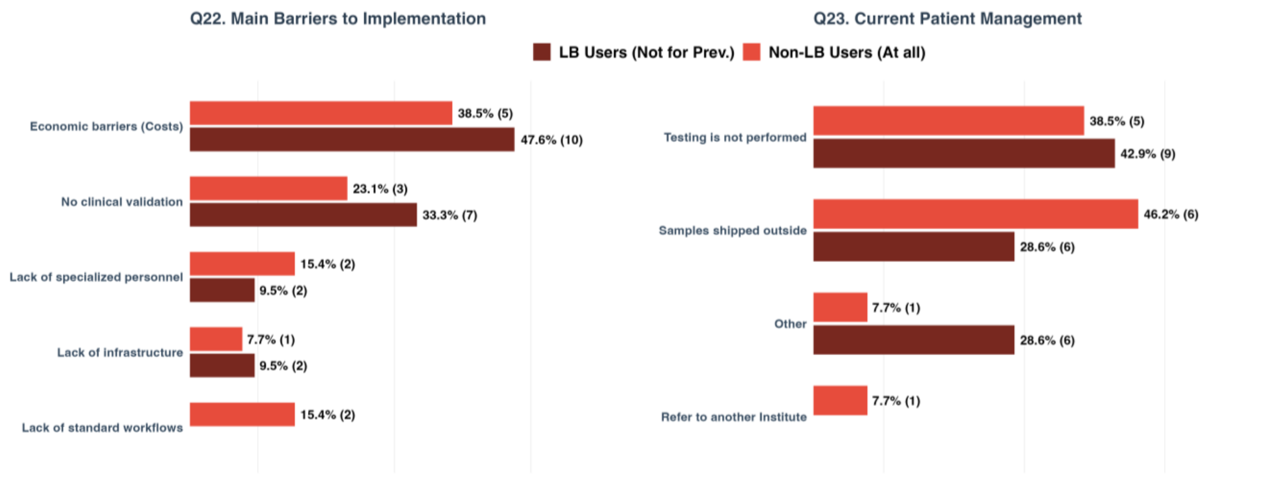

Figure 4. Focus on subgroups not performing LB for tertiary prevention. Comparison: barriers and current patient management for LB users for other scopes (n=21) vs non-LB users (n=13) (Q22, Q23, Q24, Q25).

Moreover, regional analysis (Fig. 5) reveals that while Continental and Central-Eastern institutes are primarily held back by economic factors, Mediterranean and, in part, Nordic centres, prioritize the need for clinical validation before implementation.

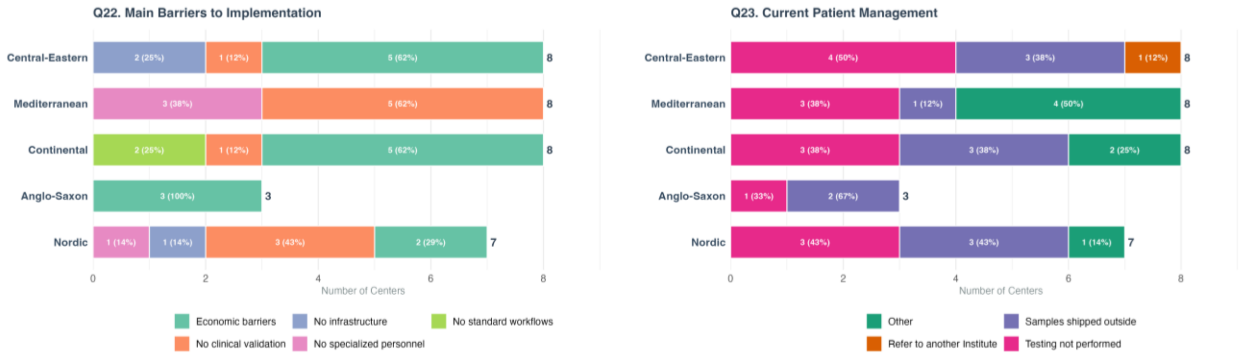

Figure 5. Barriers to LB in tertiary prevention implementation per macro region. Focus on centres not performing LB or not for tertiary prevention (n=34).

2.2.2 Barriers for LB users for tertiary prevention

While previous paragraph focused on the barriers preventing the initial adoption of LB for tertiary prevention, Fig.6 shows the factors hindering a full and standardized implementation among centres that are already active in tertiary prevention. Because these respondents have already moved past the initial adoption phase, their reported barriers reflect the obstacles to routine clinical standardization and scalability rather than mere access. However, as before, lack of clinical validation (n=12 absolute mentions) and economic barriers (12) remain the primary obstacles. Additionally, the absence of robust, evidence-based guidelines and sustainable reimbursement models prevent LB from becoming a universal standard of care.

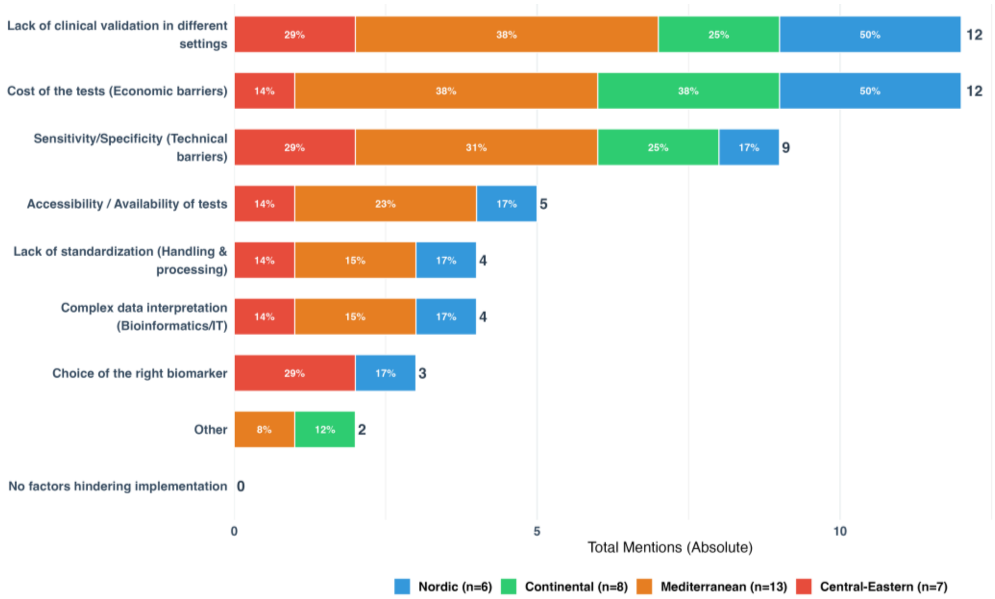

Figure 6. Barriers preventing institutes performing LB for tertiary prevention to a broad standardized application (Q21). Percentages inside bars represent penetration within the specific macro region.

2.2.3 The main economic barrier: cost analysis

Our survey showed that economic feasibility is a critical factor for the widespread adoption of LB in tertiary prevention. Specifically, it revealed disparity between the current operational costs and the target costs deemed sustainable for clinical routine (Fig.7). At present, the cost per sample (including the pre-analytical phase, w/o personnel costs) is relatively high. The largest group of centres (n=5) currently operates within the 600-1000 € bracket, while 4 centres report costs between 300-600 €. Only 2 centres are currently able to perform tests in the lower 100-300 € range. A clear consensus on the need for significant cost reduction to enable routine clinical use was documented. Indeed, the majority of participating centres (6) have identified 100-300 € as the ideal target cost per sample. The shift from the current prevailing cost (600-1000€) to the desired target (100-300€) represents a necessary step for the integration of LB and MRD monitoring into standard, equitable healthcare pathways across Europe.

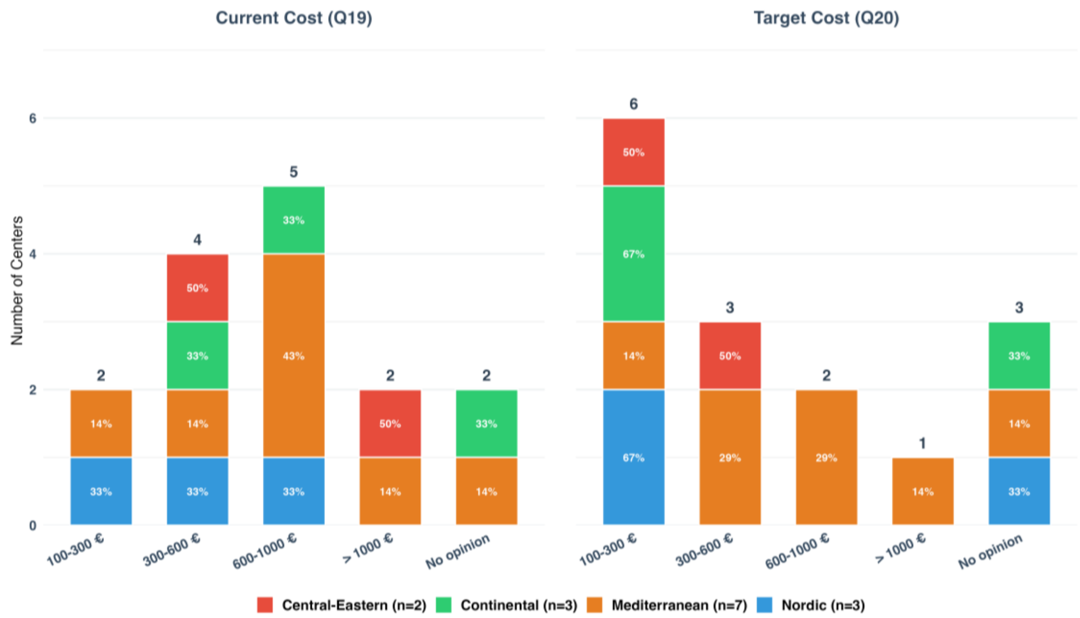

Figure 7. Cost per sample: current reality vs target (excludes personnel costs). (Q19, Q20). Percentage represent penetration within each active macro region.

2.3 Current focus and future goals

2.3.1 LB users for tertiary prevention

Centres performing LB for tertiary prevention claim to mainly focus their attention on detecting and monitoring residual disease, identifying early recurrence as well as guiding early intervention (Fig.8). Interestingly, all responders declared that their main future objective is tertiary prevention (MRD and recurrence anticipation), highlighting MRD as a key focus in the oncological field.

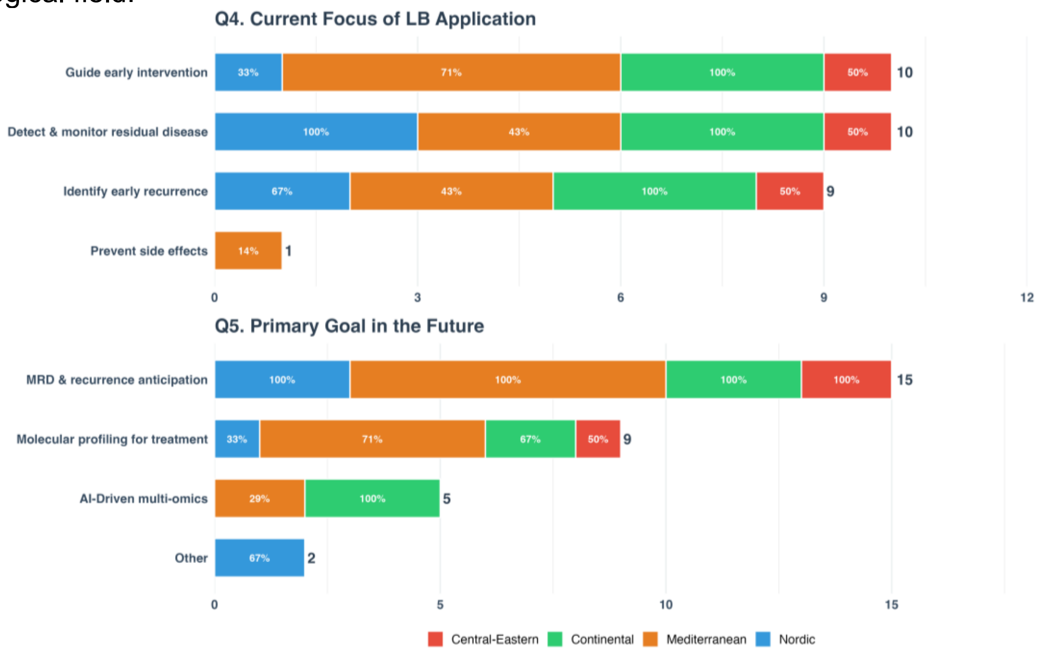

Figure 8. Current focus of LB vs future goals (n=15). (Q4, Q5). Percentages represent penetration within each specific macro region.

2.3.1.1 MRD status and monitoring

MRD analysis represents the most specialized application of LB within this task. Among the 36 centres performing LB, only 10 are actively monitoring MRD. However, as shown in the previous section, all of the centres performing tertiary prevention either work with MRD or are interested in its implementation (Fig.8). The most frequently monitored tumours were those belonging to the urogenital or digestive system followed by thoracic and lung cancers, haematological and breast tumours (Fig.9). The primary drivers for MRD assessment were therapy adjustment/intervention and early detection of relapse. The frequency of assessment showed a lack of standardization: 50% of centres report that frequency is variable according to clinical protocol, while 30% perform assessment patients every 2-3 months.

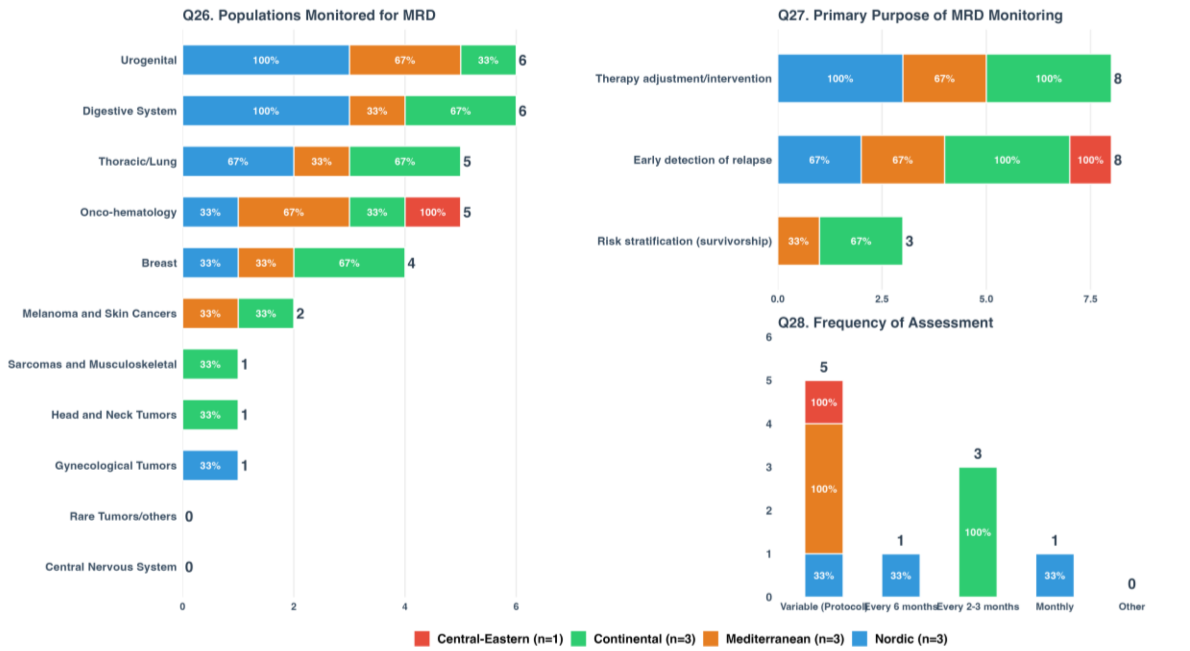

Figure 9. Analysis of the centres actively using LB for MRD detection (n=10). (Q26, Q27, Q28). Percentages represent penetration within each active region.

2.3.2 Future goals for centres non actively using LB for tertiary prevention

A clear divide exists in future planning for centres performing LB but not for tertiary prevention *vs* not performing LB at all (Fig.10). Among the latter, 38.5% declared no plans to implement it, whereas 57.1% of existing LB users (for other application) reported plans to expand into tertiary prevention within the next 2-5 years. Currently, centres lacking this capacity either do not perform the tests (41.2%) or ship samples to external service providers (35.3%) The main aim for a potential implementation would be detect and monitor MRD, identify early recurrence, guide therapy switching, while less interest was documented in preventing side effects. These results are in line with those obtained when asking to centres performing LB for tertiary prevention what's their main focus (Fig.8). The Mediterranean region, despite high technical adoption, contains the lowest percentage of centres (37%) that plans to implement LB for tertiary prevention (data not shown). This may be related to their specific concerns regarding clinical validation highlighted in Fig.5.

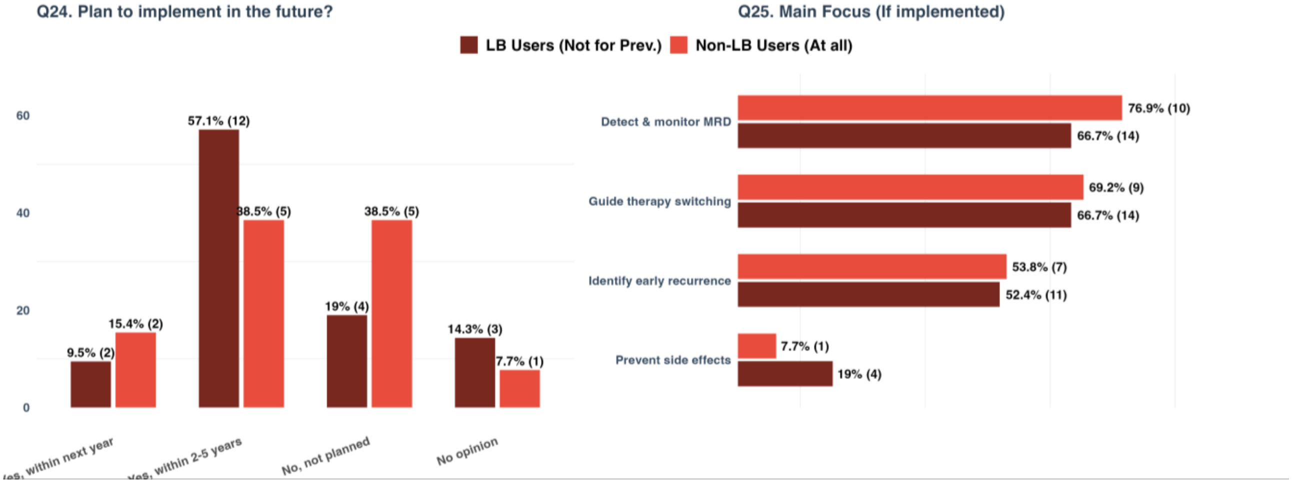

Figure 10. Comparison between LB users for other scopes (n=21) vs non LB users (n=13) (Q24, Q25): future implementation and potential main focus.

2.4 Tumour types and clinical settings

The distribution of oncology areas monitored with LB, including centres performing MRD analysis (as previously reported in Section 2.3.1.1), does not substantially differ from that observed in the subgroup of MRD users (Fig. 9).. Thoracic and lung, digestive system, onco-haematology, breast tumours, urogenital tumours were the most studied malignancies with LB (Fig.11).

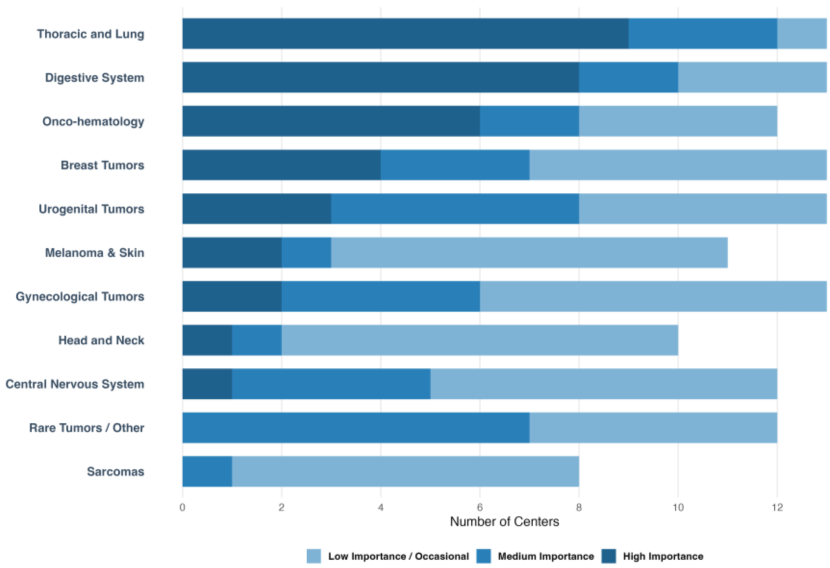

Figure 11. Oncology areas monitored for tertiary prevention. (Q8).

For each of those tumour type, we asked to indicate the clinical setting(s) (Fig.12). Molecular profiling received the most preferences, while MRD and recurrence monitoring (both related to tertiary prevention) got similar values for each type of tumour.

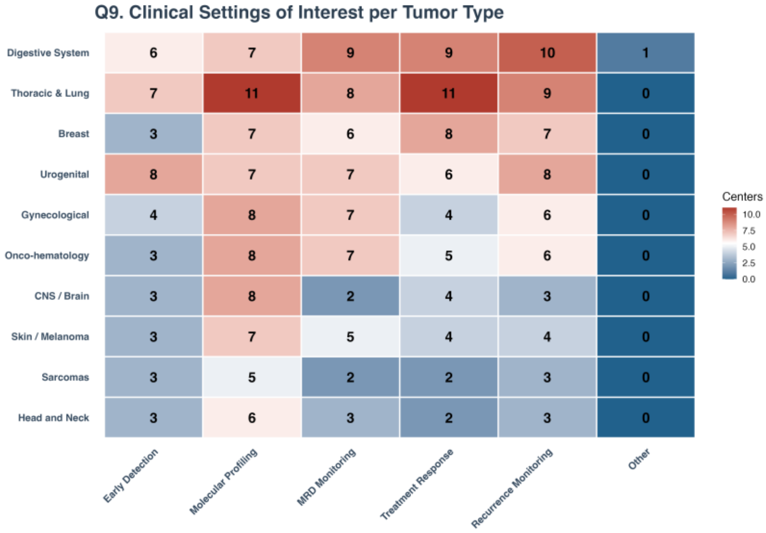

Figure 12. Clinical setting of interest per tumour type. (Q9).

2.5 Volumetric analysis of LB tests

The number of performed LB tests in 2025 for diagnostics and research is usually below 100 (13 cases, 50% of the results) (Fig.13). Despite the economic barriers underlined in section 4, there is a unanimous expectation of growth, with 100% of centres predicting an increase (73.3%) or a dramatic increase in test numbers by 2030.

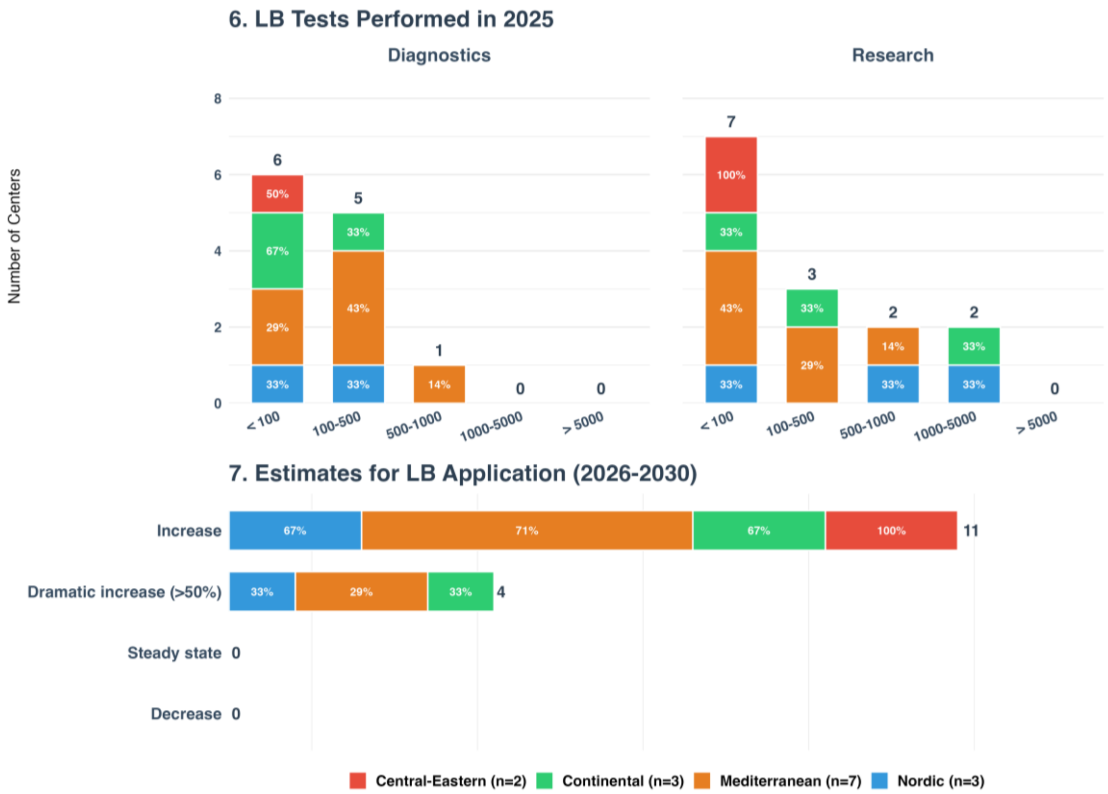

Figure 13. Volumetric analysis and future projections (Q6, Q7). Percentages represent penetration within each macro region.

2.6 Technical Infrastructure and Analytical Workflows

2.6.1 Biomaterial, biomarkers and molecular profiling

Despite plasma being by far the most analysed biofluid, CSF, pleural effusions, urine, saliva, and serum are also investigated (Fig.14). Regarding biomarkers, two main analytes appear of major interest: cfDNA and ctDNA. The most commonly employed molecular analyses are mutational profiling, followed by epigenetic analysis. Fragmentomics and proteomics are less frequently studied.

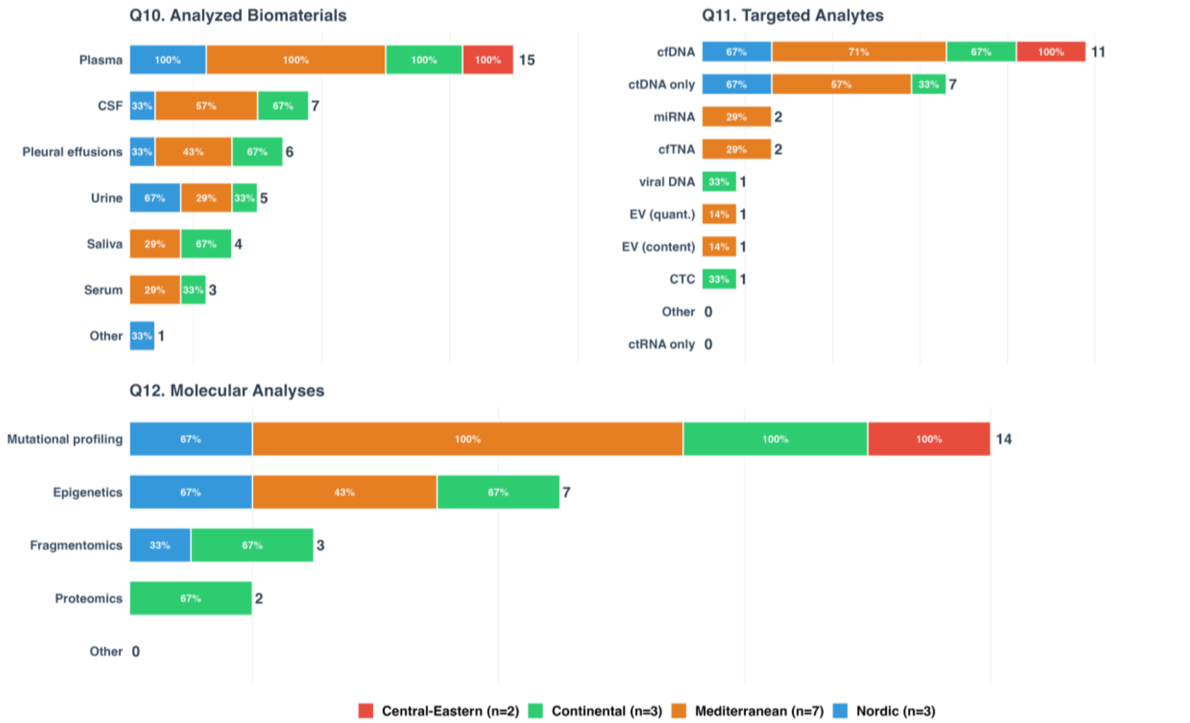

Figure 14. Analytical profiling: biomaterials and assays (Q10, Q11, Q12). Percentages represent penetration within each active macro region.

A single centre usually performs analysis on a single biomarker. Eleven institutes use multiple biomarkers (with a slight preference for tumour informed approaches over tumour agnostic), while 3 depending on clinical settings (Fig.15). Among the 11 centres, 8 analyse between 2 and 100 biomarkers, while the remaining 3 report a range from 100 to >5,000.

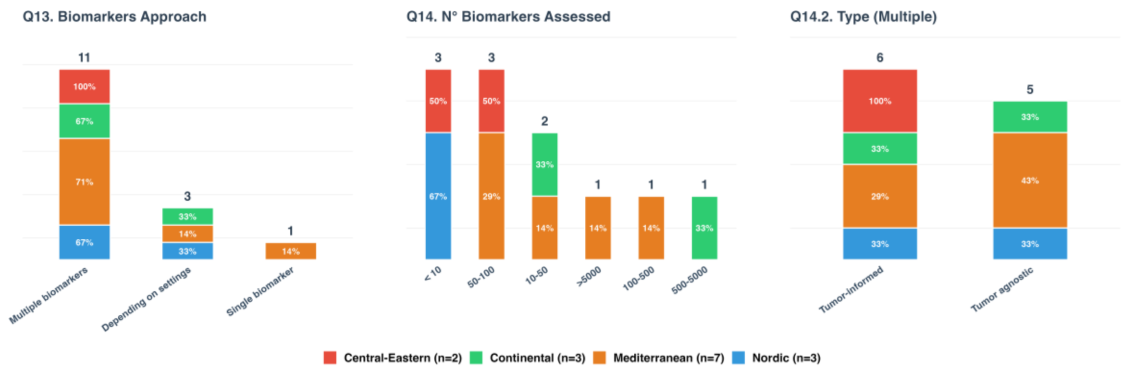

Figure 15. Strategy and implementation for active centres analysing biomarkers (Q13, Q14, Q14.2). Percentage represent penetration within each active macro region.

2.6.2 Pre-analytical workflows

The extraction phase is a fundamental step in LB workflows, with centres showing a strong preference for established commercial kits and in-house processing. Among the leading brands, Qiagen is the most widely adopted, used by 9 centres, followed by Promega (5 centres) and Thermo Fisher (3 centres) (Fig.16). Other kits such as Zymo Research and Roche/MagNA Pure are less used. Reflecting the trend seen in analytical platforms, the majority of institutes perform extraction internally. For instance, 7 out of 9 centres using Qiagen and 4 out of 5 using Promega perform the extraction in-house. Very few centres rely on external services for this stage.

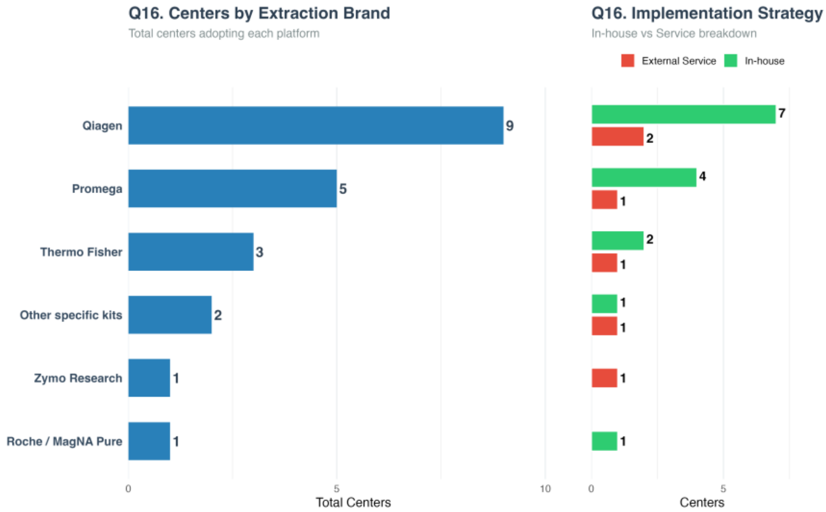

Figure 16. Pre-analytical workflows analysis. (Q16).

2.6.3 Quality control and sample requirements

Ensuring the integrity of nucleic acids is vital for downstream LB applications, particularly for the MRD setting where sensitivity is paramount. Our survey highlighted a dual-instrument approach for quality check. Qubit is the most utilized instrument for quantification (12 mentions), while Bioanalyzer/TapeStation is the preferred method for assessing fragment distribution and integrity (10 mentions) (Fig.17). Quality control is almost exclusively performed in-house: for both Qubit and Bioanalyzer/TapeStation, 100% of the reporting centers manage these checks internally. The requirements for downstream analysis demonstrate the technical challenge of performing LB with limited amount of materials. Most centres operate with low nucleic acid inputs: 7 centres declared 10-20 ng, while 5 centres can perform analyses with less than 10 ng. Only one centre reported requiring a higher input of 50-100 ng.

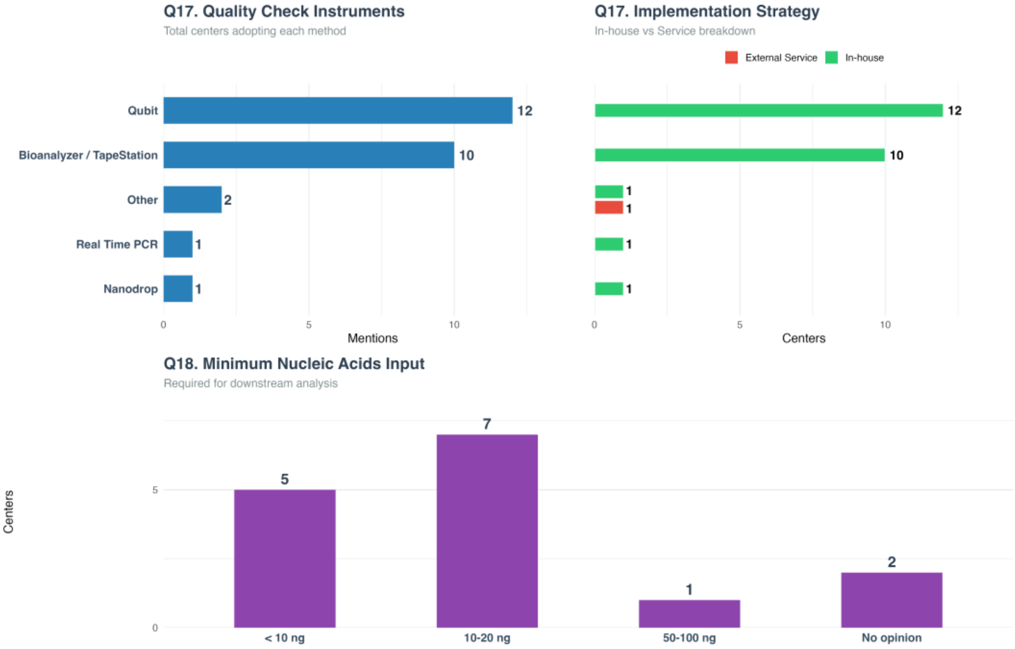

Figure 17. Quality control and input requirements. (Q17, Q18).

2.6.4 Technology platforms

NGS and dPCR were the leading technologies, both primarily managed in-house (Fig.18). For dPCR, Bio-Rad is the most used brand (7 mentions), while Illumina dominates the NGS space (10 mentions) followed by Thermo Fisher (5).

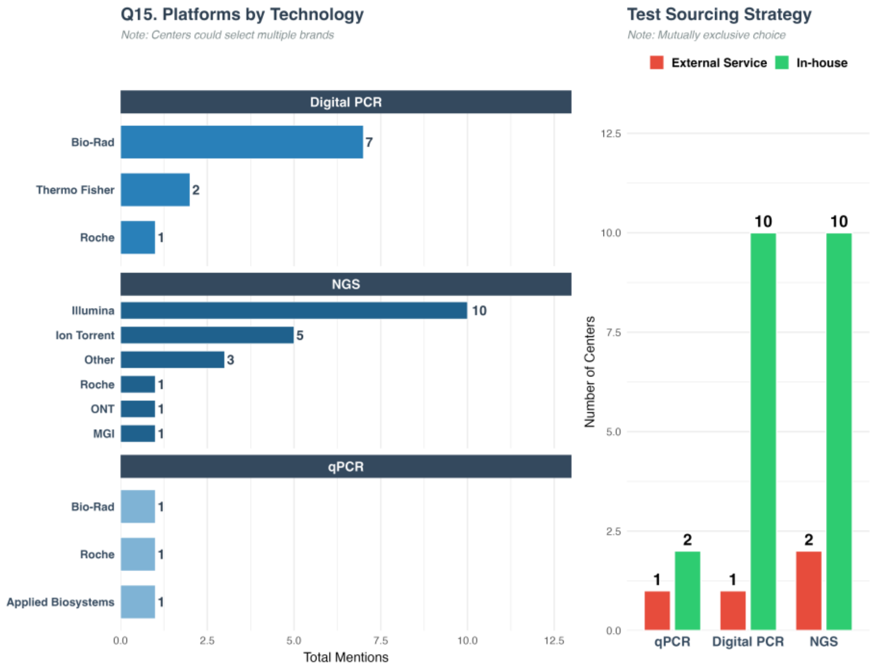

Figure 18. Technology platforms employed for LB. (Q15).

3. Conclusions and Recommendations

This mapping exercise conducted under WP10 (Task 10.1 - State of play for tertiary prevention in PCM) revealed a dual reality for LB in Europe. This has direct implications for health system equity, as unequal access to LB-based monitoring may widen disparities in post-treatment cancer care across Europe. On one hand, there is a robust technological foundation, with over 73% of institutes already equipped and performing LB analyses mainly through NGS and dPCR. On the other hand, a significant implementation gap persists: only 41.7% of these centres utilize LB for tertiary prevention (Fig.2), and active MRD monitoring remains restricted to a minority of specialized institutes (10 out of 49 responders). Therefore, a transition toward a preventative, longitudinal, real-world monitoring of cancer by LB remains incomplete.

Centres already performing LB for purpose other than tertiary prevention showed high degree of readiness to expand, with 68% planning to implement tertiary prevention within the next five years (Fig.10). As expected, non-LB users have the highest volume of centres not planning to implement LB for tertiary prevention (38%, Fig. 10).
Regardless of readiness level or current technological capacity, barriers to implementation and scaling of LB for tertiary prevention are remarkably consistent. Comparative analysis between non LB users and institutes using LB for other purposes indicates that the primary hurdles are systemic rather than operational, with both groups citing economic constraints and lack of clinical validation as the most frequent obstacles (Fig. 4). Crucially, this pattern persists even among centres already performing LB for tertiary prevention (Fig. 6). A notable exception to this general consensus on economic barriers is observed in the Mediterranean macro-region among centres not yet active in tertiary prevention. Unlike other regions that primarily cite costs, these institutes place greater emphasis on the lack of clinical validation and the need for specialised personnel as primary hurdles to implementation (Fig. 5).
Current costs per sample (often >600€) remain significantly higher than the sustainable target of 100-300€ identified as a feasible target price by the majority of centres (Fig.7). Despite this limitation, there is a unanimous consensus that LB volume will increase by 2030 (Fig.13), accompanied by a strategic shift toward MRD and early recurrence anticipation as the primary objectives (Fig. 8). Crucially, the pivotal role of MRD is reaffirmed by institutes not yet active in tertiary prevention, who identify the detection and monitoring of MRD as the absolute priority and primary driver for any future adoption of these technologies (Fig.10).

To bridge the current gap, this Joint Action should prioritize the following actionable steps:

- standardization »» develop and adopt EU-wide harmonized protocols for pre-analytical workflows and MRD assessment frequency, which are currently highly variable (Fig.14-15-16-17-18);
- evidence generation »» supporting clinical validation to justify reimbursement and the creation of formal guidelines;
- sustainability »» developing economic models that align operational costs with clinical feasibility to ensure equitable access across all European member states.

Finally, transitioning LB from a research-heavy diagnostic tool to a cornerstone of tertiary prevention is essential to improving long-term patient outcomes and advancing Precision Cancer Medicine in Europe.

4. References

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