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FROM BIOMARKERS TO PRECISION SURVEILLANCE: A SOCIO-TECHNICAL REVIEW OF NON-INVASIVE HEPATOCELLULAR CARCINOMA SCREENING IN CIRRHOSIS

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ABSTRACT

This review examines how non-invasive biomarker technologies are reshaping hepatocellular carcinoma (HCC) surveillance in cirrhosis when considered not only as diagnostic tools but also as socio-technical interventions. A structured narrative review was developed from a targeted full-text corpus covering biomarkers, precision surveillance, cost-effectiveness, surveillance harms, and disparities in access and outcomes. The literature was coded thematically across five domains: biomarker technologies, precision surveillance models, economic value, patient burden, and equity and implementation. The reviewed evidence shows that surveillance is moving from a one-size-fits-all ultrasound-based model toward hybrid, risk-stratified systems that combine blood-based biomarkers, algorithmic scores, and selective advanced imaging. Composite scores such as GALAD and HES V2.0 improve early-stage detection compared with single markers, while recent modeling studies suggest that biomarker-based or precision surveillance can be cost-effective under realistic assumptions about test performance, adherence, and price. However, adoption is constrained by assay standardization, reimbursement, false-positive workup, psychological and financial harms, and persistent disparities related to insurance, mental health, transportation, language, and digital access. The main conclusion is that the future of HCC screening is not simply a better biomarker but a better surveillance system. Research and policy should therefore evaluate analytic performance together with workflow fit, patient acceptability, equity, governance, and real-world implementation.

KEYWORDS

Hepatocellular Carcinoma, Precision Surveillance, Biomarkers, Cirrhosis, Implementation, Health Equity

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1. Introduction

Hepatocellular carcinoma (HCC) is the dominant form of primary liver cancer and remains one of the leading causes of cancer-related death worldwide. Most cases arise in the setting of cirrhosis, which makes surveillance a central component of liver care rather than a peripheral oncology task. Earlier detection changes the therapeutic horizon: patients found at a very early or early stage are more likely to receive curative-intent treatment, whereas late presentation narrows options and worsens survival. Recent reviews continue to describe HCC as a disease whose epidemiology is changing, but whose dependence on timely surveillance remains constant (Amin et al., 2025; Singal, Reig, & Villanueva, 2022).

Despite the long-standing recommendation for semiannual surveillance in high-risk groups, the dominant model of care is still built around abdominal ultrasound with or without alpha-fetoprotein (AFP). This model is attractive because it is familiar, comparatively inexpensive, and embedded in guideline language. Yet it is also vulnerable to the realities of routine practice. Ultrasound performance varies with operator expertise, body habitus, liver morphology, and local radiologic capacity, and it can be particularly compromised in people with obesity or non-viral liver disease etiologies that are becoming more common in contemporary hepatology (Huang et al., 2023; Singal et al., 2022).

These performance limitations are only part of the problem. HCC surveillance is also underused, fragmented, and socially uneven. A systematic review and meta-analysis estimated pooled surveillance use at only 24.0% among patients with cirrhosis, with substantially lower uptake outside subspecialty clinics and among patients with alcohol-associated or NASH-related disease (Wolf et al., 2021). In clinical practice, many patients never enter a reliable surveillance pathway, and others move through pathways disrupted by missed orders, scheduling barriers, transportation constraints, or inadequate follow-up. As a result, the effectiveness of surveillance in real health systems depends on far more than test sensitivity and specificity. It depends on how technologies, institutions, clinicians, and patients interact across time. That is why HCC surveillance can be understood as a socio-technical system: outcomes emerge from the combination of tools, workflows,

reimbursement rules, informational infrastructures, and the lived capacities of patients to participate in care (Huang et al., 2023; Kronenfeld & Goel, 2021; Marquardt et al., 2021).

In parallel with these challenges, the surveillance technology landscape has become much more complex. Blood-based biomarkers have moved beyond single analytes such as AFP toward multidimensional scores that combine proteins, clinical variables, and longitudinal changes over time. Composite tools such as GALAD and HES aim to reduce dependence on sonographic visualization and to support more personalized surveillance strategies. At the same time, liquid biopsy platforms, methylated DNA panels, and other emerging biomarkers promise new forms of signal extraction from peripheral samples. The important social-science question is not only whether these tools work in controlled studies, but how they alter access, workload, decision-making, costs, and patient burden once they are introduced into actual systems of care.

This review therefore shifts the center of gravity from a purely biomedical question - which biomarker is best - to a broader question that better fits the scope of the International Journal of Innovative Technologies in Social Science: how are non-invasive biomarker technologies reorganizing surveillance for HCC in cirrhosis, and what social, organizational, and policy conditions shape their value? The article argues that the next stage of HCC screening is best described as a transition from single-test evaluation to precision surveillance. In that transition, biomarkers function not only as laboratory results but as components of a larger architecture that includes risk stratification, digital decision support, advanced imaging triage, patient navigation, and resource allocation.

The objectives of the review are fourfold. First, it examines how the main non-invasive biomarker families and composite scores are positioned within contemporary HCC surveillance. Second, it synthesizes recent evidence on cost-effectiveness, risk-stratified care, and precision surveillance pathways. Third, it analyzes the literature on disparities, psychological harms, financial burden, and other patient-facing consequences of surveillance. Fourth, it proposes an explicitly socio-technical reading of innovation in this field, arguing that successful adoption depends on workflow compatibility, equity, and governance as much as on assay performance.

2. Methodology

This manuscript was prepared as a structured narrative review rather than as a formal systematic review or meta-analysis. That design was chosen because the article seeks to integrate biomedical evidence on biomarkers with implementation, health-services, and equity literature - domains that differ substantially in methods, outcome measures, and levels of analysis. A structured narrative approach made it possible to preserve methodological transparency while also enabling interpretive synthesis across heterogeneous sources.

The evidence base consisted of full-text articles assembled to capture the technological, clinical, economic, and social dimensions of HCC surveillance in cirrhosis. The review corpus combined a broad source set on HCC surveillance and biomarker technologies with nine additional publications selected to deepen coverage of socio-technical issues. These supplementary papers addressed emerging surveillance tools, cost-effectiveness modeling, disparities in access and outcomes, psychiatric comorbidity, and multidimensional biomarker scores. The final corpus therefore spanned narrative reviews, systematic reviews, prospective biomarker validation studies, economic models, and disparity-focused analyses published between 2017 and 2025.

A thematic selection strategy was used. Sources were retained if they met at least one of the following criteria: (1) they evaluated a non-invasive biomarker or biomarker score for HCC detection in populations with cirrhosis or advanced chronic liver disease; (2) they analyzed surveillance pathways, economic value, or implementation strategy; (3) they focused on patient burden, process failure, screening underuse, or social disparities relevant to HCC surveillance; or (4) they offered a contemporary synthesis of the field that could anchor the technological discussion. Articles centered exclusively on advanced therapeutic management without relevance to surveillance design were not emphasized in the synthesis.

The corpus was coded iteratively across five analytic domains: technology design, diagnostic and early detection performance, surveillance economics, patient and social burden, and implementation and governance. During coding, additional concepts were tracked when they recurred across multiple sources, including false positives, operator dependence, reimbursement, digital infrastructure, psychiatric comorbidity, insurance status, and the changing epidemiology of liver disease. These recurrent concepts were then used to organize the Results and Discussion sections.

The synthesis does not treat surveillance solely as a technical question. Instead, a socio-technical analytic lens was applied. In this framework, a surveillance technology is not just an assay or score; it is a set

of relationships connecting data capture, algorithmic interpretation, clinician action, patient adherence, and organizational response. Accordingly, the review evaluated not only reported performance metrics such as sensitivity, specificity, or area under the receiver operating characteristic curve, but also evidence on access, workflow fit, stage migration, downstream imaging, cost-utility, acceptability, and the potential for widening or narrowing disparities.

No new human or animal data were collected. The manuscript is based exclusively on published literature and therefore did not require ethics committee approval. Because the article is a structured narrative review rather than a registered systematic review, the methodology should be interpreted as transparent and purpose-driven rather than exhaustive. Its strength lies in combining technological and social dimensions that are often reviewed separately.

3. Results and interpretive synthesis

3.1. From one-size-fits-all surveillance to precision surveillance

A consistent theme across the reviewed literature is that conventional HCC surveillance is reaching the limits of a one-size-fits-all design. Ultrasound, with or without AFP, became dominant because it was cheap, familiar, and relatively easy to scale. But the evidence summarized in recent clinical reviews shows that this model underperforms in exactly those populations that are becoming more common in contemporary practice, including patients with obesity, metabolic dysfunction-associated steatotic liver disease, and non-viral cirrhosis. Singal et al. (2022) note that ultrasound combined with AFP still misses more than one-third of HCC at an early stage and that visualization problems become more likely when body habitus or parenchymal heterogeneity worsen. In other words, the test is not only imperfect in the abstract; its limitations are systematically linked to changing patient populations.

This problem is amplified by surveillance underuse and process failure. Contemporary cohort analyses show that even among patients already known to have cirrhosis, surveillance often fails before a test is ever performed. In one multicenter retrospective analysis, only 37.2% of patients with cirrhosis and HCC had regular outpatient care in the year before diagnosis, and only 24.7% of those with regular care were actually under surveillance; nearly half of surveillance failures reflected the absence of surveillance orders despite established cirrhosis (Marquardt et al., 2021). These findings are important because they show that HCC screening is partly an organizational problem. A technology with excellent analytic performance will still have limited value if ordering workflows, recall systems, and patient navigation are weak.

The literature therefore increasingly reframes surveillance around risk stratification and personalization. Rather than giving every patient the same modality at the same interval regardless of risk and expected test performance, precision surveillance seeks to tailor the surveillance pathway to the individual. This may include assigning different modalities to low-, intermediate-, and high-risk patients, or altering the pathway according to sex, obesity, liver disease etiology, decompensation status, or previous imaging quality. From a social-science perspective, this is a classic move from standardization toward adaptive technology use. It changes surveillance from a fixed service into a decision system.

Importantly, precision surveillance is not just a conceptual aspiration. Recent policy and review literature now treats it as a serious strategic direction. Lee, Fujiwara, Yang, and Hoshida (2023) describe precision HCC screening as a framework that combines risk stratification with emerging early-detection biomarkers. The ILCA white paper similarly argues that surveillance design should incorporate heterogeneity in HCC risk and test performance rather than assuming a uniform pathway for all patients with cirrhosis (Singal et al., 2023). This shift matters because it legitimizes surveillance redesign as a systems question and not merely as an exercise in biomarker discovery.

3.2. Biomarker technologies as components of surveillance infrastructure

Within this evolving landscape, biomarkers are best understood as components of surveillance infrastructure rather than as isolated laboratory curiosities. Conventional serum markers such as AFP, AFP-L3, and des-gamma-carboxy prothrombin (DCP, also referred to as PIVKA-II) remain important because they are relatively easy to collect and can be integrated into routine blood work. Yet single analytes have repeatedly shown insufficient sensitivity or inconsistent specificity when used alone. This is why the most promising developments involve composite approaches that combine multiple markers with demographic or clinical variables.

The GALAD score is a central example of this shift. GALAD combines gender, age, AFP-L3, AFP, and DCP. Earlier multinational and case-control work suggested that GALAD offered stronger early-stage

detection than AFP alone, but a major contribution of the reviewed corpus is the inclusion of a phase 3 validation study in patients with cirrhosis. In that prospective multicenter analysis, Marsh et al. (2025) followed 1,558 patients with cirrhosis and found that the area under the curve within 12 months prior to HCC diagnosis was 0.78 for GALAD versus 0.66 for AFP. At a fixed specificity of 82%, GALAD achieved 62% sensitivity at 12 months before diagnosis, compared with 41% for AFP. The socio-technical significance of these findings is substantial. A biomarker score that can be calculated from blood tests and basic demographic inputs creates a pathway toward more reproducible surveillance that is less dependent on local imaging quality.

The newer HES V2.0 score extends this logic by incorporating both static and dynamic information. As summarized by Jaber and El-Serag (2025), HES V2.0 includes current AFP, AFP-L3, DCP, age, platelet count, albumin, ALT, etiology, and changes in biomarkers over the prior year when available. In phase 3 comparisons reviewed by the authors, HES V2.0 improved sensitivity for early-stage HCC detection by 6.7 percentage points over GALAD and by 13.4% to 18.0% over ASAP at a fixed 90% specificity. Although the clinical-outcome and economic consequences of adopting HES V2.0 remain uncertain, the score illustrates a broader movement toward multidimensional surveillance technologies. These tools are less like single tests and more like modular algorithms that can be recalibrated, embedded in electronic systems, and updated as disease epidemiology changes.

This algorithmic character is especially relevant to technology-and-society scholarship. Jaber and El-Serag (2025) explicitly note that biomarker scores such as HES and GALAD lend themselves to integration into electronic health records because their constituent inputs are already generated in routine practice. That observation pushes the discussion beyond laboratory medicine. An EHR-integrated score can be used to trigger reminders, escalate follow-up imaging, identify high-risk patients who missed appointments, or alter surveillance modality when prior ultrasound quality has been poor. The technological novelty therefore lies not only in biomarker chemistry but also in the capacity for automation and organizational coordination.

The literature also shows that biomarker technologies are entering a broader ecosystem of emerging tools. Singal et al. (2022) review the growing interest in liquid biopsy approaches, including circulating tumor DNA, extracellular vesicles, and circulating RNAs. These platforms are still early from an implementation standpoint, but they signal an important social transition: surveillance may increasingly rely on high-dimensional data extracted from routine or minimally invasive samples rather than on a single operator-dependent imaging encounter. In settings where imaging access is variable, such shifts could reduce some barriers; in settings where laboratory standardization or reimbursement is poor, they could create new ones.

At the same time, biomarker technologies do not eliminate the need for multimodality pathways. The most plausible near-term model is hybrid rather than replacement. Blood-based markers and composite scores can enrich or triage surveillance, but positive results still require diagnostic confirmation and treatment planning through imaging and clinical assessment. In practical terms, this means that biomarker innovation changes the sequence and logic of care. It can alter who is prioritized, when advanced imaging is ordered, and how scarce resources are distributed. That is why biomarker scores should be evaluated not only by sensitivity but by the new forms of coordination they make possible.

Table 1. Non-invasive HCC surveillance technologies and their socio-technical characteristics.

Technology	Main inputs	Main strengths	Main constraints	Socio-technical implication
Ultrasound plus AFP	Semiannual imaging and serum AFP	Widely available; familiar to clinicians; low direct cost	Operator dependence; poor visualization in obesity and non-viral cirrhosis; underuse in practice	Works best in organized systems with dependable ordering, scheduling, and radiology capacity
GALAD	Gender, age, AFP-L3, AFP, DCP	Better early-stage detection than AFP alone; less dependent on sonographic quality	Requires validated assays and standardized calculation; still needs confirmatory imaging	Can be embedded in EHRs and used as a triage or enrichment tool

Technology	Main inputs	Main strengths	Main constraints	Socio-technical implication
HES V2.0	AFP, AFP-L3, DCP, biomarker change over time, age, platelets, albumin, ALT, etiology	Multidimensional and longitudinal; promising sensitivity at fixed specificity	Needs broader phase 4 utility evidence and recalibration across shifting etiologies	Illustrates movement toward algorithmic surveillance infrastructure rather than single tests
Liquid biopsy platforms	ctDNA, methylation panels, extracellular vesicles, circulating RNAs	Potential for earlier signal capture and higher-dimensional profiling	Cost, standardization, laboratory complexity, uncertain reimbursement	May support decentralized sampling but could widen inequity if only available in advanced centers
Abbreviated MRI	Focused MRI sequences, often non-contrast protocols	Higher sensitivity than ultrasound in selected settings; useful after poor-quality ultrasound or higher risk	Higher cost and need for imaging capacity	Most valuable as part of precision pathways that reserve imaging for patients most likely to benefit

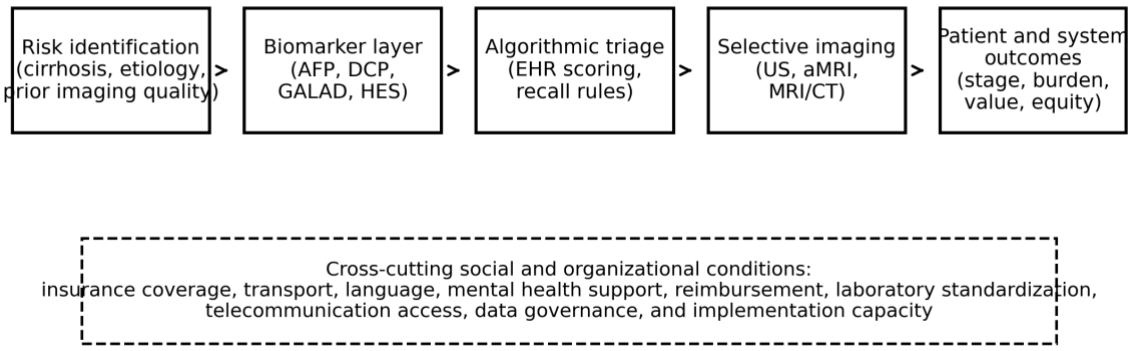

Fig. 1. *A socio-technical model of precision HCC surveillance.*

The figure summarizes how biomarker technologies, digital triage, selective imaging, and social conditions interact inside a precision-surveillance pathway.

3.3. Cost-effectiveness and the economics of precision surveillance

A major strength of the newly added articles is that they move the conversation from diagnostic promise to economic viability. In real health systems, a surveillance technology that improves detection but overwhelms budgets, increases downstream procedures, or fails to improve adherence may not deliver meaningful value. Cost-effectiveness modeling therefore becomes an essential bridge between technical performance and implementation.

Two recent studies are particularly important. First, Singal, Chhatwal, Parikh, and Tapper (2024) modeled biomarker-based screening against ultrasound plus AFP in 1,000,000 simulated patients with compensated cirrhosis. In their base case, both ultrasound/AFP and biomarker-based screening were cost-effective versus no screening, but biomarker-based screening also remained cost-effective when compared directly with ultrasound/AFP, with an incremental cost-effectiveness ratio of USD 14,800 per QALY. The

model also identified practical thresholds for implementation: biomarker sensitivity greater than 80%, test cost below USD 210, or adherence above 58% were necessary for biomarker-based screening to remain cost-effective versus ultrasound/AFP. These thresholds are socially meaningful. They show that adoption is contingent not simply on laboratory accuracy, but on price, participation, and organizational performance.

Second, Kao et al. (2024) tested a broader precision surveillance model using a modeled population of 50-year-old adults with compensated cirrhosis. They compared no surveillance, universal ultrasound plus AFP, risk-stratified surveillance, and precision surveillance that varied by both HCC risk group and patient factors affecting test performance. Precision surveillance detected a higher proportion of early-stage HCC than risk-stratified or universal ultrasound strategies - 67.6% versus 63.8% and 63.2%, respectively - and emerged as the most cost-effective strategy when willingness-to-pay thresholds exceeded USD 110,000 per QALY. Compared to no surveillance, its incremental cost-effectiveness ratio was USD 104,614 per QALY, while compared to risk-stratified surveillance it remained cost-effective with an ICER of USD 98,103 per QALY. In practical terms, this model suggests that the best-performing surveillance strategy is not the universal deployment of one modality, but a personalized mix of no surveillance, ultrasound plus AFP, GALAD, and abbreviated MRI depending on patient profile.

These findings are especially useful for a socio-technical interpretation because they show how surveillance value is co-produced by clinical and organizational variables. In Singal et al. (2024), the value of biomarkers changed when adherence changed. In Kao et al. (2024), the preferred modality changed across 48 patient types generated by combinations of risk group and factors such as obesity or likely ultrasound quality. This means that technology performance is not intrinsic in a narrow sense; it is relational. A biomarker can become more or less valuable depending on who receives it, how often, in what care environment, and what other modalities are available downstream.

Complementary modeling from Decharatanachart et al. (2024) broadens this point by showing that advanced imaging can also become economically attractive when placed within the right surveillance architecture. In their cost-utility analysis, non-contrast abbreviated MRI was cost-effective versus ultrasound with AFP in both Thailand and the United States, with incremental cost-effectiveness ratios of USD 3,667 per QALY and USD 37,062 per QALY, respectively. The probability of aMRI being the more cost-effective option was approximately 77% in Thailand and 98% in the United States. The authors also found that HCC incidence strongly influenced value, which reinforces a core precision principle: intensive technologies become easier to justify as baseline risk rises.

The cost literature also clarifies that new technologies can generate harm if they are introduced without pathway design. In the biomarker model by Singal et al. (2024), false-positive results led to CT or MRI workup and temporary reductions in utility during evaluation. Earlier work on benefits and harms in surveillance programs similarly emphasized the importance of indeterminate nodules, extra imaging, invasive follow-up, and anxiety (Atiq et al., 2017). This is one reason why cost-effectiveness cannot be reduced to a simple ratio of spending to tumors found. It must account for downstream consequences, including patient burden and non-curative diagnostic cascades.

A major lesson from this literature is that cost-effectiveness studies are not simply economic appendices to laboratory innovation. They are design tools. They clarify what conditions must be present for a technology to add value and make visible how adherence, workflow, and resource allocation are built into the success of screening innovations.

Table 2. Selected contemporary studies informing a socio-technical model of precision HCC surveillance.

Study	Design	Main finding	Relevance for IJITSS-oriented analysis
Marsh et al. (2025)	Prospective phase 3 biomarker validation	GALAD outperformed AFP for detecting HCC within 12 months before diagnosis in cirrhosis	Shows how a biomarker score can challenge the imaging-centered status quo
Jaber & El-Serag (2025)	Narrative review of multidimensional scores	HES V2.0 improved early-stage sensitivity over GALAD and ASAP at fixed specificity	Frames biomarker scores as algorithmic technologies suitable for EHR integration
Singal et al. (2024)	Decision-analytic model	Biomarker-based screening was cost-effective versus ultrasound/AFP under realistic assumptions	Demonstrates that adoption depends on cost, adherence, and false-positive workup, not only accuracy
Kao et al. (2024)	Microsimulation model	Precision surveillance produced the highest proportion of early-stage detection and was the most cost-effective strategy	Recasts surveillance as a personalized, pathway-level design problem
Decharatanachart et al. (2024)	Cost-utility analysis	Non-contrast abbreviated MRI was cost-effective in both Thailand and the United States	Shows how advanced imaging may fit within selective surveillance architectures rather than universal use
Kronenfeld & Goel (2021)	Disparities review	Insurance, income, race/ethnicity, education, and telecommunication affect screening, treatment, and survival	Expands evaluation from technical efficacy to social distribution of access and outcomes
Saleh et al. (2022)	Retrospective cohort	Patients with psychiatric illness had less recent screening despite more specialist contact and were more likely to receive palliative pathways	Illustrates how surveillance failure can persist even when health-system contact exists

3.4. Surveillance harms, patient burden, and acceptability

A strong socio-technical analysis must also ask what surveillance feels like from the patient side. Much of the biomarker literature is written in the language of improvement - higher AUC, better sensitivity, lower cost per QALY - but surveillance programs can also create physical, psychological, and financial harms. These harms matter because they influence adherence, trust, and long-term participation in care.

Atiq et al. (2017) provided an early conceptual framework for the benefits and harms of HCC surveillance in cirrhosis. They argued that surveillance should not be judged only by tumor detection, but also by false positives, indeterminate findings, overdiagnosis, procedural complications, and patient burden. More recent work has added patient-reported evidence to this framework. Narasimman, Hernaez, Cerda, Lee, Sood, et al. (2024) found that HCC surveillance may be associated with psychological harms in patients with cirrhosis, highlighting the emotional load produced by repeated testing, uncertainty, and diagnostic recall pathways. A companion analysis by Narasimman, Hernaez, Cerda, Lee, Yekkaluri, et al. (2024) documented financial burden associated with HCC screening, showing that surveillance can create costs tied to transportation, missed work, co-payments, and follow-up imaging even before cancer is diagnosed.

These findings are highly relevant to biomarker adoption. A blood-based test may appear less burdensome than imaging, but that does not automatically mean it reduces the overall experience of burden.

A highly sensitive biomarker with a substantial false-positive rate could create more recall imaging, more liver clinic visits, or more repeated laboratory testing. Conversely, a well-integrated biomarker score could reduce uncertainty by improving triage, limiting inappropriate imaging, and allowing high-risk patients to be seen earlier. The question is not whether biomarkers are burdensome in the abstract. It is whether the surrounding system is designed to translate results into proportionate and understandable action.

The literature on patient preferences supports this more human-centered view. Woolen et al. (2022) found that patients have meaningful preferences regarding surveillance parameters, including test modality and burden characteristics. Meanwhile, Singal et al. (2022) demonstrated that predictive modeling can be used in a tailored approach to promote surveillance uptake among patients with cirrhosis. Taken together, these studies suggest that surveillance technologies should be designed with behavioral and communicative layers in mind. Decision support systems, reminder systems, and biomarker-triggered pathways may all fail if they do not account for patient comprehension, fear, practical constraints, and willingness to engage in repeated monitoring.

Patient burden is also unevenly distributed. Individuals with limited transportation, unstable employment, language barriers, or competing caregiving demands are more affected by time-intensive or poorly coordinated surveillance systems. A blood-based strategy might reduce some of those burdens if it can be synchronized with routine hepatology visits or community-based phlebotomy. Yet if it depends on proprietary assays, specialist ordering, or uncovered follow-up imaging, it may merely shift burden from one form to another. The social meaning of innovation therefore lies in burden redistribution as much as in diagnostic improvement.

3.5. Disparities, social determinants, and uneven access to innovation

The most explicit evidence on the social distribution of HCC surveillance comes from disparity-focused literature. Kronenfeld and Goel (2021) argue that disparities in HCC care occur at both individual and contextual levels and extend across the full continuum from screening to treatment to survival. Their review highlights how insurance status, income, education, neighborhood context, language, and telecommunication access shape whether patients reach surveillance, how quickly they are diagnosed, and what treatment becomes available after diagnosis.

Insurance is particularly consequential. Kronenfeld and Goel (2021) summarize evidence showing that in potentially curable disease, privately insured individuals may can reach a median overall survival near 34 months, whereas patients without health insurance can have median overall survival as low as 9 months. The mechanisms are not mysterious: uninsured patients are less likely to access primary care, less likely to receive regular screening, more likely to present with advanced disease, and less able to sustain costly follow-up after diagnosis. This makes HCC surveillance a revealing case of how health technologies can reproduce broader inequalities when access to enabling services is uneven.

The study by Saleh et al. (2022) sharpens this issue by examining psychiatric comorbidity. In a safety-net hospital cohort of 393 patients with HCC, 32.5% had at least one psychiatric illness. Only 33.6% of patients with psychiatric illness underwent screening within six months before diagnosis compared with 49.8% of those without psychiatric illness. Strikingly, the psychiatric-illness group was more likely to have seen a gastroenterologist or hepatologist before diagnosis - 71.1% versus 55.1% - which means the disparity was not explained solely by a complete lack of specialist contact. Instead, it suggests breakdowns in adherence, navigation, or coordination. These patients were also more likely to be offered systemic therapy or hospice rather than curative options, consistent with more advanced disease at presentation. Biomarker innovation cannot ignore such realities. A new score will not solve surveillance inequity if mental health, follow-up, and supportive care remain disconnected.

The disparity literature also reveals a more structural issue: technologies often work best in settings that already have resources. Composite biomarker scores, proprietary assays, abbreviated MRI, and EHR-based recall systems are easier to implement in large integrated hepatology programs than in fragmented or under-resourced systems. Jaber and El-Serag (2025) note that multidimensional scores such as HES V2.0 could be integrated relatively smoothly into Western health systems with established diagnostic and EHR infrastructure. That observation is plausible, but it is also a warning. If adoption depends on mature infrastructure, then early benefits may accrue disproportionately to health systems and patient populations that are already advantaged.

This does not mean that biomarker technologies are inherently inequitable. On the contrary, they may be able to reduce some long-standing disparities. Blood-based markers are less dependent on sonographer skill, can be sampled in a wider variety of locations, and may support more standardized recall pathways. For

patients who historically receive poor-quality ultrasound because of obesity, ascites, or local imaging limitations, biomarker-guided pathways could offer more equitable risk assessment. The point is that technology alone does not determine the direction of the effect. Whether biomarkers narrow or widen disparities depends on assay availability, reimbursement, digital integration, patient outreach, language access, and the existence of coordinated follow-up systems.

For a journal focused on technology and society, this is perhaps the central message. The social value of surveillance innovation lies not only in improved detection among ideal users, but in whether innovation can be distributed across heterogeneous populations without amplifying exclusion.

Table 3. Socio-technical barriers to precision HCC surveillance and plausible design responses.

Barrier domain	Example from literature	Likely consequence	Potential design response
Patient burden	Psychological stress, travel time, out-of-pocket cost, missed work	Missed surveillance, delayed recall imaging, disengagement	Synchronize biomarker testing with routine visits; provide navigation and transparent risk communication
Provider workflow	Missed surveillance orders and fragmented follow-up	Eligible patients never enter consistent screening pathways	EHR-based registries, automated reminders, score-triggered recall protocols
Imaging variability	Poor ultrasound visualization in obesity or non-viral cirrhosis	Lower early-stage detection and more indeterminate examinations	Use biomarker scores or abbreviated MRI selectively in patients with poor expected ultrasound performance
Payment and reimbursement	Uninsured or underinsured patients have poorer access and outcomes	Technology adoption benefits already advantaged populations first	Coverage policies for biomarker assays and follow-up imaging; value-based surveillance pathways
Psychiatric and social complexity	Patients with psychiatric illness screened less despite specialist contact	Late-stage presentation and fewer curative options	Integrated hepatology-mental health coordination and proactive outreach
Algorithm governance	Need for recalibration across changing etiologies and populations	Drift, misclassification, inequitable performance	Periodic external validation, transparent thresholds, audit trails, and local recalibration policies

3.6. Digital integration, workflow redesign, and governance

A final result emerging from the reviewed corpus is that the most advanced surveillance models increasingly resemble data systems rather than stand-alone tests. Composite biomarker scores rely on multiple inputs, some of which change over time; precision surveillance models incorporate risk groups, obesity status, expected ultrasound quality, and alternative modalities such as biomarker panels or abbreviated MRI; and implementation proposals often assume some form of automated calculation or recall support. In other words, the frontier of surveillance is organizational digitization.

This is visible in both the algorithmic and implementation literature. Jaber and El-Serag (2025) argue that multidimensional scores such as HES V2.0 are well suited to integration into electronic health records because the required biomarkers and clinical inputs already exist in routine workflows. The score can therefore function as a background calculation that identifies patients who should continue with ultrasound, receive additional blood-based evaluation, or move to more advanced imaging. Singal et al. (2022) show a related logic in their work on predictive modeling to promote surveillance uptake, where data are used not merely to classify disease but to target outreach and improve completion of surveillance itself.

However, integration creates governance challenges. Any score that is embedded in an EHR becomes part of the institutional decision architecture. Questions then arise about transparency, auditability, consent, and recalibration. HES V2.0, GALAD, and similar models were derived in specific populations. As etiologies shift - for example, with declining viral hepatitis and rising MASLD-related cirrhosis - recalibration may be

necessary to preserve performance and avoid bias (Amin et al., 2025; Jaber & El-Serag, 2025). There is also the practical issue of assay standardization across laboratories. Without harmonized measurement and reporting, algorithmic portability becomes difficult.

From a workflow perspective, integration has both promise and risk. Properly implemented, scores can reduce cognitive load, prompt timely recalls, and structure referrals more consistently than ad hoc clinician memory. Poorly implemented, they can generate alert fatigue, duplicate testing, or rigid protocols that ignore local realities. The same digital infrastructure that can support precision may also obscure accountability if clinicians do not understand how scores are produced or how thresholds were chosen. This is why the governance of surveillance algorithms should be treated as part of the technology itself rather than as an external administrative concern.

4. Discussion

The reviewed literature supports a clear conclusion: non-invasive biomarkers are changing the logic of HCC surveillance, but their significance cannot be understood by diagnostic performance alone. In contemporary cirrhosis care, biomarkers are increasingly acting as coordination technologies. They help sort patients by risk, determine who should receive scarce imaging resources, structure recall intervals, and shape the burdens patients experience on the way to diagnosis. That is why a socio-technical lens is useful. It reveals that surveillance success depends on interactions among assays, algorithms, clinics, payers, and patients rather than on any single laboratory signal.

Several implications follow. First, the most realistic future for HCC screening is hybrid. The literature does not support a simple story in which blood-based biomarkers replace imaging. Instead, the direction of travel is toward layered surveillance: conventional ultrasound remains part of the pathway, blood-based scores enrich or triage the pathway, and advanced imaging is deployed more selectively for the patients most likely to benefit. This hybrid model is both technically and socially plausible because it matches the different strengths of each component. Ultrasound remains accessible and familiar; biomarker scores reduce dependence on image quality; abbreviated MRI offers a high-performance option for subsets of patients with elevated risk or poor sonographic windows (Decharatanachart et al., 2024; Kao et al., 2024; Singal et al., 2022).

Second, the field is moving from test validation to pathway validation. Early biomarker work understandably focused on whether AFP, DCP, AFP-L3, or liquid biopsy analytes could distinguish HCC from cirrhosis. But the newer studies indicate that the more consequential questions are now pathway questions: Under what conditions is biomarker-based surveillance cost-effective? Which patients should receive which modality? How should results be integrated into EHR workflows? What kinds of false-positive workup are acceptable? These are socio-technical questions because they concern the organization of care rather than just the chemistry of disease.

Third, access and equity must be treated as design criteria rather than afterthoughts. Surveillance technologies may be evaluated in elite hepatology programs, but their social value depends on performance in fragmented systems, safety-net settings, and populations facing transportation, insurance, psychiatric, or language barriers. The disparity literature reviewed here suggests that innovations can either narrow or widen inequity. A blood-based score that is inexpensive, covered, and embedded in routine phlebotomy could make surveillance easier for underserved patients. The same score, if proprietary, poorly reimbursed, or concentrated in tertiary centers, could deepen existing gaps. The relevant question for policymakers is therefore not simply whether a technology works, but for whom, at what cost, and under what institutional conditions.

Fourth, HCC surveillance offers a useful model for studying how biomedical technologies become social infrastructures. Composite scores such as GALAD and HES are not only predictive tools. Once embedded in software, reminders, registries, or reimbursement rules, they help govern the timing and intensity of clinical attention. This governance function brings with it familiar social-science concerns: algorithm transparency, trust in automated recommendations, calibration drift, and the politics of threshold setting. For example, if a health system adopts a threshold that maximizes sensitivity at the cost of many false positives, patients may absorb the burden of extra imaging and anxiety. If thresholds are too conservative, early tumors may be missed. These trade-offs are not neutral; they are choices about what kinds of error, cost, and burden a system is willing to distribute.

The literature also suggests a more human-centered agenda for innovation. Surveillance technologies are often presented as if uptake will automatically follow better performance. Yet studies on psychological harms, financial burden, patient preferences, and predictive outreach all imply the opposite. Better tests still need understandable communication, reminder systems that fit people's lives, transport and scheduling support,

and trust-building interactions with clinicians. The reason is simple: screening is repeated care, not a one-time diagnostic event. Technologies that ignore repeated burden are unlikely to achieve sustained participation.

For these reasons, the article proposes six criteria for evaluating future precision-surveillance technologies. The first is analytic validity: the technology must show acceptable discrimination and calibration in relevant populations. The second is workflow fit: it must be compatible with routine practice, including ordering, sampling, reporting, and follow-up. The third is affordability: both system-level cost-effectiveness and patient-level affordability must be considered. The fourth is patient-centeredness: burden, clarity, and acceptability should be measured alongside diagnostic outcomes. The fifth is equity: developers and implementers should explicitly assess whether the technology performs differently across etiologies, sexes, social groups, and care settings. The sixth is governance: thresholds, data flows, software integration, and recalibration rules must be transparent enough to support accountability.

These criteria also point toward a broader research agenda in technology-and-society scholarship. More studies are needed on implementation in non-tertiary settings, on surveillance completion rather than only assay performance, on digital prompts and patient navigation, on public and private reimbursement pathways, and on the social distribution of benefits and harms from precision surveillance. Pragmatic trials and mixed-methods studies may be especially valuable because they can capture how technologies behave once they leave the controlled environment of retrospective validation cohorts.

This review has limitations. It is a structured narrative synthesis rather than a formal systematic review, and it relies on a curated corpus of contemporary full-text sources rather than an exhaustive database search. The included studies also vary widely in design, from economic simulation to cohort analysis to narrative review, which means the synthesis is interpretive rather than quantitatively pooled. In addition, much of the stronger biomarker evidence still comes from specialized centers and high-income settings. These limitations, however, do not weaken the central socio-technical conclusion: surveillance value depends on the interaction of biomarker performance with access, workflow, economics, and social context.

In sum, the literature no longer supports thinking of HCC biomarkers as mere laboratory add-ons to ultrasound. They are becoming part of a larger architecture of precision surveillance. The challenge for the coming decade is to ensure that this architecture is not only accurate, but also affordable, explainable, and equitable.

5. Conclusion

Non-invasive biomarkers are moving HCC surveillance in cirrhosis away from an imaging-only, one-size-fits-all model and toward a precision-surveillance paradigm that is more algorithmic, risk-stratified, and potentially more responsive to heterogeneous patient needs. Composite scores such as GALAD and HES V2.0, together with blood-based and liquid-biopsy innovations, show that surveillance can increasingly be organized around modular technologies rather than a single dominant test.

The reviewed evidence also shows that the value of these technologies cannot be understood in purely biomedical terms. Cost-effectiveness depends on adherence, price, and downstream workflow. Patient experience depends on psychological burden, financial burden, and clarity of follow-up. Equity depends on insurance, mental health support, transportation, language access, digital infrastructure, and the organizational capacity to turn abnormal results into timely care. For that reason, HCC surveillance should be treated as a socio-technical system in which technologies, institutions, and social conditions are inseparable.

Future progress will depend on implementation studies that test not only whether biomarker technologies detect cancer earlier, but also whether they improve surveillance completion, reduce disparities, and distribute benefits without amplifying burden. The most promising path is therefore not the adoption of a single new biomarker in isolation, but the design of precision-surveillance ecosystems that combine better risk prediction with better access, better coordination, and better governance.

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