# ctDNA Liquid Biopsy in Colorectal Cancer: Where the Evidence Sits Now

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The 2026 literature positions circulating tumor DNA (ctDNA) as a viable adjunct for colorectal cancer detection, risk stratification, and treatment monitoring, but clinical integration continues to trail the evidence. Colonoscopy remains the reference standard, yet its invasiveness and bowel preparation burden constrain uptake among screening-eligible populations.

**KEY TAKEAWAYS**

- The Pivot: ctDNA and miRNA-based liquid biopsy are now framed in peer-reviewed literature as practical complements to colonoscopy and faecal testing, not merely experimental tools, across detection, risk assessment, and treatment response monitoring in CRC.
- The Data: The reviewed literature does not report trial-level HR or p-values; claims of improved sensitivity and patient adherence over conventional screening are qualitative across all three source reviews, which limits quantitative benchmarking at this stage.
- The Action: Clinicians should not substitute ctDNA testing for colonoscopy in symptomatic patients today; the current evidence supports awareness of liquid biopsy as an emerging monitoring adjunct while awaiting prospective trial data with hard endpoints.

Colorectal cancer is a major global health burden. Existing screening tools have clear limits. Colonoscopy is effective but risky, leading to patient reluctance. Fecal tests improve access, but sensitivity takes a hit. The need for better tools drives research into blood-based molecular biomarkers.1

Colorectal cancer demands better screening and early detection. Each year, an estimated 1.9 million new cases and 935,000 deaths make it the third most common cancer and the second leading cause of cancer-related mortality globally. Early detection improves prognosis; 5-year survival rates exceed 90% for localized disease but drop below 15% for metastatic disease. The stakes are high.

Current guidelines suggest screening at age 45 or 50 using colonoscopy, sigmoidoscopy, or stool tests. Adherence remains suboptimal. This often leads to advanced-stage diagnoses, driving the hunt for less invasive options.

Three 2026 reviews make the same core argument: advances in molecular biology and omics technologies have produced many candidate biomarkers. ctDNA and microRNAs represent the most clinically proximate liquid biopsy options. Other markers are also proposed for early detection and personalized treatment.1,2

The hepatocellular carcinoma literature adds a separate but instructive dimension. ctDNA and circulating free DNA are under evaluation in liver transplantation settings for HCC, where evidence is rising but clinical integration explicitly lags.3 It's a familiar tension.

## What the reviews cover

All three papers frame liquid biopsy within the broader precision oncology context, not as a standalone technology.1,2,3 CRC-focused reviews position ctDNA for three clinical moments: early detection in screening-eligible individuals, risk assessment in those with predisposing conditions, and monitoring of treatment efficacy in diagnosed patients.1,2

The OMICS review in Molecular Cancer broadly situates these tools in gastrointestinal tumor biology, emphasizing the translational pipeline from bench identification to clinical application.2 The Journal of Gastrointestinal Surgery paper takes a more cautionary register, its title signaling directly that evidence accumulation has outpaced integration into clinical workflows, a tension it examines through the HCC transplant context.3 That's a familiar story.

ctDNA in cancer detection relies on tumor-derived DNA fragments released into the bloodstream. These fragments carry genetic and epigenetic alterations characteristic of the primary tumor. Assays detect these specific alterations to identify cancer, even early, or monitor residual disease after treatment. It's how it works.

The potential for ctDNA to detect minimal residual disease (MRD) post-surgery, predict recurrence, and guide adjuvant therapy decisions is a significant investigation area. Patient populations considered span the entire disease spectrum, from asymptomatic individuals for screening to diagnosed patients for monitoring or recurrence surveillance. The reviews discuss theoretical application in average-risk individuals for primary screening, in high-risk groups for enhanced surveillance, and in diagnosed patients for assessing treatment response and detecting relapse. The applications are extensive.

The obvious caveat runs across all three sources: none provides original trial data, patient-level outcomes, or quantitative performance metrics for ctDNA assays. No sensitivity, specificity, AUC, hazard ratios, or p-values are offered.1,2,3 The abstracts describe biomarker approaches as having 'transformative potential' and offering 'effective solutions,' but these claims lack numbered endpoints. That's a qualitative problem.

And, two of the three abstracts are textually identical despite different author groups, journal titles, and subject matter. Clinicians should register these integrity questions.1,2 The evidence base for ctDNA in routine CRC practice simply cannot be quantitatively characterized from these sources. Without specific metrics, clinicians cannot assess clinical utility, cost-effectiveness, or patient management impact. Methodological details of cited studies are also missing. This lack of transparency limits definitive conclusions.

Until these quantitative and methodological gaps are filled, ctDNA in CRC remains a promising but unproven tool for clinical practice.

Future research must prioritize well-designed, prospective clinical trials with robust methodologies to generate the necessary quantitative data. These trials should evaluate ctDNA assays across diverse patient populations, comparing their performance against established screening and monitoring methods. Furthermore, studies need to address the cost-effectiveness of integrating ctDNA into existing care pathways and its impact on patient outcomes, including quality of life and survival. Only then can the true clinical utility of ctDNA liquid biopsy in colorectal cancer be fully understood and potentially integrated into routine practice.

For further exploration of oncology, including diagnostics and treatment relevant to colorectal cancer and evolving ctDNA applications, readers are directed to the Oxford Handbook of Oncology.

## CLINICAL IMPLICATIONS

The most striking consequence of reading these three papers together is not what they say about ctDNA, but what they cannot say. None provides a sensitivity figure, a false-positive rate, or a survival outcome tied to liquid biopsy use. That's no minor caveat.

Any GP or gastroenterologist hearing ctDNA is ready for integration into CRC screening or monitoring should ask, 'Compared to what? At what threshold? And validated in which population?' The answer, from this literature, is unavailable. The potential is real. The numbers are not yet on the table in these reviews.

Commercial pressure drives the diagnostics industry to position liquid biopsy products ahead of clinical evidence. This is familiar and well-funded. Companies like Guardant Health and Foundation Medicine have built substantial market positions on ctDNA-based assays. Regulatory clearances have followed in specific indications.

The 2026 review literature reflects a research community catching up with marketing, not leading it. The duplication of abstract text across two nominally distinct papers also raises a practical concern: if systematic reviewers and meta-analysts incorporate these as independent sources, any quantitative pooling will be inflated. Editors at Clinical Chimica Acta and Molecular Cancer have a problem.

Patients eligible for CRC screening deserve clarity on what liquid biopsy can and cannot replace. A blood test avoiding bowel preparation has obvious appeal. Adherence data from colonoscopy programs consistently show a non-invasive alternative would reach people the current system misses. But deploying ctDNA testing without validated sensitivity and specificity data in a screening context risks both false reassurance and unnecessary downstream investigation.

The integration gap Shoucair and colleagues name explicitly in the HCC transplant context applies equally here. The bottleneck is not enthusiasm or even emerging evidence, but the absence of prospective, outcome-linked trial data rigorous enough to anchor a guideline recommendation. Until NICE, the USPSTF, or equivalent bodies have that data in front of them, ctDNA in CRC remains a watch-and-wait technology for clinical practice, whatever the review literature implies. It's simply not ready.

## EDITORIAL & AI STANDARDS

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## REFERENCES

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