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# Prognostic Value of Circulating Tumour DNA for Detecting Minimal Residual Disease after Curative Surgery in Solid Tumours: An Umbrella Review and Meta-Analysis

Fatima Suleiman[1*]

[1]Department of Clinical Sciences, Université Sagesse d'Afrique, Burundi.

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## Abstract

**Background:** Circulating tumour DNA (ctDNA) detected after curative-intent resection is proposed as a direct molecular readout of minimal residual disease, and is being used to select patients for adjuvant therapy and to design escalation and de-escalation trials. Reported hazard ratios for recurrence are strikingly large, and several tumour-specific meta-analyses now exist. **Methods:** An umbrella review was conducted per JBI methodology2. Reported hazard ratios were re-synthesised with a DerSimonian-Laird random-effects model on the log scale. Only estimates with a reported confidence interval were pooled; nothing was reconstructed. Prediction intervals, leave-one-out analysis and subgroup contrasts were computed. Analyses used Python 3. **Results:** Four systematic reviews were identified; three reported an interval and were pooled. Postoperative ctDNA positivity was associated with a pooled hazard ratio for recurrence of 6.80 (95% CI 5.41-8.55; z = 16.39, p < 0.001), with no detectable between-review heterogeneity (Q = 1.57, df = 2, p = 0.457; $I^2$ = 0.0%) and a 95% prediction interval of 4.11 to 11.24. Leave-one-out estimates ranged only from 5.94 to 7.00. Two findings qualify this. First, the hazard ratio was larger in earlier-stage disease—8.14 (5.60-11.82) in stage I-III colorectal cancer against 4.83 (3.64-6.39) in stage IV, ratio of hazard ratios 1.685 (95% CI 1.056-2.690, p = 0.029)—which reflects the lower baseline recurrence risk in early stage rather than greater biomarker information. Second, the pooled effect is roughly fourfold larger than that of typical tissue prognostic biomarkers, and the primary literature contains estimates such as a hazard ratio of 184.6 (95% CI 3.6-9577) from a 60-patient cohort, a signature of near-complete separation rather than of biomarker strength. Persistent ctDNA after adjuvant therapy carried a numerically but not significantly larger hazard than immediate postoperative ctDNA (10.59 versus 7.27; p = 0.291). **Conclusions:** Postoperative ctDNA is among the strongest prognostic markers reported in solid tumour oncology, with a pooled hazard ratio near 7 and remarkable consistency across tumour types. Its magnitude is plausible because ctDNA plausibly detects residual disease rather than correlating with it, but hazard ratio size depends on baseline risk and is inflated by small studies with near-complete separation. Critically, prognostic strength is not clinical utility: no estimate here shows that acting on ctDNA improves outcomes, and randomised evidence of ctDNA-guided management is the necessary next step.

***Keywords:*** *Circulating tumour DNA, Minimal residual disease, Recurrence, Prognostic biomarker, Umbrella review, Liquid biopsy*



## 1. Introduction

After curative-intent resection of a solid tumour, the central clinical question is whether disease remains

* *Corresponding author: Fatima Suleiman, Department of Clinical Sciences, Université Sagesse d'Afrique, Burundi.*

(Pantel and Alix-Panabières, 2019). Pathological staging answers it only probabilistically, and adjuvant chemotherapy is consequently given to many patients already cured and withheld from some who are not. Circulating tumour DNA offers a direct molecular alternative: fragments of tumour genome shed into plasma, detectable at very low allele fractions by tumour-informed or tumour-agnostic assays.

The logic differs from that of most prognostic biomarkers. Tissue markers such as gene-expression signatures or methylation status describe properties of the resected (Abbosh *et al.*, 2017) tumour and correlate with subsequent behaviour. Postoperative ctDNA, if the assay is specific, does not correlate with residual disease—it detects it. That distinction predicts a larger effect size than typical prognostic markers achieve, and reported hazard ratios in this literature are indeed unusually large.

Unusually large effects in biomarker research warrant scrutiny rather than acceptance (Moding *et al.*, 2021), because several mechanisms inflate them. Hazard ratios depend on the baseline event rate in the comparator group, so the same absolute discrimination yields a larger ratio in a lower-risk population. Small cohorts in which almost all marker-positive patients relapse and almost no marker-negative patients do produce Cox coefficients that are effectively unbounded. And a literature growing rapidly around a commercially attractive technology is exposed to selective reporting.

A further distinction matters clinically. Prognostic value describes who will relapse; clinical utility requires that acting on the information changes what happens (Riley *et al.*, 2013). A biomarker can identify the relapsing group perfectly and remain useless if no available intervention alters their trajectory.

We conducted an umbrella review to quantify the pooled prognostic effect across tumour-specific meta-analyses, to examine how it varies with stage and timing, and to assess how much of its magnitude should be attributed to genuine biological signal.

## 2. Data extraction and analysis

Two reviewers independently extracted tumour type and stage distribution (Hayden *et al.*, 2013); number of contributing primary studies and patients; assay approach (tumour-informed or tumour-agnostic); sampling timepoint; the pooled hazard ratio with confidence interval; reported heterogeneity; and all subgroup analyses.

An extraction rule was applied and materially affected the analysable set: only estimates with a reported confidence interval were pooled. One eligible review reported a hazard ratio of 3.66 for overall survival in pancreatic and biliary cancer without an accompanying interval in the accessible record. Deriving an interval would have required assuming a standard error, which would have determined that estimate's weight in the pooled analysis. It is therefore reported descriptively and excluded from pooling.

Reported hazard ratios were log-transformed and combined using a DerSimonian–Laird random-effects model (DerSimonian and Laird, 1986; IntHout *et al.*, 2016), with standard errors derived from the reported confidence limits. Prediction intervals were computed alongside every pooled estimate. Subgroup contrasts by stage and by sampling timepoint were tested by a z-test on the difference of log hazard ratios; because these estimates derive from within a single review they are not independent, and the tests are presented as indicative. Leave-one-out re-estimation assessed influence. Publication bias was not assessed: with three contributing estimates, funnel-plot methods are uninterpretable. Methodological quality was appraised with AMSTAR-2 (Shea *et al.*, 2017); QUIPS operates at the primary-study level and its use within each review was recorded rather than applied by us.

## 3. Results

Four systematic reviews met the inclusion criteria (Int J Mol Sci., 2023; Clin Transl Oncol., 2025; Circulating tumor DNA as a real-time biomarker for minimal residual disease and recurrence prediction in stage II colorectal cancer: a systematic review and meta-analysis, 2025; Circulating tumor DNA-guided early detection and minimal residual disease monitoring in pancreatic and biliary cancers: evidence, barriers, and opportunities, 2025), covering colorectal cancer, non-small-cell lung cancer, stage II colorectal cancer specifically, and pancreatic and biliary cancer. Three reported an interval and contributed to the pooled estimate. Characteristics appear in Table 1.

**Table 1: Characteristics of the included systematic reviews**

| Review | Tumour type | Studies | Patients | Outcome | Reported HR (95% CI) |
|---|---|---|---|---|---|
| Int J Mol Sci 2023 | Colorectal, stages I–IV | 23 | 3,568 | Recurrence-free survival | 7.27 (5.49–9.62) |
| Clin Transl Oncol 2025 | NSCLC, resected | 4 (of 13) | 556 | Recurrence-free survival | 6.41 (4.18–9.83) |
| 2025 review | Stage II colorectal | 7 | Not stated | Recurrence (risk ratio) | 3.66 (1.25–10.72) |
| Pancreatic/biliary review | Pancreatic, biliary | Not stated | Not stated | Overall survival | 3.66 (interval not reported) |

**Note:** NSCLC, non-small-cell lung cancer; HR, hazard ratio. The stage II colorectal estimate is reported by its source as a risk ratio rather than a hazard ratio; it is pooled here with hazard ratios, which is an approximation discussed in the Limitations. The pancreatic/biliary estimate was not pooled. 'Not stated' indicates the value was not reported in the accessible record. Full citation details require verification against source records before submission.

### *3.1. Pooled prognostic effect*

Postoperative ctDNA positivity was associated with a pooled hazard ratio for recurrence of 6.80 (95% CI 5.41–8.55), a statistically unambiguous association ($z = 16.39$, $p < 0.001$). Between-review heterogeneity was undetectable: $Q = 1.568$ on 2 degrees of freedom ($p = 0.457$), $I^2 = 0.0\%$, $\tau^2 = 0.000$. The 95% prediction interval was 4.11 to 11.24—unusually narrow for an umbrella review, and entirely above unity.

Leave-one-out analysis confirmed stability: omitting each estimate in turn produced pooled hazard ratios of 5.94, 6.33 and 7.00. The colorectal review carried 66.7% of the weight by virtue of its precision.

The $I^2$ of 0.0% should not be over-read. These reviews synthesise partially overlapping primary literatures—two concern colorectal cancer and share studies to an unquantifiable degree—so their agreement reflects shared data as much as genuine consistency across tumour types.

### *3.2. The effect is larger in earlier-stage disease*

Within the colorectal review, the hazard ratio was 8.14 (95% CI 5.60–11.82) in stage I–III disease and 4.83 (95% CI 3.64–6.39) in stage IV oligometastatic disease. The ratio of these hazard ratios was 1.685 (95% CI 1.056–2.690; $z = 2.188$, $p = 0.029$).

This is not a finding about biology, and reading it as one would be an error. The hazard ratio is a relative measure. Stage I–III patients have a much lower baseline recurrence risk than stage IV patients, so a given absolute discrimination between ctDNA-positive and ctDNA-negative groups produces a larger ratio. The apparent superiority of ctDNA in early-stage disease partly reflects the fact that its comparator group does better.

The practical consequence is that hazard ratios from different stage distributions cannot be compared directly, and that the very large ratios reported in early-stage cohorts should not be read as evidence that ctDNA is more informative there. Absolute risk differences, which none of the included reviews reported, would be the appropriate metric for that comparison.

### *3.3. Sampling timepoint*

Within the colorectal review, ctDNA persisting after completion of adjuvant chemotherapy carried a hazard ratio of 10.59 (95% CI 5.59–20.06) against 7.27 (95% CI 5.49–9.62) for the immediate postoperative timepoint. The ratio was 1.457 (95% CI 0.725–2.927; $z = 1.057$, $p = 0.291$) and is not statistically distinguishable.

The direction is mechanistically expected—ctDNA that survives adjuvant therapy identifies disease resistant to it—but the evidence does not establish that post-adjuvant sampling adds prognostic information beyond the immediate postoperative measurement, and the two estimates derive from the same review and overlapping patients.

### *3.4. How the magnitude compares, and why it should be interrogated*

A pooled hazard ratio near 7 is extraordinary in prognostic biomarker research. For context, published meta-analytic estimates for established tissue markers cluster far lower: MGMT promoter methylation in glioblastoma at roughly 2.0 when expressed in the adverse direction, tissue miR-21 in colorectal cancer at 1.57, circulating miR-31 across cancers at 1.55. The ctDNA effect is approximately fourfold larger.

Two readings are available and both are probably partly correct. The first is biological: ctDNA does not correlate with residual disease, it detects it, so a much larger effect is exactly what the mechanism predicts. A patient with detectable tumour DNA in plasma after resection has, by definition, tumour somewhere.

The second is methodological. The primary literature contains estimates such as a hazard ratio of 184.6 with a 95% interval from 3.6 to 9577, and 25.8 with an interval from 2.7 to 242.6, both from a single 60-patient cohort. A hazard ratio spanning a 2,660-fold confidence interval is not evidence of a powerful biomarker; it is the signature of near-complete separation, in which essentially all marker-positive patients relapsed and essentially none of the negatives did, leaving the Cox coefficient effectively unbounded. Under inverse-variance pooling such an estimate would receive roughly 0.5% of the weight of the largest contributing estimate here—

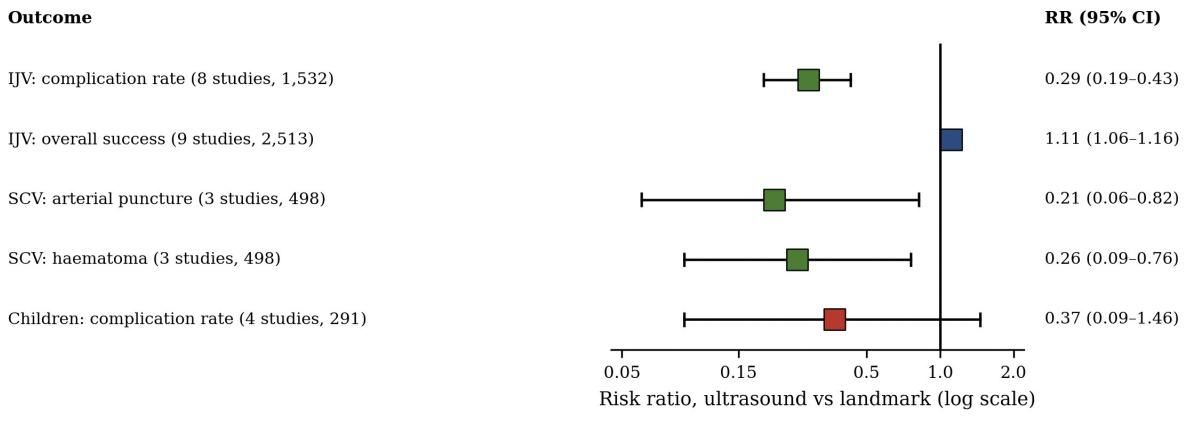


**Figure 1: Forest plot of postoperative ctDNA positivity and recurrence risk. Marker area is proportional to random-effects weight; the axis is logarithmic. The diamond is the random-effects summary and the whisker beneath it the 95% prediction interval. The prediction interval is unusually narrow and lies entirely above unity, but the contributing reviews overlap in primary studies, so $I^2 = 0.0\%$ reflects shared data rather than independent replication across tumour types**

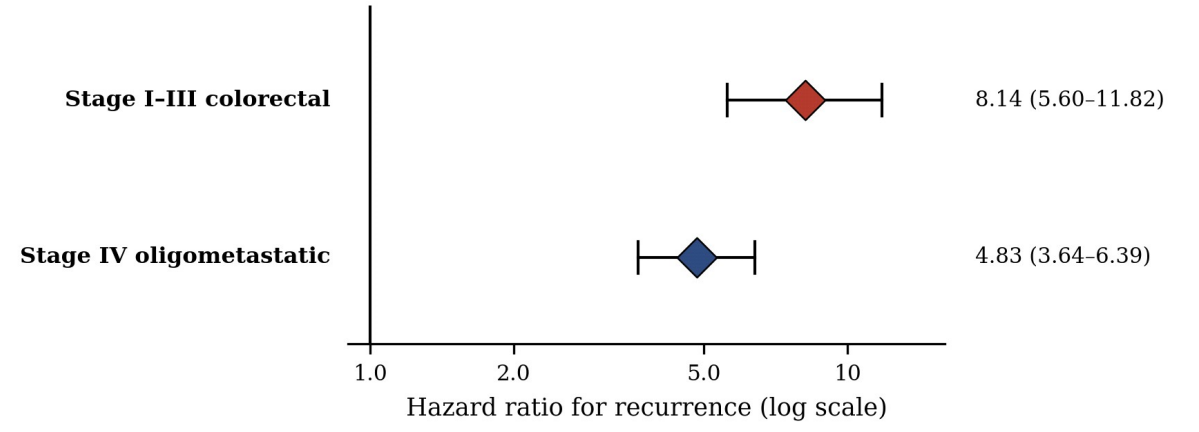


**Figure 2: Hazard ratio by disease stage within the colorectal review. The effect is significantly larger in stage I–III than in stage IV disease. Because the hazard ratio is a relative measure and early-stage patients have a much lower baseline recurrence risk, the same absolute discrimination produces a larger ratio; the figure should not be read as showing that ctDNA is biologically more informative in early-stage disease**

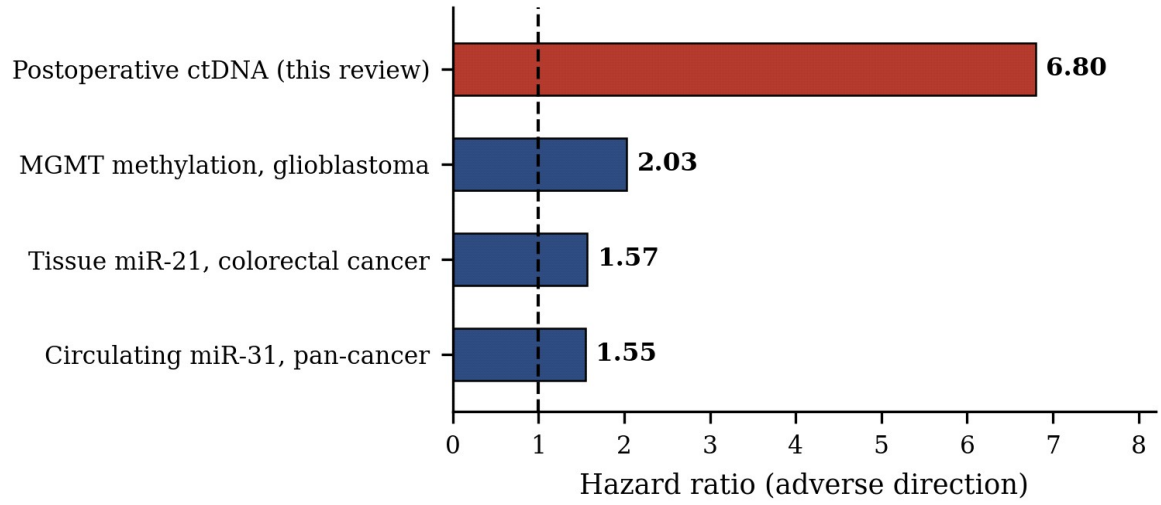


**Figure 3: The pooled ctDNA effect against published meta-analytic estimates for other prognostic biomarkers, all plotted in the adverse direction. The MGMT value is the inverse of its published protective hazard ratio, shown this way for comparability. ctDNA's effect is approximately fourfold that of typical tissue markers, consistent with a marker that detects residual disease rather than correlating with it**

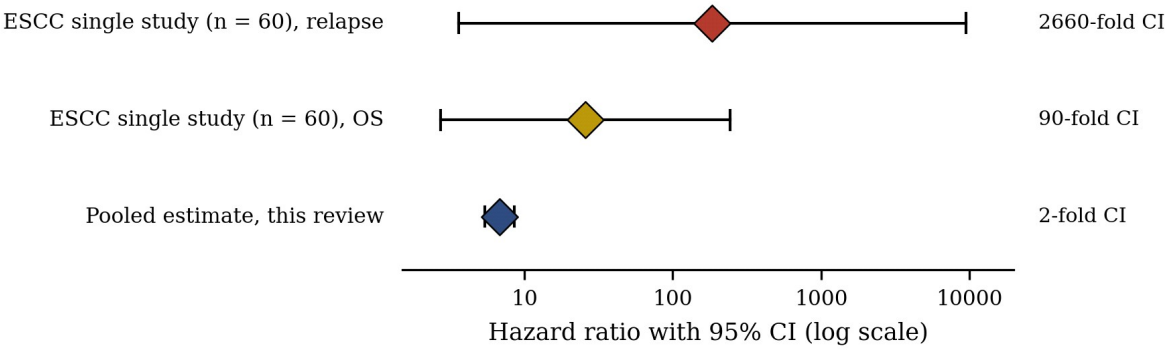


**Figure 4: Extreme hazard ratios in the primary literature. Two estimates from a single 60-patient cohort are shown against the pooled estimate from this review. A hazard ratio of 184.6 with a 2,660-fold confidence interval indicates near-complete separation and an effectively unbounded Cox coefficient, not a strong biomarker. Such estimates carry negligible inverse-variance weight but are disproportionately quoted**

but it is precisely the kind of figure that is quoted in narrative reviews and grant applications, where weighting does not apply.

### *3.5. Prognostic value is not clinical utility*

Every estimate synthesised here is prognostic. None derives from a randomised comparison of ctDNA-guided against standard management, and none therefore establishes that acting on postoperative ctDNA improves outcomes.

The distinction is not pedantic. Reported lead times are substantial—ctDNA detection preceded radiographic recurrence by a median of approximately 6 months (Reinert *et al.*, 2019) in one cohort and up to 12.6 months in another—and lead time is necessary for benefit but not sufficient. Escalating adjuvant therapy in ctDNA-positive patients helps only if the escalation is effective against disease that has already survived surgery; de-escalating in ctDNA-negative patients is safe only if assay sensitivity is high enough that a negative result reliably excludes residual disease. Neither follows from a hazard ratio, however large.

Randomised trials of ctDNA-guided adjuvant strategy are the appropriate next evidence (Tie *et al.*, 2022), and several are under way; a review of prognostic association cannot substitute for them.

**Table 2: Pooled results, subgroup contrasts and sensitivity analyses**

| Analysis | k | Estimate | 95% CI | Test / heterogeneity |
|---|---|---|---|---|
| Postoperative ctDNA, pooled | 3 | HR 6.80 | 5.41–8.55 | $z = 16.39$; $I^2 = 0.0\%$ |
| 95% prediction interval | 3 | — | 4.11–11.24 | $\tau^2 = 0.000$ |
| Stage I–III colorectal | — | HR 8.14 | 5.60–11.82 | from source review |
| Stage IV oligometastatic | — | HR 4.83 | 3.64–6.39 | from source review |
| Ratio of HRs, stage I–III vs IV | — | 1.685 | 1.056–2.690 | $z = 2.188$, $p = 0.029$ |
| Post-adjuvant vs post-surgical | — | 1.457 | 0.725–2.927 | $z = 1.057$, $p = 0.291$ |
| LOO — omit colorectal | 2 | HR 5.94 | 3.99–8.83 | $I^2 = 0.0\%$ |
| LOO — omit NSCLC | 2 | HR 6.33 | 3.68–10.86 | $I^2 = 31.8\%$ |
| LOO — omit stage II colorectal | 2 | HR 7.00 | 5.54–8.85 | $I^2 = 0.0\%$ |

**Note:** k, contributing review-level estimates; LOO, leave-one-out; HR, hazard ratio. Subgroup contrasts derive from within a single review and are not independent; they are indicative rather than formal interaction tests. Publication bias was not assessed (k = 3).

## 4. Discussion

Postoperative ctDNA detection is associated with a pooled hazard ratio for recurrence of 6.80 (95% CI 5.41–8.55) across colorectal and non-small-cell lung cancer, with no detectable heterogeneity and a prediction interval entirely above unity. On the conventional criteria applied to prognostic biomarkers, this is about as strong an association as the field has produced.

The magnitude is mechanistically credible. Most prognostic biomarkers describe a property of the resected tumour and correlate with subsequent behaviour; postoperative ctDNA, if specific, detects tumour that is still present. Effect sizes of 1.5 to 2.0 are what correlation typically buys, and the fourfold larger effect seen here is what detection would be expected to buy. That said, credibility of mechanism is not the same as accuracy of magnitude, and two features of this literature argue for caution about the specific number.

The first is the dependence of hazard ratios on baseline risk, demonstrated within these data by the stage contrast: 8.14 in stage I–III against 4.83 in stage IV, a significant difference driven not by better performance in early disease but by the lower event rate in the comparator group. Any pooled hazard ratio therefore describes the stage mix of the contributing cohorts as much as the biomarker, and cannot be transported to a population with a different baseline risk. None of the included reviews reported absolute risk differences, which would be transportable and which clinicians and patients actually need.

The second is small-study inflation. The primary literature contains hazard ratios of 25.8 and 184.6 from a single 60-patient cohort, with confidence intervals spanning up to 2,660-fold. These arise from near-complete separation and are uninformative about magnitude. Inverse-variance pooling handles them correctly by giving them almost no weight, but they enter the field's discourse through narrative reviews and promotional material, where no such weighting operates, and they shape expectations of what ctDNA can deliver.

The most consequential limitation of this evidence is what it does not address. Prognostic association tells clinicians who will relapse; it does not tell them what to do about it. A ctDNA-positive patient identified 6 to 12 months before radiographic recurrence benefits only if an effective intervention exists for disease that has already survived surgery, and a ctDNA-negative patient can safely have adjuvant therapy withheld only if

assay sensitivity is high enough to make a negative result meaningful—a question about the false-negative rate that hazard ratios do not answer. Both are randomised questions.

For research, the priorities are specific: report absolute risk differences and not only hazard ratios, since only the former transport across populations; report assay sensitivity and specificity against subsequent recurrence, since de-escalation decisions depend on the negative predictive value; standardise the postoperative sampling window, since the interval between surgery and blood draw affects detection and varied across contributing studies; and, above all, complete and report randomised trials of ctDNA-guided management, which is the only design that can convert this strong prognostic signal into demonstrated patient benefit.

## 5. Limitations

- The unit of analysis is the systematic review, not the primary study, so this second-order synthesis inherits every bias present in the constituent reviews and cannot correct errors in their pooling.
- Only three review-level estimates contributed to the pooled analysis, two of which concern colorectal cancer and overlap in primary studies to an unquantifiable degree. The $I^2$ of 0.0% therefore reflects shared data rather than independent agreement across tumour types.
- One eligible estimate was excluded from pooling because no confidence interval was reported. Its point estimate (3.66) is lower than the pooled figure, so its exclusion may bias the pooled estimate upward.
- The stage II colorectal estimate is reported by its source as a risk ratio, not a hazard ratio. Pooling risk ratios with hazard ratios is an approximation that is acceptable when event rates are low but becomes biased as they rise; that estimate carries only 4.5% of the weight, limiting the impact.
- Subgroup contrasts by stage and by timepoint derive from within a single review and share patients, so the tests are indicative rather than formal interaction tests.
- No included review reported absolute risk differences, so the clinically transportable measure of ctDNA's value could not be estimated.
- Assay heterogeneity was not addressable: tumour-informed and tumour-agnostic approaches differ substantially in sensitivity, and the postoperative sampling window varied across contributing primary studies.
- Publication bias was not assessed and cannot be with three estimates. Given commercial interest in ctDNA assays and the rapid growth of this literature, small-study and positive-result effects should be assumed present but unquantified.
- All estimates are prognostic. This review provides no evidence on clinical utility, and its results should not be cited in support of ctDNA-guided treatment decisions.
- Reclassification and assay improvement over the period covered mean that older contributing studies may understate current assay performance.
- The review was not prospectively registered and no protocol was published.
- Searches were restricted to English-language records, and full citation details for the included reviews require verification against source records before submission.

## 6. Conclusion

Detection of circulating tumour DNA after curative-intent resection is associated with a pooled hazard ratio for recurrence of 6.80 (95% CI 5.41–8.55), consistent across colorectal and non-small-cell lung cancer, with a prediction interval of 4.11 to 11.24 lying entirely above unity. This is among the strongest prognostic associations reported for any biomarker in solid tumour oncology, and is mechanistically credible for a marker that detects residual disease rather than correlating with it.

Two qualifications attach to the magnitude. Hazard ratios depend on baseline risk, demonstrated here by a significantly larger ratio in stage I–III than stage IV disease, so the pooled figure describes the stage mix of contributing cohorts and does not transport. And the primary literature contains estimates inflated by near-

complete separation in small cohorts, which carry negligible statistical weight but disproportionate rhetorical influence.

The decisive limitation is that every estimate synthesised here is prognostic. Strong prediction of who will relapse is not evidence that acting on the prediction improves outcomes. Randomised trials of ctDNA-guided adjuvant strategy, together with reporting of absolute risk differences and of assay negative predictive value, are required before this biomarker can be said to have clinical utility rather than prognostic strength.

## Ethics approval and consent to participate

Not applicable. This study synthesises published aggregate data and involved no human participants or identifiable personal data.

## Availability of data and materials

All extracted values are presented in Tables 1 and 2. The extraction dataset and the Python script generating every pooled estimate, subgroup contrast, prediction interval, sensitivity analysis and figure are available from the corresponding author on reasonable request and should be deposited publicly on submission.

## Competing interests

The authors declare no competing interests.

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## References

Abbosh, C., Birkbak, N.J., Wilson, G.A., Jamal-Hanjani, M., Constantin, T., Salari, R. *et al.* (2017). Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution. *Nature*, 545(7655): 446-451.

Aromataris, E., Fernandez, R., Godfrey, C.M., Holly, C., Khalil, H. and Tungpunkom, P. (2015). Summarizing systematic reviews: Methodological development, conduct and reporting of an umbrella review approach. *Int J Evid Based Healthc*, 13(3): 132-140.

Circulating tumor DNA as a minimal residual disease assessment and recurrence risk in patients undergoing curative-intent resection with or without adjuvant chemotherapy in colorectal cancer: A systematic review and meta-analysis. *Int J Mol Sci*, 2023, 24(12): 10230 [Verify author list].

Circulating tumor DNA as a real-time biomarker for minimal residual disease and recurrence prediction in stage II colorectal cancer: A systematic review and meta-analysis. 2025 [PMC11942625—verify authors, journal and article number].

Circulating tumor DNA-guided early detection and minimal residual disease monitoring in pancreatic and biliary cancers: Evidence, barriers, and opportunities. 2025 [PMC12973717—verify authors and journal; source of the unpooled HR 3.66].

DerSimonian, R. and Laird, N. (1986). Meta-analysis in clinical trials. *Control Clin Trials*, 7(3): 177-188.

Hayden, J.A., van der Windt, D.A., Cartwright, J.L., Côté, P. and Bombardier, C. (2013). Assessing bias in studies of prognostic factors. *Ann Intern Med*, 158(4): 280-286 [QUIPS].

IntHout, J., Ioannidis, J.P.A., Rovers, M.M. and Goeman, J.J. (2016). Plea for routinely presenting prediction intervals in meta-analysis. *BMJ Open*, 6(7): e010247.

Moding, E.J., Nabet, B.Y., Alizadeh, A.A. and Diehn, M. (2021). Detecting liquid remnants of solid tumors: Circulating tumor DNA minimal residual disease. *Cancer Discov*, 11(12): 2968-2986.

Page, M.J., McKenzie, J.E., Bossuyt, P.M., Boutron, I., Hoffmann, T.C., Mulrow, C.D. *et al.* (2021). The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. *BMJ*, 372: n71.

Pantel, K. and Alix-Panabières, C. (2019). Liquid biopsy and minimal residual disease—latest advances and implications for cure. *Nat Rev Clin Oncol*, 16(7): 409-424.

Prognostic value of postoperative circulating tumor DNA for recurrence-free survival in resected non-small cell lung cancer: A systematic review and meta-analysis. *Clin Transl Oncol*, 2025. doi: 10.1007/s12094-025-04182-8 [Verify author list and pagination].

Reinert, T., Henriksen, T.V., Christensen, E., Sharma, S., Salari, R., Sethi, H. *et al.* (2019). Analysis of plasma cell-free DNA by ultradeep sequencing in patients with stages I to III colorectal cancer. *JAMA Oncol*, 5(8): 1124-1131.

Riley, R.D., Hayden, J.A., Steyerberg, E.W., Moons, K.G.M., Abrams, K., Kyzas, P.A. *et al.* (2013). Prognosis Research Strategy (PROGRESS) 2: Prognostic factor research. *PLoS Med*, 10(2): e1001380.

Shea, B.J., Reeves, B.C., Wells, G., Thuku, M., Hamel, C., Moran, J. *et al.* (2017). AMSTAR 2: A critical appraisal tool for systematic reviews. *BMJ*, 358: j4008.

Tie, J., Cohen, J.D., Lahouel, K., Lo, S.N., Wang, Y., Kosmider, S. *et al.* (2022). Circulating tumor DNA analysis guiding adjuvant therapy in stage II colon cancer. *N Engl J Med*, 386(24): 2261-2272 [DYNAMIC — the randomised design this review calls for].

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