

Table SI. Search strategy.

A, PubMed			
Search number	Query	Search details	Results, n
1	((circulating tumor DNA [MeSH] OR ctDNA OR Tumor DNA, Circulating OR Cell-Free Tumor DNA OR Cell Free Tumor DNA) OR (Neoplasm, Residual [MeSH] OR Residual Neoplasms OR Residual Minimal Disease OR Minimal Residual Disease OR Residual Neoplasm OR Residual Cancer OR Residual Tumor OR Residual Tumour))	“circulating tumor dna”[MeSH Terms] OR (“ctdna”[All Fields] OR “ctdnas”[All Fields]) OR (“tumour dna circulating”[All Fields] OR “circulating tumor dna”[Supplementary Concept] OR “circulating tumor dna”[All Fields] OR “tumor dna circulating”[All Fields] OR “circulating tumor dna”[MeSH Terms] OR (“circulating”[All Fields] AND “tumor”[All Fields] AND “dna”[All Fields]) OR (“tumor”[All Fields] AND “dna”[All Fields] AND “circulating”[All Fields])) OR (“cell free tumour dna”[All Fields] OR “circulating tumor dna”[Supplementary Concept] OR “circulating tumor dna”[All Fields] OR “cell free tumor dna”[All Fields] OR “circulating tumor dna”[MeSH Terms] OR (“circulating”[All Fields] AND “tumor”[All Fields] AND “dna”[All Fields]) OR (“cell”[All Fields] AND “free”[All Fields] AND “tumor”[All Fields] AND “dna”[All Fields])) OR (“cell free tumour dna”[All Fields] OR “circulating tumor dna”[Supplementary Concept] OR “circulating tumor dna”[All Fields] OR “cell free tumor dna”[All Fields] OR “circulating tumor dna”[MeSH Terms] OR (“circulating”[All Fields] AND “tumor”[All Fields] AND “dna”[All Fields]) OR (“cell”[All Fields] AND “free”[All Fields] AND “tumor”[All Fields] AND “dna”[All Fields])) OR (“neoplasm, residual”[MeSH Terms] OR (“neoplasm, residual”[MeSH Terms] OR (“neoplasm”[All Fields] AND “residual”[All Fields]) OR “residual neoplasm”[All Fields] OR (“residual”[All Fields] AND “neoplasms”[All Fields]) OR “residual neoplasms”[All Fields]) OR (“neoplasm, residual”[MeSH Terms] OR (“neoplasm”[All Fields] AND “residual”[All Fields]) OR “residual neoplasm”[All Fields] OR (“residual”[All Fields] AND “minimal”[All Fields] AND “disease”[All Fields]) OR “residual minimal disease”[All Fields]) OR (“neoplasm, residual”[MeSH Terms] OR (“neoplasm”[All Fields] AND “residual”[All Fields]) OR “residual neoplasm”[All Fields] OR (“minimal”[All Fields] AND “residual”[All Fields] AND “disease”[All Fields]) OR “minimal residual disease”[All Fields]) OR (“neoplasm, residual”[MeSH Terms] OR (“neoplasm”[All Fields] AND “residual”[All Fields]) OR “residual neoplasm”[All Fields] OR (“neoplasm, residual”[MeSH Terms] OR (“neoplasm”[All Fields] AND “residual”[All Fields]) OR “residual neoplasm”[All Fields])	104,520

		Fields] AND “residual”[All Fields]) OR “residual neoplasm”[All Fields] OR (“residual”[All Fields] AND “cancer”[All Fields]) OR “residual cancer”[All Fields]) OR (“residual tumour”[All Fields] OR “neoplasm, residual”[MeSH Terms] OR (“neoplasm”[All Fields] AND “residual”[All Fields]) OR “residual neoplasm”[All Fields] OR (“residual”[All Fields] AND “tumor”[All Fields]) OR “residual tumor”[All Fields]) OR (“residual tumour”[All Fields] OR “neoplasm, residual”[MeSH Terms] OR (“neoplasm”[All Fields] AND “residual”[All Fields]) OR “residual neoplasm”[All Fields] OR (“residual”[All Fields] AND “tumor”[All Fields]) OR “residual tumor”[All Fields]))	
2	(Colorectal Neoplasms [MeSH] OR Colorectal Neoplasm OR Colorectal Tumor OR Colorectal Cancer OR Colorectal Carcinoma OR Rectal Neoplasms OR Rectal Neoplasm OR Rectum Neoplasm OR Rectal Tumor OR Cancer of Rectum OR Cancer of the Rectum OR Rectal Cancer OR Rectum Cancer)	“colorectal neoplasms”[MeSH Terms] OR (“colorectal neoplasms”[MeSH Terms] OR (“colorectal”[All Fields] AND “neoplasms”[All Fields]) OR “colorectal neoplasms”[All Fields] OR (“colorectal”[All Fields] AND “neoplasm”[All Fields]) OR “colorectal neoplasm”[All Fields]) OR (“colorectal tumour”[All Fields] OR “colorectal neoplasms”[MeSH Terms] OR (“colorectal”[All Fields] AND “neoplasms”[All Fields]) OR “colorectal neoplasms”[All Fields] OR (“colorectal”[All Fields] AND “tumor”[All Fields]) OR “colorectal tumor”[All Fields]) OR (“colorectal neoplasms”[MeSH Terms] OR (“colorectal”[All Fields] AND “neoplasms”[All Fields]) OR “colorectal neoplasms”[All Fields] OR (“colorectal”[All Fields] AND “cancer”[All Fields]) OR “colorectal cancer”[All Fields]) OR (“colorectal neoplasms”[MeSH Terms] OR (“colorectal”[All Fields] AND “neoplasms”[All Fields]) OR “colorectal neoplasms”[All Fields] OR (“colorectal”[All Fields] AND “carcinoma”[All Fields]) OR “colorectal carcinoma”[All Fields]) OR (“rectal neoplasms”[MeSH Terms] OR (“rectal”[All Fields] AND “neoplasms”[All Fields]) OR “rectal neoplasms”[All Fields]) OR (“rectal neoplasms”[MeSH Terms] OR (“rectal”[All Fields] AND “neoplasms”[All Fields]) OR “rectal neoplasms”[All Fields] OR (“rectal”[All Fields] AND “neoplasm”[All Fields]) OR “rectal neoplasm”[All Fields]) OR (“rectal neoplasms”[MeSH Terms] OR (“rectal”[All Fields] AND “neoplasms”[All Fields]) OR “rectal neoplasms”[All Fields] OR (“rectum”[All Fields] AND “neoplasm”[All Fields]) OR “rectum neoplasm”[All Fields]) OR (“rectal tumour”[All Fields] OR “rectal neoplasms”[MeSH Terms] OR (“rectal”[All Fields] AND “neoplasms”[All Fields]) OR “rectal neoplasms”[All Fields] OR	380,643

		(“rectal”[All Fields] AND “tumor”[All Fields]) OR “rectal tumor”[All Fields]) OR (“rectal neoplasms”[MeSH Terms] OR (“rectal”[All Fields] AND “neoplasms”[All Fields]) OR “rectal neoplasms”[All Fields] OR (“cancer”[All Fields] AND “rectum”[All Fields]) OR “cancer of rectum”[All Fields]) OR (“rectal neoplasms”[MeSH Terms] OR (“rectal”[All Fields] AND “neoplasms”[All Fields]) OR “rectal neoplasms”[All Fields] OR (“cancer”[All Fields] AND “rectum”[All Fields]) OR “cancer of the rectum”[All Fields]) OR (“rectal neoplasms”[MeSH Terms] OR (“rectal”[All Fields] AND “neoplasms”[All Fields]) OR “rectal neoplasms”[All Fields] OR (“rectal”[All Fields] AND “cancer”[All Fields]) OR “rectal cancer”[All Fields]) OR (“rectal neoplasms”[MeSH Terms] OR (“rectal”[All Fields] AND “neoplasms”[All Fields]) OR “rectal neoplasms”[All Fields] OR (“rectum”[All Fields] AND “cancer”[All Fields]) OR “rectum cancer”[All Fields])	
3	#1 AND #2	#1 AND #2	5,589
B, Web of Science			
Search number	Query	Search details	Results, n
1	TS=(circulating tumor DNA OR ctDNA OR Tumor DNA, Circulating OR Cell-Free Tumor DNA OR Cell Free Tumor DNA OR Neoplasm, Residual OR Residual Neoplasms OR Residual Minimal Disease OR Minimal Residual Disease OR Residual Neoplasm OR Residual Cancer OR Residual Tumor OR Residual Tumour)	TS=(circulating tumor DNA OR ctDNA OR Tumor DNA, Circulating OR Cell-Free Tumor DNA OR Cell Free Tumor DNA OR Neoplasm, Residual OR Residual Neoplasms OR Residual Minimal Disease OR Minimal Residual Disease OR Residual Neoplasm OR Residual Cancer OR Residual Tumor OR Residual Tumour)	74,748
2	TS=(Colorectal Neoplasms OR Colorectal Neoplasm OR Colorectal Tumor OR Colorectal Cancer OR Colorectal Carcinoma OR Rectal Neoplasms OR Rectal Neoplasm OR Rectum Neoplasm OR Rectal Tumor OR Cancer of Rectum OR Cancer of the Rectum OR Rectal Cancer OR Rectum Cancer)	TS=(Colorectal Neoplasms OR Colorectal Neoplasm OR Colorectal Tumor OR Colorectal Cancer OR Colorectal Carcinoma OR Rectal Neoplasms OR Rectal Neoplasm OR Rectum Neoplasm OR Rectal Tumor OR Cancer of Rectum OR Cancer of the Rectum OR Rectal Cancer OR Rectum Cancer)	280,410
3	#1 AND #2	#1 AND #2	5,882
C, EMBASE			
Search number	Query	Search details	Results, n
1	('circulating tumor dna'/exp OR 'circulating tumor dna') OR ('cell-free circulating tumor dna':ti,ab,kw OR 'cell-free circulating	('circulating tumor dna'/exp OR 'circulating tumor dna') AND [embase]/lim OR (('cell-free circulating tumor dna':ti,ab,kw OR 'cell-free	80,515

	tumour dna':ti,ab,kw OR 'cell-free tumor dna':ti,ab,kw OR 'cell-free tumour dna':ti,ab,kw OR 'circulating cell-free tumor dna':ti,ab,kw OR 'circulating cell-free tumour dna':ti,ab,kw OR 'circulating tumour dna':ti,ab,kw OR 'circulating tumor dna':ti,ab,kw) OR ('minimal residual disease'/exp OR 'minimal residual disease') OR ('disease, minimal residual':ti,ab,kw OR 'minimum residual disease':ti,ab,kw OR 'neoplasm, residual':ti,ab,kw OR 'residual disease':ti,ab,kw OR 'residual disease, minimal':ti,ab,kw OR 'residual minimal disease':ti,ab,kw OR 'residual neoplasm':ti,ab,kw OR 'minimal residual disease':ti,ab,kw)	circulating tumour dna':ti,ab,kw OR 'cell-free tumor dna':ti,ab,kw OR 'cell-free tumour dna':ti,ab,kw OR 'circulating cell-free tumor dna':ti,ab,kw OR 'circulating cell-free tumour dna':ti,ab,kw OR 'circulating tumour dna':ti,ab,kw OR 'circulating tumor dna':ti,ab,kw) AND [embase]/lim) OR (('minimal residual disease'/exp OR 'minimal residual disease') AND [embase]/lim) OR (('disease, minimal residual':ti,ab,kw OR 'minimum residual disease':ti,ab,kw OR 'neoplasm, residual':ti,ab,kw OR 'residual disease':ti,ab,kw OR 'residual disease, minimal':ti,ab,kw OR 'residual minimal disease':ti,ab,kw OR 'residual neoplasm':ti,ab,kw OR 'minimal residual disease':ti,ab,kw) AND [embase]/lim)	
2	('colorectal tumor'/exp OR 'colorectal tumor') OR ('colorectal neoplasia':ti,ab,kw OR 'colorectal neoplasm':ti,ab,kw OR 'colorectal neoplasms':ti,ab,kw OR 'colorectal tumorigenesis':ti,ab,kw OR 'colorectal tumour':ti,ab,kw OR 'neoplastic colorectal':ti,ab,kw OR 'tumor, colorectal':ti,ab,kw OR 'tumour, colorectal':ti,ab,kw OR 'colorectal tumor':ti,ab,kw)	('colorectal tumor'/exp OR 'colorectal tumor') AND [embase]/lim OR (('colorectal neoplasia':ti,ab,kw OR 'colorectal neoplasm':ti,ab,kw OR 'colorectal neoplasms':ti,ab,kw OR 'colorectal tumorigenesis':ti,ab,kw OR 'colorectal tumour':ti,ab,kw OR 'neoplastic colorectal':ti,ab,kw OR 'tumor, colorectal':ti,ab,kw OR 'tumour, colorectal':ti,ab,kw OR 'colorectal tumor':ti,ab,kw) AND [embase]/lim)	505,505
3	#1 AND #2	#1 AND #2	5,310
D, Cochrane			
Search number	Query	Search details	Results, n
1	(MeSH descriptor: [Circulating Tumor DNA] explode all trees) OR ((ctDNA OR Tumor DNA, Circulating OR Cell-Free Tumor DNA OR Cell Free Tumor DNA):ti,ab,kw) OR (MeSH descriptor: [Neoplasm, Residual] explode all trees) OR ((Residual Neoplasms OR Residual Minimal Disease OR Minimal Residual Disease OR Residual Neoplasm OR Residual Cancer OR Residual Tumor OR Residual Tumour):ti,ab,kw)	(MeSH descriptor: [Circulating Tumor DNA] explode all trees) OR ((ctDNA OR Tumor DNA, Circulating OR Cell-Free Tumor DNA OR Cell Free Tumor DNA):ti,ab,kw) OR (MeSH descriptor: [Neoplasm, Residual] explode all trees) OR ((Residual Neoplasms OR Residual Minimal Disease OR Minimal Residual Disease OR Residual Neoplasm OR Residual Cancer OR Residual Tumor OR Residual Tumour):ti,ab,kw)	12,682
2	(MeSH descriptor: [Colorectal Neoplasms] explode all trees) OR ((Colorectal Neoplasm OR Colorectal Tumor OR Colorectal Cancer OR Colorectal Carcinoma OR Rectal Neoplasms OR Rectal Neoplasm OR Rectum Neoplasm OR Rectal Tumor OR Cancer of Rectum OR Cancer of the Rectum OR Rectal Cancer OR Rectum Cancer):ti,ab,kw)	(MeSH descriptor: [Colorectal Neoplasms] explode all trees) OR ((Colorectal Neoplasm OR Colorectal Tumor OR Colorectal Cancer OR Colorectal Carcinoma OR Rectal Neoplasms OR Rectal Neoplasm OR Rectum Neoplasm OR Rectal Tumor OR Cancer of Rectum OR Cancer of the Rectum OR Rectal Cancer OR Rectum Cancer):ti,ab,kw)	32,364
3	#1 AND #2	#1 AND #2	1,089

Table SII. Additional detection method information about studies included in the meta-analysis.

First author/s, year	Chemotherapy regimens	ctDNA detection methods	Criteria for defining ctDNA positivity	(Refs.)
Kataoka <i>et al</i> , 2026	CAPOX or FOLFOX	A clinically validated, personalized, tumour-informed 16-plex PCR NGS assay	Plasma samples with at least two tumour-specific variants detected above a pre-defined threshold were defined as ctDNA-positive and the pre-defined threshold is based on Natera's proprietary variant calling method	(31)
Fan <i>et al</i> , 2024	CAPOX or FOLFOX	Targeted capture sequencing	A plasma sample with at least one variant detected was defined as ctDNA-positive	(28)
Kawashima <i>et al</i> , 2025	NA	Droplet digital PCR and NGS	Positive results were defined as variant frequency $\geq 0.1\%$	(29)
Xu <i>et al</i> , 2025	FOLFOX or FOLFIRI with or without bevacizumab or cetuximab	J25 detection panel customized based on tumour tissues	If the blood sample contained >1 mutation, it was classified as ctDNA-positive or if only one mutation was detected, the blood sample was classified as ctDNA-positive when the variant frequency was $\geq 0.1\%$	(30)
Folprecht <i>et al</i> , 2026	Capecitabine-based chemotherapy	Tumour-informed, error-reduced targeted NGS	A sample was classified ctDNA-positive if two or more of three independent replicates yielded a variant call above the mutation-specific operational cut-off	(32)

NA, not available; CAPOX, capecitabine and oxaliplatin; FOLFOX, 5-fluorouracil, leucovorin and oxaliplatin; FOLFIRI, 5-fluorouracil, leucovorin and irinotecan; ctDNA, circulating tumour DNA; PCR, polymerase chain reaction; NGS, next-generation sequencing; J25, CRLM-specific 25-gene panel.

Table SIII. Additional other information about studies included in the meta-analysis.

First author/s, year	Time for ctDNA testing	Median follow-up time (months; exposure/control)	(Refs.)
Kataoka <i>et al</i> , 2026	2-10 weeks after surgery and before the start of any adjuvant therapy	43.2	(31)
Fan <i>et al</i> , 2024	At preadjuvant and postoperative time points	19.5	(28)
Kawashima <i>et al</i> , 2025	1 month postoperative	NA	(29)
Xu <i>et al</i> , 2025	1 month postoperative	1.17/1.05	(30)
Folprecht <i>et al</i> , 2026	At a median of 21 days after resection	25	(32)

ctDNA, circulating tumour DNA; NA, not available.

Table SIV. Quality assessment of the RCT included.

First author/s, year	Sequence generation	Allocation concealment	Blinding	Incomplete outcome data	Selective outcome reporting	Free of other bias	(Ref.)
Folprecht <i>et al</i> , 2026	Low risk	Low risk	High risk	Unclear risk	Low risk	High risk	(32)

The RCT was assessed using the Cochrane Collaboration' s tool. Risk of bias was assessed as 'low risk', 'high risk' or 'unclear risk'. RCT, randomized controlled trial.

Table SV. Quality assessment of cohort studies included.

First author/s, year	Selection (out of 4)				Comparability (out of 2)	Outcomes (out of 3)			Total (out of 9)	(Refs.)
	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Outcome not present at the start of the study		Assessment of outcomes	Length of follow-up	Adequacy of follow up of cohorts		
Kataoka <i>et al</i> , 2026	1	1	1	1	2	1	1	1	9	(31)
Fan <i>et al</i> , 2024	1	1	0	1	2	1	1	1	8	(28)
Kawashima <i>et al</i> , 2025	1	1	1	1	2	1	1	0	8	(29)
Xu <i>et al</i> , 2025	1	1	1	1	1	1	0	1	7	(30)

The cohort studies were assessed using the Newcastle-Ottawa Quality Assessment Scale.