Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report [1]

TER679: Follow-up after colorectal cancer treatment in patients given treatment with curative intent

What is a Topic Exploration Report?

Topic Exploration Reports are not health technology assessments. These reports provide a high-level briefing on new topics submitted to Health Technology Wales and are not based on exhaustive or systematic literature searches. Instead, they rely on a focussed scan of key resources.

What evidence is used in a Topic Exploration Report?

Priority is given to summarising the most relevant or useful evidence, rather than covering all possible evidence. Information reported is typically based on abstracts and study authors' own conclusions, rather than detailed scrutiny of full texts.

What are the aims of a Topic Exploration Report?

Topic Exploration Reports offer an overview of the available evidence on a topic and aim to highlight any uncertainties or gaps in the evidence. These reports outline the quantity and type of evidence found, but no critical appraisal or formal evidence synthesis is conducted.

How should a Topic Exploration Report be used?

Topic Exploration Reports can be used to indicate what evidence may be available for a topic, and do not provide definitive guidance on how a technology should be used. The evidence presented within the reports should be interpreted with caution.

[1] Cyfieithu dogfennau HTW wedi'u cyhoeddi o'r Saesneg i'r Gymraeg
Translation of published technical HTW documents from English into Welsh

Topic exploration report number	TER679
Topic	Follow-up after colorectal cancer treatment in patients given treatment with curative intent
Summary of findings	Colorectal cancer follow-up recommendations are the same for all patients, regardless of risk and disease stage. Due to waiting lists, there is likely to be variation in provision across Wales. It would be useful, therefore, to identify if there is any evidence on risk-stratified follow-up, and whether there is any evidence for the use of circulating tumour DNA (ctDNA) in follow-up. HTW identified one medtech innovation briefing, four systematic reviews/ meta-analyses, four primary studies, and one report of the economic evidence from a randomised controlled trial (the effectiveness results from which had been included in the systematic review/ meta-analyses). The definition of more or less intensive treatment schedules was mixed. Due to the lack of direct frequency instructions in NICE guidelines, and therefore the likely variation across Wales, generalised comparisons are difficult. However, most evidence agreed that more intensive follow-up did not result in better overall survival or recurrence-free survival, but did result in an increased incidence of salvage surgeries. More intensive schedules also appeared to be less cost-effective. A Dutch study showed that less intensive schedule, with optional visits for patients, was acceptable to both patients and clinicians- with most patients preferring to do follow-up blood tests at home where possible, and undergo consultation by telephone. The utility of ctDNA in follow-up after treatment with curative intent was also mixed. Most evidence indicates that ctDNA can be useful in predicting risk of recurrence and therefore guiding treatment and follow-up intensity. There is some indication it may be at least as good as CEA or imaging when being used for follow-up.

Introduction and aims

In 2022, just over 2700 people were diagnosed with colorectal cancer in Wales, with around 65% of these being Stage 3 or lower, meaning curative treatment is possible. NICE guidance (NG151) on follow-up after curative treatment is generalised and does not vary depending on the stage of disease at diagnosis, or risk of recurrence. Recommended follow-up is to give a mixture of serial serum carcinoembryonic antigen (CEA) testing and CT scans for the first three years, but the suggested frequency of these is not noted. Due to long waiting lists across the NHS in Wales, there is likely to be wide variation in the schedule and duration of follow-up for patients.

Health Technology Wales researchers searched for evidence on follow-up for colorectal cancer. The aim was to identify whether a risk-based approach would be comparable to current standard of care, its acceptability to patients and clinicians, and whether ctDNA testing would be an effective alternative follow-up method.

Evidence overview

HTW identified one medtech innovation briefing, four systematic reviews/ meta-analyses, four primary studies, and one report of the economic evidence from a randomised controlled trial. No ongoing research was identified.

Health Technology Assessments

NICE published a Medtech Innovation Briefing (MIB307, NICE 2022) assessing a minimal residual disease assay called Signatera (CE marked), which measures circulating tumour DNA (ctDNA) in solid diseases, including colorectal cancer. The assay would be created via sequencing of an individual's blood and solid tumour samples to identify their tumour mutations. One of its uses could be for surveillance following the initial 6-month post-operative period alongside normal follow-up, to detect potential recurrence. The conclusion was that it may be possible to detect recurrence sooner using this technology, with one study in the identified evidence base taking place in the UK. All included studies were retrospective and therefore there was no evidence identified on the impact of Signatera on clinical decision making and outcomes. There was some evidence that the device was cost-effective from an Australian payer perspective, but no evidence in the NHS context.

Systematic reviews

Jeffery et al (2019) performed an update to a previous Cochrane review. Sixteen randomised controlled trials (RCTs) were included in the qualitative synthesis. The aim of the review was to assess the effect of different follow-up programmes; follow-up vs no follow-up, different levels of follow-up intensity, and the follow-up setting. More intensive follow-up was found to make no difference to overall survival (OS) (hazard ratio (HR) 0.91, 95% confidence interval (CI) 0.80 to 1.04), and little to no difference in relapse free survival (HR 1.05, 95% CI 0.92 to 1.21). However, salvage surgery with curative intent was more frequent in intensive follow-up regimens (risk ratio (RR) 1.98, 95% CI 1.53 to 2.56), and interval (symptomatic) recurrences were less frequent with intensive follow-up (RR 0.59, 95% CI 0.41 to 0.86). Intensive follow-up was said to probably make little or no difference to quality of life, anxiety, or depression, but may increase the complications (perforation or haemorrhage) from colonoscopies (odds ratio (OR) 7.30, 95% CI 0.75 to 70.69). There was limited data on costs, but it was noted that more intensive follow-up would likely cost more.

Lauretta et al (2023) performed a systematic review which aimed to review the impact of different follow-up tests and programmes on patients treated with curative intent. Comparisons between RCTs and meta-analyses did not allow the authors to draw conclusions

as to whether varying intensity of follow-up regimens had a significant impact on survival and recurrence detection rate. It was noted that an increased detection rate did not necessarily translate to curative surgery, and the overall conclusion was that it is not possible to determine what the ideal surveillance methods and frequency are.

Cui et al (2023) carried out a systematic review and meta-analysis comparing intensive and conventional follow-up regimens. Eighteen RCTs were included, and although there was improved OS in more intensive regimens, this was not statistically significant. Intensive follow-up resulted in an increased incidence of salvage surgery. There was no significant difference in the risk of recurrence, but a reduced risk of interval recurrence when patients underwent more intensive follow-up. Subgroup analysis indicated that the effects of intensive and conventional follow-up did seem to differ when stratified by tumour location and follow-up duration.

The use of circulating tumour DNA (ctDNA) in predicting recurrence, and therefore feeding into treatment decisions and potentially follow-up schedules on a risk-based basis, was reviewed via a meta-analyses by Mi et al (2022). Fourteen studies and 2393 patients were included. Pooled analysis showed ctDNA-positive patients were at higher risk of recurrence after surgery (RR 4.43, 95% CI 3.58 to 5.48, $p < 0.05$) and adjuvant chemotherapy (RR = 5.77, 95% CI 4.33 to 7.69, $p < 0.05$). They also had poorer prognosis after surgery (HR = 7.26, 95% CI 5,48 to 9.62, $p < 0.05$) and adjuvant chemotherapy (HR = 13.96, 95% CI 8.71-22.4, $p < 0.05$). The authors conclude that ctDNA positive patients would require closer follow-up and further treatment.

Primary research

The results of the FUTURE study (van Driel et al, 2025), which took place in the Netherlands, aimed to assess the feasibility of patient-led follow-up. Patients could vary the frequency of follow-up, the location of blood sampling (home, local facility or hospital), and communication method ('silent', telephone or in-person). Patients had seven mandatory consultations over five years, and seven optional additional 'follow-up moments'. 209 patients were analysed within the study. There were 33% of the optional 'follow-up moments' unused, and 66% of patients preferred at-home blood testing, whilst 70% patients preferred telephone consultation. The study indicated patient-led follow-up was feasible and acceptable.

A single centre prospective study in Spain, assessing ctDNA monitoring in long-term follow-up of patients with high-risk stage II and III colorectal cancer was reported by Labiano et al (2026). Utilising blood alone had sensitivity and specificity of 37.5% and 84.6%, which increased to 50% and 97.4% when tissue was used. There was, however, low concordance between tissue and plasma. This indicates there is potential for ctDNA use, but more work needs to be done.

The FIND trial (Peng et al, 2025), which took place in China, randomised 728 patients post-surgery to either ctDNA monitoring alongside standard imaging (363 patients), or standard surveillance (365 patients). No significant difference in cumulative recurrence rates was identified between groups, both in the intention-to-treat ($p = 0.671$) and per-protocol ($p = 0.738$) analysis. The proportion of patients receiving curative therapy after recurrence, however, was significantly increased (relative risk 2.214, 95%CI 1.060 to 4.780, $p = 0.034$). This indicates ctDNA guided surveillance increases likelihood of being able to treat colorectal cancer recurrences with curative intent.

A retrospective comparison of ctDNA (using Signatera), imaging and CEA results during surveillance was reported by Fakih et al (2022), 15 out of 48 included patients had a recurrence. ctDNA was not found to perform any better than imaging, with sensitivity of 53.3% vs 60.0% reported ($p > 0.99$). Imaging plus CEA was improved compared to ctDNA, but not statistically

Evidence overview

significantly so (73.3%, p = 0.55). Additionally, there was no time difference between the three methods in identifying recurrence, with medians of 14.3 months for ctDNA, 15 months for imaging, and 15 months for CEA.

Economic evidence

Mant et al (2017) performed a RCT across 39 hospitals in England and 1202 patients. The study compared minimal follow-up (one CT scan at 12-18 months if requested at study entry by treating clinician), with CEA testing every 3 months for 2 years and then every 6 months for 3 years plus a CT scan at 12-18 months, or CT scans every 6 months for 2 years then annually for 3 years, or finally CEA + CT scans (regimens as per other groups). The clinical effectiveness results have been included within the systematic reviews reported above. There was no significant difference between arms in terms of OS (p = 0.45). The additional cost per QALY gained of moving from minimum follow-up to CEA testing was £25,951 and for CT was £246,107. When compared with minimum follow-up, combined CEA + CT was more costly and generated fewer QALYs, resulting in a negative incremental cost-effectiveness ratio (-£208,347), and a dominated policy.

Areas of uncertainty

There was wide variability in follow-up schedules, and a lack of clarity on what constituted standard, less intensive, or more intensive follow-up schedules. NICE NG151 recommendations are not specific on the follow-up schedule, however NICE QS20 does give a little more information. Some clarification on the standard follow-up across Wales would be useful if this was to progress, to determine which studies may be included due to having less intensive schedules than commonly used across Wales.

There was a lack of studies and meta-analyses with subgroup analyses based on disease stage at diagnosis, or risk of recurrence. This makes it difficult to determine how a risk-stratified approach to follow-up could look.

Most analysis around ctDNA use was in predicting risk of recurrence and utilising it in determining adjuvant therapy. There was limited research on the use of ctDNA in follow-up and early detection of recurrence once treatment with curative intent has completed- especially on the impact of the use of ctDNA in this way on clinical treatment decisions and outcomes.

Literature search results

Health technology assessments and guidance

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NICE (2022). NICE Medtech Innovation Briefing (MIB307): Signatera for detecting molecular residual disease from solid tumour cancers. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/advice/mib307 [Accessed 28 July 2026]

Evidence reviews and economic evaluations

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Jeffery M, Hickey BE, Hider PN. (2019). Follow-up strategies for patients treated for non-metastatic colorectal cancer. Cochrane Database of Systematic Reviews. Issue 9. DOI: https://doi.org/10.1002/14651858.CD002200.pub4

Lauretta A, Montori G, Guerrini GP. (2023). Surveillance strategies following curative resection and non-operative approach of rectal cancer: How and how long? Review of current recommendations. World Journal of Gastrointestinal Oncology. 15(2): 177-192. DOI. https://doi/org/10.4240/wjgs.v15.i2.177

Mi J, Han X, Wang R, Ma R, Zhao D. (2022) Circulation tumour DNA in predicting recurrence and prognosis in operable colorectal cancer patients: A meta-analysis. European Journal of Clinical Investigation. 52(12):e13842. doi: https://doi.org/10.1111/eci.13842

Individual studies

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Labiano, I., Guerrero-Setas, D., Huerta, A.E. *et al.* Insights into ctDNA assessment to detect minimal residual disease (MRD) in localized colorectal cancer. *Sci Rep* (2026). https://doi.org/10.1038/s41598-026-58101-0

Mant D, Gray A, Pugh S, et al. (2017). A randomised controlled trial to assess the cost-effectiveness of intensive versus no scheduled follow-up in patients who have undergone resection for colorectal cancer with curative intent. Health Technology Assessment. 21(32):1-86. DOI: https://doi.org/10.3310/hta21320

Peng J, Ding C, Mo S, et al. (2025). LBA1 Dynamic circulating tumor DNA methylation monitoring guiding postoperative surveillance in non-metastatic colorectal cancer: Interim analysis of FIND trial. Annals of Oncology. 36(1). DoI: https://doi.org/10.1016/j.annonc.2025.05.541

van Driel MHE, Wullaert L, Voigt KR, et al. (2025). Patient-led follow-up after curative colorectal cancer surgery: The primary outcome analysis of the prospective, multicentre FUTURE-primary implementation study. European Journal of Cancer. 226:115599. DOI: https://doi.org/10.1016/j.ejca.2025.115599

Ongoing research

No evidence found

Date of search	13/07/2026
Concepts used	Colorectal cancer, follow-up, curative, ctDNA, cell-free DNA

Proposed research question and evidence selection criteria (if selected)

Proposed Research question	**What is the clinical and cost-effectiveness of less intensive, risk-stratified follow-up for colorectal cancer treated with curative intent.**

	Inclusion criteria	Exclusion criteria
Population	People who have had treatment for colorectal cancer with curative intent (Stage III or lower)	People with recurrent or metastatic colorectal cancer (Stage IV)
Intervention	Less intensive follow-up Patient led follow-up Risk stratified follow-up ctDNA testing after treatment given with curative intent	
Comparison/ Comparators	Standard/ intensive follow-up CEA/ imaging alone	
Outcome measures	Overall survival Recurrence-free survival Surgical treatment of recurrence with curative intent Acceptability Health related QoL Resource use Economic outcomes	

Proposed specialities	Cancer, digestive system