FPN 102P: Direct cost of healthcare analysis of Signatera ctDNA testing in the adjuvant setting for a hypothetical cohort of stage II and stage III colorectal cancer (CRC) patients: a UK private payer perspective.

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Background

- This study aims to evaluate and compare the annual direct healthcare costs associated with implementing a Signatera™ (Natera, Inc.) ctDNA testing protocol in the adjuvant setting for a hypothetical cohort of stage II and stage III CRC patients from the perspective of a UK private healthcare payer.
- The analysis seeks to quantify potential cost implications, identify key economic drivers, and assess the overall cost-impact of adopting ctDNA-guided treatment strategies in comparison to current standard-of-care (SoC) practices.
- The intent is to illustrate potential budget impact and not reflect observed real-world outcomes, provide management recommendations, or make claims regarding intended use.

Methods

- A hypothetical budget impact model was developed based on assumptions derived from literature and internal estimates. The model compared ctDNA-guided versus guideline-based treatment decisions in stage II and III CRC (**Figure 1**). *The results presented are illustrative only and do not constitute real-world outcomes.*
- The model simulated 1,000 stage II (396) and III (604) patients from post-surgical treatment through a 12-month surveillance protocol, using historical ctDNA data and real-world clinical patterns.
- Healthcare resource costs, including ctDNA testing (Signatera™), chemotherapy, hospital stays, consultations, pathology, and billable services, such as follow-up, and adverse events, were estimated from published literature and insurance data (**Table 1, Figure 2**).
- Sensitivity analyses evaluated the effects of ctDNA test costs, adherence to Signatera results, ctDNA predictive value, and test performance (**Figure 3**).

Table 1. Inputs for budget impact model

Cost category	Rationale	Source
Chemotherapy	Impact of Signatera-guided treatment decisions on use of chemotherapy.	NHS digital for standard-of-care chemotherapy use.[1,2]
Hospital	Impact of Signatera testing on hospital visits.	Expert judgement on decision impact of ctDNA positivity & negativity.
Pathology	Impact of Signatera testing on regular laboratory tests as part of standard-of-care.	Estimate based on claims data.
Consultation	Impact of Signatera testing on frequency of consultations required.	Expert judgement based on claims data.
Toxicity	Impact of Signatera-guided treatment strategy on chemotherapy decisions and associated side effects/toxicity.	Severe acute toxicity affects 21% of chemotherapy patients[3]; of those, almost half (10% of total patients) need to be hospitalized.
Blood test	Impact of Signatera testing on ancillary tests, such as genotyping.	Expert judgement based on claims data.
Signatera test	Impact on cadence of Signatera testing (~4 weeks post-surgery, followed by ~12 weeks post-surgery).	Natera, Inc.

ctDNA testing to guide adjuvant chemotherapy in post-surgery patients with stage II/III CRC is projected to result in cost savings for the private payer system in the UK

Figure 1: Retrospective Decision Impact Schema Overview

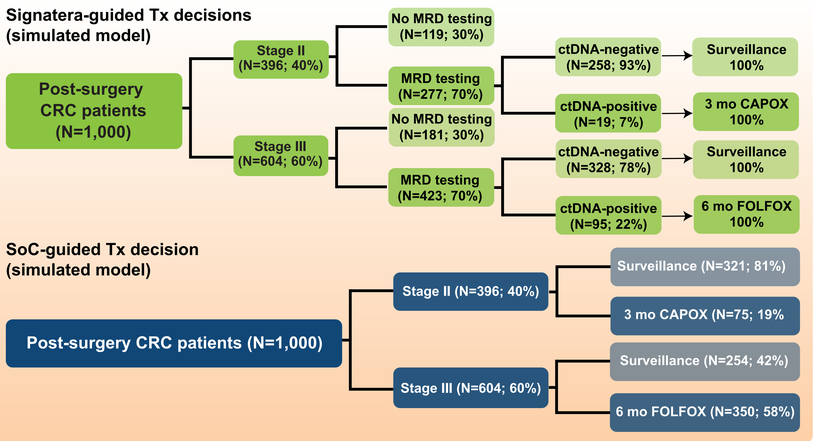

Figure 1. Simulated Treatment Decision Models Comparing Signatera-Guided vs. SoC Approaches in Post-Surgical CRC Patients. The decision trees illustrate a simulated cohort of 1,000 post-surgical CRC patients, stratified by disease stage (Stage II: 40%; Stage III: 60%) and managed using either a Signatera-guided minimal residual disease (MRD) testing strategy or SoC treatment pathways. **Abbreviations:** CRC, colorectal cancer; ctDNA, circulating tumor DNA; mo, months; MRD, molecular residual disease; SoC, standard-of-care; Tx, treatment.

Conclusions

- **Significant Cost Savings:** Implementing Signatera™ ctDNA-guided treatment in stage II/III CRC patients is projected to reduce the total healthcare costs by ~43%, from £12.02M under SoC to £6.85M, driven largely by decreased chemotherapy use in ctDNA-negative patients.
- **Personalized Care Reduces Unnecessary Treatment:** A ctDNA-guided strategy is projected to enable more personalized care by avoiding overtreatment, especially in ctDNA-negative patients, reducing costs associated with hospitalization, toxicity, and follow-up.
- **Key Cost Drivers Identified:** Sensitivity analysis, performed in conjunction with the hypothetical budget impact model demonstrated that the frequency and cost of Signatera testing, as well as chemotherapy utilization patterns, are major economic influencers, emphasizing the importance of optimizing test implementation strategies.

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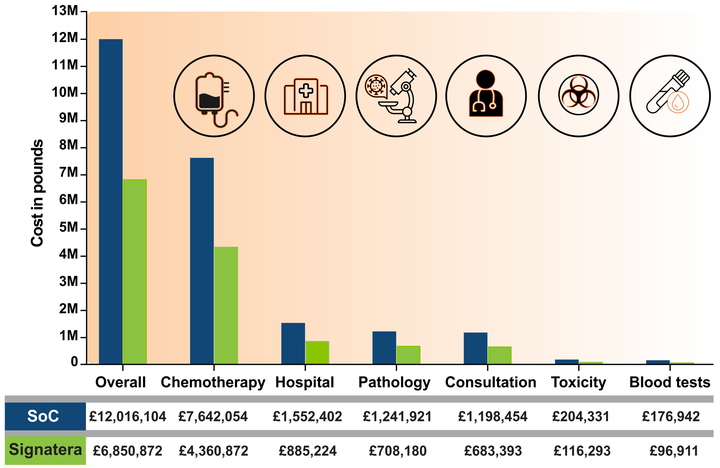
Figure 2: Comparative Cost Analysis: SoC vs. Signatera™



	Overall	Chemotherapy	Hospital	Pathology	Consultation	Toxicity	Blood tests
SoC	£12,016,104	£7,642,054	£1,552,402	£1,241,921	£1,198,454	£204,331	£176,942
Signatera	£6,850,872	£4,360,872	£885,224	£708,180	£683,393	£116,293	£96,911

Figure 2. Comparative Cost Analysis of SoC vs. Signatera-Guided Treatment in Post-Surgical CRC Patients. The bar chart compares the total and category-specific healthcare costs (in British pounds) associated with SoC and Signatera-guided treatment strategies for post-surgical CRC patients. *The results presented are illustrative only and do not constitute real-world outcomes.* **Abbreviations:** CRC, Colorectal cancer; SoC, standard-of-care.

Figure 3: Sensitivity Analysis

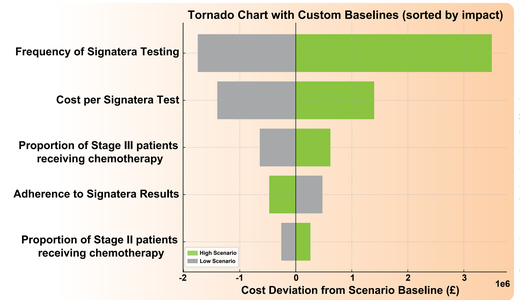


Figure 3: Tornado Chart sorted by greatest cost impact at the top using the custom scenario baselines. The chart provides a prioritized roadmap for economic impact mitigation. The model input range variations for the respective chosen parameters in the tornado chart are: 1-4, £5,000 (2 timepoints), 180-220, 50%-90%, and 22-62. Frequency of Signatera testing and cost per test are the dominant drivers of cost variation. Stage II and III chemotherapy prescribing patterns and adherence to testing results show smaller impacts, yet still significantly influence the overall budget impact of MRD testing. *The results presented are illustrative only and do not constitute real-world outcomes.* **Abbreviations:** MRD, molecular residual disease.

References
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