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Original Investigation

Budget Impact Analysis of Circulating Tumor DNA Testing for Colon Cancer in Commercial Health and Medicare Advantage Plans

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Abstract

IMPORTANCE In a randomized clinical trial, treatment guided by tumor-informed circulating tumor (ct)DNA testing reduced adjuvant chemotherapy use without compromising recurrence-free survival in patients with stage II colon cancer. The potential effects of adopting ctDNA testing into routine patient care is unknown.

OBJECTIVE To compare the total cost of patient care scenarios with and without the adoption of ctDNA testing.

DESIGN, SETTING, AND PARTICIPANTS This budget impact analysis was conducted from the perspectives of US commercial health and Medicare Advantage payers. A decision-analytical model was populated with age-specific incidence of colon cancer, use of adjuvant chemotherapy, and use of single-agent or multiagent regimens. Total cost was estimated with the costs of ctDNA testing, drug acquisition, administration, surveillance, and adverse events. The analysis was conducted from September 2023 to January 2024.

EXPOSURES The adoption of ctDNA testing.

MAIN OUTCOMES AND MEASURES The incremental cost in the first year following the adoption of ctDNA testing, where testing will affect patient treatment and costs.

RESULTS In hypothetical plans with 1 million individuals covered, 35 commercial health plan members and 102 Medicare Advantage members aged 75 years and younger were eligible for ctDNA testing. In the base case with a 50% adoption rate, total cost savings were $221 684 (equivalent to $0.02 per member per month [PMPM]) for a commercial payer and $116 720 (equivalent to $0.01 PMPM) for a Medicare Advantage payer. Cost savings were robust to variations in assumptions of all parameters in the commercial population but sensitive to variations in assumptions of adjuvant chemotherapy use rates in the Medicare Advantage population. The number needed to test to avoid 1 patient receiving adjuvant chemotherapy was 4 in the commercial population and 10 in the Medicare Advantage population. The budget-neutral cost for ctDNA testing was $16 202 for a commercial payer and $5793 for a Medicare Advantage payer.

CONCLUSIONS AND RELEVANCE Use of tumor-informed ctDNA testing to guide adjuvant chemotherapy in postsurgery patients with stage II colon cancer was projected to result in cost savings for both commercial and Medicare Advantage payers. Adoption of ctDNA testing is therefore advantageous from a budgetary perspective.

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Key Points

Question Given a landmark clinical trial showing that circulating tumor (ct)DNA-guided treatment reduced adjuvant chemotherapy for stage II colon cancer, what would be the budget impact to health insurance plans when ctDNA testing is adopted?

Finding In this budget impact analysis, compared with clinical evaluation–based treatment, ctDNA-guided treatment had lower total cost of care. Adoption of ctDNA testing was cost saving to both commercial health and Medicare Advantage payers.

Meaning The use of ctDNA testing to guide adjuvant chemotherapy for stage II colon cancer is the embodiment of precision oncology, decreasing adjuvant chemotherapy without compromising recurrence-free survival while also reducing the cost of care.

+ Supplemental content

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Introduction

Colorectal cancer is among the most commonly diagnosed cancers in the US. In 2023, an estimated 106 970 individuals were projected to be diagnosed with colon cancer,[1] with approximately 1 in 5 to 1 in 4 having stage II disease.[2] Surgery alone is associated with high overall survival (70% to 80% in 5 years).[3] Some patients also receive adjuvant chemotherapy (ACT), which may be associated with a small benefit in disease-free survival and overall survival in selected patients.[4] Traditionally, the use of ACT is guided by clinical evaluation, where only patients with high-risk factors—T4 tumors, lymphovascular invasion, poor differentiation, perineural invasion, obstruction, perforation, and/or an inadequate number of retrieved lymph nodes—are considered candidates for therapy.[5] Patient age is also a factor in the use of ACT—older patients are less likely to be offered therapy.[6] However, despite limited data supporting a survival benefit, ACT is often administered in routine care, particularly among young and middle-aged patients.[2,7,8] For example, in a retrospective analysis of a US population of 3083 patients with stage II colon cancer aged 18 to 49 years, 56% were found to have received ACT.[7]

Recent evidence from clinical trials suggests that postsurgery testing for tumor-informed circulating tumor DNA (ctDNA), a biomarker of minimal residual disease (MRD),[9,10] has the potential to help reduce unnecessary use of ACT in patients with stage II colon cancer. In a randomized clinical trial (the DYNAMIC trial), ctDNA-guided treatment, compared with clinical evaluation-based treatment, reduced the number of patients treated with ACT by 45% (15% vs 28%; relative risk [RR], 1.82; 95% CI, 1.25-2.65) without compromising disease-free survival.[11] In another clinical trial (the CIRCULATE-Japan trial), in an observational cohort of patients with stage II colorectal cancer, ctDNA status was predictive of ACT benefit in disease-free survival—patients who tested positive saw significant benefit whereas those who tested negative did not.[12] These observations portend a care scenario where postsurgery ctDNA testing is adopted to guide ACT use for patients with stage II colon cancer.

Although ctDNA testing can help patients avoid ACT and the attendant potential short- and long-term adverse effects, payers are likely to be interested in understanding the potential effects of routine adoption on budgets. This is particularly pertinent given the large number of patients and the current high cost associated with treatment—in a claims analysis of US commercial health and Medicare Advantage plans,[13] the average cost in the first year after diagnosis was more than $127 000 (in 2020 dollars) per patient with stage II colorectal cancer. Therefore, we have conducted an economic analysis on the potential adoption of tumor-informed ctDNA testing in postsurgery patients with stage II colon cancer. This analysis took the perspectives of US commercial and Medicare Advantage payers.

Methods

Reporting of this study followed the Budget Impact Analysis—Principles of Good Practice reporting guidelines. The analysis was conducted from September 2023 to January 2024.

Model Structure

A decision-tree model was developed to assess the effect of the adoption of tumor-informed ctDNA testing on the budget of health insurance plans (**Figure 1**). This model compared the total cost of patient care scenarios where the use of ACT was guided by (1) clinical evaluation only or (2) clinical evaluation for some patients and ctDNA testing for other patients.

Study Perspective and Time Horizon

Economic analyses were performed from the perspectives of commercial and Medicare Advantage payers in the US. Total costs were estimated in hypothetical plans with 1 million individuals covered in a 1-year time horizon. The total cost included the costs of ctDNA testing, drug acquisition,

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administration, surveillance, and adverse events. In ctDNA-guided treatment, patients 75 years or younger were tested for ctDNA; older patients did not receive ctDNA testing because they are less likely to be offered chemotherapy.[6] In ctDNA-guided and clinical evaluation-based treatment, patients received ACT when indicated by test results and clinical evaluation, respectively. All additional costs for ctDNA-guided treatment were assumed to incur in year 1 and would not affect a budget in subsequent years. The total cost did not include the cost of postrecurrence treatment. Because no significant differences in recurrence and recurrence-free survival were observed between clinical evaluation-based and ctDNA-guided treatments in the DYNAMIC trial,[11] recurrence and mortality-associated costs were considered to be the same in 2 patient care scenarios and cancel out the effect of the use of ctDNA testing on budget outcomes.

Input Parameters

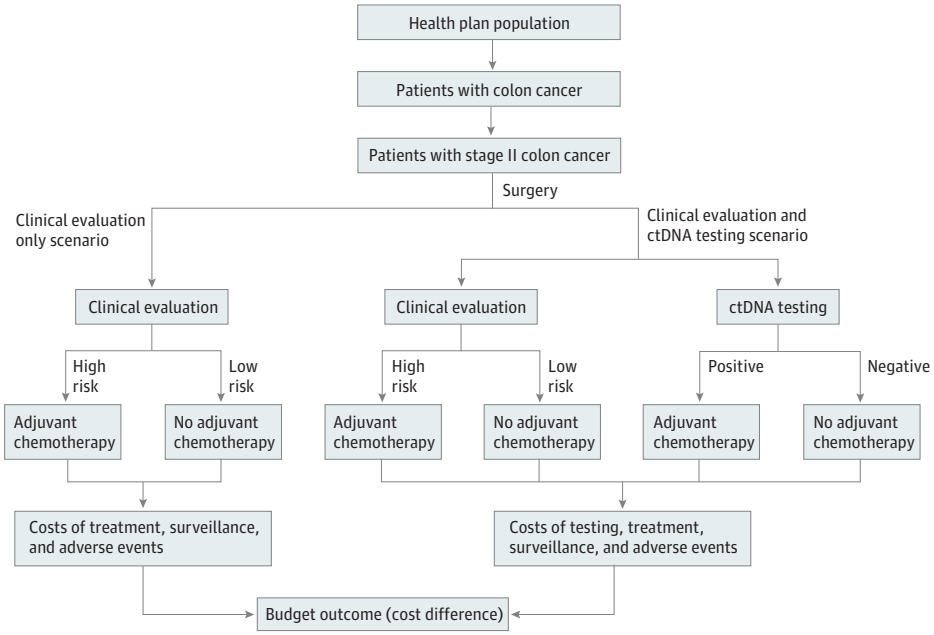
Health Plan Population

In the hypothetical commercial plan, 4% of the members were assumed to be 65 years or older based on an analysis of a self-funded health insurance. In the hypothetical Medicare Advantage plan, 87% of the members were assumed to be 65 years or older.[14] The number/proportion of members in other age groups was estimated based on the age distribution of the US population or Medicare Advantage population (**Table 1**[2,7,11,14-19]).

Patient Population

The number of patients was estimated for the health plans using the age-specific incidences of all-stage and stage II colon cancer. The age-specific incidences of colon cancer were calculated based on the estimated number of new cases in 2023 (see Table 1 in Siegel et al[1]) and the age distribution of the US population. The colon cancer incidences among members 65 to 75 years and older than 75 years were calculated based on the estimated number of new cases in 2023 in the age groups of 65 years and older (see Table 1 in Siegel et al[1]) and weighted by the proportion of cases in 2000 in these 2 age groups (see Figure 1 in Siegel et al[1]) and the US population size in 2000. The proportions of

Figure 1. Budget Analysis Framework



ctDNA indicates circulating tumor DNA.

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Table 1. Input Parameters

Variable	Base case value, %	Lower limit	Upper limit	Source
Covered individuals, No.	1 000 000	NC	NC	Hypothetical
Commercial health plan, proportion by age, y				
≥65	4.00	NC	NC	Assumed
50-64	21.92	NC	NC	US Census
≤49	74.08	NC	NC	US Census
Medicare Advantage plan, proportion by age, y				
≥65	85.50	NC	NC	Murphy-Barron, et al[14]
50-64	10.40	NC	NC	Murphy-Barron, et al[14]
≤49	3.01	NC	NC	Murphy-Barron, et al[14]
Proportion among age ≥65 y				
>75 In commercial health plan	36.4	NC	NC	US Census
>75 In Medicare Advantage	3.98	NC	NC	Murphy-Barron, et al[14]; US Census
Incidence of colon cancer by age, y				
>75	0.1833	0.1375	0.2291	Siegel, et al[1]
65-75	0.0714	0.0536	0.0893	Siegel, et al[1]
50-64	0.0474	0.0356	0.0593	Siegel, et al[1]
≤49	0.0058	0.0044	0.0073	Siegel, et al[1]
Stage II colon cancer, proportion by age in all stages, y				
≥65	24.5	18.4	30.6	Manjelievskaia, et al[2]
50-64	21.0	15.8	26.3	Manjelievskaia, et al[2]
≤49	20.1	15.1	25.1	Manjelievskaia, et al[2]
Adjuvant chemotherapy use rate by age, y				
Clinical evaluation-based treatment				
>75	7.3	NC	NC	Jiao, et al[15]
65-75	23.6	17.7	29.5	Jiao, et al[15]
50-64	40.6	30.5	50.8	Manjelievskaia, et al[2]; Kneuertz, et al[7]
≤49	56.2	42.2	70.3	Kneuertz, et al[7]
ctDNA-guided treatment	15.3	11.5	19.1	Tie, et al[11]
Proportion of single-agent regimen by age, y[a]				
Clinical evaluation-based treatment				
65-75	45.1	33.8	56.4	Manjelievskaia, et al[2]
50-64	25.7	19.3	32.1	Manjelievskaia, et al[2]
≤49	25.8	19.4	32.3	Manjelievskaia, et al[2]
ctDNA-guided treatment modifier[b]	1	0.75	1.25	Assumed
Cost, $				
ctDNA testing	3500	2625	4375	Assumed
Single-agent regimen				
Drug acquisition	16 186	12 140	20 233	Wang et al[16]; see Methods
Administration including catheter insertion/removal	14 128	10 596	17 660	Chu, et al[17]; MDSave[18]
Adverse events	13 708	10 281	17 135	Chu, et al[17]
Multiagent regimen				
Drug acquisition	39 128	29 346	48 910	Ou, et al[19]; see Methods
Administration including catheter insertion/removal	10 496	7872	13 120	Chu, et al[17]; MDSave[18]
Adverse events	16 169	12 127	20 211	Ou[19]; Chu[17]
Surveillance				
Commercial health plan	3793	NC	NC	See Methods
Medicare Advantage plan	1754	NC	NC	See Methods

Abbreviations: ctDNA, circulating tumor DNA; NC, not changed.

[a] The remaining patients receiving chemotherapy received multiagent regimens.

[b] Modifier refers to the ratio of the rate of chemotherapy regimen in ctDNA-guided vs clinical evaluation–based treatments.

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stage II colon cancer among all colon cancer cases were taken from a study with 3143 patients from 18 to 75 years.[2]

ACT Use

Age-specific use of ACT in clinical evaluation-based treatment was estimated as the following: (1) for patients older than 75 years and patients 65 to 75 years, ACT use rate was based on the number of Medicare patients who received ACT among all patients with stage II colon cancer (see Table 1 in Jiao et al[15]); (2) for patients aged 50 to 64 years, ACT use rate was assumed to be in the midpoint (40.6%) of ACT use rates between the older (≥65 years) and younger (≤49 years) patients reported in Kneuertz et al.[7] This assumption was based on ACT use in the following age groups in another study[2] (682 patients with stage II disease): 31.3% among patients aged 65 to 75 years, 52.8% among patients aged 50 to 64 years, and 71.6% among patients aged 18 to 49 years. The assumed ACT use rate for patients at age 50 to 64 years was therefore a conservative estimate; and (3) for patients 49 years or older, ACT use rate was based on the rate among 3083 patients aged 18 to 49 years reported in Kneuertz et al.[7]

Based on these age-specific ACT use rates, the weighted average rate of ACT use in the US was calculated to be 26.2% in clinical evaluation-based treatment (eTable 1 in Supplement 1). This rate is nearly identical to the 26% ACT use rate reported in a cohort of 42 971 patients with stage II colon cancer in the National Cancer Data Base[20] and similar to the 27.9% ACT use rate in the DYNAMIC trial.[11] For ctDNA-guided treatment, the ACT use rate was assumed to be the same as observed in the DYNAMIC trial.[11]

ACT Regimen

In clinical evaluation-based treatment, patients receiving ACT had 6 months of single-agent fluoropyrimidine or a multiagent regimen (combination of fluoropyrimidine and oxaliplatin) according to the age-specific rates reported in Manjelievskaia et al.[2] The rates for the patients aged 65 to 75 years were also applied to the patients older than 75 years. In ctDNA-guided treatment, the rate of chemotherapy regimen for each age group was assumed with a modifier that refers to the ratio of the rate of chemotherapy regimen in ctDNA-guided vs clinical evaluation-based treatments. The modifier was set at 1 in base case.

Costs

The costs included those for ctDNA testing, treatment and surveillance in the first year. (1) The weighted total cost of tumor-informed ctDNA testing was assumed at $3500 for each patient. (2) The cost of treatment included the cost of drug acquisition, administration including catheter insertion and removal for therapy with 5-fluorouracil (5-FU) and 5FU with oxaliplatin (FOLFOX), and treatment-related adverse events. Single-agent regimen 5-FU/ leucovorin (92% of the patients) or capecitabine (8% of the patients) was assumed to be used for 6 months.[16] The multiagent regimen oxaliplatin (CAPEOX) or FOLFOX was used as reported in Ou et al[19]: 10.0% patients received FOLFOX for 3 months, 42.1% patients received FOLFOX for 6 months, 35.3% patients received CAPEOX for 3 months, and 12.7% patients received CAPEOX for 6 months. Monthly costs of the drugs were estimated using drug prices in the Redbook and/or drugs.com. Costs for drug administration and adverse events were based on claims in Chu et al[17] and adjusted to 2023 dollars using the consumer price index for medical care.[21] Costs for catheter insertion and removal were based on the national average listed on the MDSave.com website.[18] The weighted cost of drug acquisition, administration, and adverse events for single-agent and multiagent regimens was calculated using the rate and duration of drug usage and the cost associated with individual drugs; these costs were assumed to be the same for all payers. (3) The cost of surveillance included the costs for 3 physical examinations, 3 tests of carcinoembryonic antigen, 1 computed tomographic (CT) scan, and 1 colonoscopy at a total of $3793 for a commercial payer and $1754 for a Medicare Advantage payer. These costs were estimated using a Medicare fee schedule and physician reimbursement in Medicare Advantage.[22]

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They were assumed to be the same for both ctDNA-guided and clinical evaluation–based treatment. This assumption implied no effect on budget from the cost of surveillance, but it would underestimate the effect of ctDNA testing on budget. Patients receiving ACT may have additional clinic visits compared with patients receiving no ACT. Therefore, the total cost of surveillance would be lower in ctDNA-guided treatment than in clinical evaluation-based treatment.

Analysis

The primary outcome was incremental budget in total cost for all members in a health care plan as well as per-member-per-month (PMPM) cost based on the average monthly cost for each member of a coverage plan. The effect of changes in parameter assumptions on incremental budget was examined by 1-way sensitivity analysis, where the parameter values were adjusted by plus or minus 25% (Table 1). Scenario analysis was also performed to assess the effect on budget of a conservative treatment scenario under a conservative treatment scenario according to the proposal in Iveson et al,[23] where 3-month CAPOX or 6-month single-agent fluoropyrimidine was to be used. The number needed to test (NNT) to avoid ACT use in 1 patient was calculated as:

$$NNT = \frac{1}{\mathrm{R1} - \mathrm{R2}}$$

where R1 and R2 denote ACT use rate without and with testing, respectively. All analyses were performed using TreeAge Pro (version 2023, R2.0; TreeAge Software).

Results

In hypothetical health plans with 1 million individuals covered, 191 commercial members were expected to be newly diagnosed with colon cancer in a year, with 41 having stage II disease, and 1054 Medicare Advantage members were expected to be newly diagnosed with colon cancer in a year, with 256 having stage II disease (**Table 2**). Among those with stage II colon cancer, 35 commercial members and 102 Medicare Advantage members 75 years and younger were eligible for ctDNA testing.

In clinical evaluation-based treatment, the 1-year total cost was $1 068 040 for a commercial payer and $2 550 029 for a Medicare Advantage payer. Adoption of ctDNA testing at a 50% rate would lead to cost savings of $221 684 for a commercial payer (equivalent to $0.02 PMPM) and $116 720 for a Medicare Advantage payer (equivalent to $0.01 PMPM). Higher cost savings would be expected when the rate of ctDNA testing was increased, and lower cost savings would be expected when the rate of ctDNA testing was decreased (**Table 3**; eTable 2 in Supplement 1). The NNT to avoid

Table 2. Expected Number of Incident Colon Cancer Cases in Health Plans With 1 Million Individuals Covered

		No.[a]		
Health plan	Age, y	Members	All patients	Stage II disease
Commercial	>75	14 560	27	7
	65-75	25 440	18	4
	50-64	219 200	103	22
	≤49	740 800	43	9
	All	1 000 000	191	41
Medicare Advantage	>75	344 270	631	155
	65-75	520 730	372	91
	50-64	104 000	49	10
	≤49	31 000	2	0
	All	1 000 000	1054	256

[a] Numbers may not sum up to group totals due to rounding.

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ACT use in 1 patient was estimated to be 4 in the commercial health plan population and 10 in the Medicare Advantage population.

Cost savings were robust to variations in assumptions of all parameters in a commercial population but sensitive to variations in ACT use rates in a Medicare Advantage population (**Figure 2**). As expected, the ACT use rate in clinical evaluation-based treatment had a positive and largest effect on cost savings—the higher the ACT use rate, the higher the cost savings for the payers. Conversely, the ACT use rate in ctDNA-guided treatment had a negative effect on cost savings—the higher the ACT use rate in ctDNA-guided treatment, the lower the cost savings for the payers. In the base case, the ACT use rate in ctDNA-guided treatment associated with neutral budget was estimated to be 36.6% and 19.4% in the commercial and Medicare Advantage populations, respectively (eFigure 1 in Supplement 1). Also as expected, the cost of ctDNA testing negatively affected cost savings—the higher the cost of ctDNA testing, the lower the cost savings for the payers. In the base case, the cost of ctDNA testing associated with neutral budget was estimated to be $16 202 and $5793 for the commercial and Medicare Advantage payers, respectively (eFigure 2 in Supplement 1).

In an alternative, conservative patient care scenario where a shorter duration of ACT (3 months of multiagent therapy) was to be used,[23] the budget reduction was estimated to be $0.01 PMPM for a commercial payer and $0.003 PMPM for a Medicare Advantage payer when the adoption rate of ctDNA testing was 50% (eTable 3 in Supplement 1).

Discussion

This analysis found that the adoption of ctDNA testing to guide the use of ACT for postsurgery patients with stage II colon cancer provided cost savings to both US commercial and Medicare Advantage payers. The cost savings increased further with increased adoption of the test beyond the base case where 50% of patients were tested. On a PMPM basis, the cost savings were higher to a commercial payer than they were to a Medicare Advantage payer (up to $0.04 vs $0.02 at an adoption rate of 100%). In essence, the budget reduction derived from savings in the costs associated with ACT use offset against the cost of testing. Therefore, the cost savings to payers should not be surprising because the cost associated with ACT use is high (total cost per patient is $44 022 for single-agent and $65 792 for multiagent treatment) and the NNT to avoid 1 patient receiving ACT is low (4 in the commercial population and 11 in the Medicare Advantage population).

The major driving factors of the cost savings are the higher ACT use rate in clinical evaluation-based treatment and the lower ACT use rate in ctDNA-guided treatment. Therefore, the absolute reduction in ACT use in ctDNA-guided treatment vs clinical evaluation-based treatment is expected to be the most significant factor affecting budget. In the base case, the absolute reduction in ACT use was 27.0% in the commercial population and 10.1% in the Medicare Advantage population. The larger reduction in ACT use in the commercial population compared with the Medicare Advantage

Table 3. Base-Case Budget Effects in Health Plans With 1 Million Individuals Covered

Adoption rate of ctDNA test, %	$					
	Commercial health plan			Medicare Advantage plan		
		Cost savings			Cost savings	
	Total cost	Total	PMPM	Total cost	Total	PMPM
0	1 068 040	1 [Reference]	1 [Reference]	2 550 029	1 [Reference]	1 [Reference]
25	957 198	110 842	0.009	2 491 669	58 360	0.005
50	846 356	221 684	0.018	2 433 309	116 720	0.01
75	735 514	332 526	0.028	2 374 949	175 080	0.015
100	624 672	443 368	0.037	2 316 589	233 440	0.019

Abbreviations: ctDNA, circulating tumor DNA; PMPM, per member per month.

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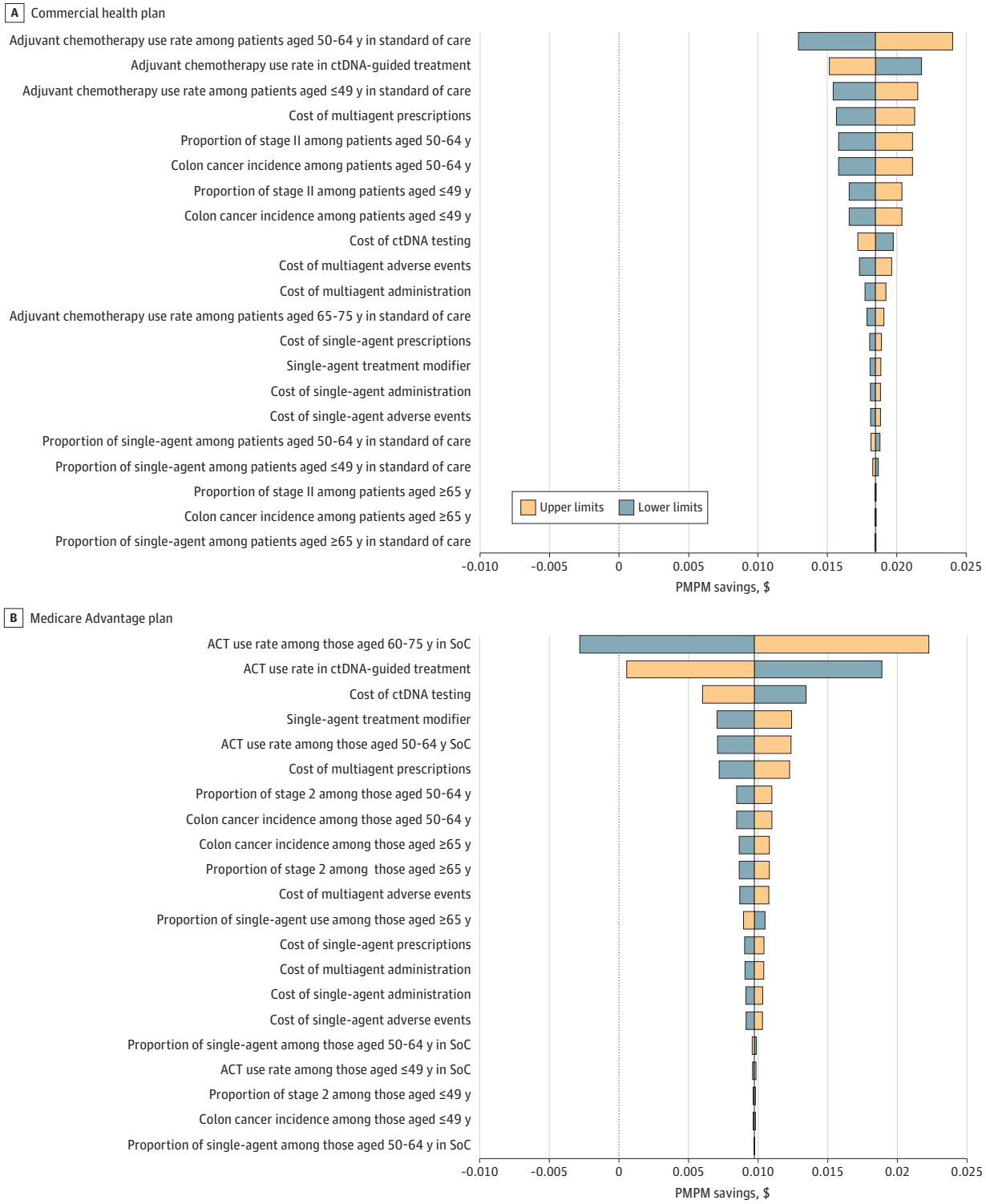
Figure 2. One-Way Sensitivity Analysis of Cost Savings per Member per Month (PMPM)



The orange bars indicate cost savings at the upper limits of the model parameters, and the blue bars indicate cost savings at the lower limits of the model parameters. The limits of the model parameters are listed in Table 1. ACT indicates adjuvant chemotherapy; ctDNA: circulating tumor DNA; SoC, standard-of-care (clinical evaluation-based treatment).

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population contributed to the larger cost savings to a commercial payer than to a Medicare Advantage payer.

These findings provide economic rationale for payers to provide insurance coverage on ctDNA testing, which varies across payers,[24] and consequently can help improve patient access to personalized care in cancer treatment. Patient insurance coverage is an important factor in treatment decision-making by oncologists and in their discussions with patients. For example, in a survey of 1049 oncologists who reported using genomic testing, 47.3% and 32.7% reported that patient insurance coverage for genomic testing was very important and somewhat important, respectively, in treatment decisions.[25] In another study including 1220 oncologists who discussed genomic testing with patients, 50.0% reported often discussing the likely costs of testing and related treatments and 26.3% reported sometimes discussing costs.[26] However, ctDNA testing is already in the clinic and increasingly being used.[27] Most oncologists surveyed showed interest in using ctDNA testing in ACT decision-making for patients with colon cancer,[28] and in a study of patient-reported outcomes from the BESPOKE trial,[29] most patients surveyed said that they valued the ctDNA testing information and would continue ctDNA testing.

Limitations

This study had some limitations. First, the modeling did not consider the costs of potential disease recurrence and mortality because these costs were not expected to be affected by ctDNA testing based on results from the DYNAMIC trial.[11] Whether recurrence and recurrence-free survival remain unchanged in clinical evaluation-based treatment vs ctDNA-guided treatment in the clinical setting, as observed in the clinical trial, is unknown. However, the relative effect on budget from a potential difference in these clinical outcomes is likely to be small and longer term than the 1-year time frame that is of interest to the payers.[30] The modeling also did not consider patient out-of-pocket cost for testing, which can be substantial for those with a high-deductible commercial health plan. Consequently, cost savings to health plans could be larger, although high out-of-pocket cost can become a barrier for patients to access the testing.

Second, the parameter estimates primarily relied on published literature and have inherent uncertainty. However, the epidemiological inputs and ACT modalities/use were derived from large studies in the US setting and are therefore likely to be reliable and relevant. In addition, conservative estimates were used in modeling when estimates were available from multiple sources; for example, the total weighted cost for multiagent used in modeling ($65 792) was lower than the 6-month total claims for CAPOX in patients with early-stage colon cancer ($71 247).[16] Cost savings also persisted (although lower) when more conservative treatment, ie, shorter duration of ACT use and a less toxic regimen (and hence less expensive treatment), was modeled. Furthermore, robust cost savings were observed across a range of estimates for all parameters in the commercial population and most of the parameters in the Medicare Advantage population.

Third, the ACT use rate in ctDNA-guided treatment was based on the DYNAMIC trial[11] in a population with a different ethnicity mix than in the US population. However, cost savings were still expected even when the ACT use rate in ctDNA-guided treatment was increased to 36.6% in the commercial population and 19.4% in the Medicare Advantage population from 15.3% in the base case.

Fourth, the analysis was conducted from the perspectives of US commercial and Medicare Advantage payers; consequently, the conclusion may not be directly applicable to other US-based payers such as Medicaid or health care systems in other locations. However, in a cost-effectiveness analysis (although not a budget impact analysis) conducted in Australia, ctDNA testing was also found to be cost saving in stage II colorectal cancer.[31] Furthermore, if interested, the conclusion can be readily reassessed with the model developed in this study using parameter inputs that are relevant to specific plans.

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Conclusions

This budget impact analysis found that adjuvant therapy–informed by ctDNA testing provides cost saving compared to clinical evaluation in patients with stage II colon cancer. Adoption of the test to US commercial health and Medicare Advantage plans should therefore be considered from a budgetary perspective. The budget impact of the adoption of the test to other payers can be assessed with the model developed in this study.

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Author Contributions: Dr Li had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Li, Heer, Sloane, Edelstein, Tie, Gibbs.

Acquisition, analysis, or interpretation of data: Li, Heer, Sloane, Edelstein, Gibbs, Barzi.

Drafting of the manuscript: Li, Heer, Gibbs.

Critical review of the manuscript for important intellectual content: All authors.

Statistical analysis: Li.

Administrative, technical, or material support: Heer, Sloane, Gibbs.

Supervision: Heer, Edelstein, Tie, Gibbs.

Other - review of background context and methods: Barzi.

Conflict of Interest Disclosures: Dr Li reported receiving employment from Quest Diagnostics. Dr Tie reported personal fees from Haystack Oncology consultancy, personal fees from Takeda advisory board, personal fees from Pierre Fabre advisory board, personal fees from MSD advisory board, personal fees from Novartis advisory board, personal fees from Merck serono advisory board, personal fees from BMS advisory board, personal fees from Daiichi Sankyo advisory board, personal fees from Gilead advisory board, and personal fees from Beigene advisory board outside the submitted work. Dr Gibbs reported personal fees from Haystack Oncology consultancy. No other disclosures were reported.

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REFERENCES

1. Siegel RL, Wagle NS, Cercek A, Smith RA, Jemal A. Colorectal cancer statistics, 2023. *CA Cancer J Clin*. 2023;73(3):233-254. doi:10.3322/caac.21772

2. Manjelievskaia J, Brown D, McGlynn KA, Anderson W, Shriver CD, Zhu K. Chemotherapy use and survival among young and middle-aged patients with colon cancer. *JAMA Surg*. 2017;152(5):452-459. doi:10.1001/jamasurg.2016.5050

3. Johnston PG. Stage II colorectal cancer: to treat or not to treat. *Oncologist*. 2005;10(5):332-334. doi:10.1634/theoncologist.10-5-332

4. Kannarkatt J, Joseph J, Kurniali PC, Al-Janadi A, Hrinczenko B. Adjuvant chemotherapy for stage II colon cancer: a clinical dilemma. *J Oncol Pract*. 2017;13(4):233-241. doi:10.1200/JOP.2016.017210

5. Baxter NN, Kennedy EB, Bergsland E, et al. Adjuvant therapy for stage II colon cancer: ASCO guideline update. *J Clin Oncol*. 2022;40(8):892-910. doi:10.1200/JCO.21.02538

6. Enofe N, Morris AD, Liu Y, et al. Receipt of adjuvant chemotherapy in stage II colon cancer and overall survival: a national cancer database study. *J Surg Res*. 2020;252:69-79. doi:10.1016/j.jss.2020.02.016

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7. Kneuertz PJ, Chang GJ, Hu CY, et al. Overtreatment of young adults with colon cancer: more intense treatments with unmatched survival gains. *JAMA Surg*. 2015;150(5):402-409. doi:10.1001/jamasurg.2014.3572

8. Schrag D, Rifas-Shiman S, Saltz L, Bach PB, Begg CB. Adjuvant chemotherapy use for Medicare beneficiaries with stage II colon cancer. *J Clin Oncol*. 2002;20(19):3999-4005. doi:10.1200/JCO.2002.11.084

9. Dasari A, Morris VK, Allegra CJ, et al. ctDNA applications and integration in colorectal cancer: an NCI Colon and Rectal-Anal Task Forces whitepaper. *Nat Rev Clin Oncol*. 2020;17(12):757-770. doi:10.1038/s41571-020-0392-0

10. Tie J, Wang Y, Tomasetti C, et al. Circulating tumor DNA analysis detects minimal residual disease and predicts recurrence in patients with stage II colon cancer. *Sci Transl Med*. 2016;8(346):346ra92. doi:10.1126/scitranslmed.aaf6219

11. Tie J, Cohen JD, Lahouel K, et al; DYNAMIC Investigators. Circulating tumor DNA analysis guiding adjuvant therapy in stage II colon cancer. *N Engl J Med*. 2022;386(24):2261-2272. doi:10.1056/NEJMoa2200075

12. Kotani D, Oki E, Nakamura Y, et al. Molecular residual disease and efficacy of adjuvant chemotherapy in patients with colorectal cancer. *Nat Med*. 2023;29(1):127-134. doi:10.1038/s41591-022-02115-4

13. McGarvey N, Gitlin M, Fadli E, Chung KC. Increased healthcare costs by later stage cancer diagnosis. *BMC Health Serv Res*. 2022;22(1):1155. doi:10.1186/s12913-022-08457-6

14. Murphy-Barron C, Pyenson B, Ferro C, Emery M. Comparing the demographics of enrollees in Medicare Advantage and fee-for-service Medicare. *Milliman*. 2020.

15. Jiao X, Hay JW, Sadeghi S, Barzi A. Outcomes and utilization of adjuvant chemotherapy for stage II colon cancer in the oxaliplatin period: a SEER-medicare analysis. *Am J Clin Oncol*. 2020;43(6):428-434. doi:10.1097/COC.0000000000000684

16. Wang X, Frohlich MM, Chu E. Suboptimal completion rates, adverse events, costs, resource utilization, and cost impact of noncompletion in oral adjuvant capecitabine-based chemotherapy in patients with early-stage colon cancer. *Clin Colorectal Cancer*. 2021;20(4):e215-e225. doi:10.1016/j.clcc.2021.05.002

17. Chu E, Schulman KL, McKenna EF Jr, Cartwright T. Patients with locally advanced and metastatic colorectal cancer treated with capecitabine versus 5-fluorouracil as monotherapy or combination therapy with oxaliplatin: a cost comparison. *Clin Colorectal Cancer*. 2010;9(4):229-237. doi:10.3816/CCC.2010.n.034

18. MDSave. Accessed December 15, 2023. https://www.mdsave.com/procedures/port-a-cath-removal/d583f8cf

19. Ou FS, Walden DJ, Larson JJ, et al. Changes in prescribing patterns in stage III colon cancer. *J Natl Compr Canc Netw*. 2023;21(8):841-850.e4. doi:10.6004/jnccn.2023.7028

20. Mukkamalla SKR, Huynh DV, Somasundar PS, Rathore R. Adjuvant chemotherapy and tumor sidedness in stage II colon cancer: analysis of the National Cancer Data Base. *Front Oncol*. 2020;10:568417. doi:10.3389/fonc.2020.568417

21. U.S. Bureau of Labor Statistics. Consumer price index for all urban consumers: medical care in U.S. city average [CPIMEDSL], retrieved from FRED, Federal Reserve Bank of St. Louis. Accessed November 8, 2023. https://fred.stlouisfed.org/series/CPIMEDSL

22. Trish E, Ginsburg P, Gascue L, Joyce G. Physician reimbursement in medicare advantage compared with traditional medicare and commercial health insurance. *JAMA Intern Med*. 2017;177(9):1287-1295. doi:10.1001/jamainternmed.2017.2679

23. Iveson TJ, Sobrero AF, Yoshino T, et al. Duration of adjuvant doublet chemotherapy (3 or 6 months) in patients with high-risk stage II colorectal cancer. *J Clin Oncol*. 2021;39(6):631-641. doi:10.1200/JCO.20.01330

24. Douglas MP, Ragavan MV, Chen C, et al. Private payer and medicare coverage policies for use of circulating tumor DNA tests in cancer diagnostics and treatment. *J Natl Compr Canc Netw*. 2023;21(6):609-616.e4. doi:10.6004/jnccn.2023.7011

25. Yabroff KR, Sylvia Shi K, Zhao J, et al. Importance f patient health insurance coverage and out-of-pocket costs for genomic testing in oncologists' treatment decisions. *JCO Oncol Pract*. 2024;20(3):429-437. doi:10.1200/OP.23.00153

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26. Yabroff KR, Zhao J, de Moor JS, et al. Factors associated with oncologist discussions of the costs of genomic testing and related treatments. *J Natl Cancer Inst*. 2020;112(5):498-506. doi:10.1093/jnci/djz173

27. Mahuron KM, Fong Y. Applications of liquid biopsy for surgical patients with cancer: a review. *JAMA Surg*. 2024;159(1):96-103. doi:10.1001/jamasurg.2023.5394

28. To YH, Gibbs P, Tie J, Loree J, Glyn T, Degeling K. Circulating tumour DNA guided adjuvant chemotherapy decision making in stage II colon cancer-a clinical vignette study. *Cancers (Basel)*. 2023;15(21):5227. doi:10.3390/cancers15215227

29. Kasi PM, Rivero S, Aushev VN, et al. Patient-reported outcomes from the BESPOKE CRC study. *J Clin Oncol*. 2024;42(3). doi:10.1200/JCO.2024.42.3_suppl.54

30. Hung A, Lugo A, Mullins CD. Modeling the budgetary impact of payer utilization management strategies: an adapted framework based on lessons learned. *J Manag Care Spec Pharm*. 2019;25(8):922-926. doi:10.18553/jmcp.2019.25.8.922

31. To YH, Degeling K, Kosmider S, et al. Circulating tumour DNA as a potential cost-effective biomarker to reduce adjuvant chemotherapy overtreatment in stage II colorectal cancer. *Pharmacoeconomics*. 2021;39(8):953-964. doi:10.1007/s40273-021-01047-0

SUPPLEMENT 1.

eTable 1. Proportion of colon cancer patients receiving adjuvant chemotherapy
eTable 2. Base-case budget impact in health plans with 1 million covered lives
eTable 3. Budget impact in health plans with 1 million covered lives with short duration of ACT
eFigure 1. The effect of adjuvant chemotherapy use rate in ctDNA-guided treatment on cost savings
eFigure 2. The effect of the cost of the ctDNA testing on cost savings

SUPPLEMENT 2.

Data Sharing Statement

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