# **ONCOPRE:** A new chemotherapy benefit prediction algorithm to assist treatment decision making

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**BACKGROUND:** Modern oncology is increasingly complex and clinical decision support tools (CDSTs) have become indispensable tools for helping physicians make correct treatment decisions and inform care. For colon cancer specifically, CDSTs such as Adjuvant! Online and Numeracy are frequently used by clinicians to estimate the benefits of adjuvant treatment. Existing CDSTs, however, have not been able to keep abreast of advancements in our understanding of colon cancer biology, such as the impact of microsatellite instability (MSI) or high risk features (HRF) in early-stage colon cancer. Existing CDSTs are also not optimized to run on mobile devices such as tablets and smartphones, and some rely on outdated technology such as Java.

**METHODS**: We present ONCOPRE, a chemotherapy benefit calculator for colon cancer that addresses the limitations of existing CDSTs. It predicts 5-year colon cancer outcomes based on epidemiological data and the results of landmark trials. To validate ONCOPRE's predictions, we will compare them with the predictions generated by existing CDSTs as well as real-world data from tertiary cancer centers in Canada.

**RESULTS**: ONCOPRE is able to predict the 5-year disease-free survival (DFS) and overall survival (OS) of colon cancer patients based on age, sex, tumor characteristics and other prognostic markers such as the presence of HRF, BRAF mutations, and MSI. Our predictions compare favorably with the outcomes of landmark trials and historical data. They are precise, generally more optimistic than historical data, and are able to handle a wider set of circumstances than existing CDSTs. We believe that these attributes make ONCOPRE the new benchmark in the area of CDSTs for colon cancer outcomes.

**CONCLUSION:** ONCOPRE represents a new CDST that can assist in treatment decision-making and patient counseling. We make the case that the next generation of CDSTs in oncology must take into account contemporary clinical, biochemical, and genetic risk factors as these elements significantly affect outcomes. The ONCOPRE platform serves as a potential model on which to develop prediction tools for other forms of cancers. It is freely accessible at http://www.oncopre.com/. See site for references.



### FIGURE 1: The inputs and outputs of the ONCOPRE application





# ONCOPRE ()

## FIGURE 2: Screenshots of the ONCOPRE application as seen on a desktop PC (accessible at http://www.oncopre.com/)

		ONCOPRE 🔾	
Chemotherapy benefit prediction model for colon cancer	Chemotherapy benefit prediction model for colon cancer	Chemotherapy benefit prediction model for colon cancer	
Calculator Calculator About terms	Calculator ABOUT TERMS	Calculator Calculator About Terms	
Patient demographics	Patient demographics	Patient demographics	
Patient's sex	Patient's current age Patient's sex	Patient's current age Patient's sex	
vu v maie v	ou v Mare v	ou viaie v	
TNM staging	TNM staging	TNM staging	
T, depth of invasion     N, nodal invasion       T3 (tumor is in the outermost layers of the colon)     N0 (no tumor is found in lymph nodes)	T, depth of invasion N, nodal invasion T3 (turnor is in the outermost layers of the colon) N0 (no turnor is found in lymph nodes)	T, depth of invasion     N, nodal invasion       T4a (tumor has breached the visceral peritoneum)     N2b (tumor is found in 7+ lymph nodes)	
M, metastatic disease	M, metastatic disease	M, metastatic disease	
M0 (there are no distant metastases)	M0 (there are no distant metastases)	M1a (turnor has spread to a distant organ or lymph node)	
Genetic markers of prognosis	Genetic markers of prognosis	Genetic markers of prognosis	
BRAF mutation status Microsatellite instability (MSI)	BRAF mutation status Microsatellite instability (MSI)	BRAF mutation status Microsatellite instability (MSI)	
Unknown 🗘 Unknown 🗘	Negative (better prognosis)	Unknown	
High-risk features for stage II	High-risk features for stage II	Metastatic disease treatment	
Unknown + High-risk features in stage II colon cancer include:	Two or more (worst prognosis)	Prior systemic treatment for metastatic disease PFS of 1st line palliative chemo < 6 months	
Bowel obstruction or perforation     Pre-operative CEA over 5 ng/ml	Bowel obstruction or perforation     Pre-operative CEA over 5 ng/ml	Progressed on 1st line systemic treatment    Not applicable	
Indeterminate or positive margins     Specimen has < 13 lymph nodes     Lymphovascular or PN invasion	indeterminate or positive margins     Specimen has < 13 lymph nodes     Lymphovascular or PN invasion	Metastatic prognostic markers	
Poorly differentiated histology     Signet ring or mucinous tumor	Poorly differentiated histology     Signet ring or mucinous tumor	Right-sided tumor ECOG ≥ 2	
T4 primary	• T4 primary	Yes (worse prognosis)     Image: No (better prognosis)	
		Histology that is poorly differentiated Peritoneal metastases	
		No (better prognosis)   No (better prognosis)	
Results	Results	LDH ≥ 400 IU/L	
The patient is male, 60 years old, and with <b>stage 2a</b> colon cancer, <b>pT3 N0 M0</b> .	The patient is male, 60 years old, and with stage 2a colon cancer, pT3 N0 M0.		
The benefit of adjuvant chemotherapy for stage 2a disease is relatively small in the absence of high-risk features. Given the potential	The benefit of adjuvant chemotherapy for stage 2a disease is relatively small in the absence of high-risk features. Given the potential		
averse energy of demonstrately, the decision of give adjuvant directionerapy must be considered on a case-by-case basis. This patient does not have an identified high risk feature, which positively affects prognosis.	ablesse elects or chemoterapy, the decision to give adjuvant chemoterapy must be considered on a case-by-case basis. This patient has one or more high risk features, which adversely affects prognosis. The benefit of adjuvant chemotherapy is believed to be more significant for patients with bird risk features.	Results	
5-year OS for a healthy person (no cancer)		The patient is male, 60 years old, and with <b>stage 4a</b> colon cancer, <b>pT4a N2b M1a</b> .	
96% 5-year 0S	5-year OS for a healthy person (no cancer)	Outcomes for patients with metastatic colon cancer have significantly improved over the past 10 years due to advances in systemic	
If this patient is healthy and has never been diagnosed with cancer or any other life-limiting illnesses, his chances of being alive in 5	96% 5-year OS	and surgical treatments. Factors that adverse impact outcomes for patients with metastatic colon cancer include: disease progression through multiple lines of palliative chemotherapy, having a right-sided primary tumor, poor ECOG performance status, product differentiated bitategress, having a patient product on a destructed to be added t	
years is about 96%, based on his age and sex alone. This survival model is based on recent data from Canada, and is comparable to the life expectancies of healthy people in highly developed countries in Asia and Europe.	If this patient is healthy and has never been diagnosed with cancer or any other life-limiting illnesses, his chances of being alive in 5 years is about 96%, based on his age and sex alone. This survival model is based on recent data from Canada, and is comparable to	poony unerentiated histology, naving perioriear netastases, and an elevated LDH.	
5-year OS and DFS without chemotherapy	the life expectancies of healthy people in highly developed countries in Asia and Europe.	5-year OS for a healthy person (no cancer)	
82% 5.000	5-year OS and DFS without chemotherapy	96% 5-year OS	
OZ 70 5-year OS	51% 5-year OS	If this patient is healthy and has never been diagnosed with cancer or any other life-limiting illnesses, his chances of being alive in 5 years is about 96%, based on his age and sex alone. This survival model is based on recent data from Canada, and is comparable to the life supercharge of bashbu cancel is blobble directioned and the foregoent data from Canada, and is comparable to the life supercharge of bashbu cancel is blobble directioned and the foregoent data from Canada.	
75% Swear DES	Without adjuvant chemotherapy, we expect this patient to have a 5-year overall survival (OS) of about 51%.	the line expectationes of nearby people in highly developed countries in Asia and Europe.	
Without adjuvant chemotherapy, we expect this patient to have a 5-year disease-free survival (DFS) of about 75%.	34% 5-year DFS	OS with optimal treatment	
	Without adjuvant chemotherapy, we expect this patient to have a 5-year disease-free survival (DFS) of about 34%.	population of patients with metastatic disease (in blue).	
5-year US and DFS with chemotherapy	5-year OS and DFS with chemotherapy	68% 1-year OS, 17 months median OS	
	FOLFOX OR CAPOX	Overall survival (0S) visualization	
OO /o 5-year US	76% 5-year OS	80	
83% 5-year DFS	67% Ever DES	80	
Adjuvant FOLFOX or CAPOX is predicted to improve 5-year OS by 6% and 5-year DFS by 8%.	Adjuvant FOLFOX or CAPOX is predicted to improve 5-year OS by 25% and 5-year DES by 33%.	70	
CAPECITABINE (CAPE) OR 5-FU WITH LEUCOVORIN (5-FU/LV)	CAPECITABINE (CAPE) OR 5-FU WITH LEUCOVORIN (5-FU/LV)	60	
85% 5-year OS	66% 5-year OS	50	
78% 5-year DFS	569	40	
Adjuvant capecitabine (CAPE) or 5-FU with leucovorin (5-FU/LV) is predicted to improve 5-year OS by 3% and 5-year DFS by 3%.	30% 5-year DFS	20	
studies have demonstrated that capecitable is non-interior to 5-FU with leucovorin and offer similar outcomes. However, please note that single-agent and combination adjuvant chemotherapy regimens are not always clinically interchangeable.	Adjuvant capecitabine (CAPE) or 5-FU with leucovorin (5-FU/LV) is predicted to improve 5-year OS by 15% and 5-year DFS by 22%. Studies have demonstrated that capecitabine is non-inferior to 5-FU with leucovorin and offer similar outcomes. However, please	10	
	note that single-agent and combination adjuvant chemotherapy regimens are not always clinically interchangeable.		
		rousey i years a years a years a years o years o years o years 7 years a years o years 10 years	
<b>3A.</b> Predictions for a 60-year-old male	<b>3B.</b> Predictions for a 60-year-old male	<b>3C.</b> Predictions for a 60-year-old male	
	=	-	

patient with stage IIA colon cancer and no high-risk features, demonstrating minimal benefit of chemotherapy



-old male patient with metastatic disease after progression on 1<sup>st</sup> line palliative chemo, with median OS and curve

### FIGURE 3: Devices compatible with ONCOPRE and system requirements

Desktop computers (any operating system) • thin clients (any operating system) • tablets (iOS, Android) • smartphones (iOS, Android) • a modern browser (Firefox, Chrome, Safari) with JavaScript is required to run ONCOPRE

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## FIGURE 4: Key assumptions and linear regression models that form the basis of ONCOPRE predictions



Each dot represents a hazard ratio extrapolated from a clinical tria

## FIGURE 5: ONCOPRE algorithm pipeline in detail



#### FIGURE 6: validation studies

Р	ATIENT CH	ARACTER	ISTICS	AJCC	ACCENT	ONC	OPRE
Age	Gender	Stage	TNM	5-year OS	5-year OS	5-year OS	5-year DFS
60	Male	1	T1 N0 M0	93%	n/a	92%	92%
60	Male	2a	T3 N0 M0	85%	n/a	88%	83%
60	Male	2b	T4a N0 M0	72%	n/a	81%	73%
60	Male	2c	T4b N0 M0	37%	n/a	62%	52%
60	Male	3a	T2 N1a M0	83%	90%	87%	82%
60	Male	3b	T3 N2a M0	64%	75%	77%	69%
60	Male	3c	T3 N2b M0	44%	68%	66%	52%
60	Male	4	Tx Nx M1a	8%	n/a	n/a	n/a

Parameters for ACCENT stage III calculator: age of 60, caucasian, male, BMI of 26, ECOG of 0, tumor grade moderately differentiated, 14 lymph nodes, single tumor, left-sided tumor, FOLFOX.

Awaiting further validation with outcomes data from the BC Cancer Agency Gastrointestinal Cancer Outcomes Unit (GICOU) database







Multiplier	HR (OS)
0.65	-
0.58	3.83
0.58	1.93
0.71	1.67
0.71	1.23

vival (stages II and III)				
	y = 12.603	3x - 7.0993		
G				
1%	80%	100%		

