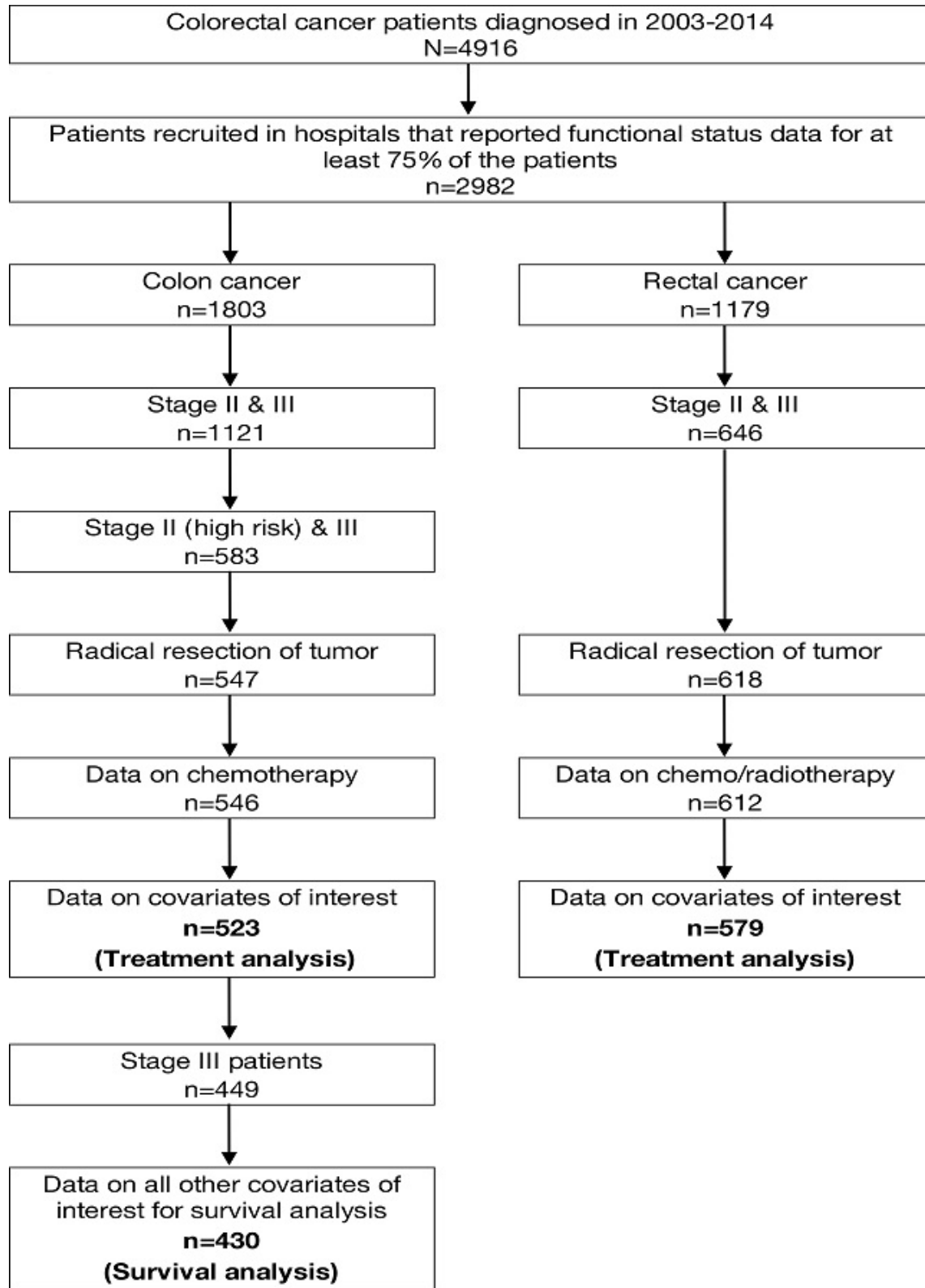


Supplementary materials

Supplementary Figure 1 Flow diagram showing selection of the analytic samplez



**Supplementary Table 1** Definition and frequency of comorbidities in the Charlson comorbidity index

Comorbidities	ICD-10 codes used	n	%	Charlson's weight
Myocardial infarction	I21.1, I21.3, I21.4, I21.9, I22, I23, I25.1, I25.2, I25.6	86	7.8	1
Congestive heart failure	I11.0, I13.0, I13.2, I50, I50.0, I50.1, I50.3, I50.4, I50.9	47	4.3	1
Peripheral vascular disease	I70, I71, I72, I73, I77, K55	82	7.4	1
Stroke & hemi/paraplegia		62	5.6	
Stroke <sup>1</sup>	G45, G46, I60 – I69, Z86.7	60		1
Hemi/paraplegia <sup>1</sup>	G11.4, G80, G81, G82, G83, I69.05	2		2
COPD	J40 – J47, J60 – J70, J84.1, J92, J96.1, 98.2, J98.3, I27.8, I27.9	80	7.3	1
Chronic renal disease	N01 – N05, N07, N11, N17 – N19, N25, I12.0, I13.1, I13.2, Z49, Z94.0, Z99.2	80	7.3	2
Chronic liver disease		62	5.6	
Mild <sup>1</sup>	K70 – K76, B18	62		1
Moderate-severe <sup>1</sup>	K70.4, K71.1, K72.1, K72.9, K76.7, B15, B16, B19, Z94.4	0		3
Diabetes mellitus		214	18.6	
Without complications <sup>1</sup>	E10.x – E14.x (where x = 0, 1 or 9)	196		1
With complications <sup>1</sup>	E10.x – E14.x (where x = 2, 3, 4, 5, 6, 7 or 8)	9		2
Gastric/duodenal ulcer	K25 – K28	5	0.5	1
Rheumatoid disease	M05, M06, M08, M30 – M36	5	0.5	1
Dementia	F00, F01, F02, F03, F05.1, G30, G30.9, G31.1	8	0.7	1
Non-colorectal cancer (except basal skin carcinoma)	C00–C17, C21–C26, C30–C34, C37– C41, C43, C45–C58, C60– C76, C81–C85, C88, C90–C97, Z85.x (where x =0, 2, 3, 4, 5, 6 or 8)	104	9.4	2
Charlson comorbidity index (CCI) score*				
Median (range)		0 (0-8)		
CCI 0		585	53.1	
CCI 1		215	19.5	
CCI 2		156	14.2	
CCI 3+		146	13.2	

ICD, International Statistical Classification of Diseases; COPD, Chronic obstructive pulmonary disease

\*HIV/AIDS did not contribute to the comorbidity scoring because none of the patients had this comorbid condition

<sup>1</sup>Are mutually exclusive (when both were present, the one with higher Charlson's weight was considered)

**Supplementary Table 2** Comorbidity and treatment patterns according to tumor stage

	Colon cancer (II* & III)			Rectal cancer (stage II & III)					
	Adjuvant chemotherapy			Neoadjuvant CRT			Adjuvant Chemotherapy		
	n	%	OR <sup>†</sup> (95% CI)	n	%	OR <sup>†</sup> (95% CI)	n	%	OR <sup>†</sup> (95% CI)
<b>Stage</b>			<i>p</i> <sub>interaction</sub> =0.531			<i>p</i> <sub>interaction</sub> =0.904			<i>p</i> <sub>interaction</sub> =0.755
<b>II</b>									
CCI 0	23	62.2	Ref <sup>1</sup>	30	28.6	Ref	40	38.1	Ref
CCI 1	2	18.2	<b>0.14 (0.03-0.72)</b>	11	25.0	0.67 (0.21-2.14)	13	29.6	1.13 (0.47-2.69)
CCI ≥2	2	7.7	<b>0.05 (0.01-0.25)</b>	11	15.5	0.62 (0.20-1.87)	20	28.2	1.19 (0.55-2.57)
<b>III</b>									
CCI 0	203	86.8	Ref	103	49.3	Ref	164	78.5	Ref
CCI 1	60	62.5	<b>0.45 (0.23-0.89)</b>	25	39.1	<b>0.42 (0.18-0.98)</b>	44	68.8	0.78 (0.38-1.57)
CCI ≥2	66	55.5	<b>0.37 (0.20-0.71)</b>	31	36.1	0.57 (0.26-1.24)	57	66.3	0.78 (0.40-1.52)

CRT, Chemoradiotherapy; OR, Odds ratio; CI, Confidence interval; CCI, Charlson comorbidity index score

<sup>†</sup>Adjusted for age, sex, tumor grade, number of lymph nodes examined, years of school education, having a partner, year of diagnosis, surgical technique, surgical volume, functional status and functional status assessment time (backward elimination of covariates with *p*>0.5; age, sex and functional status were forced into the model)

<sup>1</sup>Crude estimates

Statistically significant results are highlighted in bold

**Supplementary Table 3** Association of chemotherapy use with survival outcomes in stage III patients stratified by body mass index (BMI, kg/m<sup>2</sup>) at colon cancer diagnosis

BMI <sup>†</sup>	Outcomes	Chemo	<i>n</i>	<i>e</i>	HR* (95% CI)	<i>p</i> <sub>interaction</sub>
18.5-24.9	OS	No	49	29	Ref	
		Yes	123	36	0.80 (0.55-1.16)	
25+	OS	No	59	32	Ref	0.773
		Yes	192	60	0.75 (0.55-1.02)	
18.5-24.9	DSS	No	49	13	Ref	
		Yes	123	25	0.76 (0.44-1.30)	
25+	DSS	No	59	13	Ref	0.712
		Yes	192	38	0.81 (0.54-1.21)	

BMI, Body mass index ; Chemo, received adjuvant chemotherapy; *e*, Number of events; HR, Hazard ratio; CI, Confidence interval; *n*, Number at risk; OS, Overall survival; DSS, Disease-specific survival

<sup>†</sup>Patients with underweight (<18.5kg/m<sup>2</sup>, n=7) were excluded

\*Estimates are from propensity scores analysis and included age, sex, having a partner, years of school education, smoking status, lifetime physical activity, lifetime alcohol consumption, N-stage, T-stage, surgical technique and surgical volume, Charlson comorbidity scores, functional status and functional status assessment time

**Supplementary Table 4** Comparison of estimates for chemotherapy benefits from various propensity score methods in stage III colon cancer patients

Outcomes	Chemo	PS weighting		PS adjustment
		Original weight HR* (95% CI)	Truncated weight <sup>1</sup> HR* (95% CI)	HR* (95% CI)
OS	No	Ref		Ref
	Yes	<b>0.73 (0.58-0.92)</b>	<b>0.65 (0.52-0.83)</b>	<b>0.64 (0.43-0.97)</b>
DSS	No	Ref		Ref
	Yes	0.77 (0.56-1.06)	<b>0.71 (0.51-0.97)</b>	0.72 (0.40-1.29)
nDSS	No	Ref		Ref
	Yes	<b>0.66 (0.46-0.92)</b>	<b>0.59 (0.42-0.83)</b>	<b>0.51 (0.28-0.91)</b>
nDSS for <75 years	No	Ref	Ref	Ref
	Yes	<b>0.33 (0.17-0.63)</b>	<b>0.29 (0.15-0.54)</b>	<b>0.31 (0.10-0.93)</b>
nDSS for 75+ years	No	Ref	Ref	Ref
	Yes	1.05 (0.69-1.59)	1.05 (0.69-1.59)	0.69 (0.36-1.32)

Chemo, received adjuvant chemotherapy; HR, Hazard ratio; CI, Confidence interval; OS, Overall survival; DSS, Disease-specific survival; nDSS, Non-disease-specific survival

<sup>1</sup>Weight truncated at the 99<sup>th</sup> percentile of the chemotherapy non-recipients

\*Propensity scores were calculated from age, sex, having a partner, years of school education, body mass index, smoking status, lifetime physical activity, lifetime alcohol consumption, N-stage, T-stage, surgical technique and surgical volume, Charlson comorbidity scores, functional status and functional status assessment time (statistically significant results are highlighted in bold)

**Supplementary Table 5** Association of chemotherapy use with survival outcomes, accounted for immortal time bias and competing events

Outcome	Chemotherapy	Propensity score weighting	Accounted for immortal time bias	Accounted for competing events
		HR <sup>1</sup> (95% CI)	HR <sup>2</sup> (95% CI)	sHR <sup>3</sup> (95% CI)
OS	No	Ref	Ref	
	Yes	<b>0.73 (0.58-0.92)</b>	<b>0.75 (0.60-0.95)</b>	--
DSS	No	Ref	Ref	Ref
	Yes	0.77 (0.56-1.06)	0.78 (0.57-1.07)	0.83 (0.61-1.13)
nDSS	No	Ref	Ref	Ref
	Yes	<b>0.66 (0.46-0.92)</b>	<b>0.70 (0.50-1.00)</b>	0.73 (0.53-1.01)

HR, Hazard ratio; CI, Confidence interval; sHR, Subdistribution hazard ratio; OS, Overall survival; DSS, Disease-specific survival; nDSS, Non-disease-specific survival

<sup>1</sup>Propensity score was calculated from age, sex, having a partner, years of school education, body mass index, smoking status, lifetime physical activity, lifetime alcohol consumption, N-stage, T-stage, tumor grade, number of examined lymph nodes, surgical volume, surgical technique, Charlson comorbidity scores, functional status and functional status assessment time

<sup>2</sup>Model 1 accounted for immortal time bias

<sup>3</sup>Model 1 accounted for competing events, using the Fine and Gray model

Statistically significant results are highlighted in bold

**Supplementary Table 6** Frequency of mortality incidents from causes other than colon cancer

Cause of death	N	%	Chemotherapy		No chemotherapy	
			n	%	n	%
Cardiovascular incidents	27	39.1	9	27.3	18	50.0
<i>Cardiac problems</i>	14					
<i>Vascular</i>	8					
<i>Cerebrovascular (stroke)</i>	3					
<i>Hematologic problems</i>	2					
Other cancers	20	29.0	15	45.5	5	13.9
<i>Pulmonary</i>	4					
<i>Gastrointestinal</i>	6					
<i>Urinary</i>	3					
<i>Reproductive</i>	2					
<i>Hematologic</i>	2					
<i>Other sites or unspecified</i>	3					
Pulmonary problems	9	13.0	2	6.0	7	19.4
<i>COPD</i>	4					
<i>Embolus/bronchitis/pneumonia</i>	5					
Gastrointestinal problems	3	4.3	2	6.0	1	2.8
Parkinson disease	1	1.5	0	0.0	1	2.8
Renal failure	2	2.9	2	6.0	0	0.0
Sepsis	1	1.5	0	0.0	1	2.8
Others	6	8.7	3	9.1	3	8.3
<b>Total</b>	<b>69</b>		<b>33</b>		<b>36</b>	

COPD, Chronic obstructive pulmonary disease