

## Supplementary Online Content

Dossa F, Acuna SA, Rickles AS, et al. Association between adjuvant chemotherapy and overall survival in patients with rectal cancer and pathological complete response after neoadjuvant chemotherapy and resection. *JAMA Oncol*. Published online April 19, 2018. doi:10.1001/jamaoncol.2017.5597

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Codes Used for Cohort Development

ICD-O-3 Morphologic Codes	
8140	Adenocarcinoma, NOS
8144	Adenocarcinoma, intestinal type
8210	Adenocarcinoma in adenomatous polyp
8211	Tubular adenocarcinoma
8213	Serrated adenocarcinoma
8221	Adenocarcinoma in multiple adenomatous polyps
8261	Adenocarcinoma in villous adenoma
8262	Villous adenocarcinoma
8263	Adenocarcinoma in tubulovillous adenoma
Resectional surgery codes	
30	Wedge or segmental resection, partial proctectomy, NOS Includes: anterior resection, Hartmann's operation, low anterior resection, transsacral rectosigmoidectomy
40	Pull through with sphincter preservation (coloanal anastomosis)
50	Total proctectomy Includes: abdominoperineal resection
60	Total proctocolectomy, NOS
70	Proctectomy or proctocolectomy with resection in continuity with other organs; pelvic exenteration
80	Proctectomy, NOS

**eTable 2.** Baseline Characteristics Before and After Propensity Score Matching

Characteristic	Before matching			After matching		
	No Adjuvant Treatment n = 1,775	Adjuvant Treatment n = 680	Standardized Differences	No Adjuvant Treatment n = 667	Adjuvant Treatment n = 667	Standardized Differences
<i>Patient Characteristics</i>						
Age, median years (IQR)	61 (52-70)	57 (49-65)	-0.34	56 (49-65)	57 (49-65)	0.006
Sex, n (%)			0.11			-0.03
Male	1,088 (61.3)	381 (56.0)		370 (55.5)	379 (56.8)	
Female	687 (38.7)	299 (44.0)		297 (44.5)	288 (43.2)	
Race, n (%)			0.06			0.04
White	1,546 (87.1)	597 (87.8)		591 (88.6)	585 (87.7)	
Black	129 (7.3)	40 (5.9)		39 (5.9)	40 (6.0)	
Other	91 (5.1)	40 (5.9)		35 (5.3)	39 (5.9)	
Ethnicity, n (%)			0.05			0.02
Not Hispanic	1,592 (89.7)	610 (89.7)		598 (89.7)	599 (89.8)	
Hispanic	100 (5.6)	33 (4.9)		36 (5.4)	33 (5.0)	
Insurance status, n (%)			0.27			0.06
Uninsured	59 (3.3)	21 (3.1)		23 (3.5)	21 (3.2)	
Private	911 (51.3)	433 (63.7)		421 (63.1)	422 (63.3)	
Medicaid	97 (5.5)	35 (5.2)		38 (5.7)	35 (5.3)	
Medicare	666 (37.5)	176 (25.9)		173 (25.9)	174 (26.1)	
Area of residence, n (%)			0.14			0.08
Not metropolitan	307 (17.3)	131 (19.3)		137 (20.5)	131 (19.6)	
Metropolitan	1,417 (79.8)	542 (79.7)		530 (79.5)	534 (80.1)	
Median Income, n			0.07			0.02

(%)						
<\$38,000	283 (15.9)	107 (15.7)		106 (15.9)	107 (16.0)	
\$38,000- \$47,999	403 (22.7)	138 (20.3)		140 (20.1)	137 (20.5)	
\$48,000 – \$62,999	476 (26.8)	188 (27.7)		186 (27.9)	184 (27.6)	
\$63,000+	594 (33.5)	242 (35.6)		235 (35.2)	239 (35.8)	
No high school education <sup>†</sup> , <i>n</i> (%)			0.13			0.05
>21%	277 (15.6)	92 (13.5)		101 (15.1)	92 (13.8)	
13-20.9%	454 (25.6)	158 (23.2)		160 (24.0)	157 (23.5)	
7-12.9%	584 (32.9)	219 (32.2)		217 (32.5)	217 (32.5)	
<7%	442 (24.9)	206 (30.3)		189 (28.3)	201 (30.1)	
Charlson- Deyo Comorbidity Score, <i>n</i> (%)			0.09			0.02
0	1,401 (78.9)	560 (82.4)		544 (81.6)	547 (82.0)	
1	303 (17.1)	100 (14.7)		101 (15.1)	100 (15.0)	
≥2	71 (4.0)	20 (2.9)		22 (3.3)	20 (3.0)	
<i>Facility Characteristics</i>						
Facility type, <i>n</i> (%)			0.07			0.02
Community cancer program	892 (50.3)	318 (46.8)		316 (47.4)	314 (47.1)	
Not community cancer program	794 (44.7)	322 (47.4)		309 (46.3)	314 (47.1)	
Distance to facility,	12.1 (5.5-	13.6 (6.2-	0.03	13.0 (5.9-	13.7 (6.2-	0.01

<i>miles, median (IQR)</i>	29.8)	34.6)		31.6)	34.6)	
<i>Tumor Characteristics</i>						
Grade, <i>n (%)</i>			0.12			0.05
Well differentiated	119 (6.7)	32 (4.7)		30 (4.5)	32 (4.8)	
Moderately differentiated	1,064 (60.0)	439 (64.6)		419 (62.8)	430 (64.5)	
Poorly differentiated	107 (6.0)	45 (6.6)		41 (6.2)	43 (6.4)	
Missing	485 (27.3)	164 (24.1)		177 (26.5)	162 (24.3)	
Tumor size, <i>cm, n(%)</i>			0.23			0.05
<2	78 (4.4)	23 (3.4)		26 (3.9)	23 (3.5)	
2-4	367 (20.7)	177 (26.0)		169 (25.3)	170 (25.5)	
4-6	363 (20.5)	176 (25.9)		174 (26.1)	172 (25.8)	
>6	256 (14.4)	93 (13.7)		101 (15.1)	93 (13.9)	
Missing	711 (40.0)	211 (31.0)		197 (29.5)	209 (31.3)	
Clinical T stage, <i>n (%)</i>			0.17			0.02
1/2	199 (11.2)	62 (9.1)		59 (8.9)	60 (9.0)	
3/4	1,462 (82.4)	596 (87.7)		584 (87.6)	585 (87.7)	
Clinical N stage, <i>n (%)</i>			0.25			0.02
0	985 (55.5)	321 (47.2)		319 (47.8)	319 (47.8)	
1	647 (36.5)	319 (46.9)		311 (46.6)	309 (46.3)	
2	59 (3.3)	26 (3.8)		25 (3.8)	25 (3.8)	
Missing	84 (4.7)	14 (2.1)		12 (1.8)	14 (2.1)	

<i>Treatment Characteristics</i>						
Radiation dose, <i>n</i> (%)			0.15			0.08
4500	233 (13.1)	78 (11.5)		63 (9.5)	77 (11.5)	
5040	919 (51.8)	399 (58.7)		401 (60.1)	389 (58.3)	
5400	131 (7.4)	45 (6.6)		41 (6.2)	45 (6.8)	
Other	260 (14.7)	92 (13.5)		94 (14.1)	91 (13.6)	
Missing	232 (13.1)	66 (9.7)		68 (10.2)	65 (9.8)	
Time from end of radiation to surgery, <i>n</i> (%)			0.25			0.09
<5 weeks	103 (5.8)	45 (6.6)		36 (5.4)	45 (6.8)	
5-7 weeks	460 (25.9)	200 (29.4)		207 (31.0)	197 (29.5)	
7-9 weeks	511 (28.8)	233 (34.3)		214 (32.1)	228 (34.2)	
9-12 weeks	386 (21.8)	131 (19.3)		143 (21.4)	129 (19.3)	
>12 weeks	200 (11.3)	37 (5.4)		36 (5.4)	36 (5.4)	
Number of nodes examined, <i>n</i> (%)			0.16			0.03
<6	386 (21.8)	109 (16.0)		105 (15.7)	108 (16.2)	
6-11	469 (26.4)	176 (25.9)		164 (24.6)	172 (25.8)	
≥12	905 (50.7)	387 (56.9)		391 (58.6)	380 (57.0)	
Length of stay, median days ( <i>IQR</i> )	6 (5-8)	6 (4-7)	0.04	6 (4-8)	6 (4-7)	-0.08
30d unplanned readmission, <i>n</i> (%)			0.09			0.06
Yes	108 (6.1)	57 (8.4)		52 (7.8)	57 (8.5)	

No	1605 (90.4)	602 (88.5)		600 (90.0)	590 (88.5)	

† Represents percentage of adults within the patient's area of residence (based on zip code) that did not complete high school education

**eTable 3.** Sensitivity Analysis Evaluating the Sensitivity of Study Results to the Presence of Unmeasured Confounding

Estimates for the proportions of patients in each group with poor performance status and hazard ratio for the association between poor performance status and mortality were derived from the literature:

Estimate	Reference
Proportion of colorectal cancer patients who underwent surgery and exhibited ECOG $\geq 2$	
6%	Mathoulin-Pelissier et al. (2012)
11.5%	Dobbins et al. (2015)
Proportion of colorectal cancer patients with ECOG $\geq 2$ who received chemotherapy	
2.5-3.6%	Kabbinavar et al. (2005)
4.7-5.6%	Grothey et al. (2008)
4.2-7.8%	Giantonio et al. (2007)
Proportion of colorectal cancer patients with ECOG $\geq 2$ who did not receive chemotherapy	
10.3%	Grothey et al. (2008)
Hazard ratio for association between ECOG $\geq 2$ (vs. 0) and mortality (95% CI)	
1.60 (1.21-2.12)	Grothey et al. (2008)*
4.14 (1.56-10.95)	Ugolini et al. (2015)**

\* Based on multivariable Cox model

\*\* Based on univariable Cox model (study of patients >70 years old)

<b>Patients with poor performance status in the control group (%)</b>	<b>Patients with poor performance status in the treated group (%)</b>	<b>Hazard ratio for the association between poor performance status and mortality</b>	<b>Adjusted hazard ratio (95% confidence interval) for the association between adjuvant chemotherapy and mortality</b>
0	0	0	0.44 (0.28-0.70)
10	2.5	2.0	0.51 (0.35-0.77)
10	2.5	4.0	0.63 (0.47-0.89)
10	2.5	6.0	0.73 (0.57-0.99)
15	2.5	2.0	0.55 (0.40-0.82)
15	2.5	4.0	0.74 (0.58-1.00)
10	5	2.0	0.49 (0.33-0.75)
10	5	4.0	0.56 (0.40-0.82)
10	5	6.0	0.62 (0.46-0.88)
10	5	8.0	0.67 (0.51-0.93)
10	5	10.0	0.71 (0.55-0.97)
10	5	12.0	0.74 (0.58-1.00)
15	5	3.5	0.64 (0.48-0.90)
15	5	4.0	0.67 (0.51-0.93)
15	5	4.5	0.70 (0.54-0.96)



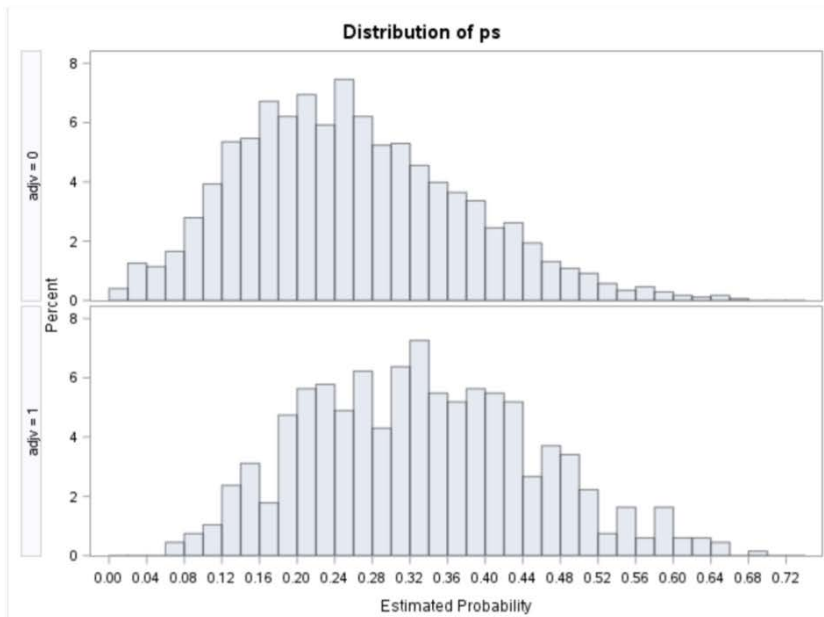
15	5	5.0	0.73 (0.57-0.99)
15	5	5.5	0.75 (0.59-1.01)

In this analysis, poor performance status was considered to be an unmeasured confounder that was more prevalent among the control group than the treated group and independently associated with overall survival. The proportions of patients with poor performance status in the control and treatment groups was varied, as was the hazard ratio for the association between poor performance status and mortality. Adjusted hazard ratios for the association between adjuvant chemotherapy and mortality were then calculated based on these values.

**eFigure.** Histograms Demonstrating the Distribution of Propensity Scores Among NonAdjuvant (upper panes) and Adjuvant (lower panes) Treated Patients

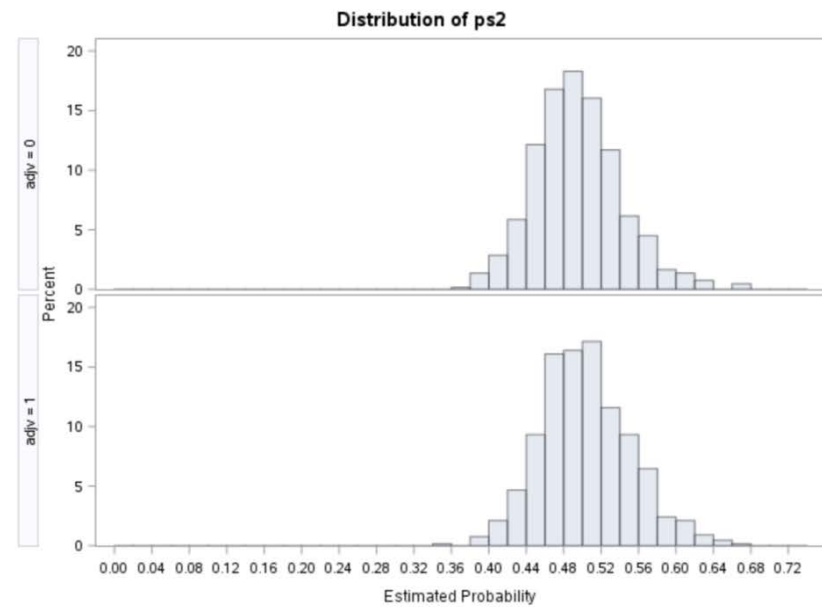
**A. Prior to propensity score matching**

a)



**B. After propensity score matching**

b)



Following propensity score matching, the distribution of propensity scores was similar between adjuvant and non-adjuvant treated patients, suggesting balance of covariates included in the propensity score model.