## **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.

ICD-O-3 Morp	hologic 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 1. Codes Used for Cohort Development

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

eTable 2. Baseline Characteristics Before and After Propensity Score Matching

$ \begin{array}{ c c c c c c c c c c c c c c c c c c c$	(%)						
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	<\$38.000	283	107		106	107	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		(15.9)	(15.7)		(15.9)	(16.0)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	\$38.000-	403	138		140	137	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	\$47.999	(22.7)	(20.3)		(20.1)	(20.5)	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	\$48,000 -	476	188		186	184	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	\$62,999	(26.8)	(27.7)		(27.9)	(27.6)	
30,0001  374  242  2.55  257    (33.5)  (35.6)  (35.2)  (35.8)  0.05    No high school education <sup>†</sup> , n (%)  0.13  0.13  0.05    >21%  277  92 (13.5)  101  92 (13.8)    (15.6)  (15.1)  (15.1)  100  (23.5)    7-12.9%  584  219  217  217    (32.9)  (32.2)  (32.5)  (32.5)  (32.5)     (24.9)  (30.3)  (28.3)  (30.1)    Charlson- Deyo Comorbidity Score, n (%)  0.09  22 (3.3)  201  0.02    1  303  100  101  100  101    11.  303  100  101  100  101    11.  303  100  101  100  101  100    12.1  14.01  260  22 (3.3)  20 (3.0)  100  101  100    12.1  14.01  20 (2.9)  22 (3.3)  20 (3.0)  100  101  100    12.1  14.01  20 (2.9)  22 (3	\$63.000±	594	242		235	239	
No high school education <sup>†</sup> , n (%)    (35.3)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (35.4)    (3	φ05,0001	(33.5)	(35.6)		(35.2)	(35.8)	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	No high	(33.5)	(33.0)	0.13	(33.2)	(33.0)	0.05
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	school			0.15			0.05
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	$education^{\dagger}$ n						
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	$\binom{0}{2}$						
$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	>21%	277	92 (13.5)		101	92 (13.8)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	>2170	(15.6)	)2(13.3)		(15.1)	)2 (13.0)	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	13 20 0%	(15.0)	158		160	157	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	13-20.970	(25.6)	(23.2)		(24.0)	(23.5)	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	7 12 00/	(23.0)	(23.2)		(24.0)	(23.3)	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	7-12.9%	384	(22.2)		(22.5)	(22.5)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	~70/	(32.9)	(32.2)		(32.3)	(32.3)	
Charlson- Deyo Comorbidity Score, $n$ (%)(30.3)(28.3)(30.1)01,4015600.090.090.0201,401560544547(78.9)(82.4)(81.6)(82.0)1303100101100(17.1)(14.7)(15.1)(15.0) $\geq 2$ 71 (4.0)20 (2.9)22 (3.3)20 (3.0) $\vdash$ $=$ $=$ $=$ $=$ Facility Characterist ics $=$ $=$ $=$ Facility type, $n$ (%) $=$ $=$ $=$ Not794322309314community cancer program $=$ $=$ $=$ Not794322309314community cancer $=$ $=$ $=$ program $=$ $=$ $=$ $=$ Distance to12.113.60.0313.013.70.01facility, concer(5.5-(6.2-(5.9-(6.2-	%</td <td>442</td> <td>206</td> <td></td> <td>189</td> <td>201</td> <td></td>	442	206		189	201	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $		(24.9)	(30.3)	0.00	(28.3)	(30.1)	0.02
Deyo Comorbidity Score, $n$ (%)Image: sector of the	Charlson-			0.09			0.02
Comorbidity Score, $n$ (%)Image: state of the state o	Deyo						
Score, $n$ (%)       0  1,401  560  544  547    (78.9)  (82.4)  (81.6)  (82.0)    1  303  100  101  100    (17.1)  (14.7)  (15.1)  (15.0)    ≥2  71 (4.0)  20 (2.9)  22 (3.3)  20 (3.0)    Facility	Comorbidity						
0  1,401  560  544  547    (78.9)  (82.4)  (81.6)  (82.0)    1  303  100  101  100    (17.1)  (14.7)  (15.1)  (15.0)    ≥2  71 (4.0)  20 (2.9)  22 (3.3)  20 (3.0)    Facility  -  -  -  -    Facility  -  -  -  -    Facility  -  -  -  -    Facility  -  0.07  -  0.02    type, n (%)  -  -  -  -  -    Not  794  322  309  314  -    community  (44.7)  (47.4)  (47.1)  -  -    not  794  322  309  314  -  -    community  (44.7)  (47.4)  (46.3)  (47.1)  -  -    program  -  -  -  -  -  -  -  -    Not  794  322  309  314  <	Score, $n(\%)$	1 404					
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	0	1,401	560		544	547	
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$		(78.9)	(82.4)		(81.6)	(82.0)	
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	1	303	100		101	100	
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		(17.1)	(14.7)		(15.1)	(15.0)	
Facility Characterist icsImage: constraint of the second se	≥2	71 (4.0)	20 (2.9)		22 (3.3)	20 (3.0)	
Facility Characterist ics  Image: Characterist ics							
Characterist ics  Image: Second system  Im	Facility						
icsImage: constraint of the second structureImage: constraint of the second structurerespectiverespectiverespectiver	Characterist						
Facility type, $n$ (%)Image: Constraint of the second straint of the second stra	ics						
type, $n$ (%)Image: second secon	Facility			0.07			0.02
892    318    316    314      Community    (50.3)    (46.8)    (47.4)    (47.1)      program    -    -    -    -      Not    794    322    309    314      community    (44.7)    (47.4)    (46.3)    (47.1)      cancer    -    -    -    -      program    -    -    -    -      Distance to    12.1    13.6    0.03    13.0    13.7    0.01      facility,    (5.5-    (6.2-    (5.9-    (6.2-    -    -	type, <i>n</i> (%)						
Community cancer  (50.3)  (46.8)  (47.4)  (47.1)    program  -  -  -  -  -    Not  794  322  309  314    community cancer  (47.4)  (46.3)  (47.1)    program  -  -  -  -    Distance to  12.1  13.6  0.03  13.0  13.7  0.01    facility,  (5.5-  (6.2-  (5.9-  (6.2-  -  -  -		892	318		316	314	
cancer  program  Image: cancer  Image: cancer  Image: cancer  309  314    Not  794  322  309  314    community  (44.7)  (47.4)  (46.3)  (47.1)    cancer  Image: cancer  Image: cancer  Image: cancer  Image: cancer    program  Image: cancer  Image: cancer  Image: cancer  Image: cancer    Distance to  12.1  13.6  0.03  13.0  13.7  0.01    facility,  (5.5-  (6.2-  (5.9-  (6.2-  1.1  1.	Community	(50.3)	(46.8)		(47.4)	(47.1)	
program    Image: scale of the sc	cancer						
Not community cancer    794 (44.7)    322 (47.4)    309 (46.3)    314 (47.1)      program	program						
community cancer  (44.7)  (47.4)  (46.3)  (47.1)    program  -  -  -  -  -    Distance to facility,  12.1  13.6  0.03  13.0  13.7  0.01	Not	794	322		309	314	
cancer    regram    regram <thre< th="">    regram    regram</thre<>	community	(44.7)	(47.4)		(46.3)	(47.1)	
program	cancer				Ì, í		
Distance to    12.1    13.6    0.03    13.0    13.7    0.01      facility,    (5.5-    (6.2-    (5.9-    (6.2- <td< td=""><td>program</td><td></td><td></td><td></td><td></td><td></td><td></td></td<>	program						
facility. (5.5- (6.2- (5.9- (6.2-	Distance to	12.1	13.6	0.03	13.0	13.7	0.01
	facility.	(5.5-	(6.2-		(5.9-	(6.2-	-

miles,	29.8)	34.6)		31.6)	34.6)	
median						
(IQR)						
Tumor						
Characterist						
ics						
Grade. <i>n</i> (%)			0.12			0.05
Well	119 (67)	32 (47)	0112	30 (4 5)	32 (4.8)	0100
differentiate	117 (017)	52(117)		55 (115)	02(110)	
d						
<u>u</u>	1.064	/39		<i>A</i> 19	430	
Moderately	(60.0)	(64.6)		(62.8)	(64.5)	
differentiate	(00.0)	(04.0)		(02.0)	(04.3)	
differentiate						
u Doorly	107 (6.0)	15 (6 6)		41 (6 2)	12 (6.1)	
POOLIY	107 (0.0)	43 (0.0)		41 (0.2)	45 (0.4)	
d .	405	164		177	1.0	
Missing	485	164			162	
	(27.3)	(24.1)	0.00	(26.5)	(24.3)	0.07
Tumor size,			0.23			0.05
cm, n(%)						
<2	78 (4.4)	23 (3.4)		26 (3.9)	23 (3.5)	
2-4	367	177		169	170	
	(20.7)	(26.0)		(25.3)	(25.5)	
4-6	363	176		174	172	
	(20.5)	(25.9)		(26.1)	(25.8)	
>6	256	93 (13.7)		101	93 (13.9)	
	(14.4)			(15.1)		
Missing	711	211		197	209	
	(40.0)	(31.0)		(29.5)	(31.3)	
Clinical T			0.17			0.02
stage, <i>n</i> (%)						
1/2	199	62 (9.1)		59 (8.9)	60 (9.0)	
	(11.2)	~ /			~ /	
3/4	1.462	596		584	585	
	(82.4)	(87.7)		(87.6)	(87.7)	
Clinical N	(02.1)	(0,11)	0.25	(07.0)	(0/11/)	0.02
stage $n(\%)$			0.20			0.02
0	985	321		319	319	
	(55 5)	(47.2)		(47.8)	(47.8)	
1	6/7	310		311	300	
1	(36.5)	(16.0)		(16.6)	(16.3)	
2	50 (2 2)	(+0.3)		(+0.0)	(+0.3) 25 (2 0)	
<u> </u>	37(3.3)	20(3.8)		23(3.0)	23(3.0)	
Iviissing	84 (4.7)	14 (2.1)		12(1.8)	14 (2.1)	

Treatment						
Characterist						
ics						
Radiation			0.15			0.08
dose, $n(\%)$						
4500	233	78 (11.5)		63 (9.5)	77 (11.5)	
1200	(13.1)	, (11.0)		00 (910)	,, (11.0)	
5040	919	399		401	389	
5010	(51.8)	(58.7)		(60.1)	(58.3)	
5400	(31.0)	45 (6 6)		41(62)	45 (6.8)	
Other	$\frac{131(7.4)}{260}$	92(13.5)		94(14.1)	91(13.6)	
Other	(14.7)	)2 (13.3)		)4 (14.1)	)1 (15.0)	
Missing	(14.7)	66 (0.7)		68 (10.2)	65(0.8)	
wiissnig	(12.1)	00 (9.7)		08 (10.2)	03 (9.8)	
Time from	(13.1)		0.25			0.00
and of			0.23			0.09
rediction to						
surgery, $n$						
( <i>70)</i>	102 (5.9)	15 (6 6)		26(5.4)	15 (6.9)	
<5 weeks	105 (5.8)	45 (0.0)		30 (5.4)	43 (0.8)	
5-7	460	200		207	197	
weeks	(25.9)	(29.4)		(31.0)	(29.5)	
7-9	511	233		214	228	
weeks	(28.8)	(34.3)		(32.1)	(34.2)	
9-12	386	131		143	129	
weeks	(21.8)	(19.3)		(21.4)	(19.3)	
>12	200	37 (5.4)		36 (5.4)	36 (5.4)	
weeks	(11.3)					
Number of			0.16			0.03
nodes						
examined, <i>n</i>						
(%)						
<6	386	109		105	108	
	(21.8)	(16.0)		(15.7)	(16.2)	
6-11	469	176		164	172	
	(26.4)	(25.9)		(24.6)	(25.8)	
≥12	905	387		391	380	
	(50.7)	(56.9)		(58.6)	(57.0)	
Length of	6 (5-8)	6 (4-7)	0.04	6 (4-8)	6 (4-7)	-0.08
stay, <i>median</i>						
days (IQR)						
30d			0.09			0.06
unplanned						
readmission,						
n (%)						
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)	

the partial 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 $\ge 2$ (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)

Patients with poor performance status	Patients with poor performance	Hazard ratio for the association	Adjusted hazard ratio (95%
in the control	status in the	between poor	confidence interval)
group (%)	treated group (%)	performance status	for the association
		and mortality	between adjuvant
			chemotherapy and
			mortality
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

b)

## A. Prior to propensity score matching

a)

## **B.** After propensity score matching



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.