

## Supplementary Online Content

Unger JM, Hershman DL, Fleury ME, Vaidya R. Association of Patient Comorbid Conditions With Cancer Clinical Trial Participation. *JAMA Oncology*. Published online January 10, 2018. doi:10.1001/jamaoncol.2018.5953

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

**eTable 1:** List of comorbid conditions

<b>Comorbid Conditions</b>
Heart attack
Heart failure
Coronary bypass surgery
Hypertension (high blood pressure)
Stroke or transient ischemic attack (TIA)
Poor kidney function
History of another type of cancer
Blood clots
Asthma
Emphysema, chronic bronchitis, or obstructive lung disease
Stomach ulcers or peptic ulcer disease
Diabetes
Moderate to severe arthritis
Alzheimer's disease or other dementia
Cirrhosis or serious liver damage
Hearing loss or impairment
Visual loss or impairment
Degenerative joint disease

**eQuestions: Clinical trial treatment decision-making questions**

**Question:** “Have you made a decision regarding treatment for your cancer in the past 3 months?”

**Response options: Yes vs. No**

*If response is “Yes”, the following question was asked: “In making your decision, did you discuss with your physician participation in a clinical trial as part of your treatment?”*

*<The following text was provided to describe a clinical trial>*

“What is a clinical trial?” Clinical trials are carefully controlled scientific research studies to test new treatments for people with cancer. The goal of this medical research is to find better ways to treat cancer and improve the lives of cancer patients. Clinical trials test the safety and potential benefits of new treatments before they are approved for widespread use. They investigate many types of approaches such as new drugs, new surgical or radiological procedures, and new ways to reduce the side effects of treatment. All medications, procedures, and treatments currently used were once investigated in clinical trials.”

**Response options: No vs. Yes, but not offered participation in a clinical trial vs. Yes, and was offered participation in a clinical trial**

*If response is “Yes, and was offered participation in a clinical trial”, the following question was asked: “Did you decide to participate in a clinical trial?”*

**Response options: Yes vs. No**

**eTable 2:** Sociodemographic and cancer characteristics of the cohort

<b>Patient Characteristics (N=5,499)</b>			
<b>Patient Factor</b>	Category	Number	Percent
<b>Age</b>	18-39	248	4.5
	40-64	4,052	73.7
	≥ 65	1,199	21.8
<b>Sex</b>	Female	3,420	62.2
	Male	2,079	37.8
<b>Race</b>	White	5,192	94.4
	African American	135	2.5
	Asian/Pacific Islander	62	1.1
	Native American	20	0.4
	Other	90	1.6
<b>Income</b>	< \$20,000	342	6.2
	\$20,000 - \$34,999	483	8.8
	\$35,000 - \$49,999	631	11.5
	\$50,000 - \$99,999	1,679	30.5
	≥ \$100,000	1,444	26.3
	Do not know	24	0.4
	Refused to answer	896	16.3
<b>Education</b>	≤ 8th grade	19	0.4
	Some high school	87	1.6
	High school diploma	554	10.1
	Some college	1,223	22.2
	2-year college degree	627	11.4
	4-year college degree	1,288	23.4
	Graduate school	1,701	30.9
<b>Cancer Type</b>	Breast	2,894	52.6
	Colorectal	408	7.4
	Lung	651	11.9
	Prostate	1,546	28.1

**eTable 3:** Prevalence of common disease conditions in study cohort versus U.S. population of similar age distribution

Condition	Study Cohort	U.S. population*	Age matching categories	Source
Arthritis**	15.3%	14.2%	18-34, 35-44, 45-54, 55-64, 65-74, 75-84, 85+	Hootman JM, Helmick CG, Barbour KE, Theis KA, Boring MA. Updated Projected Prevalence of Self-Reported Doctor-Diagnosed Arthritis and Arthritis-Attributable Activity Limitation Among US Adults, 2015-2040. <i>Arthritis Rheumatol.</i> 2016 Jul;68(7):1582-7.
Asthma	11.5%	8.5%	20-24, 35-34, 35-64, 65+	2016 National Health Interview Survey (NHIS) Data. Centers for Disease Control and Prevention. Most recent asthma data. Prevalence.
COPD	6.6%	4.6%	40-54, 55-70	Doney B, Hnizdo E, Syamlal G, Kullman G, Burchfiel C, Martin CJ, Mujuru P. Prevalence of chronic obstructive pulmonary disease among US working adults aged 40 to 70 years. <i>National Health Interview Survey data 2004 to 2011. J Occup Environ Med.</i> 2014 Oct;56(10):1088-93.
Diabetes	7.9%	9.7%	18-44, 45-64, 65+	Centers for Disease Control and Prevention. National diabetes statistics report, 2017. Estimates of diabetes and its burden in the United States. <a href="http://www.diabetes.org/assets/pdfs/basics/cdc-statistics-report-2017.pdf">http://www.diabetes.org/assets/pdfs/basics/cdc-statistics-report-2017.pdf</a>
Hearing	11.2%	13.4%	20-29, 30-39, 40-49, 50-59, 60-69	National Institute on Deafness and Other Communication Disorders. Hearing loss increases with age. <a href="https://www.nidcd.nih.gov/health/statistics/hearing-loss-increases-with-age">https://www.nidcd.nih.gov/health/statistics/hearing-loss-increases-with-age</a>
Heart failure	1.2%	3.1%	20-39, 40-59, 60-79, 80+	Mozzafarian D, Benjamin EJ, Go AS, et al. on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. <i>Circulation.</i> 2016;133:e38-e360. Chart 20-2.
Hypertension	35.0%	36.3%	18-39, 40-59, 65+	NCHS, National Health and Nutrition Examination Survey, 2015–2016; Hypertension Prevalence and Control Among Adults: United States, 2015–2016. <a href="https://www.cdc.gov/nchs/data/databriefs/db289_table.pdf#page=1">https://www.cdc.gov/nchs/data/databriefs/db289_table.pdf#page=1</a>
Stroke	2.3%	3.6%	20-39, 40-59, 60-79, 80+	Mozzafarian D, Benjamin EJ, Go AS, et al. on behalf of the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2016 update: a report from the American Heart Association. <i>Circulation.</i> 2016;133:e38-e360. Chart 14-1.

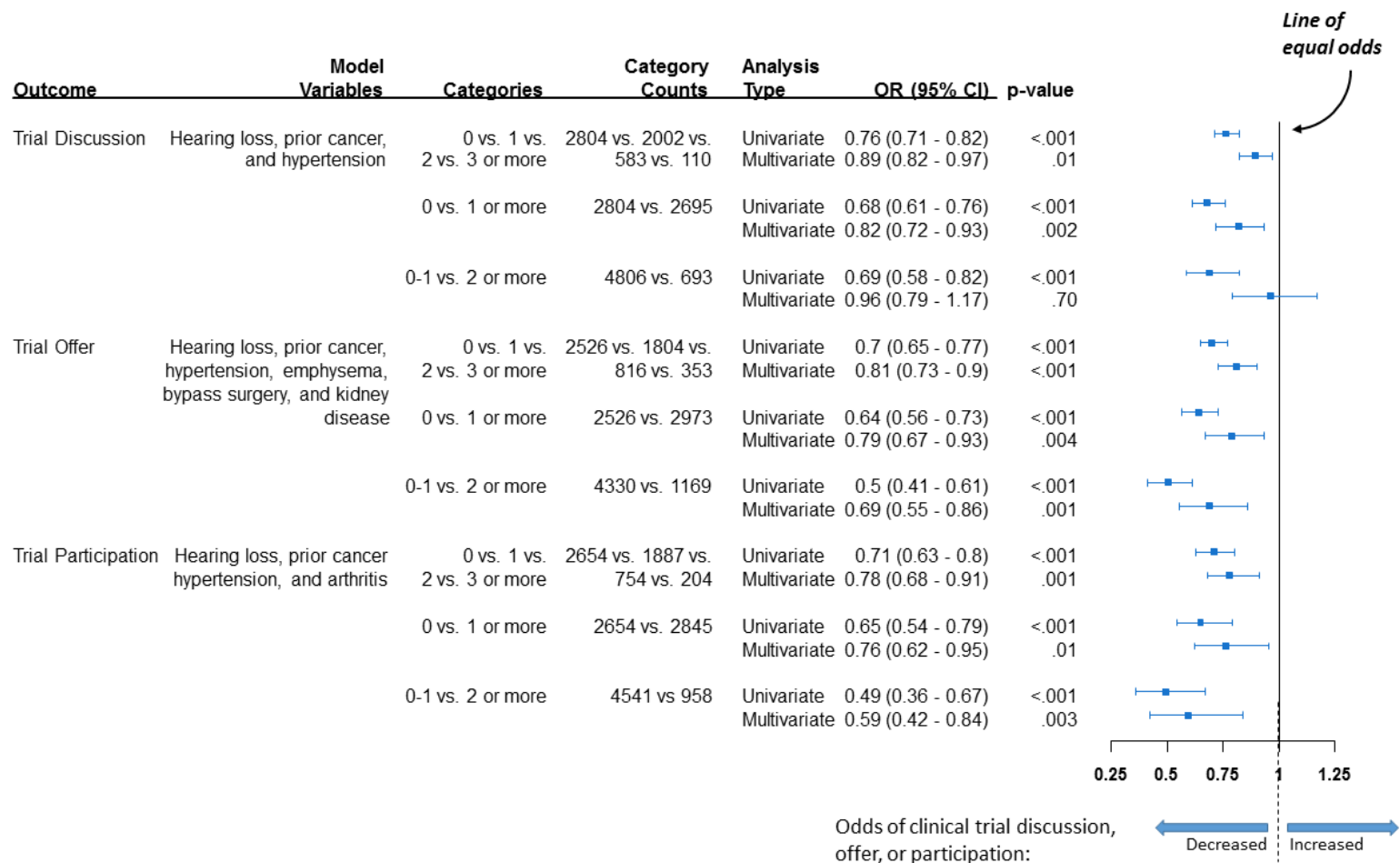
\* Age adjusted, based on the specified categories.

\*\* Based on activities limited by arthritis. Mild arthritis excluded.

**eTable 4:** Multivariable associations of individual comorbid conditions and trial discussion, offer, and participation

	Trial Discussion			Trial Offer			Trial Participation		
	Condition?*(yes vs. no)	OR (95% CI)	p-value	Condition?*(yes vs. no)	OR (95% CI)	p-value	Condition?*(yes vs. no)	OR (95% CI)	p-value
<b>Cardiovascular (any)</b>									
Blood Clots	<b>37.1%</b> vs. 39.7%	0.82 (0.61-1.1)	0.18	<b>13.1%</b> vs. 18.0%	0.75 (0.5-1.13)	0.17	<b>8.0%</b> vs. 9.1%	0.81 (0.48-1.37)	0.43
Bypass surgery	<b>28.0%</b> vs. 39.7%	0.8 (0.48-1.35)	0.4	<b>4.0%</b> vs. 18.0%	0.29 (0.09-0.95)	0.04	<b>2.0%</b> vs. 9.1%	0.19 (0.03-1.35)	0.096
Heart Attack	<b>36.0%</b> vs. 39.7%	1.46 (1.02-2.09)	0.04	<b>9.0%</b> vs. 18.1%	0.94 (0.53-1.64)	0.82	<b>5.3%</b> vs. 9.2%	1.01 (0.5-2.04)	0.99
Heart Failure	<b>28.6%</b> vs. 39.7%	0.96 (0.53-1.73)	0.89	<b>7.9%</b> vs. 17.9%	0.64 (0.25-1.64)	0.35	<b>0.0%</b> vs. 9.1%	N/A	N/A
Hypertension	<b>34.5%</b> vs. 42.2%	0.88 (0.77-1)	0.05	<b>14.0%</b> vs. 19.8%	0.78 (0.65-0.93)	0.005	<b>7.6%</b> vs. 9.8%	0.84 (0.67-1.05)	0.12
Stroke/TIA	<b>32.3%</b> vs. 39.7%	0.88 (0.58-1.34)	0.55	<b>8.1%</b> vs. 18.0%	0.47 (0.22-0.97)	0.04	<b>4.0%</b> vs. 9.1%	0.58 (0.23-1.45)	0.24
<b>Kidney Disease</b>	<b>29.8%</b> vs. 39.7%	0.74 (0.44-1.22)	0.23	<b>6.4%</b> vs. 18.0%	0.52 (0.22-1.23)	0.14	<b>4.3%</b> vs. 9.1%	0.7 (0.25-1.93)	0.49
<b>Liver (cirrhosis)</b>	<b>31.0%</b> vs. 39.6%	0.56 (0.22-1.46)	0.24	<b>13.8%</b> vs. 17.8%	1.19 (0.39-3.57)	0.76	10.3% vs. <b>9.0%</b>	1.71 (0.5-5.89)	0.39
<b>Prior Cancer</b>	<b>34.5%</b> vs. 40.1%	0.91 (0.74-1.12)	0.39	<b>13.4%</b> vs. 18.3%	0.84 (0.63-1.12)	0.24	<b>5.9%</b> vs. 9.4%	0.71 (0.47-1.05)	0.09
<b>Lung (any)</b>									
Asthma	42.5% vs. <b>39.1%</b>	1.09 (0.9-1.31)	0.39	19.0% vs. <b>17.6%</b>	1.03 (0.81-1.3)	0.83	9.2% vs. <b>9.0%</b>	0.97 (0.71-1.32)	0.84
COPD	<b>36.0%</b> vs. 39.8%	0.86 (0.66-1.11)	0.25	<b>10.4%</b> vs. 18.3%	0.63 (0.42-0.94)	0.025	<b>7.7%</b> vs. 9.1%	0.88 (0.55-1.41)	0.59
<b>Other (any)</b>									
Alzheimer's	52.6% vs. <b>39.5%</b>	2.18 (0.81-5.89)	0.12	<b>5.3%</b> vs. 17.8%	0.35 (0.05-2.66)	0.31	<b>5.3%</b> vs. 9.0%	0.71 (0.09-5.43)	0.74
Arthritis	<b>35.2%</b> vs. 40.3%	0.93 (0.78-1.11)	0.43	<b>13.8%</b> vs. 18.5%	0.8 (0.63-1.02)	0.07	<b>6.2%</b> vs. 9.5%	0.71 (0.51-0.99)	0.042
Diabetes	<b>36.0%</b> vs. 39.8%	0.95 (0.75-1.19)	0.63	<b>12.6%</b> vs. 18.2%	0.69 (0.5-0.96)	0.026	<b>6.9%</b> vs. 9.2%	0.73 (0.47-1.12)	0.15
Hearing Loss	<b>32.6%</b> vs. 40.4%	0.93 (0.76-1.15)	0.52	<b>12.2%</b> vs. 18.5%	0.92 (0.69-1.23)	0.58	<b>5.4%</b> vs. 9.5%	0.7 (0.46-1.05)	0.086
Joint Disease	<b>38.9%</b> vs. 39.6%	1.13 (0.9-1.41)	0.29	<b>15.0%</b> vs. 18.0%	0.86 (0.64-1.16)	0.33	<b>6.0%</b> vs. 9.3%	0.73 (0.48-1.11)	0.14
Ulcers	<b>33.4%</b> vs. 39.9%	0.78 (0.59-1.03)	0.075	<b>14.5%</b> vs. 18.0%	0.89 (0.62-1.27)	0.52	<b>6.9%</b> vs. 9.1%	0.83 (0.51-1.35)	0.45
Vision Loss	<b>35.3%</b> vs. 40.4%	0.89 (0.76-1.06)	0.19	<b>14.6%</b> vs. 18.4%	0.87 (0.7-1.08)	0.21	<b>7.5%</b> vs. 9.3%	0.92 (0.69-1.22)	0.56

**eFigure:** Forest plot of the association between comorbidity risk scores and outcomes.



Forest plot of the association between comorbidity risk scores and outcomes. A best model for each outcome (trial discussion, trial offer, and trial participation) was derived using the best subsets method; the model variables for each best model are listed for each outcome. For each univariate and multivariate analysis, the blue box represents the odds ratio and the vertical line through the box represents the magnitude of the 95% confidence interval. The vertical (black) line shows the line of equal odds. Odds ratios to the left of the vertical line represent decreased odds of

clinical trial discussion, offer, or participation, and odds ratios to the right represents increased odds of clinical trial discussion, offer, or participation, respectively. P-values are derived from multivariable logistic regression analyses adjusted for demographic factors and income, and stratified by cancer type.



**eTable 5:** Sensitivity analyses

<b>Outcome</b>	<b>OR (95% CI)</b>	<b>p-value</b>	<b>OR (95% CI)</b>	<b>p-value</b>
<i>Using 3-level age categorization in multivariable analysis of the association of 0 vs. <math>\geq 1</math> of any comorbidities and outcomes*</i>				
	Original (binary age categories)		Sensitivity analysis (3-level age categories)	
Discussion	0.86 (0.75-0.98)	0.02	0.87 (0.76-0.99)	0.03
Offer	0.82 (0.7-0.96)	0.02	0.84 (0.71-0.99)	0.035
Participation	0.76 (0.61-0.94)	0.01	0.78 (0.63-0.96)	0.02
<i>Using 3-level age categorization in multivariable analysis of 0 vs. 1 vs. <math>\geq 2</math> of the common predictors (hypertension, prior cancer, hearing loss) and outcomes*</i>				
	Original (Binary age cat.)		Sensitivity analysis (3-level age categories)	
Discussion	0.89 (0.81-0.98)	0.02	0.9 (0.81-0.99)	0.04
Offer	0.82 (0.72-0.94)	0.004	0.84 (0.73-0.96)	0.01
Participation	0.78 (0.65-0.93)	0.006	0.8 (0.67-0.95)	0.01
<i>Excluding prior cancers from the examination of 0 vs. <math>\geq 1</math> of any comorbidities and outcomes</i>				
	Original (all patients)		Sensitivity analysis (exclude patients with prior cancer)	
Discussion	0.86 (0.75-0.97)	0.02	0.87 (0.76-0.99)	0.04
Offer	0.82 (0.7-0.96)	0.02	0.84 (0.71-0.99)	0.04
Participation	0.76 (0.61-0.94)	0.01	0.78 (0.63-0.96)	0.02

\* Three-level age categorization: 18-39 vs. 40-64 vs.  $\geq 65$  years