Comparing the Association Between Insurance and Mortality in Ovarian, Pancreatic, Lung, Colorectal, Prostate, and Breast Cancers

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ABSTRACT

Background: Insurance coverage is associated with better cancer outcomes; however, the relative importance of insurance coverage may differ between cancers. This study compared the association between insurance coverage at diagnosis and cancer-specific mortality (CSM; insurance sensitivity) in 6 cancers. **Patients and Methods:** Using the SEER cancer registry, data were abstracted for individuals diagnosed with ovarian, pancreatic, lung, colorectal, prostate, or breast cancer in 2007 through 2010. The association between insurance coverage at diagnosis and CSM was modeled using a Fine and Gray competing-risks regression adjusted for demographics. An interaction term combining insurance status and cancer type was used to test whether insurance sensitivity differed between cancers. Separate models were fit for each cancer. To control for lead-time bias and to assess whether insurance sensitivity may be mediated by earlier diagnosis and treatment, additional models were fit adjusting for disease stage and treatment. **Results:** Lack of insurance was associated with an increased hazard of CSM in all cancers ($P < .01$). The magnitude of the effect differed significantly between cancers ($P_{\text{interaction}} = .04$), ranging from an adjusted hazard ratio of 1.13 (95% CI, 1.01–1.28) in ovarian and 1.19 (95% CI, 1.11–1.29) in pancreatic cancer to 2.19 (95% CI, 2.02–2.37) in breast and 2.98 (95% CI, 2.54–3.49) in prostate cancer. The benefit of insurance was attenuated after adjusting for stage and treatment (eg, screening/early treatment effect), with the largest reductions in prostate, breast, and colorectal cancers. **Conclusions:** Greater insurance sensitivity was seen in screening-detected malignancies with effective treatments for early-stage disease (eg, prostate, breast, and colorectal cancers). Given that this differential is significantly reduced after adjusting for stage and treatment, our results suggest that a significant portion (but not all) of the benefit of insurance coverage is due to detection and treatment of certain curable early-stage cancers.

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Background

Insurance coverage impacts many aspects of cancer care, from screening^{1,2} to treatment.^{3–5} Insurance may also affect long-term outcomes, such as cancer progression and mortality.^{6,7} The relative benefit may vary depending on the underlying malignancy. For instance, there is evidence that insurance expansion following the 2010 Patient Protection and Affordable Care Act (ACA) led to increases in recommended cancer screening for colorectal and breast cancers but not for cervical cancer.^{1,8} Regarding long-term outcomes such as mortality, some cancers have been shown to have particularly strong associations between insurance coverage and cancer-specific mortality (CSM). For example, uninsured men with testicular cancer have particularly high mortality rates.⁹

Understanding the strength of the association between insurance status and cancer outcomes has clear relevance given ongoing legislative debates about policies, which have the potential to alter insurance rates.¹⁰ Data on insurance sensitivity of different cancers may yield actionable perspectives on the policies most likely to improve patient outcomes. For example, the best strategy to improve outcomes in highly insurance-sensitive cancers may be to increase outreach and insurance coverage in at-risk populations, whereas in less insurance-sensitive cancers, basic clinical and translational research may yield the greatest benefits.

Using data from the SEER database, we assessed whether the association between insurance coverage at diagnosis and CSM varied in a statistically significant fashion among individuals with ovarian, pancreatic, lung, colorectal, prostate, or breast cancer, which constitute more than half of all cancer deaths in the United States.¹¹ For each cancer, we assessed the magnitude of the association between insurance coverage at diagnosis

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and CSM. To infer the extent to which these differences may be attributable to early detection and improved access to definitive treatment, we assessed how insurance sensitivity changed after adjusting for disease stage at diagnosis and receipt of definitive treatment.

Patients and Methods

Data Source

Data were extracted from the SEER database, which provides a population-based sample, representing approximately 26% of the US population, from sites chosen as representative of the overall US population. The SEER registry contains detailed clinical and pathologic data and tumor-specific variables, such as stage and grade, and data on CSM and death from other causes.¹²

Study Population

Study cohorts consisted of individuals aged 18 to 64 years with ovarian, pancreatic, lung, colorectal, prostate, or breast cancer in 2007 through 2010. These 6 cancers comprised 58% of all new cancer cases in the United States during the study period.¹³ This age range was chosen because most Americans aged ≥ 65 become eligible for Medicare, which is the universal insurance program for elderly individuals in the United States. The study period of 2007–2010 was chosen because 2007 was when insurance data became available within SEER, and 2010 saw the passage of the ACA, which includes a variety of policies that altered insurance coverage, such as coverage of dependents aged < 26 years, elimination of exclusions for preexisting conditions, expansion of Medicaid, the subsidized insurance Marketplace, and the “individual mandate” (with tax penalties for the uninsured starting in 2014). This period also yielded a slightly longer follow-up period, which is important for slower growing cancers, such as breast and prostate. We excluded individuals who had a preexisting cancer diagnosis besides their primary diagnosis, those with missing information on stage and grade, and those with unknown cause of death or insurance status.

Endpoints

The primary outcome was CSM, defined as death from an individual’s primary cancer diagnosis.

Predictor Variable

The main predictor variable was insurance status at the time of diagnosis, based on the “Insurance Recode (2007+)” variable in SEER. This is a dichotomously coded variable, which describes patients’ insurance status at the time of diagnosis (not after treatment, because many patients may obtain insurance coverage after a cancer diagnosis).

Covariates

Patient-level covariates included age, sex (where applicable), race (white, black, other, unknown), and marital status. Other demographic variables included income, residence type, and education (based on subjects’ county of residence). Tumor characteristics included clinical stage (derived from the 6th edition of the *AJCC Cancer Staging Manual*) and receipt of any definitive treatment, which was defined as surgery for ovarian, pancreatic, colorectal, and breast cancers, and surgery or radiation for prostate and lung cancers.

Statistical Analysis

Baseline covariates were compared between patients with each cancer with and without insurance coverage at the time of diagnosis. Means and standard deviations were calculated for all continuous variables and proportions were reported for all categorical variables. Chi-square tests were used to compare the distribution of categorical variables between patients with and without insurance, and 2-sided *t* tests were used to compare means of continuous variables.

To assess whether insurance sensitivity varied in a statistically significant fashion between cancer types, we performed a combined analysis of patients with all 6 cancers. An adjusted competing risks survival model was fit. The outcome of the model was CSM; the main predictor variable of the model was an interaction term combining cancer type and insurance status. This interaction term was used to test the hypothesis that the effect of insurance differed significantly between the 6 cancers. Because of potential effects of age, treatment, demographics, and stage in different cancer types, we included additional interaction terms between cancer type and tumor stage, receipt of treatment, and each demographic variable (age at diagnosis, sex, race, marital status, residence type, education, and income).

Cumulative incidence curves were then generated for each of the 6 cancers to estimate the effect of CSM. An adjusted Fine and Gray competing-risks regression model was fit, adjusting for the aforementioned covariates plus interaction terms, to estimate the association between insurance coverage at diagnosis and the patient level hazard of CSM.¹⁴ Competing risks were defined as death from any noncancer causes, because for malignancies with a naturally protracted course (such as prostate cancer), insurance may also reduce the risk of non-cancer-related causes of death, such as cardiovascular or pulmonary disease.

Next, to account for lead-time bias and to assess whether the protective effect of insurance was due to earlier stage at diagnosis and/or access to treatment, 2 additional adjusted models were fit. In the first, we added a term for stage at diagnosis to account for the

possibility that insured patients are diagnosed with earlier-stage cancers (eg, due to screening). Second, a term was added to adjust for receipt of definitive treatment (defined as surgery and/or radiation as appropriate for each malignancy). Using a previously described approach, the change in the protective benefit of insurance was then compared after each adjustment and the relative change in excess risk of death among the uninsured was used to infer the contribution of stage at diagnosis and treatment of all 6 cancers.^{15–18} For cancers with nonsignificant effect, a post hoc power analysis using a 2-sample comparison of exponential survivor functions was performed to estimate the achievable effect size using a β of 0.80 (corresponding to an acceptable false-negative rate of 20%) and an α of 0.01.

All analyses were performed using STATA, version 14.0 (StataCorp LLP) and SAS 9.4 (SAS Institute Inc.). The study was approved by the Brigham and Women's Hospital Institutional Review Board.

Results

Analytic cohorts were identified for the 6 cancers as summarized in Table 1. The populations ranged in size from 10,607 (ovarian cancer) to 115,606 (breast cancer), and mean ages ranged from 51 (breast cancer) to 58 years (prostate cancer). Overall, most individuals had insurance coverage, ranging from 92% (lung cancer) to 97% (prostate and breast cancer). On average, insured individuals had higher income and educational levels compared with uninsured individuals ($P<.0001$ for both variables across all 6 cancers) and were more likely to be married and less likely to be black ($P<.0001$ for both variables across all 6 cancers).

Regarding cancer stage and treatment, individuals without insurance had proportionally more advanced tumors and received less definitive therapy: for example, in breast cancer, 4.9% of insured patients had metastases (M1) at the time of diagnosis versus 13.7% of uninsured patients ($P<.0001$). Similarly, 94% of insured patients with breast cancer received definitive treatment versus only 79% of uninsured patients ($P<.0001$).

In the combined cohort ($n=332,703$), no insurance coverage was associated with worse overall CMS (hazard ratio [HR], 1.19; 95% CI, 1.14–1.23; $P<.0001$). In addition, the interaction term combining cancer type and insurance status was significantly associated with CSM ($P=.04$ for joint test across all 6 cancer types), suggesting that the effect of insurance on overall mortality varies in a statistically significant fashion across the 6 cohorts.

We next evaluated the magnitude of the effect of insurance coverage on CSM for patients with each of the cancers individually (Figure 1). In our competing-risks regression model adjusted for patient demographics (including age, sex [where appropriate], income, marital

status, race, residence type, and education), no insurance was independently associated with an increased hazard of CSM in all 6 cancer types ($P<.01$ in all cohorts). The magnitude of the effect ranged from 1.13 (95% CI, 1.01–1.28) in ovarian cancer to 2.98 (95% CI, 2.54–3.49) in prostate cancer (Table 2).

In the secondary analysis adjusting for disease stage at diagnosis, the excess risk among uninsured patients was reduced but remained statistically significant in all but ovarian cancer. The largest changes were seen in prostate (from 2.98 to 1.33) and breast cancer (from 2.19 to 1.43). After adjusting for both disease stage at diagnosis and receipt of definitive therapy, no difference was seen in mortality among patients with pancreatic (adjusted HR, 1.08; 95% CI, 0.98–1.18) or ovarian cancer (adjusted HR, 1.05; 95% CI, 0.91–1.20). The remaining 4 cancers showed persistently worse CSM in uninsured compared with insured patients. Adjusted HRs (uninsured vs insured) for all cancer types and after each adjustment are shown in Table 2 and Figure 2. Finally, to quantify the relative contribution of stage at diagnosis and definitive treatment on the excess hazard of CSM in the uninsured, we compared the excess risk of death in insured and uninsured patients after each adjustment in all 6 cancers using a previously described method.^{15–18} The individual contribution of stage and treatment on the excess risk of death in the uninsured is summarized in supplemental eTable 1 (available with this article at JNCCN.org).

Due to the lack of significance regarding the effect of insurance on ovarian and pancreatic cancer survival ($N=10,607$ and $N=11,870$, respectively) after both adjustments, a post hoc power analysis was performed. In a hypothetical cohort of 10,000 individuals with a 10:1 ratio of insured to uninsured, there would be 80% power (with a type I error rate of 5%) to detect an HR of ≥ 1.11 , which is larger than the observed effect size in the fully adjusted ovarian and pancreatic models.

Discussion

In this population-based study of individuals diagnosed with ovarian, pancreatic, lung, colorectal, breast, or prostate cancer, we found that the magnitude of the association between insurance coverage and mortality (ie, insurance sensitivity) varied significantly between cancers, with the greatest insurance sensitivity in prostate, colorectal, and breast cancers and a lesser but statistically significant effect in ovarian, lung, and pancreatic cancers. Controlling for disease stage at diagnosis (screening effect) and receipt of definitive treatment (treatment effect) reduced the magnitude of the association, with the largest reductions in breast, prostate, and colorectal cancers.

The finding that insurance coverage has the largest magnitude of association with breast and prostate cancers

Table 1. Baseline Characteristics of Individuals Based on Insurance Status at Diagnosis

	Ovarian Cancer (N=10,607)		Pancreatic Cancer (N=11,870)		Lung Cancer (N=52,730)		Colorectal Cancer (N=52,234)		Breast Cancer (N=115,606)		Prostate Cancer (N=89,656)	
	Insured	Uninsured	Insured	Uninsured	Insured	Uninsured	Insured	Uninsured	Insured	Uninsured	Insured	Uninsured
Patients diagnosed, n (%)	9,825 (92.63)	782 (7.37)	11,001 (92.68)	869 (7.32)	48,267 (91.54)	4,463 (8.46)	48,480 (92.81)	3,754 (7.19)	112,402 (97.23)	3,204 (2.77)	87,198 (97.26)	2,458 (2.74)
Patient demographics												
Mean age, y (SD)	51.03 (9.99)	49.48 (11.05)	55.38 (7.24)	54.40 (7.56)	56.28 (6.53)	54.82 (6.91)	53.35 (8.14)	52.81 (8.57)	51.59 (8.37)	50.74 (8.97)	57.65 (5.00)	57.56 (5.04)
Year of diagnosis, n (%)												
2007	2,459 (25.03)	214 (27.37)	2,624 (23.85)	189 (21.75)	12,213 (25.30)	1,090 (24.42)	12,081 (24.92)	867 (23.1)	27,638 (24.59)	780 (24.34)	22,121 (25.37)	560 (22.78)
2008	2,420 (24.63)	199 (25.45)	2,715 (24.68)	226 (26.01)	12,144 (25.16)	1,123 (25.16)	11,913 (24.57)	868 (23.12)	28,068 (24.97)	785 (24.50)	21,638 (24.81)	618 (25.14)
2009	2,493 (25.37)	185 (23.66)	2,839 (25.81)	213 (24.51)	12,101 (25.07)	1,175 (26.33)	12,229 (25.22)	981 (26.13)	28,684 (25.52)	811 (25.31)	22,159 (25.41)	594 (24.17)
2010	2,453 (24.97)	184 (23.53)	2,823 (25.66)	241 (27.73)	11,809 (24.47)	1,075 (24.09)	12,257 (25.28)	1,038 (27.65)	28,012 (24.92)	828 (25.84)	21,280 (24.40)	686 (27.91)
Sex, n (%)												
Male	—	—	6,460 (58.72)	546 (62.83)	26,603 (55.12)	2,656 (59.51)	27,285 (56.28)	2,138 (56.95)	579 (0.52)	24 (0.75)	87,198 (100.00)	2,458 (100.00)
Female	9,825 (100)	782 (100)	4,541 (41.28)	323 (37.17)	21,664 (44.88)	1,807 (40.49)	21,195 (43.72)	1,616 (43.05)	111,823 (99.48)	3,180 (99.25)	—	—
Race, n (%)												
White	7,938 (80.79)	590 (75.45)	8,433 (76.66)	608 (69.97)	37,675 (78.06)	3,250 (72.82)	36,220 (74.71)	2,528 (67.34)	87,377 (77.74)	2,134 (66.60)	66,388 (76.13)	1,530 (62.25)
Black	784 (7.98)	111 (14.19)	1,721 (15.64)	196 (22.55)	7,303 (15.13)	980 (21.96)	7,004 (14.45)	908 (24.19)	13,374 (11.90)	742 (23.16)	15,667 (17.97)	803 (32.67)
Other	1,062 (10.81)	71 (9.08)	818 (7.44)	59 (6.73)	3,195 (6.62)	222 (4.97)	4,880 (10.07)	301 (8.02)	11,062 (9.84)	284 (8.86)	3,638 (4.17)	95 (3.86)
Unknown	41 (0.42)	^b	29 (0.26)	^b	95 (0.20)	11 (0.25)	376 (0.78)	17 (0.45)	589 (0.52)	44 (1.37)	1,505 (1.73)	30 (1.22)
Marital status, n (%)												
Married	5,548 (56.47)	287 (36.70)	6,522 (59.29)	325 (37.40)	25,968 (53.80)	1,491 (33.41)	29,709 (61.28)	1,500 (39.96)	70,695 (62.89)	1,319 (41.17)	60,638 (69.54)	1,134 (46.14)
Not married	3,949 (40.19)	456 (58.31)	4,089 (37.17)	513 (59.03)	20,656 (42.80)	2,773 (62.13)	16,655 (34.35)	2,078 (55.35)	37,791 (33.62)	1,718 (53.62)	19,768 (22.67)	1,176 (47.84)
Unknown	328 (3.34)	39 (4.99)	390 (3.55)	31 (3.57)	1,643 (3.40)	199 (4.46)	2,116 (4.36)	176 (4.69)	3,916 (3.48)	167 (5.21)	6,792 (7.79)	148 (6.02)

Abbreviation: N/A, not applicable.

^aP value from chi-square test for categorical variables or analysis of variance for continuous variables.^bCells with <10 individuals were censored for privacy per data use agreement.^cBased on percentage of individuals in home county who graduated from high school.^dDefinitive treatment was defined as surgery or radiation for prostate and lung cancers, and surgery for ovarian, pancreatic, colorectal, and breast cancers.

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Table 1. Baseline Characteristics of Individuals Based on Insurance Status at Diagnosis (cont.)

	Ovarian Cancer (N=10,607)			Pancreatic Cancer (N=11,870)			Lung Cancer (N=52,730)			Colorectal Cancer (N=52,234)			Breast Cancer (N=115,606)			Prostate Cancer (N=89,656)		
	Insured	Uninsured	P Value ^a	Insured	Uninsured	P Value ^a	Insured	Uninsured	P Value ^a	Insured	Uninsured	P Value ^a	Insured	Uninsured	P Value ^a	Insured	Uninsured	P Value ^a
Residence type, n (%)	.0004			<.0001			<.0001			<.0001			<.0001			<.0001		
Rural	125 (1.27)	16 (2.05)		152 (1.38)	18 (2.07)		1,125 (2.33)	133 (2.98)		720 (1.49)	102 (2.72)		1,215 (1.08)	70 (2.18)		989 (1.13)	44 (1.79)	
Urban	829 (8.44)	97 (12.40)		1,192 (10.84)	137 (15.77)		7,035 (14.58)	850 (19.05)		5,555 (11.46)	606 (16.14)		9,823 (8.74)	418 (13.05)		7,922 (9.09)	301 (12.25)	
Metropolitan	8,855 (90.13)	668 (85.42)		9,631 (87.55)	714 (82.16)		40,019 (82.91)	3,480 (77.97)		42,083 (86.80)	3,044 (81.09)		101,197 (90.03)	2,713 (84.68)		78,235 (89.72)	2,111 (85.88)	
Unknown/ Missing	16 (0.16)	^b		26 (0.24)	^b		88 (0.18)	^b		122 (0.25)	^b		167 (0.15)	^b		52 (0.06)	^b	
Mean percentage that completed high school, % (SD) ^c	84.39 (6.26)	82.7 (6.50)	<.0001	84.20 (6.42)	83.10 (6.29)	<.0001	83.81 (6.64)	82.82 (6.66)	<.0001	83.92 (6.43)	82.41 (6.58)	<.0001	84.46 (6.26)	83.19 (6.49)	<.0001	84.73 (6.13)	83.20 (6.27)	<.0001
Mean income (SD), \$USD	60,869 (18,522)	57,072 (25,609)	<.0001	59,057 (16,539)	55,157 (14,081)	<.0001	56,351 (15,770)	52,610 (14,302)	<.0001	58,889 (16,197)	54,019 (17,285)	<.0001	60,651 (17,160)	57,168 (21,385)	<.0001	59,984 (16,696)	56,090 (18,689)	<.0001
Tumor characteristics																		
Clinical T stage, n (%)	.0044			.0259			<.0001			<.0001			<.0001			<.0001		
Tx	790 (8.04)	91 (11.64)		2,514 (22.85)	227 (26.12)		6,540 (13.55)	651 (14.59)		6,071 (12.52)	526 (14.01)		3,995 (3.55)	313 (9.77)		1,561 (1.79)	131 (5.33)	
T0	21 (0.21)	0 (0.00)		60 (0.55)	^b		277 (0.57)	28 (0.63)		59 (0.12)	10 (0.27)		233 (0.21)	10 (0.31)		12 (0.01)	2 (0.08)	
Tis	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
T1	3,063 (31.18)	244 (31.20)		369 (3.35)	21 (2.42)		7,821 (16.20)	440 (9.86)		9,988 (20.60)	481 (12.81)		62,184 (55.32)	1,160 (36.20)		24,901 (28.56)	847 (34.46)	
T2	1,210 (12.32)	99 (12.66)		1,925 (17.50)	154 (17.72)		12,215 (25.31)	975 (21.85)		5,307 (10.95)	264 (7.03)		34,300 (30.52)	1,056 (32.96)		49,993 (57.33)	1,136 (46.22)	
T3	4,741 (48.25)	348 (44.50)		3,958 (35.98)	272 (31.30)		2,808 (5.82)	311 (6.97)		20,897 (43.10)	1,720 (45.82)		7,023 (6.25)	304 (9.49)		9,601 (11.01)	264 (10.74)	
T4	—	—	—	2,175 (19.77)	189 (21.75)		18,606 (38.55)	2,058 (46.11)		6,158 (12.70)	753 (20.06)		4,667 (4.15)	361 (11.27)		1,130 (1.30)	78 (3.17)	

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^aP value from chi-square test for categorical variables or analysis of variance for continuous variables.^bCells with <10 individuals were censored for privacy per data use agreement.^cBased on percentage of individuals in home county who graduated from high school.^dDefinitive treatment was defined as surgery or radiation for prostate and lung cancers, and surgery for ovarian, pancreatic, colorectal, and breast cancers.

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	Insured	Uninsured	P Value ^a	Insured	Uninsured	P Value ^a	Insured	Uninsured	P Value ^a	Insured	Uninsured	P Value ^a	Insured	Uninsured	P Value ^a	Insured	Uninsured	P Value ^a
Clinical N stage, n (%)	<.0001			.0223			<.0001			.0004			<.0001			<.0001		
Nx	1,160 (11.81)	139 (17.77)		2,164 (19.67)	202 (23.25)		4,371 (9.06)	443 (9.93)		5,260 (10.85)	397 (10.58)		2,270 (2.02)	235 (7.33)		2,739 (3.14)	198 (8.06)	
N0	6,702 (68.21)	507 (64.38)		4,641 (42.19)	365 (42.00)		14,115 (29.24)	1,071 (24.00)		24,546 (50.63)	1,781 (47.44)		68,459 (60.91)	1,548 (48.31)		82,463 (94.57)	2,121 (86.29)	
N1	1,963 (19.98)	136 (17.39)		4,196 (38.14)	302 (34.75)		4,024 (8.34)	355 (7.95)		10,945 (22.58)	922 (24.56)		29,038 (25.83)	941 (29.37)		1,996 (2.29)	139 (5.66)	
N2	—	—		—	—		18,702 (38.75)	1,843 (41.30)		7,729 (15.94)	654 (17.42)		7,921 (7.05)	301 (9.39)		—	—	
N3	—	—		—	—		7,055 (14.62)	751 (16.83)		—	—		4,714 (4.19)	179 (5.59)		—	—	
Clinical M stage, n (%)	.0002			<.0001			<.0001			<.0001			<.0001			<.0001		
Mx	635 (6.46)	79 (10.10)		706 (6.42)	58 (6.67)		2,731 (5.66)	244 (5.47)		3,949 (8.15)	237 (6.31)		1,885 (1.68)	174 (5.43)		1,900 (2.18)	104 (4.23)	
M0	7,111 (72.38)	511 (65.35)		4,570 (41.54)	287 (33.03)		21,318 (44.17)	1,568 (35.13)		34,440 (71.04)	2,413 (64.28)		105,033 (93.44)	2,591 (80.87)		82,971 (95.15)	2,064 (83.97)	
M1	2,079 (21.16)	192 (24.55)		5,725 (52.04)	524 (60.30)		24,218 (50.18)	2,651 (59.40)		10,091 (20.81)	1,104 (29.41)		5,484 (4.88)	439 (13.70)		2,327 (2.67)	290 (11.80)	
Treatment																		
Definitive treatment, n (%) ^d	<.0001			<.0001			<.0001			<.0001			<.0001			<.0001		
Yes	8,784 (89.40)	617 (78.90)		72,567 (83.22)	1,674 (68.10)		31,521 (65.31)	2,438 (54.63)		42,078 (86.79)	2,870 (76.45)		105,786 (94.11)	2,520 (78.65)		72,567 (83.22)	1,674 (68.10)	
No	1,025 (10.43)	161 (20.59)		14,307 (16.41)	769 (31.29)		16,562 (34.31)	1,988 (44.54)		6,288 (12.97)	864 (23.02)		6,477 (5.76)	670 (20.91)		14,307 (16.41)	769 (31.29)	
Unknown/ Missing	16 (0.16)	^b		324 (0.37)	15 (0.61)		184 (0.38)	37 (0.83)		114 (0.24)	20 (0.53)		139 (0.12)	14 (0.44)		324 (0.37)	15 (0.61)	

Abbreviation: N/A, not applicable.

^aP value from chi-square test for categorical variables or analysis of variance for continuous variables.^bCells with <10 individuals were censored for privacy per data use agreement.^cBased on percentage of individuals in home county who graduated from high school.^dDefinitive treatment was defined as surgery or radiation for prostate and lung cancers, and surgery for ovarian, pancreatic, colorectal, and breast cancers.

Figure 1. Cumulative incidence of CSM in (A) ovarian, (B) pancreatic, (C) lung, (D) colorectal, (E) breast, and (F) prostate cancer by insurance status. Abbreviation: CSM, cancer-specific mortality.

is noteworthy. It was previously shown that insurance coverage increases both screening^{1,2} and receipt of definitive cancer treatment.¹⁹ Breast, prostate, and colorectal cancers were highly “insurance-sensitive,” have common screening tests, and are potentially curable at an early stage. In contrast, insurance coverage conferred a less pronounced benefit in ovarian and pancreatic cancers. Although there are known insurance-based disparities in

treatment of pancreatic^{20,21} and ovarian cancer,²² it is possible that these cancers are so aggressive that even optimum care provides only a scant benefit.

Although there is an existing body of research showing that insurance coverage is associated with better outcomes,^{19,23} our study adds several important elements that provide insight into how insurance may exert its protective effect. First, by including an interaction term

Table 2. Adjusted Hazard of Cancer-Specific Mortality for Uninsured Versus Insured Individuals

Cancer	Adjusted for Demographics ^a		Adjusted for Disease Stage at Diagnosis ^b		Adjusted for Disease Stage at Diagnosis and Receipt of Definitive Treatment ^c	
	Hazard Ratio	95% CI	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Ovarian	1.13	1.01–1.28	1.12	0.98–1.30	1.05	0.91–1.20
Pancreatic	1.19	1.11–1.29	1.12	1.03–1.22	1.08	0.98–1.18
Lung	1.29	1.23–1.35	1.14	1.09–1.20	1.13	1.07–1.18
Colorectal	1.45	1.35–1.55	1.19	1.12–1.26	1.10	1.04–1.17
Breast	2.19	2.02–2.37	1.43	1.31–1.56	1.32	1.19–1.47
Prostate	2.98	2.54–3.49	1.33	1.14–1.55	1.30	1.12–1.51

^aAge at diagnosis, sex, race, marital status, residence type (urban, rural, unknown), education (ie, county high school graduation rate), and income.

^bT, N, and M stage.

^cDefinitive treatment was defined as surgery or radiation for prostate and lung cancers, and surgery for ovarian, pancreatic, colorectal, and breast cancers.

in our models, we were able to test the hypothesis that insurance sensitivity varies between cancers and then provide estimates of the effect size across 6 major cancers. Second, by adjusting first for demographics and comorbidities, then for disease stage at diagnosis, and then for receipt of definitive treatment, we were able to generate hypotheses about possible mechanisms through which insurance coverage exerts its protective effect.

Although this study raises important questions about the role of insurance coverage in different cancers, it has key limitations. First and most importantly, patients were not randomized to insured versus uninsured groups. Thus, there may be unmeasured confounders (eg, habits, such as poor diet and smoking) that are more common among the uninsured. If these confounders exert a greater impact in prostate, colorectal, and breast cancers, then this could explain the apparently higher insurance sensitivity of these cancers.

Another important limitation is the potential for lead-time bias. Because insured patients may be diagnosed earlier (especially in screening-detected cancers), there may be a tendency toward an increased amount of time between diagnosis and any cancer-related endpoint. To account for this, we performed a mediation analysis controlling for disease stage (because insured patients tended to have earlier-stage cancer at diagnosis) and found that earlier stage at diagnosis accounted for more than half of the explainable excess risk in lung, colorectal, breast, and prostate cancers.

Additionally, although prior studies have compared different types of insurance (eg, Medicaid/Medicare vs private insurance) versus no insurance, we chose instead to treat insurance coverage as a dichotomous variable (any insurance vs no insurance), primarily because of numerous public policy debates that may affect both private and public insurance (eg, expansion of Medicare to all adults, Medicaid expansion, repeal of the ACA).

Another limitation is the inability to make nuanced judgements about the appropriateness of definitive treatment. Because the decision regarding whether a patient is a candidate for surgery and/or radiation is complex, we did not attempt to evaluate the suitability or timeliness of a definitive therapy. Similarly, in colorectal cancer, individuals with insurance may be more likely to be treated for their precancerous growths, and therefore might not ultimately ever be diagnosed with cancer and would not enter into this study cohort. We simply assessed whether a patient received definitive treatment, and whether this accounted for insurance sensitivity of certain treatments. In addition, although our use of a competing risk model should limit confounding due to competing medical risks, there may be differences in unmeasured characteristics between insured and uninsured individuals that could impact CSM. For example, individuals who are homeless and unemployed (neither of which are captured in our dataset) may have both an increased risk of being uninsured and having other cancer risk factors, such as worse diet or environmental or other risk factors. Finally, our power analysis suggests that this sample size may be too small to account for very small differences between insured and uninsured men and women with less prevalent cancers (eg, pancreatic and ovarian cancers).

It should be noted that the uninsured proportion in this study ranged from 2.74% in prostate cancer to approximately 8.50% in lung cancer. These rates are similar to those reported in other studies using the SEER database, but lower than US Census estimates. For example, Walker et al¹⁹ examined 10 major cancers from 2007 through 2010 within SEER and found uninsured rates of approximately 4.7% overall, and Grant et al²⁴ reported an uninsured rate of 4.9% in their SEER-based study of the top 25 incident cancers in the United States. These rates are lower than the census-reported uninsured rate during this period, which was approximately

Figure 2. Insurance sensitivity of 6 major cancers, defined as the magnitude of the association between adjusted CSM and insurance coverage (adjusted for demographics only), after 3 adjustments.

Abbreviation: CSM, cancer-specific mortality.

^aResidual difference in CSM after adjusting for demographics, disease stage, and receipt of definitive treatment (from gray to null).

^bChange in insurance sensitivity after adjusting for treatment and disease stage at diagnosis (from orange to gray).

^cChange in CSM after adjusting for disease stage at diagnosis (from blue to gray).

15.4%.²⁵ There are several possible reasons for this discrepancy, one being that the “Insurance Recode 2007+” variable has not, to our knowledge, been externally validated.

Although insurance coverage doubtless has a complex relationship with health outcomes, our results are consistent with a large portion of the benefit of insurance coverage arising from detection and treatment of prevalent, but curable, early-stage cancers. This may yield actionable policy goals; for example, prostate and breast cancers exert a large burden on black individuals, who also are historically underinsured. In contrast, for less insurance-sensitive cancers, such as pancreatic and ovarian, emphasizing basic, clinical, and translational research may be the best strategy. Although insurance sensitivity varies among cancers, the effect of insurance on CSM in most cancers is persistent, even after adjusting for disease stage at diagnosis and receipt of definitive treatment, suggesting that there may be ongoing unobserved differences in care beyond simply early diagnosis and treatment. The specific ingredients leading to the significant residual benefit of insurance coverage after adjusting for disease stage

and treatment receipt are uncertain, but may include factors such as greater multidisciplinary care, involvement of patient navigators, and access to more experienced clinicians.

Conclusions

Insurance coverage at the time of diagnosis is independently associated with reduced CSM among patients with ovarian, pancreatic, lung, colorectal, breast, and prostate cancers. The magnitude of this effect varies among these cancers, with greater insurance sensitivity in screening-detected cancers with effective treatments for localized disease. This differential was significantly mediated but not eliminated after adjusting for disease stage and receipt of treatment, suggesting that much (but not all) of the benefit of insurance coverage may be via detection and treatment of certain curable early-stage cancers.

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Supplemental online content for:

Comparing the Association Between Insurance and Mortality in Ovarian, Pancreatic, Lung, Colorectal, Prostate, and Breast Cancers

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eTable 1: Hazard Ratios and Explainable Excess Risk for Overall Survival

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Cancer	Adjusted for Demographics ^a HR (95% CI)	Adjusted for Demographics ^a and Disease Stage at Diagnosis ^b HR (95% CI)	Adjusted for Demographics, ^a Disease Stage at Diagnosis, ^b and Receipt of Definitive Treatment ^c HR (95% CI)
Ovarian			
Adjusted hazard ratio (U/I)	1.1 (1.01–1.28)	1.1 (0.98–1.30)	1.0 (0.91–1.20)
Excess relative risk, % (U/I)	13.2 (1–28)	12.2 (–2 to 30)	4.2 (–9 to 20)
Total explainable excess risk, %	—	7.5 (–134 to 149) ^d	68 (–98.3 to 234) ^d
Individual contribution of explainable excess risk, %	—	7.5 (–134 to 149) ^d	60.6 (–122 to 243) ^d
Pancreatic			
Adjusted hazard ratio (U/I)	1.2 (1.11–1.29)	1.1 (1.029–1.219)	1.1 (0.978–1.181)
Excess relative risk, % (U/I)	12 (12–25)	12.0 (2.9–21.9)	7.5 (–2.2 to 18.1)
Total explainable excess risk, %	—	37.8 (9.97–65.60)	61.1 (28.4–93.8)
Individual contribution of explainable excess risk, %	—	37.8 (9.97–65.60)	15.1 (–6.1 to 52.8) ^d
Lung			
Adjusted hazard ratio (U/I)	1.3 (1.234–1.346)	1.1 (1.085–1.196)	1.1 (1.072–1.180)
Excess relative risk, % (U/I)	28.9 (23.4–34.6)	13.9 (8.5–19.6)	12.5 (7.2–18.0)
Total explainable excess risk, %	—	51.9 (47.4–56.4)	56.7 (52.3–61.2)
Individual contribution of explainable excess risk, %	—	51.9 (47.4–56.4)	4.8 (1.0–8.7)
Colorectal			
Adjusted hazard ratio (U/I)	1.4 (1.350–1.547)	1.2 (1.119–1.262)	1.1 (1.040–1.171)
Excess relative risk, % (U/I)	44.5 (35.0–54.7)	18.8 (11.9–26.2)	10.4 (4.0–17.1)
Total explainable excess risk, %	—	57.8 (52.8–62.7)	76.6 (71.2–82.0)
Individual contribution of explainable excess risk, %	—	57.8 (52.8–62.7)	18.9 (16.2–21.5)
Breast			
Adjusted hazard ratio (U/I)	2.2 (2.021–2.373)	1.4 (1.308–1.557)	1.3 (1.189–1.468)
Excess relative risk, % (U/I)	219.0 (202.1–237.2)	42.7 (30.8–55.7)	32.1 (18.9–46.8)
Total explainable excess risk, %	—	64.1 (61.8–66.4)	73.0 (70.4–75.7)
Individual contribution of explainable excess risk, %	—	64.1 (61.8–66.4)	8.9 (7.5–10.3)
Prostate			
Adjusted hazard ratio (U/I)	3.0 (2.544–3.490)	1.3 (1.135–1.547)	1.3 (1.120–1.506)
Excess relative risk, % (U/I)	297.9 (254–349)	32.5 (13.5–54.7)	29.8 (12.0–50.6)
Total explainable excess risk, %	—	83.6 (77.2–90.0)	84.9 (78.5–91.4)
Individual contribution of explainable excess risk, %	—	83.6 (77.2–90.0)	1.4 (0.15–2.57)

Abbreviations: I, insured; U, uninsured.

^aAge at diagnosis, sex, race, marital status, residence type (urban, rural, unknown), education (county high school graduation rate), and income.^bT, N, and M stage.^cDefinitive treatment coded dichotomously (Y/N) and was defined as surgery or radiation for prostate and lung cancers, and surgery for ovarian, pancreatic, colorectal, and breast cancers.^dNonstatistically significant contribution to excess risk.