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Impact of Insurance Status on Stage, Treatment, and Survival in Patients with Colorectal Cancer: **A Population-Based Analysis**

Author Da Statis Data I nuscrip Lite Fur	rs' Contribution: Study Design A ata Collection B stical Analysis C nterpretation D to Preparation E rrature Search F idds Collection G	ABCD BCDE CDE ABEF	Wei Sun* Minghua Cheng* Shaohui Zhuang Zeting Qiu	Department of Anesthesiology, The First Affiliated Hospital of Shantou University Medical College, Shantou, Guangdong, P.R. China
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	Back Material/N	kground: Aethods:	This study aimed to analyze data from the Surveillance tify patients with colorectal cancer (CRC) who had sp nosis, definitive treatment, and survival outcome wit Between 2007 and 2009, SEER database analysis iden the associations between insurance status and disease the Cox model, and the Fine and Gray model were u	e, Epidemiology, and End Results (SEER) program to iden- becific insurance details and the effects of stage at diag- h insurance status. tified 54,232 patients with CRC. Logistic models examined se stage and definitive treatment. Kaplan-Meier analysis, sed to compare the tumor cause-specific survival (TCSS)
	Con	Results:	for patients with different insurance status. Insured patients were more likely to have earlier tun ceiving Medicaid (adjusted OR, 1.318; 95% CI, 1.249– tients (adjusted OR, 1.479; 95% CI, 1.352–1.618; P <c undergo definitive treatment when compared with p 0.470–0.742; P<0.001) and compared with patients who P<0.001). Insured patients had a significantly increase (HR, 1.298; 95% CI, 1.236–1.363; P<0.001) and comp CI, 1.100–1.297; P<0.001).</c 	nor stage at diagnosis when compared with patients re- 1.391; P<0.001) and when compared with uninsured pa- 0.001). Insured patients were significantly more likely to patients receiving Medicaid (adjusted OR, 0.591; 95% CI, p were uninsured (adjusted OR, 0.404; 95% CI, 0.282–0.579; ed TCSS when compared with patients receiving Medicaid pared with patients who were uninsured (HR 1.195, 95%
	Con MoSH Ko	clusions:	come and was an independent factor for TCSS in pat	ned early diagnosis, definitive treatment, and clinical out- ients with CRC.
	Full-1	text PDF:	https://www.medscimonit.com/abstract/index/idArt	/913282
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Background

Colorectal cancer (CRC), is the third most common cancer in the United States, and in 2018 there were an estimated 140.250 new cases resulting in 50,630 associated deaths [1]. CRC is the third leading cause of cancer mortality in both men and women [2]. The incidence of CRC has been declining during the past four decades, mainly due to the reduced risk factors and the use of colonoscopic screening [2]. In patients who have been diagnosed with CRC, the survival and prognosis have improved annually, partly due to the development of improved surgical management and improved systemic chemotherapy regimens [3]. The survival outcome for patients with a diagnosis of CRC has been associated with clinical and histopathological factors, including the tumor site, tumor type, histologic grade, the American Joint Committee on Cancer (AJCC) stage, tumor node metastasis (TNM) status, and a comprehensive treatment strategy [4].

Recently, clinicians have become increasingly aware of the impact of sociodemographic factors, especially the insurance status, on the diagnosis, treatment, and prognosis of patients with cancer. Previous studies have shown that patients with hepatocellular carcinoma and breast cancer who were on Medicaid or who were uninsured patients tended to have a more advanced stage at diagnosis and were more likely to refuse treatment after diagnosis [5,6]. Also, insured patients with prostate cancer have been shown to have improved prognosis when compared to patients with Medicaid and uninsured individuals [7]. However, there have been few previous studies on how insurance status impacts the stage at diagnosis, the definitive treatment, and the survival for patients with CRC, using population-based analysis [8].

This study aimed to use data from the Surveillance, Epidemiology, and End Results (SEER) program [9] to identify all patients with CRC who had specific insurance details and to analyze the effects of the stage at diagnosis, definitive treatment, and survival outcome, with insurance status.

Material and Methods

Search strategy for the Surveillance, Epidemiology, and End Results (SEER) database

The Surveillance, Epidemiology, and End Results (SEER) database is a publicly available program composed of 18 cancer registries and covers approximately 30% of the population in the United States with a typical distribution [10]. The data in the SEER database is de-identified to ensure patient confidentiality. The SEER database is considered to be representative of the entire US population, and includes patient demographic information and data from patient clinical records and followup data of survival. SEER is updated annually by the National Center for Health Statistics.

Permission was obtained to use the SEER database in November 2016 (Authorization number by Author QZT: 12738-Nov.2016). All the patient data were obtained through the SEER*Stat software version 8.3.5 (released on March 6, 2018) (*https://seer.cancer.gov/seerstat/*), including demographic, clinical and follow-up information. Detailed information of the patients with CRC diagnosed between 2007 and 2009 from the SEER-18 was performed with SEER*Stat software. This study complied with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Approval for this study was waived by the local ethics committee, and no informed consents were needed.

Inclusion criteria for patients with colorectal cancer (CRC) from the SEER database

All patients with colorectal cancer (CRC) were identified during 2007 and 2009 for analysis. The following study inclusion criteria were used: patients were included who were diagnosed with primary CRC, according to the Anatomic International Classification of Diseases for Oncology, Third Edition [ICD-O-3], codes C18.0, C18.1, C18.2, C18.3, C18.4, C18.5, C18.6, C18.7, C18.8, C18.9, C19.9, C20.9); patients were diagnosed between 2007 and 2009, because insurance status was missing in the database for patients diagnosed before 2007, and patients diagnosed after 2009 did not meet the 5-year follow-up period; patients included in the analysis were aged older than 18 years and younger than 85 years at diagnosis; patients were limited to adenocarcinoma (histologic ICD-O-3 codes: 8140, 8210, 8261, 8263, 8481), mucinous adenocarcinoma (histologic ICD-O-3 code: 8480), and signet ring cell carcinoma (histologic ICD-O-3 code: 8490).

The following study exclusion criteria were used: patients with unknown demographic information on gender, age at diagnosis, race, marital status, household income, college completion and rural/metropolitan location; patients with unknown clinical information including histologic grade, and AJCC TNM stage; patients with no information on definitive surgery or radiotherapy; patients with multiple primary tumors; patients with unknown cause of death or unknown survival time; patients with a survival time ≤ 1 month; autopsy or death certificate only.

Demographic data of patients with CRC from the SEER database

Demographic data collected for analysis included gender, age, year of diagnosis, marital status, race, insurance status, household income, completion of college education, rural or metropolitan location, cancer site, histology, histologic grade,

AJCC TNM stage, T status, N status, M status, surgical therapy, radiotherapy, chemotherapy, cause of death, and survival time (in months) from the SEER database. Gender was classified as male and female. The patients' ages were grouped as 18–54, 55–64, 65–74, and 75–85 years. The year of diagnosis was 2007, 2008, and 2009. Marital status was classified as married and unmarried. Race was classified as Asian/Pacific Islander, black, Hispanic white, and non-Hispanic white. Insurance status was classified as insured, Medicaid, and uninsured. Household income was classified into quartile 1 (<59,080 dollars), quartile 2 (59,080–66,230 dollars), quartile 3 (55,230–83,950 dollars) and quartile 4 (>83,950 dollars). College completion was classified into quartile 1 (<17.22%), quartile 2 (17.22–24.86%), quartile 3 (24.86–30.51%) and quartile 4 (>30.51%). Rural/metropolitan location was classified as rural and metropolitan.

Data on CRC from the SEER database

Cancer site was classified as the left colon (splenic flexure, descending colon, sigmoid colon), the right colon (cecum, ascending colon, hepatic flexure, transverse colon), and rectosigmoid or the rectum (rectum, rectosigmoid junction). Histologic grade was classified as grade I, II, III, and IV. AJCC TNM stage was classified as stage I, II, III and IV. AJCC T status was classified as T1, T2, T3, and T4. AJCC N status was classified as N0, N1, N2, and N3. AJCC M status was classified as MO and M1. SEER stage was classified as localized, regional and distant. Surgical treatment and radiotherapy were all defined as having received therapy or not. Chemotherapy was classified as having received chemotherapy or not/unknown. Definitive treatment was defined as receiving definitive surgery, radiotherapy or chemotherapy. Causes of death were classified as tumor cause-specific death (TCSD) and other causespecific death (OCSD).

Statistical analysis

The demographic, clinical, and pathologic features analyzed were summarized by descriptive statistical analysis. Continuous variables with normal distribution were described as the mean ± standard deviation (SD), continuous variables with skewed distribution were described as medians, first quartiles, and third quartiles, and categorical variables were described as frequencies and percentages. For categorical variables, Pearson's chi-squared (χ^2) test and Fisher's exact tests were used to determine statistical significance. Multinomial logistic regression models were used to detect associations between insurance status and multifactor disease stage at diagnosis by R package of MASS, with the greater the odds ratio (OR) values, the more advanced the cancer stage. Binomial logistic regression models were used to detect associations between insurance status and definitive treatment, with the greater the OR values, the greater the possibility of receiving definitive treatment.





Bar plots were drawn by R package of ggplot2. For tumor causespecific survival (TCSS), deaths caused by CRC were considered as events. Kaplan-Meier analysis and the multivariate Cox proportional hazard model were selected to distinguish independent risk factors by the R package of KMsurv and survival. When displaying Kaplan-Meier curves based on raw data by the survminer R package, due to disequilibrium among different types of insurance, the curves were reproduced after propensity score matching (PSM) by R packages of MatchIt. In the competing risk analysis, OCSD was regarded as the competing event of TCSD. The Fine and Gray proportional sub-distribution hazard model was chosen to predict TCSD by R package cmprsk and riskRegression [11,12]. All analysis was performed using R statistical software version 3.3.1 (released June 2016) (www.r-project.org). All P-values were two-sided and P<0.05 was considered significant.

Results

Baseline characteristics of patients with colorectal cancer (CRC) from the Surveillance, Epidemiology, and End Results (SEER) database

As shown in Figure 1, there were 54,232 patients with colorectal cancer (CRC) diagnosed between 2007 and 2009 in the Surveillance, Epidemiology, and End Results (SEER) database. Among these cases, 46,774 patients (86.2%) were insured, 5,651 patients (10.4%) had Medicaid, and 1,807 patients (3.3%) were uninsured. Table 1 showed the overall baseline

	Overall	Insured	Medicaid	Uninsured
Characteristic	N=54232	N=46774	N=5651	N=1807
Gender				
Male	28798 (53.1)	25117 (53.7)	2676 (47.4)	1005 (55.6)
Female	25434 (46.9)	21657 (46.3)	2975 (52.6)	802 (44.4)
Age (years)	64.42±12.58	65.00±12.43	62.85±13.06	54.36±9.74
Age group (years)				
18–54	12504 (23.1)	10139 (21.7)	1521 (26.9)	844 (46.7)
55–64	13328 (24.6)	11098 (23.7)	1407 (24.9)	823 (45.5)
65–74	14585 (26.9)	12993 (27.8)	1505 (26.6)	87 (4.8)
75–85	13815 (25.5)	12544 (26.8)	1218 (21.6)	53 (2.9)
Year of diagnosis				
2007	18317 (33.8)	15926 (34.0)	1801 (31.9)	590 (32.7)
2008	18060 (33.3)	15607 (33.4)	1856 (32.8)	597 (33.0)
2009	17855 (32.9)	15241 (32.6)	1994 (35.3)	620 (34.3)
Marital status				
Married	32777 (60.4)	29911 (63.9)	2095 (37.1)	771 (42.7)
Unmarried	21455 (39.6)	16863 (36.1)	3556 (62.9)	1036 (57.3)
Race				
Asian/Pacific Islander	4689 (8.6)	3675 (7.9)	865 (15.3)	149 (8.2)
Black	6427 (11.9)	4902 (10.5)	1085 (19.2)	440 (24.3)
Hispanic white	5420 (10.0)	3953 (8.5)	1152 (20.4)	315 (17.4)
Non-Hispanic white	37696 (69.5)	34244 (73.2)	2549 (45.1)	903 (50.0)
Household income				
Quartile 1	13873 (25.6)	12507 (26.7)	1104 (19.5)	262 (14.5)
Quartile 2	13393 (24.7)	12045 (25.8)	948 (16.8)	400 (22.1)
Quartile 3	13991 (25.8)	11591 (24.8)	1915 (33.9)	485 (26.8)
Quartile 4	12975 (23.9)	10631 (22.7)	1684 (29.8)	660 (36.5)
College completion				
Quartile 1	13890 (25.6)	12449 (26.6)	1085 (19.2)	356 (19.7)
Quartile 2	15496 (28.6)	12992 (27.8)	2011 (35.6)	493 (27.3)
Quartile 3	11483 (21.2)	10151 (21.7)	971 (17.2)	361 (20.0)
Quartile 4	13363 (24.6)	11182 (23.9)	1584 (28.0)	597 (33.0)
Rural/metropolitan location				
Rural	6963 (12.8)	5894 (12.6)	773 (13.7)	296 (16.4)
Metropolitan	47269 (87.2)	40880 (87.4)	4878 (86.3)	1511 (83.6)
Cancer site				
Left colon	16243 (30.0)	13776 (29.5)	1835 (32.5)	632 (35.0)
Right colon	22669 (41.8)	19944 (42.6)	2110 (37.3)	615 (34.0)
Rectosigmoid/rectum	15320 (28.2)	13054 (27.9)	1706 (30.2)	560 (31.0)

Table 1. Baseline characteristics of included patients with colorectal cancer, overall and by insurance status.

2400

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Characteristic	Overa	ıll	Ins	Insured		Medicaid		Uninsured	
Characteristic	N=542	32	N=4	6774	N=!	5651	N= 1	1807	
Histology									
Adenocarcinoma	50353 (9	92.8)	43435	(92.9)	5242	(92.8)	1676	(92.8)	
Mucinous adenocarcinoma	3434 ((6.3)	2957	(6.3)	363	(6.4)	114	(6.3)	
Signet ring cell carcinoma	445 ((0.8)	382	(0.8)	46	(0.8)	17	(0.9)	
Grade									
I	4790 ((8.8)	4207	(9.0)	445	(7.9)	138	(7.6)	
II	39484 (7	2.8)	33918	(72.5)	4218	(74.6)	1348	(74.6)	
III	9135 (1	.6.8)	7933	(17.0)	913	(16.2)	289	(16.0)	
IV	823 ((1.5)	716	(1.5)	75	(1.3)	32	(1.8)	
AJCC stage									
I	14054 (2	25.9)	12696	(27.1)	1095	(19.4)	263	(14.6)	
ll	15441 (2	28.5)	13212	(28.2)	1698	(30.0)	531	(29.4)	
III	16866 (3	31.1)	14444	(30.9)	1797	(31.8)	625	(34.6)	
IV	7871 (1	.4.5)	6422	(13.7)	1061	(18.8)	388	(21.5)	
AJCC-T									
T1	8976 (1	.6.6)	8065	(17.2)	728	(12.9)	183	(10.1)	
T2	8444 (1	.5.6)	7599	(16.2)	681	(12.1)	164	(9.1)	
Т3	30181 (5	5.7)	25775	(55.1)	3319	(58.7)	1087	(60.2)	
T4	6631 (1	.2.2)	5335	(11.4)	923	(16.3)	373	(20.6)	
AJCC-N									
NO	31282 (5	57.7)	27286	(58.3)	3104	(54.9)	892	(49.4)	
N1	13582 (2	25.0)	11615	(24.8)	1450	(25.7)	517	(28.6)	
N2	9368 (1	.7.3)	7873	(16.8)	1097	(19.4)	398	(22.0)	
AJCC-M									
MO	46361 (8	35.5)	40352	(86.3)	4590	(81.2)	1419	(78.5)	
M1	7871 (1	.4.5)	6422	(13.7)	1061	(18.8)	388	(21.5)	
SEER stage									
Localized	22571 (4	1.6)	20047	(42.9)	1991	(35.2)	533	(29.5)	
Regional	23160 (4	2.7)	19814	(42.4)	2502	(44.3)	844	(46.7)	
Distant	8501 (1	.5.7)	6913	(14.8)	1158	(20.5)	430	(23.8)	
Surgery									
Yes	52215 (9	96.3)	45252	(96.7)	5299	(93.8)	1664	(92.1)	
No	2017 ((3.7)	1522	(3.3)	352	(6.2)	143	(7.9)	

Table 1 continued. Baseline characteristics of included patients with colorectal cancer, overall and by insurance status.

Chamataviatia	Overall	Insured	Medicaid	Uninsured
Characteristic	N=54232	N=46774	N=5651	N=1807
Radiotherapy				
Yes	8588 (15.8)	7179 (15.3)	1012 (17.9)	397 (22.0)
No	45644 (84.2)	39595 (84.7)	4639 (82.1)	1410 (78.0)
Chemotherapy				
Yes	23929 (44.1)	20242 (43.3)	2576 (45.6)	1111 (61.5)
No	30303 (55.9)	26532 (56.7)	3075 (54.4)	696 (38.5)

 Table 1 continued.
 Baseline characteristics of included patients with colorectal cancer, overall and by insurance status.

N - number; AJCC - the American Joint Committee on Cancer; SEER - the Surveillance, Epidemiology and End Results.

characteristics of the patients and their insurance status. There were 28,798 male patients (53.1%), 32,777 married patients (60.4%), 37,696 non-Hispanic white patients (69.5%), and 47,269 patients who lived in metropolitan conditions (87.2%). Analysis of the clinicopathological data showed that the majority of patients, 50,353, had a colorectal adenocarcinoma (92.8%), of which, 39,484 were grade II (72.8%), 16,866 were AJCC stage III (31.1%), 30,181 were T3 (55.7%), 31,282 were N0 (57.7%), 46,361 were M0 (57.7%) and 23,160 were SEER regional stage (42.7%). There were 52,215 patients (96.3%) who received surgical treatment, 8,588 patients (15.8%) receiving radiotherapy, and 23,929 patients (44.1%) received chemotherapy. The median follow-up period was 66.0 months (range, 36.0–80.0 months).

Cancer stage at diagnosis

As shown in Figure 2, insured patients were more likely to have an earlier SEER stage at diagnosis when compared with Medicaid or uninsured patients. However, uninsured patients had the lowest proportion of SEER localized stage, as well as the highest proportion of SEER distant stage. Univariate analysis, shown in Table 2, identified sociodemographic factors associated with SEER stage at diagnosis, including age group, marital status, race, insurance status, income, and education. After adjusting the multivariate logistic analysis, insurance status was still an independent influencing factor of SEER stage. Insured patients had an earlier SEER stage at diagnosis compared with other patients, including patients with Medicaid compared with insured patients (adjusted OR, 1.318; 95% Cl, 1.249-1.391) and uninsured patients compared with insured patients (adjusted OR, 1.479; 95% CI, 1.352–1.618 P<0.001). Married patients and non-Hispanic white patients were diagnosed at an early stage, with unmarried compared with married patients (adjusted OR, 1.110; 95% CI, 1.073-1.148; P<0.001) and non-Hispanic white patients compared with Asian/Pacific Islanders (adjusted OR, 0.896; 95% CI, 0.846-0.949; P<0.001). Supplementary Table 1 showed the findings of the impact of





insurance status on SEER stage stratified by age group, race, or cancer site, which showed that insured patients had an earlier stage at diagnosis. Table 3 showed the association between insurance status and AJCC stage, T status, N status and M status stratified by cancer site after changing the response variables in the multivariate logistic models. Finally, insured patients were found to be significantly more likely to be diagnosed with an earlier cancer stage and TNM status when compared with Medicaid or uninsured patients.

Definitive treatment

Figure 3 showed that insured patients were more likely to receive definitive treatment when compared with Medicaid or uninsured patients. The chi-squared analysis data shown in Table 4 summarized the sociodemographic and clinical factors associated with definitive treatment, including gender, age group, marital status, race, insurance status, income, education, residence, cancer site, and SEER stage. After adjustment

 Table 2. Multivariate logistic regression analysis of the association between the Surveillance, Epidemiology and End Results (SEER) stage at diagnosis and sociodemographic factors, including insurance status.

Chana shanisti s		Univariate	e analysis		Mu	ltivariate analy	sis
Characteristic	Localized	Regional	Distant	P-value	Adjusted OR	95% CI	P-value
Gender							
Male	12044	12194	4560	0.175			
Female	10527	10966	3941				
Age group (years)				<0.001			<0.001
18–54	4327	5633	2544		Refei	rence	
55–64	5420	5638	2270		0.781	0.746–0.818	
65–74	6469	6042	2074		0.668	0.638–0.700	
75–85	6355	5847	1613		0.599	0.571–0.628	
Year of diagnosis				0.114			
2007	7532	7957	2828				
2008	7510	7691	2859				
2009	7529	7512	2814				
Marital status				<0.001			<0.001
Married	14004	13826	4947		Refei	rence	
Unmarried	8567	9334	3554		1.110	1.073–1.148	
Race				<0.001			<0.001
Asian/Pacific Islander	1790	2134	765		Refei	rence	
Black	2491	2705	1231		0.976	0.908–1.049	
Hispanic white	2112	2418	890		0.938	0.871-1.009	
Non-Hispanic white	16178	15903	5615		0.896	0.846–0.949	
Insurance status				<0.001			<0.001
Insured	20047	19814	6913		Refei	rence	
Medicaid	1991	2502	1158		1.318	1.249–1.391	
Uninsured	533	844	430		1.479	1.352–1.618	
Income				0.001			
Quartile 1	5781	6012	2080				
Quartile 2	5637	5748	2008				
Quartile 3	5793	5946	2252				
Quartile 4	5360	5454	2161				
Education				0.02			
Quartile 1	5735	6051	2104				
Quartile 2	6470	6636	2390				
Quartile 3	4726	4917	1840				
Quartile 4	5640	5556	2167				
Residence				0.294			
Rural	2866	2962	1135				
Metropolitan	19705	20198	7366				

 Table 2 continued. Multivariate logistic regression analysis of the association between the Surveillance, Epidemiology and End Results (SEER) stage at diagnosis and sociodemographic factors, including insurance status.

Charactovictic		Univariate	e analysis	Multivariate analysis			
Characteristic	Localized	Regional	Distant	P-value	Adjusted OR	95% CI	P-value
Cancer site				<0.001			<0.001
Left colon	6634	6800	2809		Refere	ence	
Right colon	9533	9564	3572		1.010	0.971–1.050	
Rectosigmoid/rectum	6404	6796	2120		0.892	0.855–0.930	

SEER – the Surveillance, Epidemiology and End Results; OR – odds ratio; CI – confidence interval.

Table 3. Multivariate logistic regression models evaluating the impact of insurance status on AJCC stage, T status, N status andM status stratified by cancer site in patients with colorectal cancer.

Cancer site	Response variable	Insurance status (versus Insured)	Adjusted OR	95% CI	P-value
		Medicaid	1.359	1.244–1.484	<0.001
	AJCC Stage	Uninsured	1.494	1.461–1.527	
		Medicaid	1.570	1.426–1.728	<0.001
Loft colon	AJCC-1	Uninsured	2.159	2.113-2.206	
		Medicaid	1.173	1.066–1.291	<0.001
	AJCC-N	Uninsured	1.208	1.179–1.237	
	ALCC M	Medicaid	1.326	1.160–1.515	<0.001
	AJCC-IM	Uninsured	1.393	1.139–1.704	
	AICC stage	Medicaid	1.168	1.076–1.269	<0.001
	AJCC Stage	Uninsured	1.375	1.365–1.386	
	ALCC T	Medicaid	1.251	1.144–1.370	<0.001
Right colon	AJCC-1	Uninsured	1.566	1.553–1.578	
Right Colon		Medicaid	1.040	0.952-1.137	0.014
	AJCC-N	Uninsured	1.251	1.240–1.263	
	ALCC M	Medicaid	1.206	1.066–1.365	<0.001
	AJCC-M	Uninsured	1.214	0.992–1.486	
	AICC stage	Medicaid	1.392	1.268–1.528	<0.001
	AJCC Stage	Uninsured	1.433	1.404–1.463	
	ALCC T	Medicaid	1.481	1.337–1.640	<0.001
Rectosigmoid/	AJCC-1	Uninsured	1.992	1.955–2.030	P-value <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001 <0.001
rectum		Medicaid	1.121	1.014–1.239	0.052
	AJCC-N	Uninsured	1.119	1.095–1.144	
	ALCC M	Medicaid	1.603	1.397–1.839	<0.001
		Uninsured	1.516	1.220–1.884	

AJCC – the American Joint Committee on Cancer; OR – odds ratio; CI – confidence interval. The multivariate logistic model included age group, gender, year of diagnosis, marriage, race, household income, college completion and residence for adjustment.



Figure 3. The proportion of patients with or without definitive treatments, by insurance status.

in the multivariate analysis, insurance status remained as a significant relevant factor of definitive treatment. The insured patient group tended to receive definitive treatment when compared with Medicaid (adjusted OR, 0.591; 95% CI, 0.470–0.742; P<0.001) and uninsured patients (adjusted OR, 0.404; 95% CI, 0.282–0.579; P<0.001). Unmarried, black, or rural patients were more likely to refuse definitive treatment (unmarried vs. married, adjusted OR, 0.634; 95% CI, 0.531–0.757; P<0.001) (black vs. Asian/Pacific Islander, adjusted OR, 0.558; 95% CI, 0.379–0.823; P=0.003) (rural vs. metropolitan, adjusted OR, 0.723; 95% CI, 0.557–0.938; P=0.015). As shown in Supplementary Table 2, to reduce the bias among groups, a subgroup analysis stratified by age group, race or cancer site, and showed that the impact of insurance status on definitive treatment persisted, in most cases.

Table 4. Multivariate	logistic r	egression	analysis of	of association	between	definitive	treatment	and insurance sta	tus.
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Charactoristic	U	nivariate analys	is	Multivariate analysis			
	No	Yes	P-value	Adjusted OR	95% CI	P-value	
Gender			<0.001				
Female	238	25196		Refe	rence		
Male	330	28468		0.728	0.611-0.867	<0.001	
Age group (years)			<0.001				
18–54	95	12409		Refe	rence		
55–64	111	13217		0.821	0.621–1.084	0.165	
65–74	134	14451		0.587	0.446-0.773	<0.001	
75–85	228	13587		0.275	0.213-0.357	<0.001	
Year of diagnosis			0.301				
2007	176	18141					
2008	191	17869					
2009	201	17654					
Marital status			<0.001				
Married	258	32519		Refe	rence		
Unmarried	310	21145		0.634	0.531–0.757	<0.001	
Race			<0.001				
Asian/Pacific Islander	39	4650		Refe	rence		
Black	117	6310		0.558	0.379–0.823	0.003	
Hispanic white	75	5345		0.693	0.465–1.034	0.073	
Non-Hispanic white	337	37359		1.086	0.765–1.541	0.645	

Charactoristic	U	nivariate analys	is	Multivariate analysis			
	No	Yes	P-value	Adjusted OR	95% CI	P-value	
Insurance status			<0.001				
Insured	421	46353		Refe	rence		
Medicaid	108	5543		0.591	0.470-0.742	<0.001	
Uninsured	39	1768		0.404	0.282-0.579	<0.001	
Income			<0.001				
Quartile 1	114	13759		Refe	rence		
Quartile 2	107	13286		0.773	0.559–1.068	0.119	
Quartile 3	151	13840		0.667	0.481–0.923	0.015	
Quartile 4	196	12779		0.510	0.348–0.749	<0.001	
Education			<0.001				
Quartile 1	136	13754		Refe	rence		
Quartile 2	146	15350		1.405	1.049–1.883	0.023	
Quartile 3	100	11383		1.809	1.280–2.558	<0.001	
Quartile 4	186	13177		1.400	0.978–2.003	0.066	
Residence			<0.001				
Metropolitan	461	46808		Refe	rence		
Rural	107	6856		0.723	0.557–0.938	0.015	
Cancer site			<0.001				
Left colon	139	16104		Refe	rence		
Right colon	168	22501		1.278	1.016-1.607	0.036	
Rectosigmoid/rectum	261	15059		0.442	0.358–0.545	<0.001	
SEER stage			<0.001				
Distant	209	8292		Refe	rence		
Localized	302	22269		1.980	1.648–2.379	<0.001	
Regional	57	23103		10.998	8.180–14.785	<0.001	

 Table 4 continued.
 Multivariate logistic regression analysis of association between definitive treatment and insurance status.

OR - odds ratio; CI - confidence interval; SEER - the Surveillance, Epidemiology and End Results.

Tumor cause-specific survival (TCSS)

As shown in Supplementary Table 3, the 3-year and 5-year TCSS rates were 81.92% and 74.91% in the insured group, 72.71% and 63.46% in the Medicaid group, and 74.36% and 64.85% in the uninsured group, respectively. As shown in Table 5, Cox analysis adjusted all the significant prognostic factors detected by univariate Kaplan-Meier analysis and showed that insurance status remained as an independent prognostic factor for tumor cause-specific survival (TCSS). Insured patients

had a significantly increased TCSS when compared with patients receiving Medicaid (HR, 1.298; 95% Cl, 1.236–1.363; P<0.001) and compared with patients who were uninsured (HR 1.195, 95% Cl, 1.100–1.297; P<0.001). Kaplan-Meier survival curves shown in Figure 4, demonstrated that the prognosis of the insured group was significantly better than that of the other two groups when using the raw data. After the adjustment of propensity score matching (PSM) (Supplementary Table 4), the effect of the insured group still existed with the balancing data as shown in Figure 4B. Following the Fine and

Table 5. The multivariate Cox model and the Fine and Gray proportional sub-distribution hazard model for tumor cause-specific survival in patients with colorectal cancer.

	M	ultivariate Cox mo	del	F	ine and Gray mode	əl
Characteristics	HR	95% CI	P-value	sHR	95% CI	P-value
Gender						
Female	Ref	erence				
Male	1.096	1.060–1.133	<0.001			
Age group (years)						
18–54	Ref	erence		Refe	erence	
55–64	1.126	1.075-1.180	<0.001	1.111	1.059–1.164	<0.001
65–74	1.351	1.288–1.416	<0.001	1.261	1.200–1.325	<0.001
75–85	1.910	1.819–2.006	<0.001	1.634	1.549–1.723	<0.001
Marital status						
Married	Ref	erence		Refe	erence	
Unmarried	1.161	1.122–1.201	<0.001	1.110	1.071–1.151	<0.001
Race						
Asian/Pacific Islander	Ref	erence		Refe	erence	
Black	1.380	1.283–1.486	<0.001	1.385	1.283–1.495	<0.001
Hispanic white	1.058	0.980-1.143	0.147	1.070	0.986–1.160	0.100
Non-Hispanic white	1.094	1.028–1.163	0.005	1.109	1.041-1.182	0.002
Insurance status						
Insured	Ref	erence		Refe	erence	
Medicaid	1.298	1.236–1.363	<0.001	1.260	1.192–1.332	<0.001
Uninsured	1.195	1.100–1.297	<0.001	1.143	1.041-1.256	0.005
Income						
Quartile 1	Ref	erence				
Quartile 2	1.050	0.990–1.114	0.102			
Quartile 3	1.039	0.977–1.104	0.228			
Quartile 4	1.086	1.010–1.167	0.025			
Education						
Quartile 1	Ref	erence		Refe	erence	
Quartile 2	0.995	0.941–1.052	0.861	1.012	0.966–1.061	0.610
Quartile 3	1.054	0.988–1.124	0.110	1.072	1.018–1.128	0.008
Quartile 4	1.110	1.035–1.189	0.003	1.139	1.086–1.195	<0.001
Cancer site						
Left colon	Ref	erence		Refe	erence	
Right colon	1.059	1.017–1.102	0.005	1.027	0.985–1.070	0.210
Rectosigmoid/rectum	1.137	1.081–1.197	<0.001	1.128	1.070–1.189	<0.001
Histology						
Adenocarcinoma	Refe	erence		Refe	erence	
Mucinous adenocarcinoma	1.084	1.019–1.152	0.011	1.074	1.006–1.147	0.033
Signet ring cell carcinoma	1.446	1.275-1.640	<0.001	1.269	1.060-1.520	0.010

Characteristics	M	ultivariate Cox mo	del	Fine and Gray model			
Characteristics	HR	95% CI	P-value	sHR	95% CI	P-value	
Grade							
I	Ref	erence		Ref	erence		
II	1.192	1.107–1.284	<0.001	1.179	1.094–1.270	<0.001	
III	1.531	1.413–1.658	<0.001	1.491	1.374–1.617	<0.001	
IV	1.517	1.333–1.726	<0.001	1.481	1.274–1.721	<0.001	
AJCC stage							
I	Ref	erence		Ref	erence		
ll	1.306	1.170–1.457	<0.001	1.290	1.153–1.444	<0.001	
III	2.095	1.832–2.396	<0.001	2.035	1.767–2.344	<0.001	
IV	5.329	4.497–6.313	<0.001	4.560	3.813-5.453	<0.001	
AJCC-T							
T1	Ref	erence		Ref	erence		
T2	0.837	0.764–0.917	<0.001	0.856	0.780–0.940	0.001	
Т3	1.315	1.210–1.429	<0.001	1.347	1.230–1.475	<0.001	
T4	2.026	1.858–2.209	<0.001	1.977	1.792–2.180	<0.001	
AJCC-N							
NO	Ref	erence		Ref	erence		
N1	1.148	1.073–1.228	<0.001	1.122	1.040–1.211	0.003	
N2	1.939	1.814–2.072	<0.001	1.836	1.701–1.981	<0.001	
SEER stage							
Localized	Ref	erence		Ref	erence		
Regional	1.314	1.212–1.424	<0.001	1.298	1.198–1.407	<0.001	
Distant	2.257	1.967–2.589	<0.001	2.325	2.015-2.682	<0.001	
Surgery							
Yes	Ref	erence		Ref	erence		
No	2.970	2.782-3.169	<0.001	2.530	2.320–2.760	<0.001	
Radiotherapy							
Yes	Ref	erence		Ref	erence		
No	0.891	0.844–0.940	<0.001	0.897	0.845-0.953	<0.001	
Chemotherapy							
Yes	Ref	erence		Ref	erence		
No	1.251	1.201–1.303	<0.001	1.120	1.069–1.173	<0.001	

 Table 5 continued.
 The multivariate Cox model and the Fine and Gray proportional sub-distribution hazard model for tumor cause-specific survival in patients with colorectal cancer.

HR – hazard ratio; CI – confidence interval; sHR – sub-distribution hazard ratio; AJCC – the American Joint Committee on Cancer; SEER – the Surveillance, Epidemiology and End Results.

Gray analysis, insurance status remained as an independent predictive factor of TCSS. Medicaid or uninsured individuals had significantly worse prognosis when compared with insured patients. Medicaid patients compared with insured patients (sub-distribution HR, 1.260; 95% CI, 1.192-1.332; P<0.001), uninsured patients compared with insured patients (sub-distribution HR 1.195; 95% CI, 1.041-1.256; P=0.005). As shown in Figure 5, the patients were stratified by age group, race,



Figure 4. Kaplan-Meier survival curves for tumor cause-specific survival, by insurance status, with or without propensity score matching (PSM). (A) Kaplan-Meier survival curves without propensity score matching (PSM). (B) Kaplan-Meier survival curves with PSM. The x-axis represents survival times; the y-axis represents survival rates.

and cancer site, which showed that insured patients always had the best TCSS outcomes.

Discussion

A retrospective cohort study used data from the Surveillance, Epidemiology, and End Results (SEER) database, and investigated the influence of insurance status on the disease stage at diagnosis, the definitive treatment, and the survival outcome in 54,232 patients with colorectal cancer (CRC). Among these patients, 86.2% were insured, 10.4% had Medicaid, and 3.3% were uninsured. Insurance status was a significant influencing factor of SEER stage. The SEER stage at diagnosis in Medicaid or uninsured patients was more advanced than insured patients. Insured patients had significantly earlier cancer stage and TNM status. As for definitive treatment, insurance status remained as a relevant factor, and insured patients were more likely to receive definitive treatment when compared with Medicaid or uninsured patients. Also, in terms of prognosis, the 5-year tumor cause-specific survival (TCSS) rates were 74.91% in the insured group, 63.46% in the Medicaid group, and 64.85% in the uninsured group. Both the Cox regression model and the Fine and Gray model showed that insurance status was an independent prognostic factor for TCSS. Insured patients had a better prognosis than either Medicaid or uninsured patients.

Socioeconomic factors, including household income, education level, and marital status, have previously been confirmed to affect tumor prognosis [13–16]. CRC is the third most common

cancer and the third leading cause of cancer death in the United States. However, the relationship between CRC and insurance status has not been previously studied in detail. In the present study, insurance status was found to be an independent predictive factor for disease stage, definitive treatment, and prognosis, which is consistent with the findings from previous studies in other cancers [6]. Tantraworasin et al. studied the effect of insurance type in Asian patients with lung cancer and found that uninsured or Medicaid Asian patients were more likely to be diagnosed with advanced disease, less likely to undergo treatment, and had shorter overall survival [17]. Similar results have been found for hepatocellular carcinoma and prostate cancer [5,7]. In 2016, Rima et al. identified the association between race and insurance in patients with CRC, with similar findings to those of the present study, but only took into account limited patient demographic data, including only age, sex, race, marital status and insurance, probably due to problems with data acquisition [18]. The present study analyzed more variables, including income, education, residence or cancer site, to adjust for the complicated effects, and included stratified analysis to reduce bias, and adopted reasonable multinomial logistic models to detect the association between insurance and cancer stage [8]. However, in this stratified analysis, the effect of insurance status was not statistically significant in the subgroup aged more than 65 years. This finding may have been because the numbers of uninsured persons in those subgroups were less than 100, resulting in less adequate sample sizes [17].

There are other potential reasons for the impact of insurance on the cancer stage at diagnosis. The results of this study

Figure 5. Kaplan-Meier survival curves for tumor cause-specific survival, by insurance status, with stratification by age group, race, or cancer site. Stratified by age group (A–D); stratified by race (E–G); stratified by cancer site (H–K). The x-axis represents survival times; the y-axis represents survival rates.

showed that insured patients tended to be initially diagnosed at an early stage, probably because these patients were more likely to attend regular medical screening appointments and procedures, including colonoscopies or computed tomography (CT) colonography [4,19,20]. Therefore, CRC can be found at an earlier stage in insured patients [21]. CRC screening rates have increased between 2008 to 2015 in the United States, but the uninsured patient population continues to be screened for cancer at below the recommended levels [22].

The disparities between treatment in Medicaid or uninsured patients compared with insured patients have been previously reported [23,24]. In this study, the majority of patients with CRC received definitive treatment during the follow-up period, but the possibility of insured patients receiving treatment was significantly increased when compared with other patient groups. This finding may be because healthcare organizations preferentially admit, diagnose, and treat insured patients instead of Medicaid or uninsured patients [25]. Also, low income and weak social networks, which may be relevant factors of Medicaid or uninsured status, strongly hamper treatment [26]. Because of high treatment costs, uninsured patients may not seek treatment or screening for early diagnosis due to inability to pay the healthcare costs.

The differences in prognosis and patient survival among the patient groups with CRC and different insurance status were closely related to cancer stage and treatment. The data analyzed in this study demonstrated that uninsured or Medicaid patients were probably diagnosed at a more advanced stage, resulting in a worse survival outcome. Also, these patients tend to refuse definitive treatment, which also results in a poor prognosis. In this study, propensity score matching (PSM) was used to balance baseline variance among groups, and insured patients remained as having the optimal prognosis using Kaplan-Meier analysis. The traditional Kaplan-Meier analysis and Cox regression analysis often overestimate the risk of the tested event, which is overcome by the Fine and Gray proportional sub-distribution hazard analysis [27]. In this study, the Fine and Gray model was used to correct the hazard of predictive factors. Therefore, even if the effect of insurance status on prognosis was reduced by the Fine and Gray competing risk model, the results were still statistically significant.

Globally, human cancer results in a large medical and socioeconomic burden. The significance of the findings of this study indicates that medical insurance coverage should increase as part of healthcare reform to ensure that individuals have health insurance. Only in this way can the early diagnosis of cancer, including CRC, treatments, and prognosis be improved. In the USA, the government initiated Medicaid for partial uninsured individuals or minorities with low incomes and low education levels [28]. The original intention of Medicaid was to protect the insurance benefits of vulnerable groups and reduce the racial and socioeconomic imbalance in health care [7,28]. However, according to the findings of this study, no significant difference was detected in TCSS between Medicaid and uninsured patients with CRC. The Medicaid patients had even more adverse survival outcomes than uninsured patients, after PSM. Therefore, whether it is a developed or developing country, expanding the coverage of medical insurance will be an important measure for government healthcare reform [26]. For CRC, private insurance for high-income individuals, and increasing the prevalence of Medicaid for low-income individuals, with the encouragement of screening programs using colonoscopy is recommended.

This study had several limitations. During the screening process of the SEER database, more than half of the original identified 100,000 patients were excluded, because of missing demographic, clinical and pathologic information, which might have resulted in selection bias. Some risk factors, including smoking status, alcohol use, medical comorbidities, and clinical complications, can affect the diagnosis, treatment and survival of patients with CRC. However, the SEER program did not collect these data for the target population. Also, the variables of household income and education level provided by the SEER database are not at patient-level, but at regional level. Detailed therapeutic regimens, including the use of specific chemotherapy, were not directly available from the SEER database, which was a limitation of the study, as chemotherapy has become a routine treatment for patients with advanced CRC. Insurance status, as the key variable, has been in the SEER database since 2007, but only consists of insured, Medicaid, and uninsured status. However, even insured status might be subdivided into private insurance, government Medicare, and coverage from the military or Veterans Affairs, which were inaccessible in the SEER database. The disparities among these different insurance states should be investigated in future studies. Also, given that this was a retrospective cohort study, based on the statistical methods, it was only possible to demonstrate correlations, instead of causality, between insurance status and cancer stage as well as definitive treatment. It is not possible to determine whether insured patients had an earlier cancer stage at diagnosis and inevitably received definitive treatment, and further studies are needed.

Conclusions

A large population-based analysis of patients with colorectal cancer (CRC) used data from the Surveillance, Epidemiology, and End Results (SEER) database. Insurance status was a significant factor that determined early diagnosis, definitive treatment, and was an independent factor for tumor cause-specific survival (TCSS) in patients with CRC. Insured patients

had a significantly earlier cancer stage at diagnosis, were significantly more likely to receive definitive treatment, and had a better prognosis than either patients with Medicaid or uninsured patients. In the USA, increased health insurance coverage may facilitate early diagnosis, promote definitive treatment, and improve the outcome for patients with CRC.

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Conflict of interests

None.

Supplementary Tables

Supplementary Table 1. Adjusted odds ratios (OR) for impact of insurance status on the Surveillance, Epidemiology and End Results (SEER) stage, stratified by age group, race or cancer site.

Subgroup	Insurance status (versus Insured)	Adjusted OR	ljusted OR 95% Cl		
Age group (years)					
18–54	Medicaid	1.642	1.476–1.827	<i>(</i> 0.001	
	Uninsured	1.447	1.266–1.655	<0.001	
FF 64	Medicaid	1.466	1.315-1.635	<0.001	
55-04	Uninsured	1.540	1.346–1.762	20.001	
65.74	Medicaid	1.142	1.030–1.266	0.005	
05-74	Uninsured	1.547	1.544–1.549	0.005	
75 95	Medicaid	1.051	0.936-1.179	0 5 7 9	
75-07	Uninsured	1.192	1.191–1.193	0.578	
Race					
Acian/Dacific Islandor	Medicaid	1.387	1.203–1.599	<0.001	
ASIAN/Pacific Islander	Uninsured	1.702	1.668–1.736	20.001	
Black	Medicaid	1.318	1.160–1.497	(0.001	
	Uninsured	Uninsured 1.380		<0.001	
Hispanic white	Medicaid	1.335	1.179–1.511	<0.001	
Hispanic white	Uninsured	1.138	1.052–1.231	<0.001	
Non Hisponis white	Medicaid	1.295	1.199–1.398	<i>x</i> 0 001	
Non-Hispanic White	Uninsured	1.614	1.595–1.633	<0.001	
Site					
Left colon	Medicaid	1.385	1.262–1.519	<i>4</i> 0 001	
	Uninsured	1.566 1.532–1.601		<0.001	
Right colon	Medicaid	1.188	1.090-–.295	<i>x</i> 0.001	
	Uninsured	1.343	1.332–1.353	<0.001	
Destesion oid /Dest	Medicaid	1.428	1.294–1.575	<i>(</i> 0.001	
kectosigmoid/kectum	Uninsured	1.558	1.525–1.592	<0.001	

SEER – the Surveillance, Epidemiology and End Results; OR – odds ratio; CI – confidence interval. Multivariable logistic models were adjusted for age group, gender, year of diagnosis, marriage, race, household income, college completion, residence and cancer site.

Supplementary Table 2. Adjusted odds ratios (ORs) for the impact of insurance status on definitive treatment stratified by age group, race, or cancer site.

Subgroup	Insurance status (versus Insured)	Adjusted OR	95% CI	P-value
Age group (years)				
	Medicaid	0.433	0.254–0.741	0.002
18-54	Uninsured	0.304	0.171–0.543	<0.001
	Medicaid	0.372	0.229–0.603	<0.001
55-64	Uninsured	0.391	0.218–0.703	0.002
<5 7 A	Medicaid	0.638	0.396–1.027	0.064
65-74	Uninsured	0.549	0.124–2.436	0.431
75.05	Medicaid	0.839	0.559–1.260	0.398
/5-85	Uninsured	0.340	0.101–1.143	0.081
Race				
A -: /D: 6: -	Medicaid	0.610	0.288–1.291	0.196
Asian/Pacific Islander	Uninsured	0.213	0.065–0.700	0.011
	Medicaid	0.492	0.311-0.776	0.002
Black	Uninsured	0.265	0.142–0.495	<0.001
Hispanic white	Medicaid	0.734	0.426–1.265	0.266
	Uninsured	0.679	0.254–1.817	0.441
N	Medicaid	0.589	0.420–0.826	0.002
Non-Hispanic white	Uninsured	0.480	0.271–0.850	0.012
Canser site				
Left colon	Medicaid	0.646	0.402-1.037	0.070
	Uninsured	0.510	0.235–1.108	0.089
Right colon	Medicaid	0.567	0.409–0.786	<0.001
	Uninsured	0.438	0.258-0.743	0.002
Rectosigmoid/Rectum	Medicaid	0.577	0.372–0.895	0.014
	Uninsured	0.287	0.151–0.548	<0.001

OR – odds ratio; CI – confidence interval. Multivariable logistic models were adjusted for age group, gender, marriage, race, household income, college completion, residence, cancer site, histology and the Surveillance, Epidemiology and End Results (SEER) stage.

Characteristics	3-year	5-year	Log rank	Divoluo	
Characteristics	TCSS rate	TCSS rate	χ^2 test	P-value	
Gender			4	0.045	
Female	80.70%	73.87%			
Male	80.75%	73.01%			
Age group (years)			134	<0.001	
18–54	81.50%	73.41%			
55–64	82.55%	75.04%			
65–74	81.68%	75.09%			
75–85	77.18%	70.02%			
Year of diagnosis			2	0.365	
2007	80.75%	73.42%			
2008	80.41%	73.10%			
2009	81.02%	73.73%			
Marital status			284	<0.001	
Married	82.81%	75.91%			
Unmarried	77.50%	69.50%			
Race			200	<0.001	
Asian/Pacific Islander	82.50%	74.97%			
Black	74.99%	66.35%			
Hispanic white	81.06%	73.19%			
Non-Hispanic white	81.43%	74.45%			
Insurance status			436	<0.001	
Insured	81.92%	74.91%			
Medicaid	72.71%	63.46%			
Uninsured	74.36%	64.85%			
Income			84.1	<0.001	
Quartile 1	82.53%	75.47%			
Quartile 2	81.31%	74.13%			
Quartile 3	80.31%	73.00%			
Quartile 4	78.63%	70.89%			
Education			58.9	<0.001	
Quartile 1	82.11%	74.97%			
Quartile 2	81.33%	74.40%			
Quartile 3	79.87%	72.26%			
Quartile 4	79.30%	71.63%			
Residence			20.1	<0.001	
Metropolitan	80.94%	73.69%			
Rural	79.27%	71.51%			
Cancer site			42.4	<0.001	
Left colon	82.70%	75.03%			
Right colon	79.05%	73.28%			
Rectosigmoid/rectum	81.11%	71.97%			

Supplementary Table 3. Univariate survival analysis for tumor cause-specific survival in patients with colorectal cancer.

2414

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Control (Control) TCSS rate 2 ¹ test 2 ¹ test Histology 434 <0.01 Adenocarcinoma 81.38% 74.07% Mucinous adenocarcinoma 75.22% 67.88% Signet ring cell carcinoma 48.28% 40.94% Grade 1577 <0.001 II 83.03% 75.47% III 83.03% 57.07% V 65.93% 57.07% <t< th=""><th>Characteristics</th><th>3-year</th><th>5-year</th><th>Log rank</th><th>P-value</th></t<>	Characteristics	3-year	5-year	Log rank	P-value
Histology 434 0.001 Adencarcinoma 81.38% 74.07% Mucinous adencarcinoma 75.22% 67.88% Signet ring cell carcinoma 48.28% 40.94% Grade 1577 c0.001 I 90.17% 85.20% II 80.33% 75.47% III 67.06% 59.66% IV 65.93% 57.70% ACC stage 25127 c0.001 I 96.35% 93.66% III 91.08% 85.73% III 91.08% 85.73% III 91.08% 85.19% V 33.08% 18.41% AICC-T 6734 60.001 T1 91.38% 88.19% T2 94.34% 90.79% T3 79.74% 71.06% NO 90.53% 85.33% NI 75.96% 66.75% NQ 88.77% 82.07% AICC-M 23127	Characteristics	TCSS rate	TCSS rate	χ² test	F-Value
Adenocarcinoma 81.38% 74.07% Mucinous adenocarcinoma 75.22% 67.88% Signet ring cell carcinoma 48.28% 40.94% Grade 1577 <0.001	Histology			434	<0.001
Mucinous adenocarcinoma 75.22% 67.88% Signet ring cell carcinoma 48.28% 40.94% Grade 1577 <0.001	Adenocarcinoma	81.38%	74.07%		
Signet ring cell carcinoma 48.28% 40.94% Grade 1577 <0.001	Mucinous adenocarcinoma	75.22%	67.88%		
Grade 1577 <0.001	Signet ring cell carcinoma	48.28%	40.94%		
I 90.17% 85.20% II 83.03% 75.47% III 67.06% 59.66% V 65.93% 57.70% AICC stage 25127 <0.001	Grade			1577	<0.001
II 83.03% 75.47% II 67.06% 59.66% V 65.93% 57.70% ALCC stage 25127 <0.001	I	90.17%	85.20%		
III 67.06% 59.66% IV 65.93% 57.70% AICC stage 25127 <0.001	II	83.03%	75.47%		
IV 65.93% 57.70% AICC stage 25127 <0.001	III	67.06%	59.66%		
AICC stage 25127 <0.001	IV	65.93%	57.70%		
I 96.35% 93.66% II 91.08% 85.73% III 80.37% 70.88% IV 33.08% 18.41% AICC-T 6734 <0.001	AJCC stage			25127	<0.001
II 91.08% 85.73% III 80.37% 70.88% IV 33.08% 18.41% AICC-T 6734 <0.001	I	96.35%	93.66%		
III 80.37% 70.88% IV 33.08% 18.41% AICC-T 6734 <0.001	II	91.08%	85.73%		
IV 33.08% 18.41% AICC-T 6734 <0.001	111	80.37%	70.88%		
AJCC-T 6734 <0.001 T1 91.38% 88.19% T2 94.34% 90.79% T3 79.74% 71.06% T4 53.28% 41.76% AJCC-N 8891 <0.001	IV	33.08%	18.41%		
T1 91.38% 88.19% T2 94.34% 90.79% T3 79.74% 71.06% T4 53.28% 41.76% AICC-N 8891 <0.001	AJCC-T			6734	<0.001
T294.34%90.79%T379.74%71.06%T453.28%41.76%AICC-N8891<0.001	T1	91.38%	88.19%		
T379.74%71.06%T453.28%41.76%AICC-N8891<0.001N090.53%85.83%N175.96%66.75%N254.93%41.79%AICC-M23177<0.001M088.77%82.70%M133.08%18.41%SEER stage23652<0.001Localized95.06%91.50%Regional83.35%74.99%Distant35.37%20.99%Surgery3945<0.001Yes82.37%75.11%No35.71%63.15%No86.39%81.88%Chemotherapy114<0.001Yes79.50%69.01%No80.96%74.27%	T2	94.34%	90.79%		
T4 53.28% 41.76% AICC-N 8891 <0.001 N0 90.53% 85.83% N1 75.96% 66.75% N2 54.93% 41.79% AICC-M 23177 <0.001 M0 88.77% 82.70% M1 33.08% 18.41% SEER stage 23652 <0.001 Localized 95.06% 91.50% Poistant 35.37% 20.99% Surgery 3945 <0.001 Yes 82.37% 75.11% No 35.71% 26.47% Radiotherapy 2353 <0.001 Yes 73.77% 63.15% No 86.39% 81.88% Chemotherapy 114 <0.001 Yes 79.50% 69.01% No 80.96% 74.27%	Т3	79.74%	71.06%		
AICC-N 8891 <0.001 N0 90.53% 85.83% N1 75.96% 66.75% N2 54.93% 41.79% AICC-M 23177 <0.001	T4	53.28%	41.76%		
N0 90.53% 85.83% N1 75.96% 66.75% N2 54.93% 41.79% AJCC-M 23177 <0.001	AJCC-N			8891	<0.001
N1 75.96% 66.75% N2 54.93% 41.79% AJCC-M 23177 <0.001	NO	90.53%	85.83%		
N2 54.93% 41.79% AJCC-M 23177 <0.001	N1	75.96%	66.75%		
AJCC-M 23177 <0.001 M0 88.77% 82.70% M1 33.08% 18.41% SEER stage 23652 <0.001	N2	54.93%	41.79%		
M0 88.77% 82.70% M1 33.08% 18.41% SEER stage 23652 <0.001	AJCC-M			23177	<0.001
M1 33.08% 18.41% SEER stage 23652 <0.001	MO	88.77%	82.70%		
SEER stage 23652 <0.001 Localized 95.06% 91.50% Regional 83.35% 74.99% Distant 35.37% 20.99% Surgery 3945 <0.001	M1	33.08%	18.41%		
Localized 95.06% 91.50% Regional 83.35% 74.99% Distant 35.37% 20.99% Surgery 3945 <0.001	SEER stage			23652	<0.001
Regional 83.35% 74.99% Distant 35.37% 20.99% Surgery 3945 <0.001	Localized	95.06%	91.50%		
Distant 35.37% 20.99% Surgery 3945 <0.001 Yes 82.37% 75.11% No 35.71% 26.47% Radiotherapy 2353 <0.001 Yes 73.77% 63.15% No 86.39% 81.88% Chemotherapy 114 <0.001 Yes 79.50% 69.01% No 80.96% 74.27%	Regional	83.35%	74.99%		
Surgery 3945 <0.001 Yes 82.37% 75.11% No 35.71% 26.47% Radiotherapy 2353 <0.001	Distant	35.37%	20.99%		
Yes 82.37% 75.11% No 35.71% 26.47% Radiotherapy 2353 <0.001	Surgery			3945	<0.001
No 35.71% 26.47% Radiotherapy 2353 <0.001	Yes	82.37%	75.11%		
Radiotherapy 2353 <0.001 Yes 73.77% 63.15% No 86.39% 81.88% Chemotherapy 114 <0.001	No	35.71%	26.47%		
Yes 73.77% 63.15% No 86.39% 81.88% Chemotherapy 114 <0.001 Yes 79.50% 69.01% No 80.96% 74.27%	Radiotherapy			2353	<0.001
No 86.39% 81.88% Chemotherapy 114 <0.001	Yes	73.77%	63.15%		
Chemotherapy 114 <0.001 Yes 79.50% 69.01% No 80.96% 74.27%	No	86.39%	81.88%		
Yes 79.50% 69.01% No 80.96% 74.27%	Chemotherapy			114	<0.001
No 80.96% 74.27%	Yes	79.50%	69.01%		
	No	80.96%	74.27%		

TCSS – tumor cause-specific survival; AJCC – the American Joint Committee on Cancer; SEER – the Surveillance, Epidemiology and End Results.

Supplementary Table 4. Baseline characteristics by insurance status in patients with colorectal cancer after propensity score matching (PSM).

Characteristic	Insured		Ме	Medicaid		nsured	Duralius
	N =	1795	N =	1776	N =	1776	P-value
Gender							0.872
Male	999	(55.7)	973	(54.8)	982	(55.3)	
Female	796	(44.3)	803	(45.2)	794	(44.7)	
Age group (years)							0.857
18–54	858	(47.8)	828	(46.6)	836	(47.1)	
55–64	797	(44.4)	809	(45.6)	800	(45.0)	
65–74	80	(4.5)	91	(5.1)	87	(4.9)	
75–85	60	(3.3)	48	(2.7)	53	(3.0)	
Year of diagnosis							0.710
2007	579	(32.3)	548	(30.9)	580	(32.7)	
2008	613	(34.2)	602	(33.9)	585	(32.9)	
2009	603	(33.6)	626	(35.2)	611	(34.4)	
Marital status							
Married	784	(43.7)	738	(41.6)	743	(41.8)	0.378
Unmarried	1011	(56.3)	1038	(58.4)	1033	(58.2)	
Race							0.988
Asian/Pacific Islander	156	(8.7)	157	(8.8)	149	(8.4)	
Black	416	(23.2)	423	(23.8)	430	(24.2)	
Hispanic white	330	(18.4)	323	(18.2)	315	(17.7)	
Non-Hispanic white	893	(49.7)	873	(49.2)	882	(49.7)	
Household income							0.907
Quartile 1	274	(15.3)	259	(14.6)	261	(14.7)	
Quartile 2	401	(22.3)	376	(21.2)	382	(21.5)	
Quartile 3	482	(26.9)	506	(28.5)	484	(27.3)	
Quartile 4	638	(35.5)	635	(35.8)	649	(36.5)	
College completion							0.712
Quartile 1	360	(20.1)	336	(18.9)	343	(19.3)	
Quartile 2	473	(26.4)	509	(28.7)	490	(27.6)	
Quartile 3	356	(19.8)	366	(20.6)	354	(19.9)	
Quartile 4	606	(33.8)	565	(31.8)	589	(33.2)	
Rural/metropolitan location							0.924
Rural	288	(16.0)	286	(16.1)	293	(16.5)	
Metropolitan	1507	(84.0)	1490	(83.9)	1483	(83.5)	
Cancer site							0.938
Left colon	644	(35.9)	639	(36.0)	618	(34.8)	
Right colon	605	(33.7)	589	(33.2)	603	(34.0)	
Rectosigmoid/rectum	546	(30.4)	548	(30.9)	555	(31.2)	

Charactoristic	Insured		Me	Medicaid		nsured	D value
	N =	= 1795	N =	= 1776	N =	1776	r-value
Histology							0.932
Adenocarcinoma	1671	(93.1)	1646	(92.7)	1645	(92.6)	
Mucinous adenocarcinoma	111	(6.2)	113	(6.4)	114	(6.4)	
Signet ring cell carcinoma	13	(0.7)	17	(1.0)	17	(1.0)	
Grade							0.870
I	146	(8.1)	140	(7.9)	135	(7.6)	
II	1315	(73.3)	1330	(74.9)	1321	(74.4)	
III	294	(16.4)	269	(15.1)	288	(16.2)	
IV	40	(2.2)	37	(2.1)	32	(1.8)	
AJCC stage							0.663
l	248	(13.8)	263	(14.8)	261	(14.7)	
II	568	(31.6)	514	(28.9)	522	(29.4)	
III	601	(33.5)	624	(35.1)	609	(34.3)	
IV	378	(21.1)	375	(21.1)	384	(21.6)	
AJCC-T							0.603
T1	159	(8.9)	180	(10.1)	181	(10.2)	
T2	163	(9.1)	155	(8.7)	164	(9.2)	
Т3	1106	(61.6)	1050	(59.1)	1064	(59.9)	
T4	367	(20.4)	391	(22.0)	367	(20.7)	
AJCC-N							0.668
NO	913	(50.9)	865	(48.7)	881	(49.6)	
N1	511	(28.5)	514	(28.9)	502	(28.3)	
N2	371	(20.7)	397	(22.4)	393	(22.1)	
AJCC-M							0.903
MO	1417	(78.9)	1401	(78.9)	1392	(78.4)	
M1	378	(21.1)	375	(21.1)	384	(21.6)	
SEER stage							0.946
Localized	541	(30.1)	518	(29.2)	529	(29.8)	
Regional	839	(46.7)	837	(47.1)	821	(46.2)	
Distant	415	(23.1)	421	(23.7)	426	(24.0)	
Surgery							0.355
Yes	1675	(93.3)	1646	(92.7)	1635	(92.1)	
No	120	(6.7)	130	(7.3)	141	(7.9)	
Radiotherapy							0.446
Yes	366	(20.4)	379	(21.3)	393	(22.1)	
No	1429	(79.6)	1397	(78.7)	1383	(77.9)	
Chemotherapy							0.725
Yes	1071	(59.7)	1071	(60.3)	1083	(61.0)	
No	724	(40.3)	705	(39.7)	693	(39.0)	

N - number; AJCC - the American Joint Committee on Cancer; SEER - the Surveillance, Epidemiology and End Results.

References:

- 1. Siegel RL, Miller KD, Jemal A: Cancer statistics, 2018. Cancer J Clin, 2018; 68(1): 7–30
- 2. Arnold M, Sierra MS, Laversanne M et al: Global patterns and trends in colorectal cancer incidence and mortality. Gut, 2017; 66(4): 683–91
- 3. Siegel RL, Miller KD, Fedewa SA et al: Colorectal cancer statistics, 2017. Cancer J Clin, 2017; 67(3): 177–93
- Fedewa SA, Sauer AG, Siegel RL, Jemal A: Prevalence of major risk factors and use of screening tests for cancer in the United States. Cancer Epidemiol Biomarkers Prev, 2015; 24(4): 637–52
- 5. Wang J, Ha J, Lopez A et al: Medicaid and uninsured hepatocellular carcinoma patients have more advanced tumor stage and are less likely to receive treatment. J Clin Gastroenterol, 2018; 52(5): 437–43
- Churilla TM, Egleston B, Bleicher R et al: Disparities in the local management of breast cancer in the US according to health insurance status. Breast J, 2017; 23(2): 169–76
- Mahal AR, Mahal BA, Nguyen PL, Yu JB: Prostate cancer outcomes for men aged younger than 65 years with Medicaid versus private insurance. Cancer, 2018; 124(4): 752–59
- Tawk R, Abner A, Ashford A, Brown CP: Differences in colorectal cancer outcomes by race and insurance. Int J Environ Res Public Health, 2015; 13(1): ijerph13010048
- 9. Hankey BF, Ries LA, Edwards BK: The surveillance, epidemiology, and end results program: a national resource. Cancer Epidemiol Biomarkers Prev, 1999; 8(12): 1117–21
- Hayat MJ, Howlader N, Reichman ME, Edwards BK: Cancer statistics, trends, and multiple primary cancer analyses from the Surveillance, Epidemiology, and End Results (SEER) program. Oncologist, 2007; 12(1): 20–37
- 11. Fine JP, Gray RJ: A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc, 1999; 94(446): 496–509
- Scrucca L, Santucci A, Aversa F: Regression modeling of competing risk using R: An in-depth guide for clinicians. Bone Marrow Transplant, 2010; 45(9): 1388–95
- 13. Lin D, Gold HT, Schreiber D et al: Impact of socioeconomic status on survival for patients with anal cancer. Cancer, 2018; 124(8): 1791–97
- 14. Sun W, Qiu Z, Tan W et al: The influence of marital status on survival in patients with oral tongue squamous cell carcinoma. Oncotarget, 2017; 8(47): 82092–102
- Katsnelson J, Barnes RJ, Patel HA et al: Effect of median household income on surgical approach and survival in renal cell carcinoma. Urol Oncol, 2017; 35(9): 541.e1–.e6

- Liu L, Chi YY, Wang AA, Luo Y: Marital status and survival of patients with hormone receptor-positive male breast cancer: A Surveillance, Epidemiology, and End Results (SEER) population-based study. Med Sci Monit, 2018; 24: 3425–41
- Tantraworasin A, Taioli E, Liu B et al: The influence of insurance type on stage at presentation, treatment, and survival between Asian American and non-Hispanic White lung cancer patients. Cancer Med, 2018; 7(5): 1612–29
- Purim O, Gordon N, Brenner B: Cancer of the colon and rectum: Potential effects of sex-age interactions on incidence and outcome. Med Sci Monit, 2013; 19: 203–9
- Halpern MT, Romaire MA, Haber SG et al: Impact of state-specific Medicaid reimbursement and eligibility policies on receipt of cancer screening. Cancer, 2014; 120(19): 3016–24
- 20. Smith MA, Weiss JM, Potvien A et al: Insurance coverage for CT colonography screening: Impact on overall colorectal cancer screening rates. Radiology, 2017; 284(3): 717–24
- Foley KL, Song EY, Klepin H et al: Screening colonoscopy among colorectal cancer survivors insured by Medicaid. Am J Clin Oncol, 2012; 35(3): 205–11
- 22. de Moor JS, Cohen RA, Shapiro JA et al: Colorectal cancer screening in the United States: Trends from 2008 to 2015 and variation by health insurance coverage. Prev Med, 2018; 112: 199–206
- Markt SC, Tang T, Cronin AM et al: Insurance status and cancer treatment mediate the association between race/ethnicity and cervical cancer survival. PloS One, 2018; 13(2): e0193047
- Parikh AA, Robinson J, Zaydfudim VM et al: The effect of health insurance status on the treatment and outcomes of patients with colorectal cancer. J Surg Oncol, 2014; 110(3): 227–32
- Pulte D, Jansen L, Brenner H: Disparities in colon cancer survival by insurance type: A population-based analysis. Dis Colon Rectum, 2018; 61(5): 538–46
- Ahmed A, Walters RW, Tahseen AI, Silberstein PT: The association between insurance status and survival in patients with stage III colon cancer. J Clin Oncol, 2017;35(Suppl. 4): 535
- Kattan MW, Heller G, Brennan MF: A competing-risks nomogram for sarcoma-specific death following local recurrence. Stat Med, 2003; 22(22): 3515–25
- 28. Sommers BD, Bindman AB: New physicians, the Affordable Care Act, and the changing practice of medicine. JAMA, 2012; 307(16): 1697–98