

Supplementary Information

Age- and Stage-Specific Transitions Between Colorectal Cancer-Specific and Other-Cause Mortality After Resection

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2 **Supplementary Table S1. Cohort eligibility, variable definitions, and SEER coding used in the analysis**

Domain		Analysis variable	SEER source field(s)	Definition and coding	Analytical use
Cohort eligibility		Diagnosis period	Year of diagnosis	Cases diagnosed during 2004–2018 were eligible; follow-up was available through 2023.	Defines the study period and permits long-term follow-up.
Cohort eligibility		Colorectal primary site	Primary Site – labeled; Site recode ICD-O-3/WHO 2008	ICD-O-3 topography codes C18.0–C18.9 (colon), C19.9 (rectosigmoid junction), and C20.9 (rectum).	Eligibility criterion and derivation of tumor location.
Cohort eligibility		Eligible histology	ICD-O-3 Hist/behav; ICD-O-3 Hist/behav, malignant	Conventional adenocarcinoma: 8140/3, 8210/3, and 8260/3–8263/3; mucinous adenocarcinoma: 8480/3 and 8481/3; signet-ring cell carcinoma: 8490/3.	Eligibility criterion and derivation of histologic subtype.
Cohort eligibility		First or only malignant primary	Sequence number	One primary only or the first of two or more malignant primaries; later-sequence malignant primaries were excluded.	Reduces ambiguity in attribution of stage and cause-specific death.
Cohort eligibility		Stage I–III and M0 disease	Derived AJCC Stage Group, 6th ed.; Derived AJCC Stage Group, 7th ed.; Derived SEER Cmb Stg Grp; Derived EOD 2018 Stage Group Recode; corresponding derived M fields	Stage I–III was harmonized across calendar periods. Stage IV, unknown/not applicable stage, missing stage, or documented M1 disease in the applicable derived M field was excluded.	Eligibility criterion and stage effect modifier.
Cohort eligibility		Cancer-directed resection	RX Summ–Surg Prim Site (1998–2022)	Codes 30–80 were classified as qualifying cancer-directed resection. Codes 00–29, 90, 99, and missing values were excluded. Site-specific procedure labels were interpreted separately for colon, rectosigmoid-junction, and rectal primaries.	Eligibility criterion; identifies segmental or more extensive resection of the primary tumor.
Cohort eligibility		Known cause-of-death classification	Vital status recode; SEER cause-specific death classification; SEER other cause of death classification; COD to site recode	Alive patients and deaths classifiable as CRC-specific or other-cause were retained. Dead patients with missing or unknown cause-of-death classification were excluded.	Eligibility criterion for competing-risk analysis.
Outcome and follow-up		Follow-up time	Survival months	Time from diagnosis to death or last recorded follow-up, measured in months; follow-up available through 2023.	Time scale for cumulative incidence, Fine–Gray, and cause-specific Cox analyses.
Outcome and follow-up		Competing-risk outcome	Vital status; SEER cause-specific death classification; SEER other cause of death classification; COD to site recode	0 = alive or censored; 1 = CRC-specific death; 2 = death from causes other than CRC. The two causes of death were mutually competing events.	Primary competing-risk outcome.
Primary exposure		Age group	Age recode with <1 year olds and 90+ Derived AJCC Stage Group, 6th ed. (2004–2009); Derived AJCC Stage Group, 7th ed. (2010–2015); Derived SEER Cmb Stg Grp (2016–2017); Derived EOD 2018 Stage Group Recode (2018)	<65, 65–74, 75–84, 85–89, and ≥90 years. Patients aged <65 years served as the reference group.	Primary exposure variable.
Effect modifier		AJCC stage		SEER-derived stage groups were harmonized as stage I, II, and III. Stage IV, unknown/not applicable stage, missing stage, and documented M1 disease were excluded.	Prespecified effect modifier.
Interaction term		Age group × AJCC stage	Derived from age group and AJCC stage	Product interaction between the five-category age-group variable and the three-category stage variable.	Tests whether age-related mortality associations differ according to stage.
Demographic covariate		Sex	Sex	Male and female.	Adjustment covariate.
Demographic covariate		Race	Race recode (W, B, AI, API)	White, Black, Asian or Pacific Islander, American Indian/Alaska Native, and Unknown.	Adjustment covariate.
Demographic covariate		Marital status	Marital status at diagnosis	Married, unmarried, and unknown. Unmarried included never married, divorced, separated, widowed, and unmarried or domestic partner categories.	Adjustment covariate.
Diagnosis covariate		Diagnosis period	Year of diagnosis	2004–2009, 2010–2014, and 2015–2018; entered as a categorical variable.	Adjustment for temporal changes in diagnosis, treatment, and supportive care.
Tumor characteristic		Tumor location	Primary Site – labeled; Site recode ICD-O-3/WHO 2008	Right colon, left colon, rectosigmoid junction, and rectum, grouped from ICD-O-3 primary-site codes.	Adjustment covariate.
Tumor characteristic		Histologic subtype	ICD-O-3 Hist/behav	Conventional adenocarcinoma, mucinous adenocarcinoma, and signet-ring cell carcinoma.	Adjustment covariate.
Tumor characteristic		Tumor grade	Grade Recode (thru 2017); Grade Clinical; Grade Pathological; Derived Summary Grade 2018	Well differentiated, moderately differentiated, poorly differentiated, undifferentiated, and unknown; applicable grade fields were harmonized across diagnosis years.	Adjustment covariate.
Treatment covariate		Chemotherapy	Chemotherapy recode (yes, no/unk)	Yes versus no/unknown. SEER chemotherapy information indicates whether chemotherapy was recorded as part of the first course of therapy.	Adjustment covariate; not interpreted as a causal treatment effect.
Sensitivity analysis		Three-month landmark cohort	Derived from Survival months and vital status	Patients were required to be alive and under observation for more than 3 months. Follow-up was reset by subtracting 3 months from the original survival time.	Reduces the influence of very early deaths.

3 Note: The final analytic cohort included 175,184 patients with stage I–III colorectal cancer diagnosed during 2004–2018. CRC-specific death and other-cause death were treated as mutually competing events. Unknown categories were retained where
4 prespecified. SEER treatment information reflects the first course of therapy and should not be interpreted as a causal treatment effect. Surgery codes should be interpreted using the site-specific labels in the SEER coding manual.
5 Abbreviations: AJCC, American Joint Committee on Cancer; CRC, colorectal cancer; ICD-O-3, International Classification of Diseases for Oncology, Third Edition; SEER, Surveillance, Epidemiology, and End Results.

2 **Supplementary Table S2. Cause-specific Cox regression analyses of age-group associations with colorectal cancer-specific and other-cause mortality within AJCC stage**

		CRC-specific death		Other-cause death	
AJCC stage	Age group, years	HR (95% CI)	<i>P</i> value	HR (95% CI)	<i>P</i> value
Stage I	<65	1.00 (Reference)	—	1.00 (Reference)	—
	65–74	1.56 (1.45–1.68)	<0.001	3.23 (3.09–3.39)	<0.001
	75–84	2.53 (2.35–2.72)	<0.001	7.97 (7.62–8.33)	<0.001
	85–89	3.90 (3.47–4.37)	<0.001	15.02 (14.10–15.99)	<0.001
	≥90	6.43 (5.43–7.63)	<0.001	23.42 (21.31–25.74)	<0.001
Stage II	<65	1.00 (Reference)	—	1.00 (Reference)	—
	65–74	1.38 (1.32–1.45)	<0.001	2.84 (2.72–2.97)	<0.001
	75–84	1.96 (1.87–2.05)	<0.001	6.32 (6.07–6.59)	<0.001
	85–89	2.86 (2.69–3.05)	<0.001	11.25 (10.68–11.86)	<0.001
	≥90	4.43 (4.07–4.82)	<0.001	16.38 (15.28–17.55)	<0.001
Stage III	<65	1.00 (Reference)	—	1.00 (Reference)	—
	65–74	1.34 (1.30–1.39)	<0.001	3.34 (3.20–3.50)	<0.001
	75–84	2.10 (2.03–2.17)	<0.001	7.14 (6.83–7.48)	<0.001
	85–89	3.00 (2.83–3.17)	<0.001	12.19 (11.43–13.01)	<0.001
	≥90	4.57 (4.22–4.95)	<0.001	17.32 (15.78–19.02)	<0.001
Age group × AJCC stage interaction		Wald $\chi^2 = 57.72$; df = 8	<0.001	Wald $\chi^2 = 114.61$; df = 8	<0.001

3 Note: Values are presented as hazard ratios with 95% confidence intervals. Within each AJCC stage, patients aged <65 years served as the reference group. For the CRC-specific death model, deaths from other causes were treated as censored observations.
4 For the other-cause death model, CRC-specific deaths were treated as censored observations. The models included the main effects of age group and AJCC stage and their interaction and were adjusted for sex, race, marital status, diagnosis period, tumor
5 location, histologic subtype, tumor grade, and chemotherapy. P values were obtained using Wald tests; reference-category P values are not applicable.

6 Abbreviations: AJCC, American Joint Committee on Cancer; CI, confidence interval; CRC, colorectal cancer; HR, hazard ratio.

2 **Supplementary Table S3. Three-month landmark sensitivity analysis of age-group associations with colorectal cancer-specific and other-cause mortality using**
3 **multivariable Fine–Gray models within AJCC stage**

		CRC-specific death		Other-cause death	
AJCC stage	Age group, years	sHR (95% CI)	<i>P</i> value	sHR (95% CI)	<i>P</i> value
Stage I	<65	1.00 (Reference)	—	1.00 (Reference)	—
	65–74	1.40 (1.31–1.49)	<0.001	3.00 (2.86–3.14)	<0.001
	75–84	1.82 (1.68–1.97)	<0.001	6.37 (6.07–6.68)	<0.001
	85–89	2.22 (1.94–2.53)	<0.001	9.78 (9.16–10.44)	<0.001
	≥90	2.46 (1.98–3.06)	<0.001	12.72 (11.51–14.06)	<0.001
Stage II	<65	1.00 (Reference)	—	1.00 (Reference)	—
	65–74	1.27 (1.22–1.33)	<0.001	2.57 (2.48–2.67)	<0.001
	75–84	1.48 (1.41–1.56)	<0.001	4.82 (4.64–5.00)	<0.001
	85–89	1.68 (1.55–1.82)	<0.001	6.91 (6.53–7.30)	<0.001
	≥90	1.92 (1.73–2.14)	<0.001	7.93 (7.36–8.54)	<0.001
Stage III	<65	1.00 (Reference)	—	1.00 (Reference)	—
	65–74	1.22 (1.17–1.27)	<0.001	2.85 (2.74–2.97)	<0.001
	75–84	1.64 (1.58–1.71)	<0.001	4.60 (4.40–4.81)	<0.001
	85–89	1.94 (1.80–2.08)	<0.001	5.76 (5.44–6.10)	<0.001
	≥90	2.43 (2.18–2.72)	<0.001	5.66 (4.98–6.42)	<0.001
Age group × AJCC stage interaction		Wald χ^2 = 68.98; df = 8	<0.001	Wald χ^2 = 343.27; df = 8	<0.001

4 Note: The three-month landmark cohort included patients who were alive and remained under observation for more than 3 months after diagnosis. The time origin was reset to 3 months after diagnosis by subtracting 3 months from the original follow-up
5 time. Values are presented as subdistribution hazard ratios with 95% confidence intervals. Within each AJCC stage, patients aged <65 years served as the reference group. The models included the main effects of age group and AJCC stage and their
6 interaction and were adjusted for sex, race, marital status, diagnosis period, tumor location, histologic subtype, tumor grade, and chemotherapy. CRC-specific death and other-cause death were treated as mutually competing events. P values were obtained
7 using Wald tests; reference-category P values are not applicable.
8 Abbreviations: AJCC, American Joint Committee on Cancer; CI, confidence interval; CRC, colorectal cancer; sHR, subdistribution hazard ratio.