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ORIGINAL RESEARCH

The Outcome of Unscreened Population in Colorectal Cancer: The Impact of Sex and Other Determinants on Cancer Stage

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Background: In Saudi Arabia, there is no population-based colorectal cancer (CRC) screening, and more than two-thirds of patients are diagnosed with a late stage. We assessed the association between sex and distant metastasis CRC and hypothesize that females, younger age, non-married, and patients with colon cancer would present with metastatic tumors.

Patients and Methods: The retrospective cohort study used data from the Ministry of National Guard Cancer Registry. Logistic regression was used to assess the association between sex and metastatic CRC adjusting for patient covariates. In a sensitivity analysis, the association between sex and late-stage CRC was evaluated.

Results: A total of 1016 CRC patients met the eligibility criteria, with 37.59% of females and 30.26% of males diagnosed with metastatic CRC. After adjusting for marital status, grade, and morphology, females were 20% more likely than males to present with a metastatic tumor 1.20 (95% CI, 1.04–1.38).

Conclusion: Although the entire Saudi population would benefit from CRC screening, women may benefit the most from targeted screening.

Keywords: colorectal cancer, registry, survival, Saudi Arabia

Background

Colorectal cancer (CRC) is the third most common cancer and the second cause of cancer death globally.[1,2] CRC risk factors, including poor diet, smoking, alcohol intake, and visceral fat, are more common in males and reflects the higher CRC morbidity and mortality in males compared to females.[1,3] In Saudi Arabia, CRC remains the most prevalent cancer in males and the third most prevalent in females causing 2047 new cases and 1090 deaths in 2014.[4–6] Despite the higher CRC incidence in Saudi males, the increased consumption of fatty diet, the increased percentage of overweight, and the lower rates of physical activities in Saudi females are characteristics more frequently associated with poor CRC outcomes.[6]

CRC survival, as a critical CRC outcome, is determined by several factors, including demographics (age, sex, and marital status), tumor characteristics (size, grade, and stage at diagnosis), comorbidities, treatment, and the existence of population-based screening.[3] Currently, there is no population-based CRC screening in Saudi Arabia. Of all the other factors contributing to CRC survival, the most determinant factor is the stage at diagnosis, a more predictive CRC survival factor than treatment.[7] Evidence indicates that lower CRC survival is associated with

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a later stage at diagnosis, and there is an inverse relationship between an advanced stage at diagnosis and CRC survival.[3,8,9]

Previous studies in the Saudi population reported a 9.6% sex difference in the 5-year overall survival in CRC patients, favoring females.[10,11] However, after adjustment for patient characteristics, the same studies reported a survival advantage in males, an obscure finding. Whether there is a difference between Saudi males and females in terms of the stage at diagnosis, remains unknown.

Prior international research reported controversial results regarding the association between sex and stage at diagnosis. In the US, Nguyen et al conducted a systematic review and meta-analysis to assess the association between sex and advanced colorectal neoplasia. They found that males had an 83% higher risk of developing advanced neoplasia compared to females.[12] However, a UK-based national study assessing the same association found no overall differences, but males were more likely to be diagnosed at Stage I compared to females.[13] A possible explanation that males are more likely to be diagnosed at an earlier stage is they have higher distal colon cancer that is characterized by polypoid tumors, opposed to flat tumors that is more common in the proximal colon and prevalent in females and easily missed on the initial colonoscopy.[14–17] Evidence is unclear about the association between sex and the stage at diagnosis, especially in a population with no systematic CRC screening such as the Saudi population.

Our objective was to study the association between sex and distant metastasis (ie, late-stage) versus non-metastasis (ie, early-stage) CRC diagnosis, after adjusting for other independent patient-related covariates. Our primary hypothesis was that women because they have less access to healthcare, would be more likely than men to be diagnosed at a late rather than the early stages of CRC. Secondly, based on prior literature, we expected a late-stage CRC diagnosis to be more frequent in younger patients,[18] in non-married patients,[19,20] and colon cancer patients due to fewer visible bleeding symptoms before diagnosis compared with rectal cancer patients.[21,22]

Patients and Methods

Data Sources

The current study is a retrospective cohort study using data from the Cancer Registry of the Ministry of National Guard-Health Affairs (MNG-HA). The registry captures cancer information about patient demographics, clinical characteristics such as cancer type, location, and extent at the time of diagnosis. The registry records all cases diagnosed and treated at King Abdulaziz Medical City (KAMC) in Riyadh. King Abdullah International Medical Research Center approved this study (IRB#RC19/029/R).

Study Population

Patients included in the current study were all from the MNG-HA population with histopathologically confirmed CRC diagnosis between January 1, 2009, and December 31, 2017, and ≥18 years old at the time of diagnosis. The MNG-HA population consists of military service members and their dependents, civilian workforce, and healthcare students from the MNG-HA healthcare system. The population of more than one million individuals is served by tertiary care hospitals and four main primary and secondary care clinics.

Study Variables

Patient and Tumor Characteristics

The patient demographics retrieved from the medical records include age at diagnosis, sex, and marital status. The clinical variables, including tumor topography, morphology, behavior, grade, and extent, were extracted from the pathology reports and surgical specimens. The anatomic tumor location was categorized according to the ICD for Oncology-third edition topography as follows: right colon (ie, cecum, ascending colon, hepatic flexure of the colon and transverse colon), left colon (ie, splenic flexure of the colon, descending colon, and sigmoid), rectum (rectosigmoid junction and rectum) and colon not otherwise specified (NOS).[23–25]

Outcome Variable

The outcome of the study was the stage at diagnosis. Distant metastasis at the time of diagnosis designates non-curable disease, and the goal of treatment is palliative. However, an in-situ, localized, or regional stage at diagnosis is considered curable.[26] Given the distinction between a treatable vs curable stage at diagnosis, patients diagnosed with distant metastasis were categorized as late-stage-at-diagnosis, and patients presenting with an in situ, localized, or regional stage were classified as early-stage-at-diagnosis. The Surveillance, Epidemiology, and End Results (SEER) Summary Staging (In situ, localized, regional, distant metastasis) was used in this study.[27]

Sensitivity Analysis

Two sensitivity analyses were conducted. Firstly, to compare our findings with prior studies, the outcome variable was also categorized as follows: In-situ and stage I were considered early tumors while stages II, III and IV were considered late-stage tumor.[28] Secondly, the anatomic tumor location was defined differently in three separate models. For the first model, the right bowel segment (cecum, appendix, ascending colon, hepatic flexure, transverse colon, and splenic flexure) and the left bowel segment (descending colon, sigmoid, rectosigmoid, and rectum) definitions were used. In the second model, the proximal colon (cecum, appendix, ascending colon, hepatic flexure, transverse colon, splenic flexure, and descending colon) and the distal colon (sigmoid, rectosigmoid, and rectum) definition were used. For the third model, the cecum and appendix were designated as one category with the distal (sigmoid, rectosigmoid, and rectum) bowel in the other category. The two sensitivity analyses were used to assess the robustness of our results under various definitions.

Data Analysis

The demographic and clinical characteristics were assessed using chi-square statistics, and Wald tests were used to determine the association between covariates and stage at diagnosis. Logistic regression models were used to determine the univariate association between the stage at diagnosis and covariates, and the multivariate association between stage at diagnosis and sex adjusting for all potential covariates. Backward elimination was used during the multivariate analysis to retain all variables with a $P \leq 0.20$. These variables were marital status, topography, grade, and morphology. We assessed the interaction between sex and other covariates and found no significant interaction. All statistical tests were 2-sided, and findings were considered statistically significant at $P < 0.05$. All analyses were conducted using SAS statistical software version 9.4 (SAS Institute Inc. Cary, NC).

Results

After applying the eligibility criteria, the total sample was 1016 CRC patients diagnosed between 2009 and 2017. Table 1 displays the demographic and clinical features of the patients according to sex. Women were diagnosed at a younger age but were less married compared to men.

Table 2 displays the results of the univariate and multivariate logistic regression analyses. At the univariate level, patients who presented with moderately differentiated tumors were 41.40% less likely to be diagnosed at the metastatic stage (OR= 0.586; 95% CI: 0.452, 0.760), compared to patients diagnosed with poorly differentiated tumors.

At the multivariate level, after adjustment for marital status, topography, grade, and morphology, women were 20% more likely than men to be diagnosed with metastatic stage tumors (OR= 1.204; 95% CI: 1.048, 1.384). Patients who presented with moderately differentiated tumors were 44% less likely than patients with poorly differentiated tumors to be diagnosed at a metastatic stage (OR= 0.562; 95% CI: 0.424, 0.747). Moreover, compared with patients diagnosed with signet ring cell carcinoma, patients diagnosed with adenocarcinoma, mucinous adenocarcinoma, adenocarcinoma with villous/tubulovillous adenoma, and others were 77.1%, 86.0%, 86.7%, and 87.3% less likely to present with metastatic stage tumors, respectively. Table 3 displays the significant increase in a metastatic stage diagnosis in both sexes throughout the diagnosis periods. In the sensitivity analyses (Supplementary Table 1 and 2), we found no differences in metastatic stage at diagnosis according to tumor subsites.

Discussion

In a population with no systematic CRC screening, we investigated the association between sex and metastatic stage at diagnosis after controlling for potential covariates. We hypothesized that because women have less access to healthcare, they were more likely than men to be diagnosed with distant metastatic CRC. We also hypothesized that younger patients, non-married, and patients with colon cancer (compared to rectal cancer patients) would be more likely to be diagnosed at a metastatic stage. We reported an increase in the diagnosis of distant metastatic CRC between 2009 and 2017 in both sexes, with a higher proportion of metastatic or late-stage diagnosis in women. We also demonstrated that women were 20% more likely than men to be diagnosed at a metastatic stage. We were unable to detect a difference in the diagnosis of metastatic CRC by age and marital status, as reported previously.[18,21,22,29] A diagnosis of CRC at the metastatic stage, especially non-resectable metastatic tumors, is associated with increased morbidity and mortality[3] and is a substantial burden to healthcare.[30,31]

Table 1 Demographic and Clinical Characteristics by Sex, MNG-HA, 2009–2017 *

Characteristics	Total (n=1016)		Women (n=431)		Men (n=585)		P
	N	%, SD	N	%, SD	N	%, SD	
Age (years)							
Mean (SD)	60.46	14.28	59.09	13.94	61.46	14.45	
≤40	84	8.27	39	9.05	45	7.69	**0.04**
41–50	142	13.98	65	15.08	77	13.16	
51–60	293	28.84	138	32.02	155	26.50	
61–70	242	23.82	102	23.67	140	23.93	
71–80	178	17.52	58	13.46	120	20.51	
≥81	77	7.58	29	6.73	48	8.21	
Marital status							
Married	760	74.80	300	69.61	460	78.63	**<0.01**
Non-married	256	25.20	131	30.39	125	21.37	
Tumor site							
Right colon	182	17.91	77	17.87	105	17.95	0.66
Left colon	291	28.64	132	30.63	159	27.18	
Colon-non specified	168	16.54	69	16.01	99	16.92	
Colon (all)	641	63.09	278	64.51	363	64.05	
Rectum	375	36.91	153	35.50	222	37.95	
Tumor morphology							
Adenocarcinoma (AC)	857	84.35	362	83.99	495	84.62	0.48
Mucinous AC	63	6.20	27	6.26	36	6.15	
Mucin-producing AC	12	1.18	3	0.70	9	1.54	
Signet ring cell	14	1.38	4	0.93	10	1.71	
AC in villous adenoma	16	1.57	9	2.09	7	1.20	
Others	54	5.31	26	6.03	28	4.79	
Tumor grade							
Well differentiated	33	3.25	16	3.71	17	2.91	0.73
Moderately differentiated	776	76.38	326	75.64	450	76.92	
Poorly differentiated	68	6.69	32	7.42	36	6.15	
Unknown	139	13.68	57	13.23	82	14.02	
Stage at diagnosis							
In situ	3	0.30	2	0.46	1	0.17	0.06
Localized	228	23.22	83	19.26	145	24.79	
Regional	412	41.96	169	39.21	243	41.54	
Distant metastasis	339	34.52	162	37.59	177	30.26	
Missing	34	3.35	15	3.48	19	3.25	

Note: *Bold numbers indicate significant results at p=0.05.

The majority of prior research found no significant differences in metastatic or late-stage diagnosis by sex, contrary to other studies.[13,18,28,32–39] Congruent with our findings, Charlton et al assessed the association between sex and late-stage diagnosis in a Medicare population and found women to be 64% more likely than men to be diagnosed at a late stage. However, the association was reduced to a non-significant 3% when the authors stratified the results by having had a colonoscopy, differentiating patients diagnosed with a colonoscopy from others (eg, emergency admission).[28] Similarly, Morgan et al reported that Californian women had a 6% higher odds of late-stage after adjustment for age, race, SES, and bowel segment.[29] In contrast, Amri et al compared the odds of a metastatic stage diagnosis by sex and found no significant difference; however, other authors reported unscreened women are more likely to be diagnosed at a metastatic stage than screened women.[32] Given the fact that our population is

Table 2 Logistic Regression of Metastatic vs Non-Metastatic Colorectal Cancer Diagnosis by Sex and Other Determinants, MNG-HA, 2009–2017*

Characteristics	Univariate			Multivariate	
	OR	95% CI	P	OR	95% CI
Sex					
Male	1.0		**0.01**	**1.0**	
Female	**1.182**	**(1.035,1.350)**		**1.204**	**(1.048,1.384)**
Age					
≤40	1.0		0.40	-	-
41–50	1.037	(0.753,1.429)		-	-
51–60	0.855	(0.663,1.102)		-	-
61–70	1.110	(0.856,1.440)		-	-
71–80	1.025	(0.760,1.383)		-	-
≥81	0.851	(0.554,1.306)		-	-
Marital status					
Married	1.0		0.17	-	-
Non-married	1.109	(0.954,1.290)		-	-
Tumor site				-	-
Right colon	1.0		0.25	-	-
Left colon	1.021	(0.820,1.272)		-	-
Rectum	0.840	(0.681,1.037)		-	-
Colon-non specified	1.193	(0.918,1.549)		-	-
Colon (all)	1.0		0.10	-	-
Rectum	0.894	(0.779,1.027)			
Tumor grade					
Poorly differentiated	1.0		**<0.01**	1.0	
Moderately differ.	**0.586**	**(0.452,0.760)**		**0.562**	**(0.424,0.747)**
Well differ.	0.789	(0.453,1.372)		0.898	(0.508,1.588)
Unknown	**1.603**	**(1.141,2.253)**		**1.855**	**(1.275,2.699)**
Morphology					
Signet ring cell carc.	1.0		0.11	1.0	
Adenocarcinoma (AC)	0.687	(0.467,1.011)		0.987	(0.648,1.503)
Mucin-producing AC	1.340	(0.495,3.621)		1.491	(0.529,4.203)
Mucinous AC	0.591	(0.330,1.058)		0.554	(0.300,1.023)
AC Villous, Tubuvillous adenoma	0.447	(0.165,1.207)		0.572	(0.203,1.609)
Others	0.835	(0.460,1.517)		**0.514**	**(0.268,0.984)**

Note: *Bold numbers indicate significant results at p=0.05.

an unscreened population, a null association between sex and metastatic diagnosis could be expected, because the women in the study, compared to men, presented with fewer rectal tumors and had slightly better tumor characteristics (less signet ring cell carcinoma and more well-differentiated tumors). It remains unclear why more women present at metastatic stage. The reason for this disparity cannot be inferred from the current study data, as it may range from behavioral, cultural (eg, inability for women to drive causing a delay or even lack of access to healthcare), and socioeconomic factors, to sex-specific factors such as fewer communication with the provider during a clinic visit.[40]

We also hypothesized that younger patients, the non-married, and patients diagnosed with colon cancer would be more likely than their counterparts to present at a metastatic stage. With regard to age, we did not find a difference in a metastatic diagnosis by age, a finding similar to several studies,[21,28,33] but not to others.[18] The hypothesis that younger patients are more likely to be diagnosed at a late

Table 3 CRC Among Women and Men by Year and Stage at Diagnosis, 2009–2017

Sex	Stage	Diagnosis Year									
		2009 N (%)	2010 N (%)	2011 N (%)	2012 N (%)	2013 N (%)	2014 N (%)	2015 N (%)	2016 N (%)	2017 N (%)	P
Women											
	Non-Metastatic	26 (77.22)	23 (63.89)	30 (56.60)	25 (58.14)	36 (69.23)	34 (56.67)	31 (62.00)	33 (62.26)	16 (48.48)	0.21
	Metastatic	10 (27.78)	13 (36.11)	23 (43.40)	18 (41.86)	16 (30.77)	26 (43.33)	19 (38.00)	20 (37.74)	17 (51.52)	
Men											
	Non-Metastatic	42 (80.77)	33 (60.00)	33 (64.71)	65 (77.38)	54 (70.13)	45 (64.29)	37 (61.67)	52 (74.29)	28 (59.57)	0.24
	Metastatic	10 (19.23)	22 (40.00)	18 (35.29)	19 (22.62)	23 (29.87)	25 (35.71)	23 (38.33)	18 (25.71)	19 (40.43)	
Women											
	Early stages (In situ, localized)	9 (25.00)	12 (33.33)	12 (22.64)	8 (18.60)	15 (28.85)	13 (21.67)	9 (18.00)	4(7.55)	3(9.09)	0.002
	Late stage	27 (75.00)	24 (66.67)	41 (77.36)	35 (81.40)	37 (71.15)	47 (78.33)	41 (82.00)	49 (92.45)	30 (90.91)	
Men											
	Early stages (In situ, localized)	15 (28.85)	14 (25.45)	13 (25.49)	25 (29.76)	31 (40.26)	20 (28.57)	10 (16.67)	11 (15.71)	7 (14.89)	0.01
	Late stage	37 (71.15)	41 (74.55)	38 (74.51)	59 (70.24)	46 (59.74)	50 (71.43)	50 (83.33)	59 (84.29)	40 (85.11)	

stage is based on prior findings that younger patients (<50 years) tend to present with aggressive disease that develops into an advanced stage faster than the older population,[41,42] however; this was not found in the current study. The univariate analysis indicated that non-married patients were more likely to be diagnosed at a metastatic stage compared to married patients, but the finding was insignificant. Prior research showed that social support through marriage is positively associated with CRC detection and treatment.[19,43] In terms of tumor location (ie, left vs right, etc.), the analyses showed no differences between men and women who presented with left-sided-colon or rectal-tumor and metastatic stage, inconsistent with prior literature.[1,3] In a sensitivity analysis that is limited to individuals presenting with right-sided or left-sided tumors and proximal or distal tumors (Supplementary Table 1), there was also no significant association between tumor location and metastatic stage. It should be noted that in the current study, in addition to sex, other tumor characteristics were associated with a metastatic stage at diagnosis, including tumor grade and morphology. Patients diagnosed with moderately differentiated tumors or non-signet ring cell carcinoma were less likely to be diagnosed at a metastatic stage compared to their counterparts.

In a sensitivity analysis (Supplementary Table 2), we categorized the stage at diagnosis in early-stage (in situ and localized tumors) and late-stage (regional and distant metastasis) similar to a previous publication,[28] and the proportion of patients classified as late-stage exceeded 76%. Considering that the stage at diagnosis is the most predictive factor for CRC outcome, it is disheartening that the majority of our population present at a late stage, in view of the preventive nature of CRC. The prognosis of late-stage CRC is poor because it is associated with increased morbidity and mortality, irrespective of the patient's characteristics. On a positive note, though women tend to present with more metastatic disease than men, the survival rates are similar, suggesting an improvement in CRC treatment.

Evidence suggests a link between the lack of population-based CRC screening and the detrimental CRC outcomes.[44–47] Not only does the absence of CRC screening prevent the detection of polyps and CRC during the early development, but it has a negative impact on the entire continuum of CRC, especially among female.[32] For instance, during the diagnosis phase, 86.1% of the non-screened women and 4.2% of the screened women present with symptoms. Likewise, while 13.6% of the non-screened women undergo emergency admission, only 2.5% of the screened women do. During the treatment phase, compared to non-screened women, screened women suffer from longer surgery duration and subsequent longer length of hospital stay (118 vs 105 minutes), higher multivisceral resections (20% vs 5%), higher node involvement (47.6% vs 21%) and higher distant metastasis (12.3% vs 1.7%). The long-term benefits of CRC screening are, in essence, pertinent to the medical and surgical

oncologists since positive CRC outcomes are higher among screened patients.

While there is no population-based screening in Saudi Arabia, different groups endorsed screening for average-risk asymptomatic patients 45–70 years old.[48,49] They have also recommended the use of a colonoscopy every 10 years, followed by sigmoidoscopy every 5 years with Guaiac Fecal Occult Blood Test (gFOBT) or Fecal Immunochemical Test (FIT). Nonetheless, the implementation of screening in Saudi Arabia is challenging because of the several factors influencing the screening. Among the known factors are age, gender, race, socioeconomic status, the availability of health insurance, the usual source of care, level of communication with the provider, knowledge of CRC screening, and geographic access to screening centers.[40,50]

While the effective implementation of screening requires a usual source of care, Primary Care Physician (PCP) is the source of care associated with the increased uptake of CRC screening.[40] For instance, a 10% increase in PCP supply is associated with a 5% reduction in late-stage CRC. PCP initiates the discussion and recommendation about screening, perform the non-invasive stool-based tests (eg, FOBT), and do a specialist referral for endoscopic testing.[51] However, not all PCPs are alike since evidence suggests that male PCPs are less likely than female PCPs to practice patient-centered communication or spend more time with the patient during clinic visits to discuss preventive services such as screening.[52,53] Given the higher proportion of male healthcare providers in Saudi Arabia pertinent to the existing culture,[54] the challenge will remain in the uptake of screening. Accordingly, policies advocating for increasing the number of female PCP should be prioritized.

A strength of the current study is the use of the Cancer Registry from a diverse population diagnosed with CRC. Although most of the MNG-HA population are military personnel, some are professional workers or students. The study has some limitations that should be considered when interpreting the findings. Firstly, the generalizability of the results should be limited to an MNG-HA population or other similar populations. Secondly, we were unable to assess the reasons for the differences in stage at diagnosis. However, given the absence of population-based screening and the fact that none of our samples was diagnosed with a death certificate, the potential explanations for the differences in stage at diagnosis could be whether individuals were diagnosed during an emergency or elective visit, a delay due to a long waiting time or GP referral, factors that should be explored in future studies. Thirdly, our registry lacks information about potential confounders such as socioeconomic status. However, given the universal access to healthcare in our population, these factors should have a negligible effect on our findings. Fourthly, there were also limitations to the classification of the metastatic stage at diagnosis, a classification that was solely based on treatable versus curable disease. This classification would have been problematic had there been referral bias (eg, more severe cases referred to our institutions), and the distribution of metastatic stage was higher among women.

Nonetheless, the sensitivity analysis corroborated our main findings and showed that women still present with late-stage tumors compared to men. Lastly, covariates such as BMI, comorbidities, and physical activities were not captured in the data. Therefore, we were unable to compare these characteristics by sex. Nonetheless, prior studies showed that 40% of Saudi women and approximately 30% of Saudi men were considered obese (BMI $\geq$ 30).[4] Moreover, 50% of Saudi men and 66% of Saudi women were found to be physically inactive.

Conclusion

Although a preventable disease, we have shown that 34.56% of our sample presented with metastatic CRC, 76% presented with late-stage CRC, and the majority of late-stage cases were women. The findings clearly show the disparities in CRC stage at diagnosis in the Saudi population. The current study, therefore, provides a framework for future population-based screening by extending the positive impact of the overall CRC screening to people with the highest likelihood of presenting with late-stage CRC.

Abbreviations

CRC, Colorectal Cancer; MNG-HA, Ministry of National Guard-Health Affairs; ICD, International Classification of Diseases; SEER, Surveillance, Epidemiology, and End Results; AJCC, American Joint Committee on Cancer; NOS, Non Otherwise Specified.

Data Sharing Statement

The data are available from the Oncology Department but restrictions applies to the availability of these data due to sensitive identifier that have been used in this study, which were used under license for the current study, and so are not publicly available.

Ethics Approval

King Abdullah International Medical Research Center approved this study (IRB#RC19/029/R).

Consent for Publication

De-identified patient information was used in this study, and consent was obtained from the study participants prior to study commencement.

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest for this work.

References

1. Keum N, Giovannucci E. Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. *Nat Rev Gastroenterol Hepatol*. 2019;1–20.
2. Ferlay J, Colombet M, Soerjomataram I, et al. Estimating the global cancer incidence and mortality in 2018: globocan sources and methods. *Int j Cancer*. 2019;144(8):1941–1953.
3. Siegel RL, Miller KD, Fedewa SA, et al. Colorectal cancer statistics, 2017. *CA Cancer J Clin*. 2017. doi:10.3322/caac.21395
4. World Health Organization. Cancer country profile. 2014.
5. KFSHRC OCRU. Tumor registry annual report 2014. 2017.
6. Alyabsi M, Alhumaid A, Allah-Bakhsh H, Alkelya M, Aziz MA. Colorectal cancer in saudi arabia as the proof-of-principle model for implementing strategies of predictive, preventive, and personalized medicine in healthcare. *EPMA J*. 2019;1–13.
7. Lai Y, Wang C, Civan JM, et al. Effects of cancer stage and treatment differences on racial disparities in survival from colon cancer: A united states population-based study. *Gastroenterology*. 2016;150 (5):1135–1146. doi:10.1053/j.gastro.2016.01.030
8. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin*. 2016;66(1):7–30. doi:10.3322/caac.21332
9. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394–424.
10. Al-Ahwal MS, Shafik YH, Al-Ahwal HM. First national survival data for colorectal cancer among saudis between 1994 and 2004: what's next? *BMC Public Health*. 2013;13(73). doi:10.1186/1471-2458-13-73
11. Alsanea N, Abduljabbar AS, Alhomoud S, Ashari LH, Hibbert D, Bazarbashi S. Colorectal cancer in saudi arabia: incidence, survival, demographics and implications for national policies. *Ann Saudi Med*. 2015;35(3):196–202. doi:10.5144/0256-4947.2015.196
12. Nguyen SP, Bent S, Chen Y-H, Terdiman JP. Gender as a risk factor for advanced neoplasia and colorectal cancer: A systematic review and meta-analysis. *Clinical Gastroenterol Hepatol*. 2009;7(6):676–681. e673. doi:10.1016/j.cgh.2009.01.008
13. White A, Ironmonger L, Steele RJC, Ormiston-Smith N, Crawford C, Seims A. A review of sex-related differences in colorectal cancer incidence, screening uptake, routes to diagnosis, cancer stage and survival in the UK. *BMC Cancer*. 2018;18(1):906. doi:10.1186/s12885-018-4786-7
14. Singh H, Nugent Z, Demers AA, Bernstein CN. Rate and predictors of early/missed colorectal cancers after colonoscopy in manitoba: A population-based study. *Am J Gastroenterol*. 2010;105 (12):2588–2596. doi:10.1038/ajg.2010.390
15. Singh H, Nugent Z, Mahmud SM, Demers AA, Bernstein CN. Predictors of colorectal cancer after negative colonoscopy: A population-based study. *Am J Gastroenterol*. 2010;105(3):663–673. doi:10.1038/ajg.2009.650
16. Kaku E, Oda Y, Murakami Y, et al. Proportion of flat-and depressed-type and laterally spreading tumor among advanced colorectal neoplasia. *Clinical Gastroenterol Hepatol*. 2011;9(6):503–508. doi:10.1016/j.cgh.2011.03.018
17. Saunders BP, Fukumoto M, Halligan S, Jobling C, Moussa ME, Bartram CI. Why is colonoscopy more difficult in women? *Gastrointest Endosc*. 1996;43(2):124–126. doi:10.1016/S0016-5107(06)80113-6
18. Mandelblatt J, Andrews H, Kao R, Wallace R, Kerner J. The late-stage diagnosis of colorectal cancer: demographic and socioeconomic factors. *Am J Public Health*. 1996;86(12):1794–1797. doi:10.2105/ajph.86.12.1794
19. Li Q, Gan L, Liang L, Li X, Cai S. The influence of marital status on stage at diagnosis and survival of patients with colorectal cancer. *Oncotarget*. 2015;6(9):7339. doi:10.18632/oncotarget.3129
20. Liu M, Li L, Yu W, Chen J, Xiong W. Marriage is a dependent risk factor for mortality of colon adenocarcinoma without a time-varying effect. *Oncotarget*. 2017;8(12):20056. doi:10.18632/oncotarget.15378
21. Sankaranarayanan J, Watanabe-Galloway S, Sun J, Qiu F. Rurality and other determinants of early colorectal cancer diagnosis in nebraska: A 6-year cancer registry study, 1998–2003. *J Rural Health*. 2009;25(4):358–365. doi:10.1111/j.1748-0361.2009.00244.x
22. Beahrs OH, Sanfelippo PM. Factors in prognosis of colon and rectal cancer. *Cancer*. 1971;28(1):213–218. doi:10.1002/1097-0142-(197107)28:1<213::AID-CNCR2820280142>3.0.CO;2-I
23. Murphy G, Devesa SS, Cross AJ, Inskip PD, McGlynn KA. Sex disparities in colorectal cancer incidence by anatomic subsite, race and age. *Int J Cancer*. 2011;128(7):1668–1675. doi:10.1002/ijc.25481
24. Lee YC, Lee YL, Chuang JP, Lee JC. Differences in survival between colon and rectal cancer from seer data. *PLoS One*. 2013;8(11): e78709. doi:10.1371/journal.pone.0078709
25. Chen VW, Hsieh MC, Charlton ME, et al. Analysis of stage and clinical/prognostic factors for colon and rectal cancer from seer registries: ajcc and collaborative stage data collection system. *Cancer*. 2014;120(Suppl 23):3793–3806. doi:10.1002/cncr.29056
26. Andrilla CHA, Moore TE, Wong K M. Investigating the impact of geographic location on colorectal cancer stage at diagnosis: A national study of the seer cancer registry. *J Rural Health*. 2019. doi:10.1111/jrh.12392
27. Young JL. Seer summary staging manual 2000: codes and coding instructions. *National Cancer Institute, National Institutes Health*. 2001.
28. Charlton ME, Matthews KA, Gaglioti A, Bay C, McDowell BD, Ward MM. Is travel time to colonoscopy associated with late-stage colorectal cancer among medicare beneficiaries in iowa? *J Rural Health*. 2015. doi:10.1111/jrh.12159
29. Morgan JW, Cho MM, Guenzi CD, et al. Predictors of delayed-stage colorectal cancer: are we neglecting critical demographic information? *Ann Epidemiol*. 2011;21(12):914–921. doi:10.1016/j.annepidem.2011.09.002

30. Scalo JF, Rascati KL. Trends and issues in oncology costs. *Expert Rev Pharmacoecon Outcomes Res*. 2014;14(1):35–44. doi:10.1586/14737167.2014.864561
31. Mariotto AB, Robin Yabroff K, Shao Y, Feuer EJ. Projections of the cost of cancer care in the united states: 2010–2020. *J Natl Cancer Inst*. 2011;103(2):117–128. doi:10.1093/jnci/djq495
32. Amri R, Bordeianou LG. The fate of unscreened women in colon cancer: impact on staging and prognosis. *Am J Surg*. 2015;209(6):927–934. doi:10.1016/j.amjsurg.2014.09.033
33. Scoggins JF, Fedorenko CR, Donahue SM, Buchwald D, Blough DK. Is distance to provider a barrier to care for medicaid patients with breast, colorectal, or lung cancer? *J Rural Health*. 2012;28(1):54–62. doi:10.1111/j.1748-0361.2011.00371.x
34. McArdle CS, McMillan DC. Male gender adversely affects survival following surgery for colorectal cancer. *Br J Surg*. 2003;90(6):711–715. doi:10.1002/bjs.4098
35. Alyabsi M, Charlton M, Meza J, Islam KMM. The impact of travel time on colorectal cancer stage at diagnosis in a privately insured population. *BMC Health Serv Res*. 2019;19(1):172. doi:10.1186/s12913-019-4004-6
36. Althans AR, Brady JT, Keller DS, Stein SL, Steele SR. Are we catching women in the safety net? Colorectal cancer outcomes by gender at a safety net hospital. *Am J Surg*. 2017;214(4):715–720. doi:10.1016/j.amjsurg.2017.07.022
37. Innos K, Padrik P. Sex differences in cancer survival in estonia: A population-based study. *BMC Cancer*. 2015;15(72). doi:10.1186/s12885-015-1080-9
38. Kotake K, Asano M, Ozawa H. Gender differences in colorectal cancer survival in japan. *Int J Clin Oncol*. 2016;21(1):194–203. doi:10.1007/s10147-015-0868-6
39. Majek O, Gondos A, Jansen L, et al. Sex differences in colorectal cancer survival: population-based analysis of 164,996 colorectal cancer patients in germany. *PLoS One*. 2013;8(7):e68077. doi:10.1371/journal.pone.0068077
40. Beydoun HA. Predictors of colorectal cancer screening behaviors among average-risk older adults in the united states. *Cancer Causes Control*. 2008;19(4):339–359. doi:10.1007/s10552-007-9100-y
41. Ahnen DJ, Wade SW, Jones WF, et al. The increasing incidence of young-onset colorectal cancer: A call to action. *Mayo Clin Proc*. 2014;89(2):216–224. doi:10.1016/j.mayocp.2013.09.006
42. Amri R, Bordeianou LG. The conundrum of the young colon cancer patient. *Surgery*. 2015;158(6):1696–1703. doi:10.1016/j.surg.2015.07.018
43. Aizer AA, Chen M-H, McCarthy EP, et al. Marital status and survival in patients with cancer. *J clin oncol*. 2013;31(31):3869. doi:10.1200/JCO.2013.49.6489
44. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA. Global cancer statistics 2018: globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394–424. doi:10.3322/caac.21492
45. DeSantis CE, Lin CC, Mariotto AB, et al. Cancer treatment and survivorship statistics. *CA Cancer J Clin*. 2014;64(4):252–271. doi:10.3322/caac.21235
46. Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics. *CA Cancer J Clin*. 2020.
47. Lindholm E. Survival benefit in a randomized clinical trial of faecal occult blood screening for colorectal cancer. *British J Surgery*. 2008;95(8):1029–1036. doi:10.1002/bjs.6136
48. Alsanea N, Almadi MA, Abduljabbar AS, et al. National guidelines for colorectal cancer screening in saudi arabia with strength of recommendations and quality of evidence. *Ann Saudi Med*. 2015;35(3):189–195. doi:10.5144/0256-4947.2015.189
49. Aljumah AA. Policy of screening for colorectal cancer in saudi arabia: A prospective analysis. *Saudi J Gastroenterol*. 2017;23(3):161–168. doi:10.4103/sjg.SJG_468_16
50. McLachlan SA. Patients' experiences and reported barriers to colonoscopy in the screening context–a systematic review of the literature. *Patient Educ Couns*. 2012;86(2):137–146. doi:10.1016/j.pec.2011.04.010
51. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: A joint guideline from the american cancer society, the us multi-society task force on colorectal cancer, and the american college of radiology. *CA Cancer J Clin*. 2008;58(3):130–160. doi:10.3322/CA.2007.0018
52. Flocke SA. Physician and patient gender concordance and the delivery of comprehensive clinical preventive services. *Med Care*. 2005;486–492. doi:10.1097/01.mlr.0000160418.72625.1c
53. Roter DL, Hall JA. Physician gender effects in medical communication: A meta-analytic review. *JAMA*. 2002;288(6):756–764. doi:10.1001/jama.288.6.756
54. Albejaidi F, Nair KS. Building the health workforce: saudi arabia's challenges in achieving vision 2030. *Int J Health Plann Manage*. 2019;34(4):e1405–e1416. doi:10.1002/hpm.2861