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Marital Status and Survival in Patients With Cancer

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ABSTRACT

Purpose
To examine the impact of marital status on stage at diagnosis, use of definitive therapy, and cancer-specific mortality among each of the 10 leading causes of cancer-related death in the United States.

Methods
We used the Surveillance, Epidemiology and End Results program to identify 1,260,898 patients diagnosed in 2004 through 2008 with lung, colorectal, breast, pancreatic, prostate, liver/intrahepatic bile duct, non-Hodgkin lymphoma, head/neck, ovarian, or esophageal cancer. We used multivariable logistic and Cox regression to analyze the 734,889 patients who had clinical and follow-up information available.

Results
Married patients were less likely to present with metastatic disease (adjusted odds ratio [OR], 0.83; 95% CI, 0.82 to 0.84; $P < .001$), more likely to receive definitive therapy (adjusted OR, 1.53; 95% CI, 1.51 to 1.56; $P < .001$), and less likely to die as a result of their cancer after adjusting for demographics, stage, and treatment (adjusted hazard ratio, 0.80; 95% CI, 0.79 to 0.81; $P < .001$) than unmarried patients. These associations remained significant when each individual cancer was analyzed ($P < .05$ for all end points for each malignancy). The benefit associated with marriage was greater in males than females for all outcome measures analyzed ($P < .001$ in all cases). For prostate, breast, colorectal, esophageal, and head/neck cancers, the survival benefit associated with marriage was larger than the published survival benefit of chemotherapy.

Conclusion
Even after adjusting for known confounders, unmarried patients are at significantly higher risk of presentation with metastatic cancer, undertreatment, and death resulting from their cancer. This study highlights the potentially significant impact that social support can have on cancer detection, treatment, and survival.

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INTRODUCTION

Fifty-one percent of Americans are married.[1] Studies assessing the impact of marital status on disease-specific survival among patients with cancer have yielded conflicting results, with protective,[2-9] mixed,[10-13] and nonsignificant[14,15] effects identified by prior investigations, most of which involved a single malignancy.[2,4-10,13] In addition, some[3,10] but not all[4,5] studies have identified a differential effect of marriage in men versus women, although a meta-analysis did not identify such effect modification.[16] Ultimately, from prior studies, it is difficult to draw meaningful conclusions regarding the impact of marital status on survival among patients with cancer.

The presence of a consistent association between marital status and outcome across multiple cancers would support the notion that unmarried patients with any malignancy represent an at-risk population that might benefit from targeted, support-based interventions. Given that the National Institutes of Health/National Cancer Institute spends approximately $5 billion per annum[17] on cancer research focused mainly on biologic investigations, targeted social support interventions could prove to be a cost-effective method of improving survival among at-risk patients with cancer. We used the Surveillance, Epidemiology and End Results (SEER) database[18] to study nearly 1 million contemporary patients and make generalizable conclusions regarding the impact of marital status on stage at presentation, use of definitive therapy, and disease-specific survival among each of the 10 leading causes of cancer-related death in the United States.

METHODS

Patient Population and Study Design

We used the SEER database to identify 1,260,898 patients diagnosed in 2004 through 2008 with one of the 10 leading causes of cancer-related death (ie, lung, colorectal, breast, pancreatic, prostate, liver/intrahepatic bile duct, non-Hodgkin lymphoma, head/neck, ovarian, and esophageal cancer), each of which results in more than 15,000 deaths per annum in the United States.[19] Sponsored by the National Cancer Institute, the SEER program collects and publishes cancer incidence, treatment, and survival data from population-based cancer registries; the program captures approximately 97% of incident cancers, and the tumor registries cover approximately 26% of the United States population.[18] The year 2004 was selected as the first year of the study given that several employed covariates were introduced in SEER in 2004.[20] Patients were excluded if age at diagnosis was less than 18 years, a diagnosis of cancer was made at autopsy, a prior malignancy had been diagnosed, clinical information was incomplete, or if the cause of death was unknown, leaving 734,889 patients in the final cohort.

Statistical Analysis

Baseline patient characteristics were compared with the t test or χ^2 test, as appropriate. For each malignancy, multivariable logistic regression was used to determine the association of marital status on stage at diagnosis (metastatic *v* nonmetastatic) after adjustment for demographic factors (age, sex, race, residence type [urban *v* rural], education, and median household income). Race was classified as white, African American, Hispanic, or Asian American, as determined by SEER.[18] Residence type, educational status (ie, percentage of adults $\geq$ 25 years of age with a high school education), and median household income were determined at the county level by linkage to the 2003 US Department of Agriculture rural–urban continuum codes,[21] 2000 US Census,[22] and 2004 small area income and poverty estimates from the US Census, respectively.[23]

After excluding patients with metastatic disease and those for whom the tumor stage, nodal stage, and therapy used was unknown (including all patients with non-Hodgkin lymphoma, given that information regarding chemotherapy, the primary management modality for such patients, is not available in SEER), 562,758 patients remained eligible for analysis of receipt of definitive therapy. Multivariable logistic regression was used to determine the association of marital status on use of appropriate definitive therapy after adjustment for demographic factors, tumor stage, and nodal stage. Tumor and nodal stage, delineating the local and regional extent of disease progression, respectively, were determined per the American Joint Committee on Cancer sixth edition.[20] Appropriate definitive therapy was defined as surgery and/or radiation for prostate, lung, pancreatic, liver/intrahepatic bile duct, esophageal, and head/neck cancer. In contrast, only surgery was considered to be the appropriate definitive therapy for breast, colorectal, and ovarian cancer.

For the outcome measure of cancer-specific mortality, Cox proportional hazards multivariable regression was used to assess the impact of marital status on cancer-specific mortality after adjustment for demographic factors, tumor stage, nodal stage, and use of definitive therapy. Among patients with breast cancer, only female patients were included in the analysis.

Marital status was classified as either married or unmarried and then also reanalyzed as married versus single, separated, divorced, or widowed. All logistic regression analyses were performed in a multilevel fashion to account for intracorrelations on the county level; for the Cox regression, a γ frailty model[24] was used. The median follow-up among surviving patents for the cohort analyzed for cancer-specific mortality was 3.1 years (range, 0.1 to 5.9 years). All P values are two-sided. The threshold of .05 was used to determine significance. Statistical analyses were performed by authors M.C. and A.A. using SAS version 9.3 (SAS Institute, Cary, NC). This study was approved by our institutional review board; informed consent was waived.

RESULTS

Patient Characteristics

Baseline patient characteristics are displayed in Table 1. Married patients were, on average, 2.5 years younger than unmarried patients and were more likely to be both male and white ($P < .001$). In addition, patients who were married were more likely to be from counties that were rurally situated and that displayed higher income and education levels ($P < .001$), although such differences were small in magnitude. Married patients were also less likely to present with advanced tumor and nodal stage than unmarried patients ($P < .001$).

Impact of Marital Status on Outcomes of Interest

As displayed in Figure 1, after adjustment for demographics, married patients were less likely to present with metastatic disease than those who were unmarried (odds ratio [OR] 0.83; 95% CI, 0.82 to 0.84; $P < .001$), an association that remained significant when each cancer was evaluated individually (adjusted OR range for each cancer: 0.52 to 0.93; $P < .05$ in all cases). After adjusting for demographics and tumor and nodal stage, married patients with nonmetastatic disease were more likely to undergo definitive surgical and/or radiotherapeutic management than unmarried patients (adjusted OR, 1.53; 95% CI, 1.51 to 1.56; $P < .001$), an effect that was significant in all cancers evaluated (adjusted OR range for each cancer, 1.42 to 1.76; $P < .05$ in all cases).

On Cox regression for cancer-specific mortality, after adjusting for demographics, tumor and nodal stage, and use of definitive therapy, patients who were married were significantly less likely to die of their disease (adjusted hazard ratio [HR], 0.80; 95% CI, 0.79 to 0.81; $P < .001$), an association that remained significant in all cancers evaluated (adjusted HR range, 0.67 to 0.88; $P < .05$ in all cases). When the unmarried cohort was stratified among its respective components (never married, separated, divorced, and widowed), all subgroups of unmarried patients were more likely to present with metastatic disease, be undertreated, and die of their cancer than their married counterparts ($P < .001$ for all associations, see Table 2). As shown in Table 3, among all patients evaluated, the effect of marriage on stage at presentation, use of definitive therapy, and cancer-specific mortality was greater for men than women ($P_{\text{interaction}} < .001$ in all cases).

DISCUSSION

We found that unmarried patients, including those who are widowed, are at significantly greater risk of presentation with metastatic cancer, undertreatment, and death resulting from their cancer than patients who are married. The association between marital status and each of these outcomes was significant for every malignancy evaluated. After adjusting for demographics, stage, and treatment, marriage remained associated with a relative reduction in cancer death ranging from 12% to 33%. In Table 4, for each solid malignancy, we compare the published HRs for the overall survival benefit of chemotherapy from landmark randomized trials, meta-analyses, and systematic reviews with the observed HRs for the survival benefit associated with marriage in our study. For five cancers studied (prostate, breast, colorectal, esophageal, and head/neck cancers), the survival benefit associated

Table 1. Baseline Demographic and Clinical Characteristics

Characteristic*	Unmarried (n = 275,728)† No.	%	Married (n = 459,161)† No.	%
Age, years				
Mean	66		63	
SD	14		12	
Income, USD‡				
Mean	48,000		49,000	
SD	11,000		11,000	
Percent that completed high school‡				
Mean	79		80	
SD	8		8	
Sex				
Male	109,321	40	272,225	59
Female	166,407	60	186,936	41
Race				
White	190,320	69	344,883	75
Black	46,048	17	38,330	8
Hispanic	24,248	9	40,143	9
Asian	13,670	5	33,945	7
Native American	1,442	1	1,860	0
Residence‡				
Rural	33,549	12	59,899	13
Urban	242,179	88	399,262	87
Tumor stage§				
1	95,716	37	192,535	45
2	71,362	28	127,611	30
3	45,795	18	62,018	14
4	42,946	17	47,071	11
Not applicable	19,909		29,926	
Nodal stage§				
0	162,930	64	304,837	71
1	43,651	17	62,948	15
2	39,095	15	49,058	11
3	10,143	4	12,392	3
Not applicable	19,909		29,926	
Metastatic disease at diagnosis‖				
No	222,539	81	393,416	86
Yes	53,189	19	65,745	14
Malignancy				
Prostate	44,344	16	146,304	32
Breast	75,689	27	107,907	24
Lung	57,303	21	67,277	15
Colorectal	44,526	16	61,483	13
Pancreatic	7,795	3	11,430	2
Liver, IHBD	5,884	2	8,185	2
Esophageal	3,630	1	5,373	1
Ovarian	7,096	3	8,426	2
Head/neck	9,552	3	12,850	3
Non-Hodgkin lymphoma	19,909	7	29,926	7

Abbreviations: IHBD, intrahepatic bile duct; SD, standard deviation; USD, United States dollars.

*All *P* values comparing characteristics of married and unmarried patients were < .001.

†Percentages may not add up to 100 because of rounding.

‡County-level data.

§Patients with non-Hodgkin lymphoma could not be classified as having a tumor or nodal stage and are listed as not applicable.

‖In patients with non-Hodgkin lymphoma, metastatic refers to stage IV.

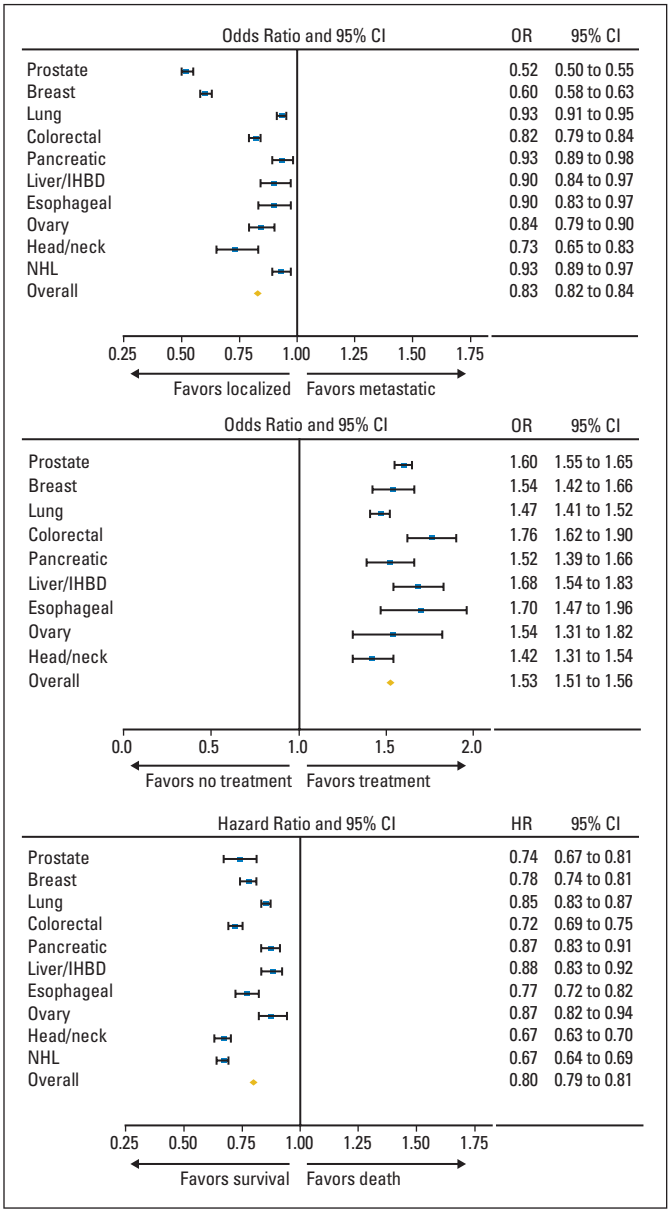

Fig 1. Forest plots depicting odds ratios and 95% CIs for the (A) association between marital status (married *v* unmarried) and presentation with metastatic disease, (B) use of definitive therapy, and (C) cancer-specific mortality for each of the 10 cancers evaluated and among the entire cohort. Odds ratios for the outcome measure of presentation with metastatic disease are adjusted for the demographics of age, sex, race, income, education, and urban versus rural residence (exceptions: prostate, breast, and ovarian, no adjustment for sex; overall, also adjusted for primary site). Odds ratios for the outcome measure of use of definitive therapy are adjusted for demographics (age, sex, race, income, education, and urban *v* rural residence), tumor stage, and nodal stage (exceptions: prostate, also adjusted for Gleason score and prostate-specific antigen [PSA], no adjustment for nodal stage or sex; breast and ovarian, no adjustment for sex; overall, excludes patients with non-Hodgkin lymphoma [NHL] and also adjusted for cancer stage and primary site but not tumor stage or nodal stage). Hazard ratios for the outcome measure of cancer-specific mortality are adjusted for demographics (age, sex, race, income, education, and urban *v* rural residence), tumor stage, nodal stage, and whether definitive treatment was administered (exceptions: prostate, also adjusted for Gleason score and PSA, no adjustment for nodal stage or sex; breast and ovarian, not adjusted for sex; NHL, also adjusted for cancer stage and histology but not tumor stage, nodal stage, or use of definitive therapy; overall, excludes patients with NHL and also adjusted for cancer stage and primary site but not tumor stage or nodal stage). IHBD, intrahepatic bile duct.

Table 2. Associations Between Specific Subgroups of the Unmarried Population and Outcomes of Presentation With Metastatic Disease, Use of Definitive Therapy, and CSM*

	Metastatic Disease at Dx			Definitive Treatment†			CSM†		
Population	OR‡	95% CI	*P*	OR§	95% CI	*P*	HR‖	95% CI	*P*
Married	Ref		—	Ref		—	Ref		—
Never married	1.28	1.25 to 1.30	< .001	0.57	0.55 to 0.58	< .001	1.33	1.30 to 1.36	< .001
Separated	1.25	1.18 to 1.32	< .001	0.67	0.61 to 0.73	< .001	1.21	1.14 to 1.29	< .001
Divorced	1.21	1.18 to 1.23	< .001	0.70	0.68 to 0.72	< .001	1.24	1.21 to 1.27	< .001
Widowed	1.12	1.10 to 1.14	< .001	0.70	0.68 to 0.72	< .001	1.24	1.22 to 1.26	< .001

Abbreviations: CSM, cancer-specific mortality; Dx, diagnosis; HR, hazard ratio; OR, odds ratio.
*Includes patients from all 10 evaluated cancers for outcome of presentation with metastatic disease and all cancers except non-Hodgkin lymphoma for outcomes of selection of definitive therapy and cancer-specific mortality.
†Excludes patients with metastatic disease.
‡OR adjusted for demographics of age, sex, race, income, education, urban versus rural residence, and primary site.
§OR adjusted for demographics (age, sex, race, income, education, and urban *v* rural residence), cancer stage, and primary site.
‖HR adjusted for demographics (age, sex, race, income, education, and urban *v* rural residence), cancer stage, primary site, and whether definitive surgical or radiotherapeutic treatment administered.

with marriage was larger than the published survival benefit of chemotherapy. The importance of this study is that it highlights the consistent and substantial impact that features of marriage, particularly social support, can have on cancer detection, treatment, and survival. It raises the possibility that investments in targeted social support interventions aimed at vulnerable populations, such as unmarried patients, could significantly improve the likelihood of achieving cure. Pending further investigations, including cost-benefit analyses, such interventions may prove to be a cost-effective method of improving outcomes among unmarried patients with cancer.

The association between married status and earlier stage at presentation identified in this study may reflect better access to care for married versus unmarried patients,[34] although even in nations with universal access to free care, such as Denmark, sociodemographic factors affect outcome in a multitude of health conditions.[35-37] Marital status may also impact stage at diagnosis for patients with cancer given possible encouragement by spouses to seek medical attention for worrisome symptoms. Spouses also may encourage patients to undergo definitive versus expectant management,[38] potentially accounting for the discrepancies in definitive treatment we identified. There are many explanations for the vital question of why marriage is associated with improved cancer-specific survival after adjustment for demographics, stage, and treatment, but the most likely reason is that married patients have better adherence with prescribed treatments than unmarried patients.[39] Impaired adherence has been associated with poorer outcomes in patients with cancer. For example, in head/neck cancers, missed or delayed radiation treatments are associated with increased rates of locoregional recurrence and death.[40] Interestingly, in our study, married patients with head/neck cancers displayed the greatest relative reduction in cancer death (33%). Investigations relating adherence to outcome in patients with breast, hematologic, and other cancers have yielded similar results.[41-43]

The benefits of marriage on all of the outcomes evaluated in this study have additional potential underlying etiologies. Psychologically, the diagnosis of cancer may result in more distress than other diagnoses.[44] Patients who are married display less distress, depression, and anxiety than their unmarried counterparts after a diagnosis of cancer, as a partner can share the emotional burden and provide appropriate social support.[45] Depression may, in part, be a mediator of the association between marital status and adherence to medical recommendations. DiMatteo et al[46] demonstrated a strong relationship between depression and nonadherence, and married patients display lower risk of major depression.[47] Other studies have shown that women with depression who are diagnosed with breast cancer undergo definitive treatment less often and display poorer survival.[48] Physicians should consider screening for depression among unmarried patients with cancer and refer patients to mental health specialists if symptoms are identified. In addition, physicians should consider closer observation of unmarried patients with cancer to maximize adherence. Given that patients who lack emotional support mechanisms do poorly after diagnosis with numerous health-related conditions,[49] the importance of adequate support cannot be understated.

Physiologically, select studies have linked marriage to improvements in cardiovascular, endocrine, and immune function, although marriage quality may be a determinant of the magnitude and presence of this effect.[50,51] Cortisol levels seem to be lower in patients with cancer who have adequate support networks, and diurnal cortisol patterns have been linked with natural-killer cell count and survival in patients with cancer,[52,53] potentially providing a physiologic basis for the psychologically based data described previously.[54] Further investigations on this subject are warranted.

If the benefits of marriage on survival are mediated through improved support, then the most effective way to combat the increased risks associated with unmarried status in patients with cancer would be to aggressively promote support mechanisms. Some of the available literature supports such an approach. In patients with heart failure, provision of informational, emotional, and affectionate support were associated with minimization of functional decline[55] and improved health-related quality of life.[56] Among patients with metastatic breast cancer, a randomized controlled trial conducted by Spiegel et al revealed that a psychosocial support-based intervention was associated with a near doubling of overall survival.[57] It is important to note, however, that a randomized, controlled trial published by Goodwin et al, in which patients with metastatic breast cancer were randomly assigned in a 2:1 fashion to either receive weekly supportive-expressive group therapy or no such intervention, did not identify survival differences between the two arms, even though women in the

Table 3. Assessment of Effect Modification Between Marital Status and Sex for the Outcomes of Presentation With Metastatic Disease, Employment of Definitive Therapy, and CSM

	Metastatic Disease at Dx				Definitive Treatment*			CSM*		
Cancer and Sex	OR for Marriage†	95% CI	*P*‡	Definition of Definitive Treatment	OR for Marriage§	95% CI	*P*‡	HR for Marriage‖	95% CI	*P*‡
Lung										
Interaction			.02	S, RT			< .001			.87
Male	0.91	0.88 to 0.93	< .001	S, RT	1.57	1.49 to 1.65	< .001	0.85	0.83 to 0.88	< .001
Female	0.95	0.93 to 0.98	.003	S, RT	1.36	1.28 to 1.44	< .001	0.85	0.82 to 0.88	< .001
Colorectal										
Interaction			< .001	S			.003			< .001
Male	0.75	0.72 to 0.78	< .001	S	1.95	1.76 to 2.17	< .001	0.66	0.63 to 0.70	< .001
Female	0.89	0.86 to 0.93	< .001	S	1.54	1.37 to 1.73	< .001	0.79	0.75 to 0.83	< .001
Pancreatic										
Interaction			.46	S, RT			.93			.02
Male	0.91	0.85 to 0.98	.01	S, RT	1.51	1.32 to 1.73	< .001	0.82	0.76 to 0.87	< .001
Female	0.95	0.89 to 1.01	.12	S, RT	1.52	1.35 to 1.71	< .001	0.91	0.85 to 0.96	.002
Liver, IHBD										
Interaction			.61	S, RT			.25			.35
Male	0.89	0.82 to 0.98	.01	S, RT	1.73	1.57 to 1.92	< .001	0.86	0.81 to 0.92	< .001
Female	0.93	0.81 to 1.08	.36	S, RT	1.56	1.34 to 1.82	< .001	0.91	0.83 to 1.00	.05
Esophagus										
Interaction			.48	S, RT			.08			.75
Male	0.89	0.81 to 0.97	.009	S, RT	1.82	1.55 to 2.14	< .001	0.76	0.71 to 0.83	< .001
Female	0.95	0.79 to 1.15	.61	S, RT	1.34	1.00 to 1.80	.05	0.78	0.68 to 0.91	.001
Head/neck										
Interaction			.15	S, RT			.80			.007
Male	0.70	0.62 to 0.80	< .001	S, RT	1.42	1.29 to 1.57	< .001	0.64	0.60 to 0.68	< .001
Female	0.86	0.67 to 1.10	.24	S, RT	1.39	1.21 to 1.61	< .001	0.75	0.68 to 0.84	< .001
NHL										
Interaction			.28				—			.26
Male	0.91	0.86 to 0.96	< .001	—	—		—	0.66	0.63 to 0.69	< .001
Female	0.95	0.90 to 1.00	.07	—	—		—	0.68	0.65 to 0.72	< .001
Overall¶										
Interaction			< .001	Per site			< .001			< .001
Male	0.87	0.85 to 0.89	< .001	Per site	1.60	1.55 to 1.66	< .001	0.77	0.76 to 0.79	< .001
Female	0.94	0.92 to 0.96	< .001	Per site	1.43	1.37 to 1.49	< .001	0.84	0.82 to 0.86	< .001

Abbreviations: Dx, diagnosis; CSM, cancer-specific mortality; HR, hazard ratio; IHBD, intrahepatic bile duct; NHL, non-Hodgkin lymphoma; OR, odds ratio; RT, radiation; S, surgery.

*Excludes patients with metastatic disease.

†OR for marriage adjusted for demographics of age, race, income, education, and urban versus rural residence (exception: overall, also adjusted for primary site).

‡*P* values for interaction terms test whether there is a significant difference in the OR (or HR) between male and female patients.

§OR for marriage adjusted for demographic factors (age, race, income, education, and urban *v* rural residence), tumor stage, and nodal stage (exceptions: prostate, also adjusted for Gleason score and prostate-specific antigen, no adjustment for nodal stage; overall, also adjusted for cancer stage and primary site but not tumor stage or nodal stage).

‖HR for marriage adjusted for demographic factors (age, race, income, education, and urban *v* rural residence), tumor stage, nodal stage, and whether definitive treatment administered (exceptions: prostate, also adjusted for Gleason score and prostate-specific antigen, no adjustment for nodal stage; NHL, also adjusted for cancer stage and histology but not tumor stage, nodal stage, or use of definitive therapy; overall, also adjusted for cancer stage and primary site but not tumor stage or nodal stage).

¶Includes data from the seven preceding cancers for outcome of presentation with metastatic disease and all preceding cancers except NHL for outcomes of selection of definitive therapy and cancer-specific mortality.

intervention arm experienced greater improvement in both psychological symptoms and pain control.[59] In addition, in a second randomized study by Spiegel et al,[59] no significant benefit of supportive-expressive group therapy was noted on overall survival. Subsequent reviews of the literature have indicated that group psychological therapies do not confer survival benefits to women with metastatic breast cancer.[60-62] More recently, a randomized trial of patients with metastatic non–small-cell lung cancer showed that early implementation of supportive measures/palliative care along with standard oncologic care improved the median survival of patients relative to standard oncologic care alone.[63] Patients in the intervention arm underwent aggressive symptom management (including assessment/management of depression and anxiety), received assistance with decision making, and were provided with coping strategies. This study suggests that provision of these support mechanisms to unmarried patients with serious medical conditions including cancer might significantly reduce mortality and help close the "survival gap" identified in the current study.

Prior investigations examined the impact of marriage on patients with largely a single malignancy.[2,4-10,13] Two large, population-based studies in the United States, however, have previously evaluated the impact of marriage on outcomes in patients with numerous

Table 4. Comparison of HRs for Overall Survival Associated With Chemotherapy (based on prior literature) With Cancer-Specific Survival Associated With Marriage (in the present study) in Patients With Solid Malignancies

Cancer	Type of Chemotherapy Study	Population Evaluated in Chemotherapy Study	Chemotherapy	Reference	HR for Chemotherapy	HR* for Marriage in Present Study
Prostate	Randomized trial[25]	Metastatic, hormone-resistant prostate cancer	Docetaxel every 3 weeks	Mitoxantrone	0.79	0.74
Breast	Meta-analysis[26]	Early breast cancer	Anthracycline-based	No chemotherapy	0.84	0.78
Lung	Systematic review[27]	Stage I-III non–small-cell lung cancer	Any	No chemotherapy	0.71	0.85
Colorectal	Randomized trial[28]	T3-T4, resectable rectal cancer	Adjuvant fluorouracil and leucovorin	No adjuvant chemotherapy	0.85	0.72
Pancreatic	Randomized trial[29]	Resectable pancreatic cancer	Fluorouracil	No chemotherapy	0.71	0.87
Liver, IHBD	Randomized trial[30]	Advanced hepatocellular carcinoma	Sorafenib	No chemotherapy	0.69	0.88
Esophageal	Meta-analysis[31]	Resectable esophageal cancer	Any	No chemotherapy	0.87	0.77
Ovarian	Systematic review[32]	Early-stage epithelial ovarian cancer	Any	No chemotherapy	0.74	0.87
Head/neck	Meta-analysis[33]	Nonmetastatic head and neck cancer	Any	No chemotherapy	0.87	0.67

Abbreviations: HR, hazard ratio; IHBD, intrahepatic biliary duct.
*Adjusted as per Table 2.

cancers.[11,12] In a study by Goodwin et al,[11] which included 25,706 patients from New Mexico diagnosed with cancer between 1969 and 1982, unmarried patients with certain cancers displayed poorer overall survival than patients who were married. However, for the majority of the individual cancers evaluated, the association with marriage did not achieve statistical significance, limiting the conclusions that can be drawn from the study. In addition, given that all patients were from New Mexico, the results may not be generalizable to all Americans. In a later study by Lai et al,[12] the association between marital status and overall survival was assessed for 261,070 patients with cancer. For some but not all cancers, the effect of marital status proved significant. Notably, in both studies, the primary outcome was overall survival, as opposed to cancer-specific survival, increasing the likelihood that an unidentified confounding variable was the driver of the results. Our study, which uses cancer-specific survival as the primary end point, minimizes this possibility. The greater power of our study to detect significant differences in outcome among married versus unmarried patients likely allowed us to find significant associations between marital status and stage at presentation, use of definitive therapy, and cancer-specific mortality for every cancer evaluated. Our study shows a clear and consistent protective effect of marriage among patients harboring one of the 10 most clinically significant malignancies affecting Americans. In addition, given that SEER now represents 26% of the United States population, our results, based on nearly 1 million contemporary patients, may be more generalizable than those of prior investigations.

Interestingly, the impact of marriage on both stage at presentation, use of definitive therapy, and cancer-specific mortality seemed to be greater in men than in women ($P_{\text{interaction}} < .001$ in all cases). In addition, among individual cancers, when a significant interaction was present between sex and marital status for these outcome measures, male patients benefitted more from marriage than did female patients. The exact reasons for this will need to be explored further, but it could, for example, reflect that unmarried women receive greater social support from their relatives (eg, their own children), friends, or the community than unmarried men.

Potential limitations of our study should be considered. First, our results may not apply to cancers not evaluated in this study. Second, data related to chemotherapy are not available in SEER. Third, although all patients eligible for the analysis of appropriate definitive therapy had localized disease for which surgery and/or radiation offered the only option for cure, it may have been appropriate to withhold such therapy in select cases (eg, impaired performance status, low-risk prostate cancer). Fourth, it is possible that some patients cohabitated with a partner in the absence of marriage, although the percentage of Americans engaged in such a living arrangement was likely small.[64] Moreover, such patients would be categorized as unmarried by SEER yet would be expected to display better outcomes than the unmarried population at large, thereby biasing our results toward the null. Data from the 2010 US Census indicate that approximately 90 million unmarried Americans more than 15 years old live "with other persons," whereas only approximately 30 million live alone.[65] Although SEER does not record such information (including cohabitation with adult children), our data suggest that living with someone other than a spouse (eg, a roommate, child) does not confer the same protective effect on cancer outcome as marriage. Fifth, data relating to past/present smoking and alcohol use, factors linked to survival among patients with cancer,[66-70] are not available in SEER, and some studies have suggested that unmarried patients may be at greater risk of such habits.[71,72] Physicians should inquire about smoking and alcohol use, particularly in unmarried patients. Lastly, it is possible that unmarried patients are innately different from married patients in ways that cannot be accounted for by our multivariable analysis and that the associations between marital status and outcome identified in this study reflect the influence of an unmeasured confounder. This possibility is mitigated, however, by the fact that widowed patients also displayed poorer outcomes than patients who were married, suggesting that the lack of social support, and not the presence of an unmeasured confounder, is the true driver of the results presented in this study. However, given these limitations, caution should be exerted before assuming that improved social support would significantly improve outcomes in unmarried patients.

Despite these potential limitations, our study indicates that unmarried patients are at greater risk of presentation with metastatic disease, undertreatment, and cancer-specific mortality. Physicians caring for unmarried patients with cancer should be aware of the poorer outcomes seen in this population, and health care systems should consider investing in highly targeted social support services and interventions that may help to reduce the significant survival differences between married and unmarried patients with cancer.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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