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ORIGINAL ARTICLE

Health literacy and all-cause mortality among cancer patients

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Abstract

Background: The association between health literacy and all-cause mortality among cancer patients remains unclear.

Methods: This is a retrospective cohort study of 9603 patients diagnosed with prostate, lung, breast, renal, colorectal, brain, head and neck, bladder, pancreatic, liver, sarcoma, and gastric cancers who were screened for health literacy between 2008 and 2018, using the Brief Health Literacy Screen (BHLS). Higher scores (range, 3–15) indicate higher health literacy. The association between all-cause mortality and health literacy was estimated using multivariable Cox proportional hazards models.

Results: A total of 8608 (89%) patients were non-Hispanic White. The median follow-up was 3.1 years. Patients with a BHLS score of 15 had a median survival improvement of 9.4 months (95% confidence interval [CI], 6.0–13.2 months) compared to those with a score of 9. Lower BHLS scores (9 vs. 15) were associated with higher mortality in stages II (adjusted hazard ratio [aHR], 2.6 [95% CI, 1.5–5.1]) and III (aHR 2.9 [95% CI, 1.4-6.0]) prostate cancer; stages I (aHR 1.7 [95% CI, 1.1–2.5]) and IV (aHR, 1.6 [95% CI, 1.2–2.1]) lung cancer; stage I colorectal cancer (aHR, 2.2 [95% CI, 1.3–4.7]); stage I renal cancer (aHR, 1.8 [95% CI, 1.1–3.4]); stages I (aHR, 2.6 [95% CI, 1.3–7.1]) and IV (aHR, 1.7 [95% CI, 1.2–2.7]) head and neck cancer; stage II bladder cancer (aHR, 1.6 [95% CI, 1.0–2.8]); stage I liver cancer (aHR, 4.1 [95% CI, 1.9–9.3]); and all stages of breast cancer.

Conclusions: Lower health literacy was associated with higher all-cause mortality among patients with 12 different types of cancer, varying by cancer type and stage.

KEYWORDS
brief health literacy screen, cancer, health literacy

Bashir Al Hussein Al Awamlh and Kelvin A. Moses contributed equally to this article.

INTRODUCTION

Health literacy, or the degree to which individuals have the ability to find, understand, and use information to inform health-related decisions, is an important determinant of health.[1]

Across the United States, only 12% of the adult population report proficient health literacy.[2] Despite recognition by health care professionals and policymakers of health literacy as a costly and significant public health problem since 2000,[3] it is estimated that in 2017, only 27% of adults had their understanding checked by their health care providers.[4,5]

Approximately 2 million US patients are diagnosed with cancer annually,[6] necessitating an understanding of unfamiliar concepts and the navigation of complex decision-making among various treatment options.[7] Although the impact of health literacy on outcomes, including mortality, has been studied across medical conditions such as diabetes, heart failure, and renal transplant,[8–14] studies in cancer care are limited to decision-making regarding screening, quality-of-life outcomes, and treatment choices.[15–19] Consequently, a gap remains in the literature regarding the association of health literacy and mortality among cancer patients, which may be partly due to the paucity of large-scale data on individuals' health literacy levels.

In 2010, our institution incorporated routine health literacy screening into clinical assessment and electronic health records (EHR) for all admitted patients, including cancer patients, using the validated Brief Health Literacy Screen (BHLS).[20] Now, with health literacy data on more than 450,000 patients across the medical center, we conducted a retrospective cohort study to evaluate the association between health literacy and all-cause mortality among patients diagnosed with 12 different types of cancer.

MATERIALS AND METHODS

Study cohort

In this retrospective study, we used the Vanderbilt Ingram Cancer Center registry and EHR system to extract records of 9603 patients older than 18 years who were both diagnosed with cancer between 2008 and 2015 and screened for health literacy information. The cohort included patients who were diagnosed or previously treated elsewhere and were referred for further care. Data on disease characteristics and outcomes were retrieved from the cancer registry and linked with data from EHR, including health literacy information. We queried our cancer registry and only included solid tumors with a sufficient number of patients (>250 patients per cancer) with available BHLS scores, as well as complete cancer staging and treatment information to allow for multivariable analysis. The types of cancer included were prostate, lung, breast, renal, colorectal, brain, head and neck, bladder, pancreatic, liver, sarcoma, and gastric cancers. Institutional review board approval was obtained at Vanderbilt University Medical Center and waived informed consent for chart review.

Exposure (health literacy)

Health literacy was measured using the validated BHLS at the time of the initial hospital encounter in both inpatient and outpatient settings.[21–23] Beginning in 2010, nurses routinely administered the BHLS as part of the admission intake and documented scores in the EHR, as previously described.[20,24] The BHLS contains the following three questions: 1) How confident are you in filling out medical forms by yourself?; 2) How often do you have someone help you read hospital materials?; and 3) How often do you have problems learning about your medical condition because of difficulty understanding written information? Higher scores (range, 3–15) indicate higher health literacy. BHLS scores were analyzed as a continuous variable to avoid loss of information and minimize bias.[21,22] To make findings more interpretable, model outputs were expressed comparing a priori determined BHLS scores of 15 versus 9 consistent with prior studies that considered a score of 15 to represent adequate health literacy and a score ≤ 9 to represent low health literacy.[9,25]

Outcome (all-cause mortality)

The primary outcome was all-cause mortality. Vitality data was abstracted from the cancer registry, EHR, or patient contact. Follow-up data were obtained through December 2, 2018. Time to mortality was calculated from the time of diagnosis.

Statistical and patient analysis

Patient age, self-reported gender and race/ethnicity, marital status, highest level of education, insurance status, Elixhauser comorbidity score,[26] treatments received (chemotherapy, surgery, radiation therapy, immunotherapy, hormonal therapy, observation, or palliative care), and clinical cancer staging were reviewed from the EHR. Cancer staging was determined using the American Joint Committee on Cancer (AJCC) 8th edition for each respective malignancy.[27]

Patient and cancer characteristics were summarized using median and interquartile ranges or mean and standard deviation for continuous variables and counts and percentages for categorical variables. The association between health literacy and all-cause mortality was estimated using Cox proportional hazards models for each of the 12 cancer types. Models were adjusted for age, gender, race/ethnicity, AJCC cancer stage, Elixhauser comorbidity score, treatment type, and insurance status. To account for potential nonlinear associations with the outcome, age and health literacy were included using restricted cubic splines with three knots, and AJCC stage was included as a second-degree polynomial. An interaction term between stage and health literacy score was also included in the model. For some cancer types, not all variables were meaningful and were excluded from the analysis. For example, gender was excluded when analyzing breast and prostate cancer, and AJCC stage was excluded in the model for brain cancer. Education attainment was not included in the models because

health literacy and years of education are on the same causal pathway.[28] Last, this was a complete case analysis; patients with missing covariates were excluded from the analysis.

To assess the association between health literacy and all-cause mortality in each cancer type, a model-based summary measure (median survival time) on an absolute scale, rather than a relative scale, was calculated. The difference in median survival between a priori selected BHLS scores 15 versus 9 was reported and was marginalized over the observed sample covariate distribution. Standard errors were estimated from 100 bootstrap replicates. An overall measure of the association between health literacy and mortality was calculated by weighting and averaging the difference in median survival estimates across cancer types. The individual cancer-specific estimate was weighted by the inverse variance of the estimate.

Moreover, we calculated the summary quantity of interest, model-based relative hazard of mortality, by comparing the a priori selected BHLS score of 9 versus 15 for each AJCC stage with each cancer type where applicable. Standard errors and corresponding confidence intervals were generated from 500 bootstrap replicates. Multiple comparisons adjustments were not applied.

Last, partial effect plots of the log relative hazard were constructed to visualize potentially nonlinear associations between BHLS score, AJCC cancer stage, and all-cause mortality. Confidence intervals were calculated from model-based standard errors. Predictor variables for the other covariates in the model were set to a reference value, where median values were used for the continuous covariates and mode values for categorical covariates. All analyses were performed in R version 4.2.2, the RMS package, and the survival package.[29,30]

RESULTS

Baseline characteristics

Demographics and baseline characteristics are summarized in Table 1 ($n = 9603$). The median age was 62.2 years (interquartile range [IQR], 53.7–69.6). The cohort included 8608 (89%) non-Hispanic White patients, 859 (9%) non-Hispanic Black patients, 81 (1%) Hispanic patients, and 81 (1%) Asian patients. In total, there were 3775 (39%) female patients, and most patients (96%) had health insurance at the time of diagnosis. Prostate cancer was the most common type of cancer (20% of cohort), whereas gastric cancer was the least common (3% of cohort). For the entire cohort (excluding brain cancer), 4867 (55%) patients were diagnosed with either AJCC stage I or II cancers. Most patients were managed with surgery (75%), chemotherapy (35%), and/or radiation therapy (26%). Characteristics of patients stratified by cancer type are shown in Tables S1–S12.

BHLS scores

The median BHLS score for the entire cohort was 13 (IQR, 10–15). A total of 2210 (26.5%) patients had a BHLS score of ≤9. The

TABLE 1 Patient demographics, cancer characteristics, and treatments.

Variable	
Median age (years)	62.2 (53.7,69.6)
Sex, No. (%)	
Male	5828 (60.7)
Female	3775 (39.3)
Race/ethnicity, No. (%)	
Non-Hispanic White	8608 (88.9)
Non-Hispanic Black	859 (9.0)
Asian	136 (1.4)
Hispanic	81 (0.8)
American Indian/Alaska Native	9 (0.1)
Native Hawaiian	5 (0.1)
Unknown	2 (0.0)
Insurance, No. (%)	
Federal	4911 (51.1)
Private	3366 (35.1)
Insurance NOS	960 (10.0)
Uninsured	366 (3.8)
Marital status, No. (%)	
Married/partnered	6530 (68.0)
Separated/divorced	1204 (12.5)
Single	958 (10.0)
Widowed	829 (8.6)
Unknown	73 (0.8)
Missing	9 (0.1)
Year of diagnosis, No. (%)	
2008	365 (3.8)
2009	479 (5.0)
2010	1014 (10.6)
2011	1878 (19.6)
2012	1868 (19.5)
2013	1830 (19.1)
2014	1550 (16.1)
2015	619 (6.5)
Education level, No. (%)	
Less than high school	643 (6.7)
High school/GED	2308 (24.0)
Some college	1386 (14.4)
College degree	1091 (11.4)
Graduate/professional degree	676 (7.0)
Unknown	3499 (36.4)

(Continues)

TABLE 1 (Continued)

Variable	
Median BHLS score (IQR)	13 (10,15)
Mean Elixhauser comorbidity score, SD	3.57 (7.45)
Stage at diagnosis, No. (%)	
Stage I	2394 (26.9)
Stage II	2473 (27.8)
Stage III	1768 (19.8)
Stage IV	1971 (22.1)
In situ (unstaged)	305 (3.4)
Treatment, No. (%)	
Chemotherapy	3358 (35.0)
Hormone	776 (8.1)
Immunotherapy	221 (2.3)
Observation	319 (3.3)
Palliative care	508 (5.3)
Radiation	2461 (25.6)
Surgery	7180 (74.8)
Cancer type, No. (%)	
Prostate	1629 (20.0)
Lung	1482 (15.4)
Breast	1053 (11.0)
Renal	939 (9.8)
Colorectal	911 (9.5)
Brain	718 (7.5)
Head and neck	703 (7.3)
Bladder	578 (6.0)
Pancreatic	475 (5.0)
Liver	395 (4.1)
Sarcoma	391 (4.1)
Gastric	329 (3.4)

Abbreviations: BHLS, Basic Health Literacy Screen; GED, general edicational developement; IQR, interquartile range; No., Number; NOS, Not Otherwise Specified; SD, standard deviation.

distribution of health literacy scores by quartiles for all patients is shown in Table S13. Figure 1 shows the median BHLS scores stratified by AJCC stage for patients with prostate, lung, breast, colorectal, and pancreatic cancer. Scores for the remainder of the study cohort are shown in Figure S1.

Health literacy and all-cause mortality

The median follow-up for all patients included in the study was 3.1 years (IQR, 1.3–4.9). At the time of the last follow-up, 3941 (41%) had died. The difference in median survival time comparing scores of 15 to 9 for each cancer is reported in Figure 2. An adjusted weighted average of the differences, combining all cancer types in the analysis, showed an improved median survival of 9.4 months (95% CI, 6.0–13.2 months) in patients with a BHLS score of 15 compared to 9.

Higher health literacy was associated with longer survival in most cancer types. When restricting the analysis by cancer type, a BHLS score of 15 compared to 9 was associated with a significantly higher overall survival among those with head and neck cancer (adjusted difference in median survival, 2.0 years [95% CI, 0.8–3.1]), prostate cancer (adjusted difference in median survival, 1.6 years [95% CI, 0.2–3.0]), brain cancer (adjusted difference in median survival, 1.0 years [95% CI, 0.3–1.8]), bladder cancer (adjusted difference in median survival, 1.0 years [95% CI, 0.2–1.8]), lung cancer (adjusted difference in median survival, 1.0 year [95% CI, 0.1–1.6]), colorectal cancer (adjusted difference in median survival, 0.8 years [95% CI, 0.2–1.5) and breast cancer (adjusted difference in median survival, 0.7 years [95% CI, 0.3–1.5]).

Health literacy score was also associated with survival within specific stages of certain cancer types (Figures 3 and 4; Figures S2 and S3). In adjusted analyses that stratified by AJCC stage, a BHLS score of 9 compared to 15 was associated with a higher risk of mortality among all AJCC stages of breast cancer patients (e.g., stage I breast cancer: adjusted HR, 3.3 [95% CI, 2.0–5.3]); AJCC stage II (adjusted hazard ratio [HR], 2.6 [95% CI, 1.5–5.1]) and stage III (adjusted HR, 2.9 [95% CI, 1.4–6.0]) prostate cancer patients; AJCC stage I (adjusted HR, 1.7 [95% CI, 1.1–2.5]) and stage IV (adjusted HR, 1.6 [95% CI, 1.2–2.1]) lung cancer patients; stage I colorectal cancer patients (adjusted HR, 2.2 [95% CI, 1.3–4.7]); stage I renal cancer patients (adjusted HR, 1.8 [95% CI, 1.1–3.4]); stage I (adjusted HR, 2.6 [95% CI, 1.3–7.1]) and stage IV (adjusted HR, 1.7 [95% CI, 1.2–2.7]) head and neck cancer patients; stage II bladder cancer patients (adjusted HR, 1.6 [95% CI, 1.0–2.8); stage I liver cancer patients (adjusted HR, 4.1 [95% CI, 1.9–9.3]); and brain cancer patients (adjusted HR, 1.5 [95% CI, 1.1–2.3]). However, there were no significant differences in all-cause mortality and BHLS scores (9 vs 15) by AJCC stages among patients with sarcoma, gastric cancer, and pancreatic cancer.

DISCUSSION

To our knowledge, the current study is the first to assess the association between health literacy and all-cause mortality among different cancer types. In this analysis, which included almost 10,000 patients with 12 different types of malignancies, health literacy was found to be associated with all-cause mortality in some cancers. Averaged across 12 cancer types, high health literacy (BHLS score 15 vs. 9) was associated with improved overall survival by almost 9 months. Among individual cancers, higher health literacy was associated with increased overall survival in head and neck, prostate, brain, bladder, lung, colorectal, and breast cancers. Specifically, when analyzing individual cancers by stage, high health literacy was associated with higher survival rates in stage I lung, breast, colorectal,

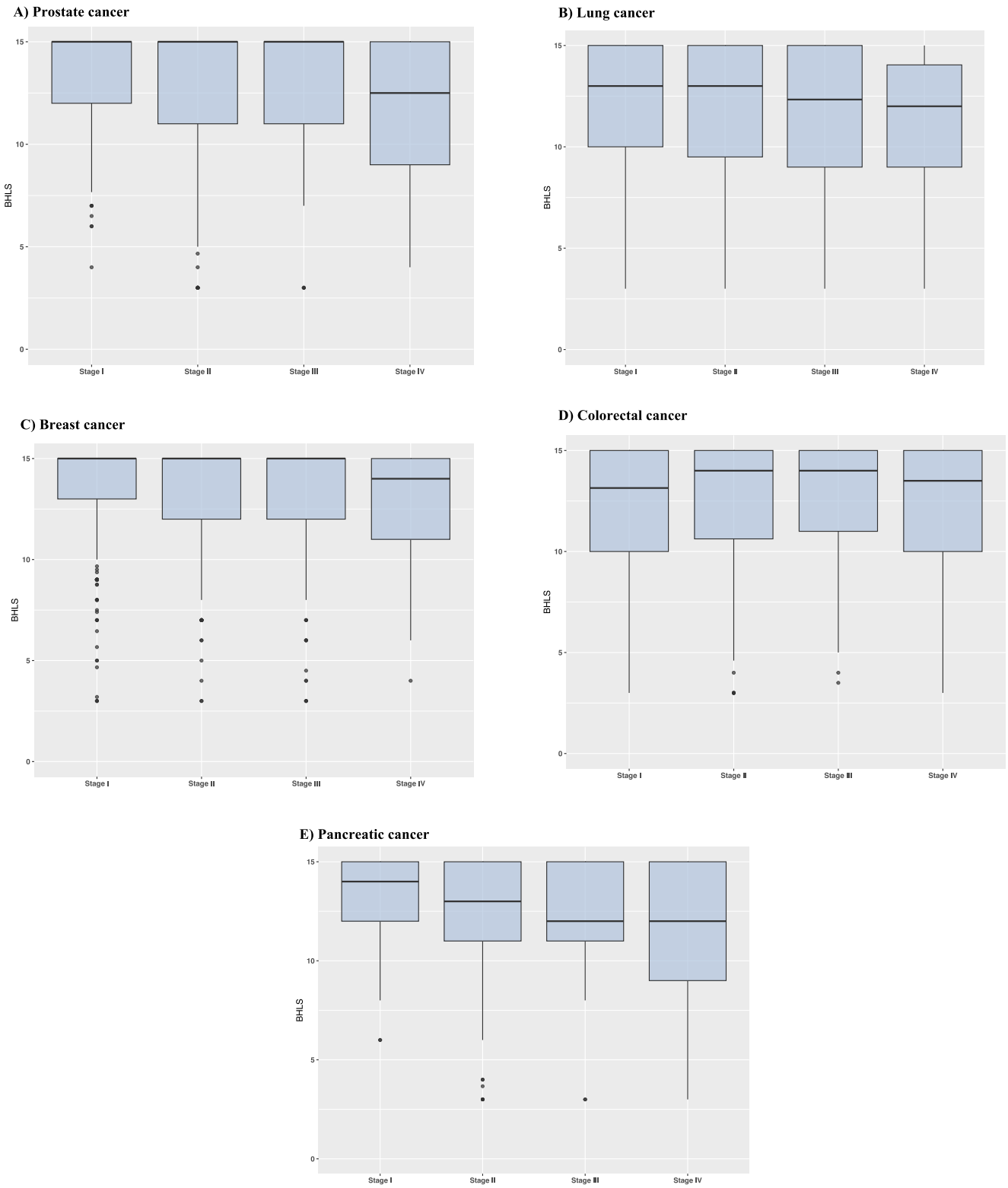

FIGURE 1 BHLS score among patients diagnosed with prostate, lung, breast, colorectal, and pancreatic cancer. Box plots demonstrating BHLS scores in patients by cancer stage among patients diagnosed with (A) prostate, (B) lung, (C) breast, (D) colorectal, and (E) pancreatic cancer. BHLS, Brief Health Literacy Screen.

renal, head and neck, and liver cancers; stage II prostate, bladder, and breast cancers; stage III prostate and breast cancers; and stage IV prostate, breast, and head and neck cancers.

The differential mortality outcomes observed in this study among cancer patients with lower health literacy compared with those with higher health literacy are likely multifactorial.

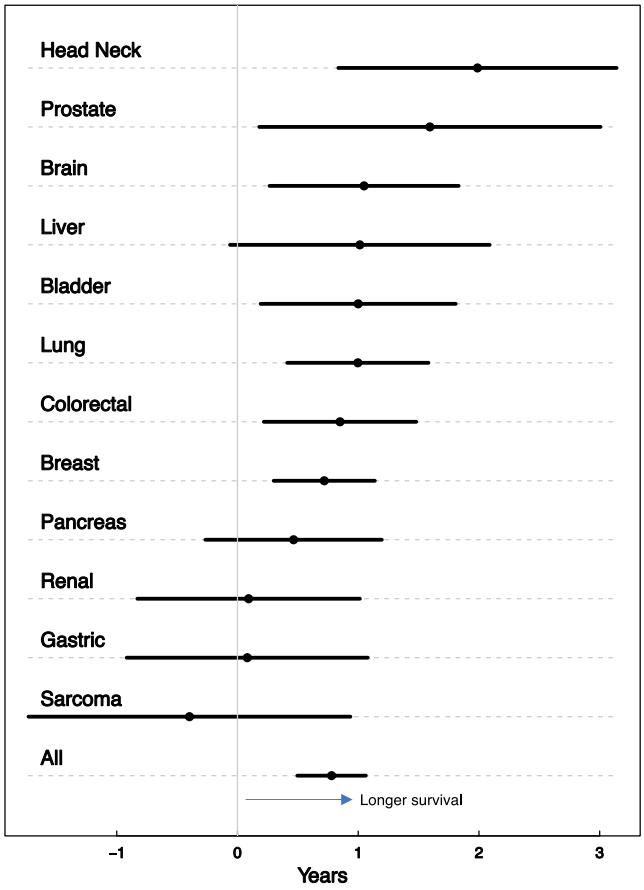

FIGURE 2 Adjusted differences in median survival between cancer patients with adequate health literacy compared to those with low health literacy. Difference in overall survival in years between patients with adequate health literacy relative (BHLS score 15) to low health literacy (BHLS score 9) in all cancer patients and among 12 individual cancer types, ordered by the magnitude of increased overall survival. The dot indicates the point estimate, and the line represents the confidence interval. BHLS, Brief Health Literacy Screen.

Differences in mortality outcomes were seen within both early and advanced stages in certain cancers, suggesting worse treatment-related outcomes across different stages among those with lower health literacy. Higher mortality among patients with lower health literacy in early-stage diseases, such as breast, prostate, renal, and colorectal cancers, may be due to inadequate comprehension of early-stage interventions, involvement in self-management practices,[31] and/or worse outcomes following surgical treatment and active surveillance.[24,32] Specifically, previous studies have demonstrated that among surgical patients, lower health literacy was associated with higher rates of postoperative complications and longer index hospitalization. The reason for these outcomes is likely multifactorial and related to limited understanding, compliance to pre- and postoperative instructions, more substantial comorbidities, less chronic disease control, as well as more social risk factors such as lack of transportation and social support.[33,34]

This study also demonstrated poorer outcomes in late-stage cancers which may relatively exhibit more indolent disease features and involve multiple lines of therapies compared to others, including head and neck, breast, and prostate cancers. Specifically, these cancers require patients to engage in complex decision-making, behavior modifications (e.g., smoking cessation), and long-term treatment adherence.[35–38] The differences observed among patients with lower health literacy with a relatively slowly progressing late-stage disease could be, in part, attributed to low adherence to treatment plans, including hormonal therapy or chemotherapy, and reduced participation in clinical trials.[39,40]

Conversely, in most advanced cancer stages or in malignancies with high lethality, such as gastric or pancreatic cancers, aggressive disease biology may play a larger role in determining outcomes, attenuating the potential association between health literacy and survival.[6] Moreover, although this study did not specifically assess for the association between health literacy and stage of cancer diagnosis, studies have shown that patients with lower health literacy have lower screening rates and less general cancer-related knowledge among patients with low health literacy, possibly resulting in missed opportunities for earlier diagnoses.[16,41–43]

Although prior studies have demonstrated worse survival outcomes among specific groups that might be included in our cohort, such as older adults, individuals with heart failure, or those with end-stage renal disease, our findings indicate that a cancer diagnosis uniquely subjects individuals with low health literacy to worse outcomes. This is further highlighted by the variation observed in the association between health literacy and mortality by cancer type and stage, such as low health literacy being associated with mortality in stage III prostate cancer but not in stage I.

From an epidemiological standpoint, health literacy emerged as a significant social determinant of health, elucidating disparities in outcomes among individuals with chronic medical conditions.[44] As such, policymakers and governmental agencies have prioritized setting forth strategies to improve health literacy. Such efforts encompass the National Action Plan to improve health literacy and the establishment of health literacy as an overarching goal in Healthy People 2030.[45] Our results have several important implications for cancer patients. First, we endorse the routine collection of health literacy information in patients diagnosed with cancer. Second, we encourage the adoption of strategies to improve organizational health literacy in facilities providing care for cancer patients.[46] Third, our findings highlight that not all cancer patients with low health literacy experience worse outcomes. As such, observational studies are needed to explore the reasons or mechanisms by which health literacy impacts outcomes for each cancer type individually, recognizing that these mechanisms may vary across different cancers and stages. Ultimately, these studies could inform hybrid effectiveness-implementation research, including in nontertiary facilities, to test interventions targeting potential mechanisms by which low health literacy affects outcomes across the cancer care continuum. These may include focused education on cancer surveillance, decision-making, or treatment adherence tailored to specific cancer types and stages.

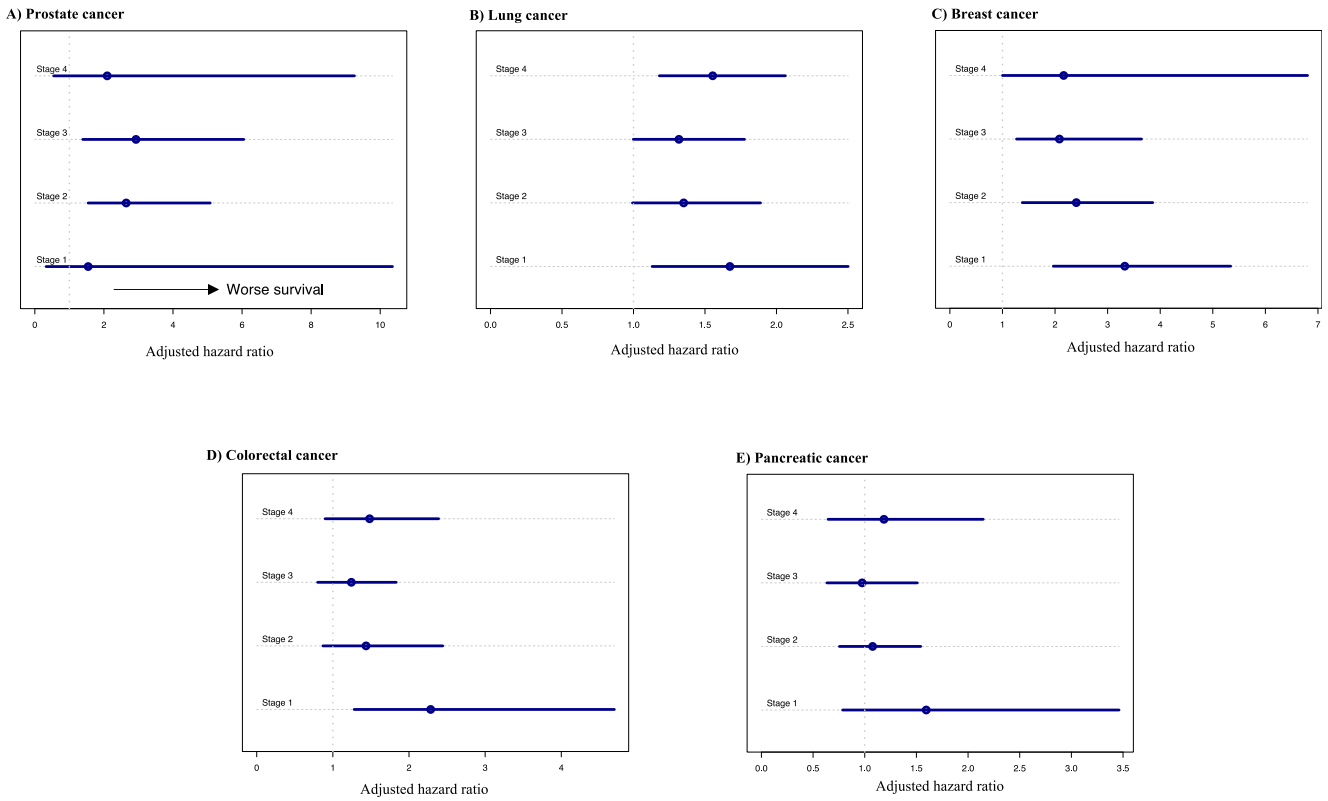

FIGURE 3 Differences in survival in prostate, lung, breast, colorectal, and pancreatic cancer among patients with a low health literacy compared to adequate health literacy by cancer stage. Adjusted hazard ratio for all-cause mortality among different stages of (A) prostate, (B) lung, (C) breast, (D) colorectal, and (E) pancreatic cancer for patients with a BHLS score of 15 compared to 9. BHLS, Brief Health Literacy Screen.

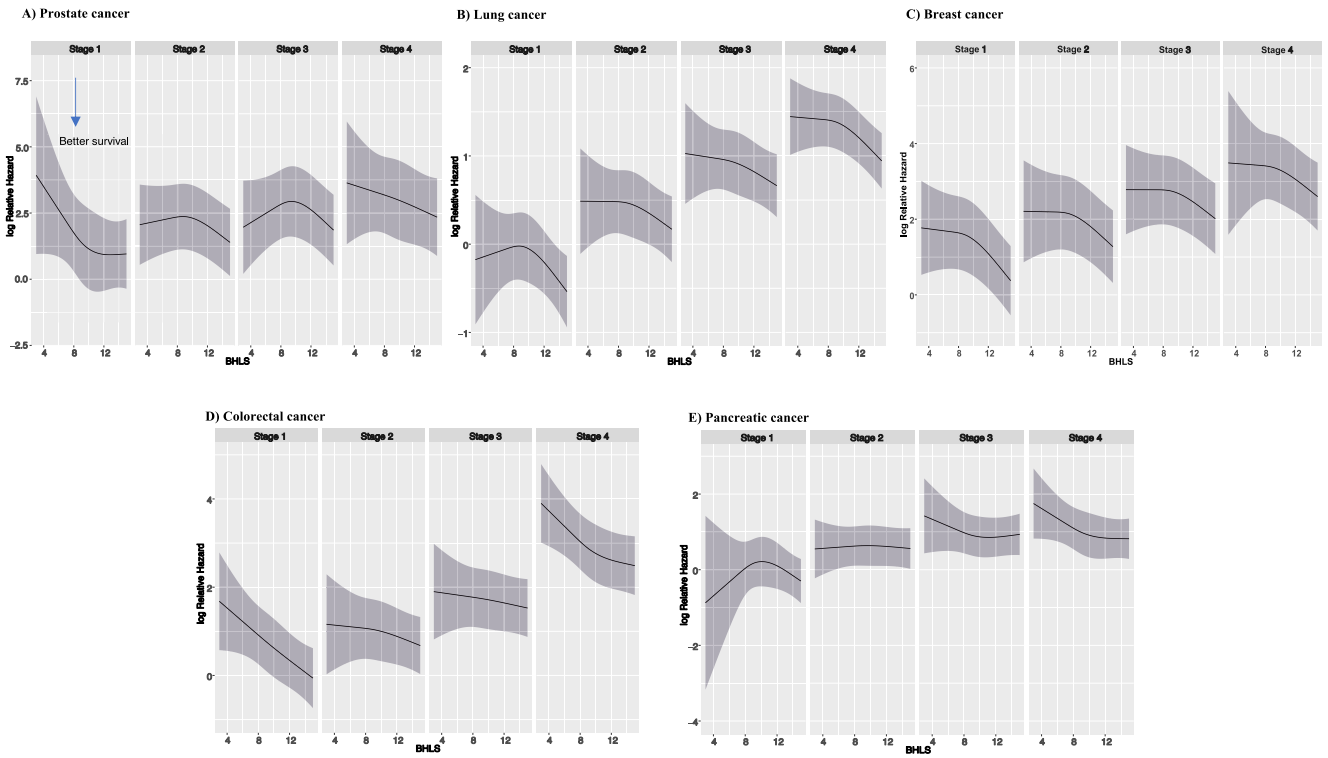

FIGURE 4 Association between health literacy score and all-cause mortality by cancer stage. Partial effect plots of adjusted log relative hazard of all-cause mortality over BHLS scores within each stage for patients with (A) prostate, (B) lung, (C) breast, (D) colorectal, and (E) pancreatic cancer. BHLS, Brief Health Literacy Screen.

Limitations

This study has several limitations. First, the findings in this observational study are not causal. Randomized clinical trials are needed to answer the causal question as to whether an intervention that improves or effectively mitigates low health literacy would impact survival rates. Second, although overall survival is perhaps the most salient outcome, the study did not ascertain disease-specific survival. Although overall survival might serve as a surrogate for cancer-specific survival in advanced-stage disease, it may overestimate the relationship between health literacy and cancer-specific outcomes. Third, this is a single tertiary institution retrospective study with a relatively homogeneous cohort (90% non-Hispanic White patients). Nonetheless, it represents one of the largest studies assessing health literacy and survival outcomes.[13,39,47–50] Fourth, the study cohort had a relatively high health literacy, likely because patients are from a tertiary referral center, and results might be different in other health care delivery systems, such as safety-net hospitals. Fifth, health literacy was not measured at the time of diagnosis for all patients. Additionally, due to the extensive referral base of our cancer center and the complexity of cancer care, which often involves multiple steps and treatment modalities, we were unable to quantify the number of patients who were referred for treatment or had previously received treatment elsewhere. Health literacy scores are stored in an institutional database, which includes all BHLS data collected since 2010; we and others generally consider health literacy a stable trait in adulthood.[51] It is not known if health literacy changes following diagnosis or treatment. However, we were not able to harmonize the time of diagnosis and assessment of health literacy in every patient. Future work among patients with cancers that have prolonged survival can present an opportunity to reassess health literacy improves during survivorship. Sixth, the study did not include other cancers that may have an association with literacy, such as cervical or ovarian cancer, due to the low availability of eligible patients. Seventh, although the study included detailed information on comorbidity status and insurance type, it lacked information on other potential confounders, such as smoking or alcohol use and primary language, as well as detailed information on treatments delivered, treatment plan adherence or refusal, urban versus rural residence, income, and access to digital health information and digital health literacy that are important areas for future study. Notwithstanding these limitations, the study is one of the first to assess health literacy in relation to all-cause mortality among cancer patients and is bolstered by its large size and diverse range of cancer types and stages.

In conclusion, among patients with 12 different types of cancer, lower health literacy, measured with BHLS, was associated with higher all-cause mortality that differed across many cancer types and stages.

AUTHOR CONTRIBUTIONS

Bashir Al Hussein Al Awamlh: Writing–original draft; writing–review and editing; methodology; and investigation. **Kelvin A. Moses**: Conceptualization; writing–original draft; writing–review and editing; project administration; supervision; and investigation. **Julia Whitman**: Data curation; software; methodology; writing–review and editing; and formal analysis. **Thomas Stewart**: Methodology; software; data curation; writing–review and editing; and formal analysis. **Sunil Kripalani**: Investigation; conceptualization; writing–review and editing; supervision; and resources. **Kamran Idrees**: Conceptualization; investigation; writing–review and editing; supervision; resources; and funding acquisition.

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CONFLICT OF INTEREST STATEMENT

Sunil Kripalani reports consulting fees from Bayer and Gilead Sciences Inc. Kelvin A. Moses reports participation on a data and safety monitoring board for Boston Scientific Corporation; and fees for other professional activities from the End Point Review Committee, National Comprehensive Cancer Network. Thomas Stewart reports participation on data and safety monitoring boards for Eli Lilly and Company and the National Institutes of Health. The other authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author on reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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