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Original Article

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Time to Treatment Initiation of Lung, Breast, Colorectal, and Prostate Cancers and Contributing Factors From 2015 to 2020 Utilizing Surveillance, Epidemiology, and End Results Program Database

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Abstract

Background: The aim of the study was to identify the factors that cause delays in treatment initiation, such as race, gender, education, income status, and associated health comorbidities, as these can increase mortality.

Methods: We utilized the Surveillance, Epidemiology, and End Results (SEER) database to identify contributing factors such as sociodemographics that impact time from diagnosis to treatment initiation (TTI) in lung cancer, breast cancer, colorectal cancer (CRC) and prostate cancer from 2015 to 2020 in 991,772 patients. Variables studied included age, sex, race, marital status, geographic location, household income, stage, and grade. Two-way analysis of variance (ANOVA) was utilized to determine if significant differences existed between the effects on TTI with respect to the variables. TTI was measured in months. Based on the aforementioned variables, propensity scores were created for odds of receiving late treatment exceeding 1 month from diagnosis. Patients were matched 1:1. Based on the propensity score, a competing risk regression model was utilized to determine risk factors associated with late treatment.

Results: Similar trends were noted among all cancers. With respect to gender, in breast cancer, TTI was shorter in males (1.02 months) compared to females at 1.24 ($P < 0.001$). A longer time to TTI was noted in patients greater than 65 years with lung cancer (1.38 months, $P < 0.001$). Shorter TTI was evident across all cancers for White patients ($P < 0.001$). Shorter TTI was noted among married versus widowed, divorced, or single patients. Patients with lower income and non-metropolitan regions had shorter TTI among all cancers. More aggressive cancers had shorter TTI. Propensity matched competing risks hazard analysis revealed similar results with younger patients, those living in metropolitan regions, those earning greater than $35,000, and localized and well-differentiated cancers being at greater risk of having a treatment delay greater than 1 month.

Conclusion: Health disparities still exist today, and this becomes more evident in our study as age, sex, and race, among other factors, can cause delays in time from diagnosis of cancer to treatment initiation, potentially negatively affecting survival in these populations.

Keywords: Cancer; Time to treatment initiation; Health disparities; Sociodemographics; SEER

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Introduction

The timespan between a confirmed cancer diagnosis and initiation of treatment is referred to as time to treatment initiation (TTI). Khorana et al performed an observational study in 2019 that found that TTI has increased in the United States with an absolute increased risk of mortality ranging from 1.2% to 3.2% per week in early-stage breast, lung, renal, and pancreatic cancers [1]. Delays in cancer treatment initiation are multifactorial and have been associated with advanced age, low socioeconomic status, distance to the treatment center, low health literacy, additional comorbidities, cultural stereotypes, and negative perceptions of disease. In 2020, Cone et al performed a cohort study to assess TTI in patients with non-metastatic breast cancer, prostate cancer, non-small cell lung cancer, and colorectal cancer (CRC) from 2004 to 2015 with data obtained from the National Cancer Database. Their findings were as follows: median TTI was 32 (21 - 48) days for breast cancer, 79 (55 - 117) days for prostate cancer, 41 (27 - 62) days for non-small cell lung cancer, and 26 (16 - 40) days for colon cancer [2]. The primary aim of this study was to utilize the Surveillance, Epidemiology, and End Results (SEER) database, which is a national cancer registry that collects data on cancer incidence from population-based cancer registries in many states across the United States, covering about 50% of the country. It includes data on patient

demographics, primary tumor site, tumor morphology, stage at diagnosis, and first course of treatment [3]. The purpose of this study was to identify how contributing factors such as sociodemographics and cancer staging impact the time from diagnosis to treatment initiation in different cancer types in the studied patient population from 2015 to 2020 and identify trends. This effect will be analyzed in the most common cancers, such as lung cancer, breast cancer, CRC, and prostate cancer.

Materials and Methods

Study design and study population

This was a retrospective observational cohort study conducted by a review of the SEER database. Participants included 991,772 adults aged 20 and older diagnosed with lung cancer, breast cancer, CRC, or prostate cancer during the years 2015 - 2020 in the United States. Variables contributing to TTI studied included age, sex, race, marital status, geographic location, household income, stage, and grade. TTI was measured in months, ranging from 0 to 24 months. Age was divided into two categories: younger than 65 and older than 65. Sex was defined as female or male. Race was divided as White and non-White to differentiate between the White population and minorities. The minority group included Hispanic, Black Asian, Pacific Islander, American Indian, and Alaska Native. Unknown race was excluded. Marital status at diagnosis was defined as single, domestic partner, married, widowed, separated, and divorced. Geographic location was defined as metropolitan, non-metropolitan, or unknown. Grades were classified as well differentiated (grade I), moderately differentiated (grade II), poorly differentiated (grade III), undifferentiated or anaplastic (grade IV), and unknown. Staging was classified as *in situ*, localized, regional, distant, and unknown/unstaged. Variables that were not studied due to not being available on the database were education level and insurance status. Pediatric patients were excluded, as well as cases diagnosed outside of the studied time frame, January 2015 to December 2020. The sample size was large and thus more representative of the population. There were 187,961 subjects with CRC, 217,249 with prostate cancer, 373,954 with breast cancer, and 212,607 with lung cancer, for a total of 991,772 adults.

Ethical issues

This research study was reviewed and approved by Rutgers Health Community Medical Center's Institutional Review Board (IRB), IRB #24-001. The study was conducted according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association.

Data collection and analysis

The database utilized for data collection is SEER*Stat 8.4.3. Patients were selected based on the variables previously mentioned. A case listing session was created to visualize individual cancer cases utilizing data from Incidence - SEER Research Data, 17 Registries, Nov 2022 Sub (2000 - 2020). Cases were narrowed down by year of diagnosis, from 2015 to 2020, and cancer site (prostate, breast, colorectal, and lung). Variables included in the table were patient ID, cancer site, sex, age, race, marital status, median household income, geographic location, grade, stage, and months from diagnosis to treatment. Patients with unknown months from diagnosis to treatment were excluded, as the purpose of the study was to identify the length from diagnosis to treatment in different cancer types and populations and pinpoint factors affecting delays, if any. A delay was defined as greater than 30 days or 1 month.

The case listing obtained from the database was exported to BlueSky Statistics, version 10.3.1, for analysis. Analysis of variance (ANOVA) was the chosen statistical method to determine if any differences existed between variables and their effect on TTI. Categorical variables were expressed as percentages and continuous variables were expressed as means and standard deviations. A statistically significant value was defined as P less than 0.05.

To obtain propensity scores for each late treatment (greater than 1 month after diagnosis) and non-late treatment, we created a logistic regression analysis which included age, sex, marital status, geographic location, type of cancer, tumor grade, cancer stage, economic status, and race/ethnicity (Supplementary Material 1, wjon.elmerpub.com). We then employed 1:1 nearest neighbor matching technique without replacement. The caliper width used for matching was 0.05. The effectiveness of matching was confirmed by employing mean bias, median bias, standardized bias, pseudo R-squared, likelihood ratio of Chi-squared, and variance ratio (Supplementary Materials 2 and 3, wjon.elmerpub.com).

As death was a competing hazard, we employed a multivariable competing risk hazards analysis on the propensity-matched dataset with late treatment as the primary outcome adjusted for age, sex, marital status, geographic location, type of cancer, tumor grade, cancer stage, economic status, and race/ethnicity. StrataCorp 16 (College Station, Texas, USA) was utilized.

Results

A total of 991,772 subjects were included in this study, with demographics and trends summarized in Table 1. Across all common cancers, similar patterns were observed in TTI. White patients had consistently shorter TTI across all cancer types, with the shortest delays seen in colon cancer. Married individuals experienced less delay compared to widowed, divorced, or single patients, regardless of race, with widowed patients over 65 having the longest TTI. Interestingly, patients with lower income and those living in non-metropolitan regions had shorter TTI across all cancers. Localized and well-differentiated cancers were observed to have longer TTI, whereas more distant and aggressive cancers were associated with shorter TTI. Table 1 shows cancer-specific TTI of factors studied. Propensity matched competing risks hazard analysis

Table 1. Cancer-Specific TTI of Factors Studied

Demographics	Cancer type	Group 1	TTI (months)	Group 2	TTI (months)	P-value
Gender	Breast	Males (2,878) 0.77%	1.02 ± 0.040	Females (371,076) 99.3%	1.24 ± 0.014	< 0.001
	CRC	Males (99,522) 52.9%	0.82 ± 0.008	Females (88,439) 47.1%	0.74 ± 0.0075	< 0.001
	Lung	Males (106,883) 50.3%	1.30 ± 0.009	Females (105,724) 49.7%	1.31 ± 0.010	0.0381
	Prostate	Males (217,249) 100%	2.53 ± 0.010	-	-	-
Age	Breast	> 65 years (168,067) 44.9%	1.23 ± 0.006	< 65 years (205,887) 55.1%	1.25 ± 0.005	0.0002
	CRC	> 65 years (97,690) 52.0%	0.81 ± 0.008	< 65 years (90,271) 48.0%	0.76 ± 0.0078	< 0.001
	Lung	> 65 years (144,645) 68.0%	1.38 ± 0.008	< 65 years (67,962) 32.0%	1.14 ± 0.016	< 0.001
	Prostate	> 65 years (134,618) 62.0%	2.30 ± 0.013	< 65 years (82,631) 38.0%	2.91 ± 0.017	< 0.001
Race	Breast	White (245,517) 65.7%	1.18 ± 0.005	Non-White (128,437) 34.3%	1.36 ± 0.008	< 0.001
	CRC	White (120,909) 64.3%	0.75 ± 0.0061	Non-White (67,052) 35.7%	0.85 ± 0.010	< 0.001
	Lung	White (159,925) 75.2%	1.26 ± 0.007	Non-White (52,682) 24.8%	1.44 ± 0.015	< 0.001
	Prostate	White (146,352) 67.4%	2.43 ± 0.012	Non-White (70,897) 32.6%	2.75 ± 0.019	< 0.001
Marital status	Breast	Married (205,336) 54.9%	1.19 ± 0.004	Divorced (39,790) 10.6%	1.30 ± 0.012	< 0.05
				Single (57,349) 15.3%	1.35 ± 0.011	< 0.05
				Separated (4,148) 1.1%	1.39 ± 0.041	< 0.05
				Widowed (47,316) 12.7%	1.25 ± 0.011	< 0.05
				Domestic partner (2,157) 0.6%	1.28 ± 0.049	< 0.05
				Unknown (17,858) 4.8%	1.32 ± 0.022	< 0.05
	CRC	Married (98,271) 52.3%	0.77 ± 0.0075	Divorced (17,649) 9.4%	0.84 ± 0.018	< 0.05
				Single (34,747) 18.5%	0.81 ± 0.014	< 0.05
				Separated (2,050) 1.1%	0.93 ± 0.057	< 0.05
				Widowed (23,132) 12.3%	0.78 ± 0.015	< 0.05
				Domestic partner (988) 0.5%	0.86 ± 0.070	< 0.05
				Unknown (11,124) 5.9%	0.69 ± 0.024	< 0.05
	Lung	Married (109,620) 51.6%	1.24 ± 0.009	Divorced (26,710) 12.6%	1.36 ± 0.020	< 0.001
				Single (31,585) 14.9%	1.34 ± 0.018	< 0.001
				Separated (2,448) 1.2%	1.38 ± 0.064	< 0.001
				Widowed (32,322) 15.2%	1.44 ± 0.018	< 0.001
				Domestic partner (1,137) 0.5%	1.32 ± 0.088	< 0.001
				Unknown (8,785) 4.1%	1.27 ± 0.035	< 0.001
	Prostate	Married (146,322) 67.4%	2.50 ± 0.012	Divorced (14,686) 6.8%	2.56 ± 0.040	< 0.05
				Single (25,893) 11.9%	2.65 ± 0.032	< 0.05
				Separated (1,679) 0.8%	2.71 ±0.125	< 0.05
				Widowed (9,250) 4.3%	1.91 ± 0.048	< 0.05
				Domestic partner (1,039) 0.5%	2.58 ± 0.150	< 0.05
				Unknown (18,380) 8.5%	2.86 ± 0.043	< 0.05
Income	Breast	< $35,000 (2,868) 0.77%	1.01 ± 0.010	> $35,000 (371,074) 99.2%	1.24 ± 0.010	< 0.001
	CRC	< $35,000 (2,275) 1.2%	0.74 ± 0.048	> $35,000 (185,678) 98.8%	0.79 ± 0.005	< 0.001
	Lung	< $35,000 (3,082) 1.4%	1.22 ± 0.057	> $35,000 (209,515) 98.6%	1.33 ± 0.006	< 0.001

Table 1. Cancer-Specific TTI of Factors Studied - *(continued)*

Demographics	Cancer type	Group 1	TTI (months)	Group 2	TTI (months)	P-value
	Prostate	< $35,000 (1,874) 0.9%	2.22 ± 0.097	> $35,000 (215,366) 99.1%	2.53 ± 0.010	< 0.001
Geographic data	Breast	Non-metropolitan (49,235) 16.8%	1.12 ± 0.010	Metropolitan (228,391) 77.8%	1.31 ± 0.005	< 0.001
	CRC	Non-metropolitan (24,377) 13.0%	0.73 ± 0.014	Metropolitan (163,137) 86.8%	0.79 ± 0.006	0.1233
	Lung	Non-metropolitan (37,793) 17.8%	1.24 ± 0.014	Metropolitan (113,737) 53.5%	1.34 ±0.009	< 0.001
	Prostate	Non-metropolitan (32,580) 15.0%	2.33 ± 0.014	Metropolitan (125,288) 57.7%	2.64 ± 0.014	0.12
Cancer stage	Breast	*In situ* (3) 0.001%	1.67 ± 1.306	Localized (248,921) 66.6%	1.31 ± 0.009	< 0.001
				Regional (102,774) 27.5%	1.14 ± 0.008	< 0.001
				Distant (19,970) 5.3%	0.90 ± 0.017	< 0.001
				Unknown (2,286) 0.6%	1.62 ± 0.100	< 0.001
	CRC	*In situ* (44) 0.02%	0.32 ± 0.199	Localized (73,733) 39.2%	0.65 ± 0.008	< 0.001
				Regional (73,880) 39.3%	0.85 ± 0.008	< 0.001
				Distant (36,951) 19.7%	0.91 ± 0.012	< 0.001
				Unknown (3,353) 1.8%	0.060	< 0.001
	Lung	*In situ* (8) 0.004%	1.63 ± 0.823	Localized (61,557) 29.0%	1.71 ± 0.004	< 0.001
				Regional (50,438) 23.7%	1.37 ± 0.013	< 0.001
				Distant (98,646) 46.4%	1.01 ± 0.008	< 0.001
				Unknown (1,958) 0.9%	1.67 ± 0.106	< 0.001
	Prostate	*In situ* (5) 0.002%	1.40 ± 2.286	Localized (147,626) 68.0%	2.73 ± 0.013	< 0.001
				Regional (42,836) 19.7%	2.69 ± 0.020	< 0.001
				Distant (23,167) 10.7%	0.96 ± 0.020	< 0.001
				Unknown (3,615) 1.7%	2.80 ± 0.119	< 0.001
Cancer grade	Breast	Well-differentiated (41,105) 11.0%	1.25 ± 0.011	Moderately differentiated (79,524) 21.3%	1.27 ± 0.001	< 0.001
				Poorly differentiated (51,767) 13.8%	1.14 ± 0.010	< 0.001
				Undifferentiated (126) 0.03%	0.87 ± 0.150	< 0.001
				Unknown (201,432) 53.9%	1.26 ± 0.005	< 0.001
	CRC	Well-differentiated (11,745) 6.2%	0.53 ± 0.020	Moderately differentiated (57,807) 30.8%	0.79 ± 0.009	< 0.001
				Poorly differentiated (12,046) 6.4%	0.72 ± 0.019	< 0.001
				Undifferentiated (2,765) 1.5%	0.67 ± 0.038	< 0.001
				Unknown (103,598) 55.1%	0.82 ± 0.007	< 0.001
	Lung	Well-differentiated (7,449) 3.5%	1.42 ± 0.038	Moderately differentiated (20,282) 9.5%	1.46 ± 0.021	< 0.001
				Poorly differentiated (23,885) 11.2%	1.33 ± 0.018	< 0.001
				Undifferentiated (2,382) 1.1%	0.94 ± 0.046	< 0.001
				Unknown (158,609) 74.6%	1.28 ± 0.006	< 0.001
	Prostate	Well-differentiated (17,267) 7.9%	2.56 ± 0.044	Moderately differentiated (51,337) 23.6%	2.89 ± 0.020	< 0.001
				Poorly differentiated (31,485) 14.5%	1.95 ± 0.021	< 0.001
				Undifferentiated (58) 0.03%	0.78 ± 0.309	< 0.001
				Unknown (117,102) 53.9%	2.53 ± 0.014	< 0.001

CRC cancer (N = 187,961), lung cancer (N = 212,607), breast cancer (N = 373,954), prostate cancer (N = 217,249). CRC: colorectal cancer; TTI: time to treatment initiation.

revealed that patients younger than 65 years old, those living in metropolitan regions, earning greater than $35,000, localized, well-differentiated cancers were at greater risk of having a delay greater than 1 month (Supplementary Material 2, wjon.elmerpub.com).

Discussion

There have been multiple studies published over the years that have shown delays in the diagnosis or treatment of cancer based on sociodemographic factors. These differences were clearly delineated in our findings, making it evident that health disparities continue to play a role in cancer management, including mortality rates.

Gender

Our results indicate gender differences in TTI, with women having higher TTI for breast cancer, while men have higher TTI for CRC. This suggests that gender-specific differences exist in treatment decisions. Behavioral differences can play a role. Harris and Jenkins highlighted that men are more likely to partake in risky behaviors across various domains, including health [4]. Rana et al conducted a systematic literature review to examine the gender differences in healthcare utilization of cancer patients and found that women tend to get diagnosed at an earlier stage, likely due to a higher probability of using inpatient cancer-care services and surgical treatments [5]. Regarding colon cancer, there is a higher incidence in men compared to females, and therefore, men tend to undergo more colonoscopies than women. Yet females also tend to have right-sided colon cancers that are more difficult to detect on colonoscopies as well as BRAF tumors which can present with a higher stage or grade at diagnosis and thus, less delay to treatment compared to males [6].

TTI was shorter in men with breast cancer at 1.02 months compared to women at 1.24 months ($P < 0.001$). Men often have advanced staging on diagnosis and worse 5-year survival rates compared to women with breast cancer due to delayed diagnosis. Stigma regarding men with breast cancer plays a role in delaying diagnosis due to lack of awareness of breast cancer in men among providers and patients as well as embarrassment associated with the diagnosis in men [7]. Thus, when men are diagnosed with breast cancer, it is often at a more advanced stage, which can lead to quicker TTI compared to women. This emphasizes the importance of breast cancer education in men and society.

Age

There is increased utilization of active surveillance (AS) and watchful waiting (WW) in low-grade prostate cancer, especially among older patients. The percentage of men with low-grade prostate cancer managed with AS and WW was 6.2% in the year 2000 and increased to 40.4% in 2010 in patients older than 75 [8]. Therefore, it is surprising that our results indicate a lower TTI of 2.30 months in patients 65 years and older compared to 2.91 months in patients younger than 65 ($P < 0.001$). Higher TTI in younger than 65 years old is also surprising as Harlan et al found that age at diagnosis is inversely proportional to the chance of receiving aggressive treatment due to younger patients generally having fewer comorbidities and thus avoiding delays due to comorbidity treatment [9]. Regardless of age, there is a longer TTI in prostate cancer in comparison to other cancers due to localized prostate cancer having low mortality regardless of active monitoring or pursuing treatment such as prostatectomy and radiotherapy [10].

In breast cancer, our results indicate a similarly lower TTI among patients older than 65 years. However, unlike breast and prostate cancers, our findings show the opposite relationship for CRC and lung cancer, with older age corresponding to higher TTI. This finding can be explained by the fact that comorbidities might have a greater effect on the aggressiveness of treatment for certain cancers like lung cancer and CRC [11]. Another interesting nuance that must be discussed is that, ultimately, the difference in TTI between the age groups for CRC might be due to differences in time to diagnosis versus TTI. Castelo et al found that younger patients less than 50 years old often presented emergently with stage IV disease and rectal involvement, and thus, had shorter TTI. However, there was no significant difference between the time of presentation and treatment among age groups due to significantly longer diagnostic intervals in younger patients [12]. Therefore, future researchers should elucidate the importance of this difference in time to diagnosis and TTI between age cohorts and how it affects outcomes.

In lung cancer, a positive association was observed between age and TTI, but this might be beneficial among the older cohort, as Azzouqa et al showed that shorter TTI had worse outcomes in advanced lung cancer, with most elderly being diagnosed with cancer at an advanced stage [13]. The explanation for this again has to do with comorbidities present at diagnosis. By aggressively treating advanced-stage lung cancer instead of taking care of other comorbidities, earlier TTI results in worse outcomes. Meanwhile, in younger populations, shorter TTI was associated with better outcomes in stage I and II cancers since they tend to have fewer comorbidities.

Race

Among all cancers, shorter TTI was noted in White patients compared to non-White, but patients who were included in SEER were mostly White. Many different studies emphasize this difference in common cancers. Caraballo et al utilized the National Health Interview Survey to identify different barriers affecting medical care and found that Latino and African American patients reported delaying care in comparison to their White counterparts due to longer wait times and difficulties in obtaining transportation [14]. Schermerhorn et al conducted a retrospective analysis of patients with stage I-III breast cancer who underwent surgical resection utilizing the National Cancer Database to identify the role of race and ethnicity in treatment delay. Black, Hispanic, and other non-

White patients had increased odds of having treatment delay relative to White patients, respectively [15]. Regardless of cancer type, there is an increasing disparity in treatment delays, as seen in our results.

In prostate cancer, we noted a delay in treatment initiation in non-Whites at 2.75 months compared to 2.43 months in Whites. Imm et al studied the perception of prostate cancer in the African American population and found that the idea of masculinity might be more prominent in this population, delaying medical care. A diagnosis of prostate cancer can cause urinary or sexual dysfunction, impacting the dominant male role in this society [16]. Meanwhile, African American women experienced the most delays in initial diagnosis and breast cancer treatment relative to women of other racial/ethnic subgroups [17-19]. We observed a delay to treatment in non-White women with breast cancer of 1.36 months compared with White women, 1.18 months.

Interestingly, when removing confounders, propensity matching demonstrated that non-White patients had a decreased hazard ratio in comparison to White patients, 0.8829 in Black patients and 0.0038 in Hispanic patients, meaning that White patients had a delay in treatment greater than 30 days. A reason for this can be that race is often influenced by other sociodemographic factors such as education level, insurance level, and income level, among other factors. Patients of non-White race often are diagnosed at more advanced levels, leading to less delay in treatment, but decreased survival. Miller-Kleinhenz et al found that Black women with breast cancer were often diagnosed at later stages due to delay in diagnostic evaluation including biopsies [18]. Mootz et al noted that minorities were more likely to receive a diagnosis of stage 3 disease or greater compared to non-Whites, and also experienced higher mortality [19]. These disparities among minorities emphasize the need for more interventions to address social, economic, and educational determinants of health.

Marital status

Overall, less TTI was noted in married patients compared to divorced, separated, or widowed patients. This is expected due to the presence of a support system. Interestingly, separated as compared to other categories exhibited longer TTI, potentially due to additional stressors involved in balancing separation/divorce and health. Huang et al reported that prostate cancer patients who were divorced or separated at the time of their study reported worse survival outcomes independent of age, ethnicity, grade, and stage [20]. Furthermore, in a meta-analysis of marital status and survival in cancer patients, Krajc et al found that being unmarried was associated with worse cancer-specific outcomes, with divorced/separated men being the most vulnerable [21].

Wang et al studied patients with colon cancer using SEER to analyze survival based on marital status. Married patients were diagnosed at earlier stages and more likely to undergo surgery compared to single, separated, and divorced patients. Married patients were also found to have lower death rates [22]. This can explain why after propensity matching, married patients were more likely to experience a treatment delay greater than 30 days compared to non-married patients, as married patients are often diagnosed earlier with less aggressive cancers compared to unmarried counterparts [23]. These results potentiate the importance of having a core support system, which can play a protective role in cancer screening and diagnosis.

Income

Most surprisingly, higher TTI was noted in incomes greater than $35,000, possibly due to more time spent looking for specialists and second opinions. Another potentiating factor could be insurance status. Since higher income is correlated with having insurance, those with lower incomes or unstable insurance may present to doctors with worse cancer presentation, therefore requiring a more aggressive approach. Our results following propensity matching also showed that as income increased, the hazard ratio was greater for delay in treatment over 30 days. Gupta et al found that low socioeconomic status level and education level are strongly associated with advanced disease at diagnosis. In this study, half of the population in the lowest-income group identified as Black. Patients living in areas of lower education levels and lower-income areas were more likely to have advanced-stage cancer at diagnosis compared to those living in areas with a higher education level and higher-income areas [24].

Although education level is not included in SEER, per the National Center for Education Statistics, in 2022, the median income of a person who completed high school was $41,800 compared to a person who had a bachelor's degree at $66,600. Based on these values, a person's education level can be assumed, with patients earning less than $35,000 likely having a low education level [25]. Mootz et al studied health disparities in breast cancer in the United States and concluded that patients living in poverty had higher breast cancer incidence rates, higher cancer stage at diagnosis, inferior 5-year survival rates, and higher mortality for all cancer types. Within the same cancer stage, patients who were uninsured, underinsured, or living in poverty had worse cancer outcomes compared to patients who were insured and living in a higher socioeconomic status. Socioeconomic factors such as lack of access to paid sick leave, transportation, and difficulties in obtaining child care contribute to delays in cancer diagnosis [19].

Geographic region

Surprisingly, our study shows that patients in non-metropolitan regions have a shorter time to treatment compared to patients in metropolitan regions for lung and breast cancers. This could be due to many reasons; one reason is that in non-metropolitan areas, despite the lower per-capita access to healthcare providers, there could be a more intimate patient-provider relationship, leading to more personalized and quicker care. However, this finding is still shocking as non-metropolitan areas generally face disparities in access to medical care. Andrilla et al

utilized 2010 - 2014 SEER incidence data to study the effect of geographic location on CRC stage at diagnosis and found that patients living in remote, small rural counties had a higher rate of having stage IV disease [26]. Obeng-Gyasi et al studied differences in breast cancer presentation and surgical management in rural and urban areas utilizing the National Cancer Database from 2004 to 2015 and found that the cancer stage increased in more rural areas [27]. This highlights the difficulties in access to care that can lead to more advanced cancers at presentation in rural areas, likely leading to shorter time to treatment.

Grade and stage

With the exception of CRC, across all cancer types, distant and undifferentiated cancers had shorter time to treatment. Caplan studied women with invasive breast cancer and found that symptomatic cancers diagnosed at stage III or IV had shorter diagnostic wait times compared to those diagnosed at stage I. Likely as the tumor burden increases or as cancers metastasize, patients become more symptomatic and seek medical care sooner and thus, receive earlier treatment compared to asymptomatic cancers. This was also observed after propensity matching. Once confounders were removed, the risk of treatment delay over 30 days was 34% lower in the distant stage group and 50% lower in the anaplastic group [28].

Other

In our study, we report on factors influencing the TTI of breast cancer, lung cancer, CRC, and prostate cancer based on sociodemographic factors such as gender, age, race, marital status, income, and geographic region, as well as clinical grade and stage. Overall, less TTI was noted in CRC and breast cancer, likely due to the availability of screening modalities. In fact, our results indicate a consistently low TTI among all sociodemographic factors for CRC, similar to previous studies as reported by Khorana et al [1]. There are a couple of probable reasons for this finding. Cone et al reported a particularly long diagnostic interval for colon cancer, which means that oftentimes, there is a delay from when symptoms first appear to when the diagnosis is made, which can also delay the time from cancer incidence to treatment. The study found that for every additional 60-day delay, the risk of dying increases by 0.9% to 4.6% for stage I colon cancer and by 3.2% to 6.0% for stage III colon cancer [2]. These findings partly explain the urgency for treatment observed in our low TTI for CRC. Furthermore, Hanna et al showed that delays in CRC treatment potentiate a higher risk of death, with adjuvant systemic treatment delays in CRC raising the risk of death by 13% [29]. Finally, Torring et al found that a longer time to diagnosis of CRC leads to the cancer being found in more advanced stages when it is finally diagnosed. They also found that delays, even from the primary care processes, can affect outcomes [30]. Therefore, it is crucial to diagnose CRC as early as possible to avoid advanced stages of the disease. Hence, it is not surprising that TTI for CRC is low among all sociodemographic factors since clinicians have become influenced by these studies.

Limitations

Our study is limited by what SEER offers; for example, it does not give information on educational level and insurance status and does not offer subjective data like patients' attitudes or thoughts on cancer diagnosis that could have also contributed to delay in treatment or lack of treatment which limits generalizability and reliability of our conclusions. Other factors that are not considered are physician recommendations and patients' comorbidities, which can also cause a delay in treatment. Noone et al stated that certain data in SEER involving treatment status may be incomplete. The overall sensitivity reported was 80% in patients receiving radiation therapy and 68% in patients receiving chemotherapy. However, the study found that the SEER database was mostly accurate, with an overall positive predictive value of over 85% in treatment detection in all groups and cancer sites, except for identifying chemotherapy in prostate cancer patients [31]. Furthermore, relevant comorbidities are not always included in SEER, which could explain some gaps in treatment. According to the SEER database, cancer treatments are now mostly administered in an outpatient setting, which makes it more difficult to obtain data.

The time period studied is until 2020, which is around the time the COVID-19 pandemic began. There is no distinction in the SEER database on which patients might have been affected by the pandemic, thus causing a longer delay in treatment. During this time, many outpatient offices, screening centers, and treatment centers were closed, causing treatment delays. Black and Latino patients also experienced a greater delay due to concerns with food security, financial stability, and affordability of cancer treatment [32]. These are all important factors that are not taken into account in the database.

Lastly, in all cancers studied, greater than two-thirds of the population was of White race. This does not accurately represent the general US population. In our study, we divide races into two groups: White and non-White. Generally, the White population experiences better outcomes compared to minorities, but within the non-White strata, there are also differences in outcomes. This is a limitation in our research that should be studied further.

Conclusion

Our study reveals the health disparities affecting TTI across various cancer types. Factors such as age, sex, race, marital status, income, and geographic location contribute significantly to delays, potentially impacting patient outcomes. These findings emphasize the need for targeted intervention, including policy changes and community-based programs, to reduce delays and improve access to timely cancer care. Future research should further explore the long-term effects of treatment delays and create strategies to address these disparities

effectively. Addressing these gaps may be essential to ensuring equitable cancer treatment and improving overall survival.

Supplementary Material

Suppl 1. Logistic regression used for propensity score matching.

Suppl 2. The Fine and Gray proportional subdistribution hazard model.

Suppl 3. Test of propensity matching.

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Conflict of Interest

The authors have no conflict of interest to declare that are relevant to the content of this article.

Informed Consent

Informed consent was not deemed necessary as the data were obtained from the SEER database.

Author Contributions

MD and MK drafted the manuscript. SS and JI assisted with editing. MD designed the study, and with the assistance of JI, performed data collection and analysis with statistics. SPA assisted in statistical analysis including logistic regression and propensity matching. JI carefully supervised manuscript preparation and writing.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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