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Research Article

Temporal Trends and Burden of Gastric Cancer in the United States: A SEER-Based Analysis

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Abstract

Background: Gastric cancer is the third leading cause of cancer death worldwide and is diagnosed in 27,000 Americans each year. It accounts for about 1.5% of all new cancers diagnosed in the US each year. We investigated the burden of gastric cancer in United States and temporal trends in cancer-specific incidence and mortality.

Methods: Using data from Surveillance, Epidemiology, and End Results (SEER) areas, we assessed gastric-cancer mortality and linked deaths from gastric cancer to incident cases in SEER cancer registries. This allowed us to evaluate population-level mortality trends attributed to specific subtypes (incidence-based mortality). We also evaluated gastric-cancer incidence and survival according to cancer subtype, sex, and calendar year. Joinpoint software was used to assess changes in incidence and trends in incidence-based mortality.

Results: The overall trend of incidence and mortality of gastric cancer is decreasing from 2000-2019. The incidence rate of gastric carcinoma has been steadily declining at 1.4% and 0.5% annually among males and females respectively. Among males, the incidence-based mortality rate of gastric carcinoma increased from 2001 to 2003 with an Annual Percentage Change (APC) of 7.2 and decreased from 2003 through 2019 with an APC of 1 while in females trend increased from 2001 to 2005 with APC of 3.8 and then trended down through 2019 with APC of 0.9. This decrease in incidence and improvement in survival was found across all races and ethnic groups. This result correlates with an increase in awareness regarding risk factors, early screening and treatment advances for gastric cancer in the time frame we examined.

Conclusions: Population-level mortality from gastric cancer in the United States decreases from 2003 to 2016, and survival after diagnosis improved substantially. Our analysis suggests that a reduction in incidence along with increased screening with esophagogastroduodenoscopy, H. pylori eradication therapy and treatment advances — is likely to explain the reduction in mortality observed during this period.

Keywords

Gastric cancer, Gastric carcinoma, Gastric cancer incidence, Gastric cancer mortality.

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Introduction

Gastric cancer accounts for almost 8% of all new cancer cases and 10% of all cancer-related deaths in 2020 [1]. The incidence and mortality rates of gastric cancer vary widely across regions due to various risk factors such as Helicobacter pylori infection, dietary habits, smoking status, genetic susceptibility, and socioeconomic status [2]. Unfortunately, gastric cancer is often diagnosed at advanced stages, limiting curative treatment options [3]. Therefore, prevention strategies, early detection methods, and effective therapies are crucial to reducing the burden of this disease.

The standard treatment for localized gastric cancer is surgical resection followed by adjuvant chemotherapy or chemoradiotherapy [4]. However, the recurrence rate after surgery is high, and the survival benefit of adjuvant therapy is modest [5]. In metastatic gastric cancer, the first-line chemotherapy regimen involves fluoropyrimidine plus platinum-based agents, with or without trastuzumab, for HER2-positive tumors [6]. Unfortunately, the response rate to chemotherapy is low, and the median overall survival is less than one year. Recently, significant advances have been made in novel therapies for gastric cancer, including immune checkpoint inhibitors, targeted agents, and molecular profiling, which have shown promise in improving progression-free survival and overall survival in selected subgroups of patients with relapsed or refractory disease [7-9].

Despite these advances, there is limited evidence on how they have influenced population mortality trends over time and space. Most studies on gastric cancer survival outcomes are based on clinical trials or single-center cohorts that may not reflect real-world practice and heterogeneity across different regions and settings [10-12]. Additionally, comprehensive data on how changes in treatment patterns affect mortality rates at various stages of disease progression still needs to be included [1,13]. Therefore, evaluating the effect of advances in gastric cancer treatment on population mortality using large-scale observational data from diverse sources is crucial.

Methods

We used the database from the United States (U.S.) Surveillance, Epidemiology, and End Results (SEER) Program from the website (www.seer.cancer.gov). We used the software: Surveillance Research Program, National Cancer Institute SEER*Stat software (www.seer.cancer.gov/seerstat) version 8.4.0.1 for the calculation of incidence and incidence-based mortality rate, and survival rate.

We included only gastric cancer patients with ages 15 years and older from 2001-2019 using the selection tab in SEER*Stat as malignant behavior, with known Age, and the first matching record for each person. The session type in the SEER*Stat was a rate session for incidence and incidence-based mortality rates and a survival session for survival rates, Geographical areas covered include San Francisco-Oakland SMSA, Connecticut, Hawaii, Iowa, New Mexico, Seattle (Puget Sound), Utah, Atlanta (Metropolitan), San Jose-Monterey, Los Angeles, Rural Georgia California excluding SF/SJM/LA, Kentucky, Louisiana, New Jersey, Greater Georgia.

Incidence-SEER Research Data, 17 registries (excl AK), Nov 2021 sub (2000-2019) which covers approximately 26.5 % of the U.S. population (based on the 2010 census) for calculation of incidence and incidence-based mortality rates based on gender and race. Incidence rates were calculated by the number of new gastric cancers occurring in a specified population during a year, usually expressed as the number of cancers per 100,000 population at risk.

We used SEER Research Data, 17 registries for the calculation of overall and gastric adenocarcinoma incidence-based mortality. Only patients who have died of gastric cancer by the study cut-off date are included in the study. The incidence-based mortality for gastric cancer is calculated using the number of gastric cancer-specific deaths among persons with gastric cancer as the numerator and the general population with gastric cancer at the time of death as the denominator. Incidence-based mortality rate measures the efficacy of an intervention comparing it with historical patterns and helps to assess the impact of an intervention by classifying the stage at diagnosis. The death certificate mortality rates were obtained from National Center for Health Statistics, which is ascertained by state death records.

Two-year gastric-cancer-specific survival and one-year gastric-adenocarcinoma-specific survival were calculated from the registry. Cause-specific survival is defined as the length of time from either the date of diagnosis or the start of treatment for gastric cancer to the date of death from the disease. It is one way to monitor the effectiveness of new treatments in clinical trials.

We used Joinpoint software, version 4.9.1.0 by National Cancer Institute to create log-linear time trends annually. We classified the above rates based on gender and rates obtained from the SEER database to report the trend from 2001 to 2019. Kaplan-Meier method was used for survival analysis.

P-value was used for statistical significance with a level of significance less than 0.05.

Results

Our study consisted of 117,461 total cases of gastric carcinoma from 2001 to 2019 with ages 15 and above, which includes 71,101

males and 46,360 females. Overall, rate of gastric carcinoma among males was 12.7 and females was 6.7 per 100,000 population. Gastric Adenocarcinoma had 67,098 indexed cases (Table 1).

Table 1: Baseline characteristics for study population.

Variables		Total number (n)	Overall rate (per 100,000 and age adjusted to 2000 US Standard Population. (95% CI, Upper CI-Lower CI)
Incidence rates of gastric carcinoma			
Total		117,461.00	9.3 (9.3-9.4)
	Male	71,101.00	12.7 (12.6-12.8)
Gender	Female	46,360.00	6.7 (6.6-6.8)
	White	84,297.00	8.3 (8.3-8.4)
	Black	15,468.00	13.7 (13.5-13.9)
	American Indian/ Alaska Native	786	6.9 (6.4-7.4)
Races	Asian or Pacific Islander	16,910.00	14.2 (14-14.4)
Incidence -based mortality rates of gastric carcinoma			
Total		90,370.00	7.2 (7.2-7.3)
Gender	Male	56,365.00	10.4 (10.3-10.5)
	Female	34,005.00	4.8 (4.8-4.9)
Races	White	65,715.00	6.5 (6.4-6.5)
	Black	11,895.00	11.1 (10.9-11.3)
	American Indian/ Alaska Native	885	7.4 (6.8-7.9)
	Asian or Pacific Islander	11,875.00	10.2 (10.1-10.4)
Incidence rates of gastric adenocarcinoma			
Extent of disease	Localized disease	17,091.00	1.4 (1.3-1.4)
	Regional disease	22,041.00	1.7 (1.7-1.8)
	Distant disease	27,966.00	2.2 (2.2-2.2)

Mortality estimates from gastric cancer were lower in National Center for Health Statistics death-certificate mortality records than incidence-based mortality based on the SEER database. The figure shows the incidence-based mortality increased from 2001 to 2003 with an annual percentage change of 7.7 (95% CI, 0.4 to 15.5, P=0.04) and started to decline from 2003 through 2019 at 0.8% annually (95% CI, -1 to -0.5, P <0.001). However, the death rate based on death certificates declined gradually throughout the study.

Gender-based Analysis of gastric Carcinoma

The incidence rate of gastric carcinoma has been steadily declining at 1.4% (95% CI, -1.4 to -1.7, P <0.001) and 0.5% (95% CI, -0.7 to -0.3, P <0.001) annually among males and females respectively. However, the incidence rate was significantly higher among males (Figure 1).

Among males, the incidence-based mortality rate of gastric carcinoma increased from 2001 to 2003 with an APC of 7.2, (95% CI, -0.3 to 15.3, P =0.06) and decreased from 2003 through 2019 with an APC of 1* (95% CI, -1.3 to -0.7, P <0.001), while in females trend increased from 2001 to 2005 with APC of 3.8* (95% CI, 0.6 to 7.1, P =0.02) and then trended down through 2019 with APC of 0.9*(95% CI, -1.4 to -0.5, P <0.001) (Figure 2).

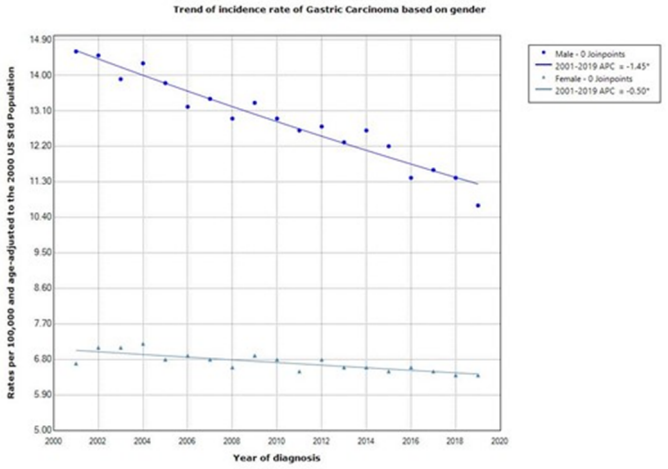

Figure 1: Trend of the incidence rate of gastric carcinoma based on gender.

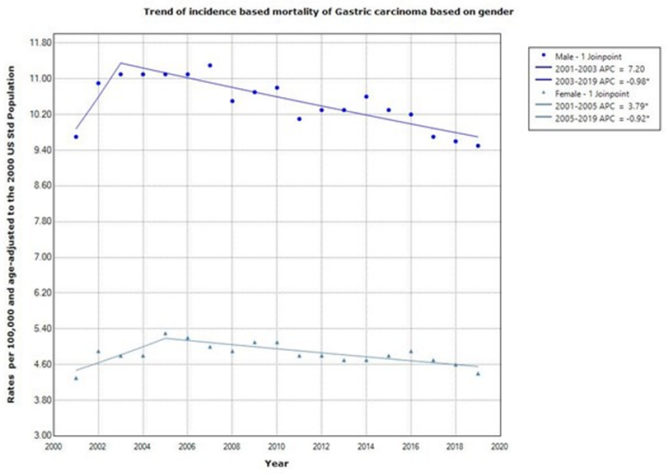

Figure 2: Trend of incidence-based mortality of gastric carcinoma based on gender.

Among males, an improved 2-year survival trend was noted from 2001 to 2009 with an APC of 2.4%* (95% CI, 1.7 to 3.2, P <0.001) which relatively plateaued from 2009 to 2017 with an APC of 1* (95% CI, 0.4 to 1.7, P =0.005). Among females, there was a steady improvement in survival trend from 2001 to 2017 with an APC of 1.9% over the studied years (95% CI, 1.6 to 2.2, P <0.001) (Figure 3).

Race-based Analysis of gastric carcinoma

The incidence rate of gastric cancer has been declining steadily annually at 0.7%* (95% CI, -0.8 to -0.5, P<0.001) among whites, 2.1% (95% CI, -2.4 to -1.9, P<0.001) among blacks, 2.4% (95% CI,

-3.6 to -1.1, P=0.001) among American Indians/Alaska Natives and 3.2% (95% CI, -3.6 to -2.9, P<0.001) among Asian or Pacific Islanders (Figure 4).

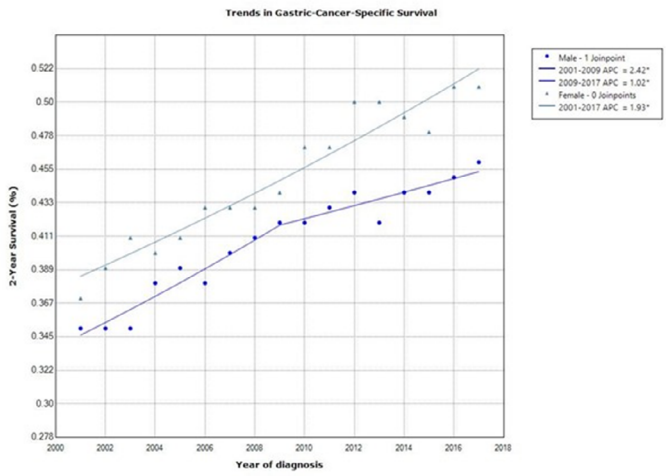

Figure 3: Trends in gastric cancer-specific survival based on gender.

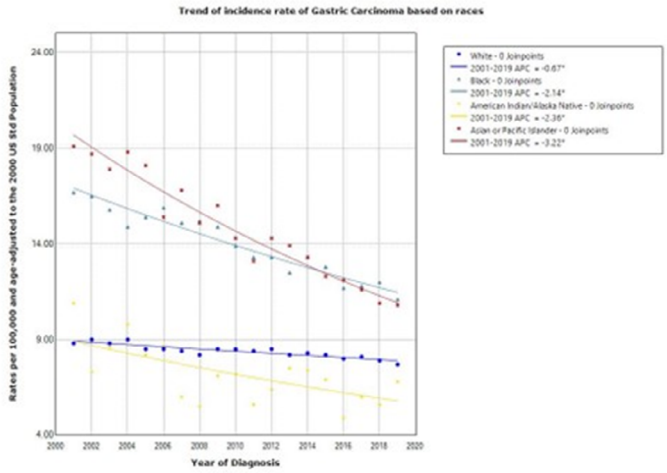

Figure 4: Trend of the incidence rate of gastric carcinoma based on races.

Among the white population, Incidence based mortality increased by 7.2% annually from 2001 to 2003 (95% CI, -0.1 to 15, P =0.054) and declined from 2003 to 2019 by 0.5% annually (95% CI, -0.7 to -0.2, P =0.001). Similarly, in Asian or Pacific Islanders, there was an increase in incidence-based mortality trend from 2001 to 2005 annually by 4.2% (95% CI, -1.7 to 10.4, P =0.151) and then gradually declined by a faster rate of 3% annually (95% CI, -3.7 to -2.4, P <0.001) from 2005 to 2019. While in black and American Indian/Alaska Native, there was a gradual decrease from 2001 to 2019 by 1.5% (95% CI, -2.1 to -0.9, P <0.001) and 1.6% (95% CI, -3 to -0.2, P =0.026). The highest rate of decline was noted among Asian or Pacific Islanders (Figure 5).

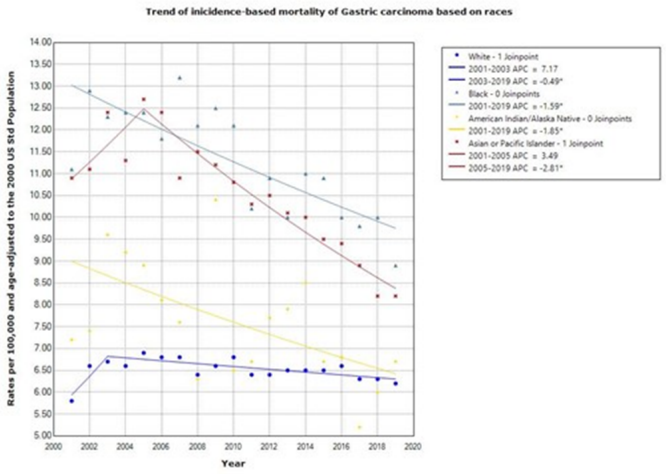

Figure 5: Trend of incidence-based mortality of gastric carcinoma based on races.

A two-year survival analysis revealed white population had substantial improvement in cause-specific survival with APC of 2.4* (95% CI, 2.1 to 2.7, P <0.001) from 2001 to 2012 and plateaued from 2012 through 2017. However, there was gradual improvement in survival from 2001 through 2017 in black, Asian or Pacific Islanders and American Indian/Alaska Natives by APC of 2.3* (95% CI, 2 to 2.7, P <0.001), 0.6 (95% CI, -1.5 to 2.6, P =0.56) and 0.5* (95% CI, 0.1 to 1, P =0.02) respectively (Figure 6).

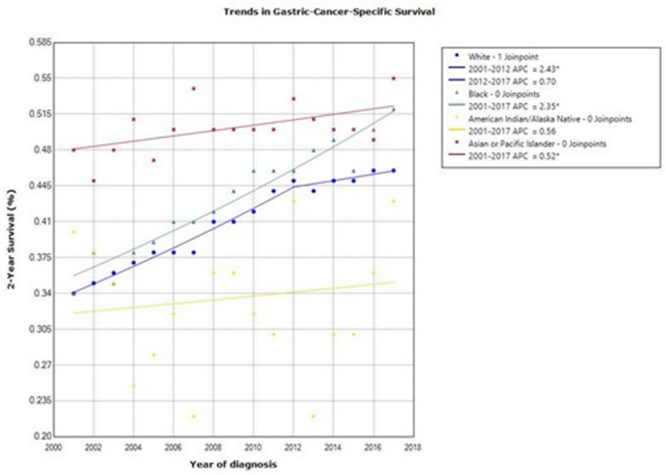

Figure 6: Trend of gastric cancer-specific survival based on races.

Subgroup analysis of Gastric Carcinoma

Gastric Adenocarcinoma

The incidence rate for localized, regional metastatic, and distant metastatic disease has been declining from 2004 to 2017 at 2.2%* (95% CI, -3 to -1.3, P <0.001), 2.8%* (95% CI, -3.2 to -2.3, P <0.001), and 0.5% (95% CI, -0.9 to 0, P=0.03) every year respectively. However, the most significant decline was noted in

regional metastatic gastric adenocarcinoma (Figure 7).

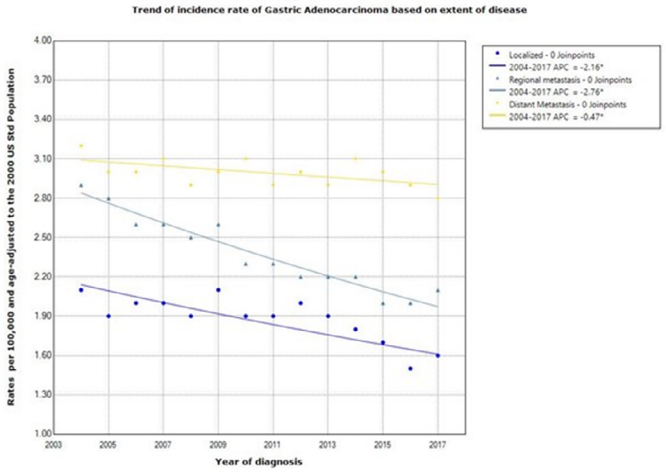

Figure 7: Trend of the incidence rate of gastric adenocarcinoma based on the extent of the disease.

For localized malignancy, incidence-based mortality increased from 2004 at an APC of 26.55* (95% CI, 10.3 to 45.3, P =0.004) to 2007 and plateaued through 2017 and declined further at an APC of 27.3* (95% CI, -41.1 to -10.3, P =0.008). Similarly, incidence-based mortality for regional metastatic disease there was a rise in rate from 2004 to 2006 by APC of 59.4* (95% CI, 37.6 to 82.3, P <0.001) and decreased from 2006 to 2017 at 1.5% annually (95% CI, -2.3 to -0.7, P =0.003) and further at a soaring rate of 28.1% annually (95% CI, -36 to -19.2, P <0.001). In distant metastatic gastric adenocarcinoma, there was a significant rise at a rate of 19.4% (95% CI, 6.6 to 33.7, P=0.007) annually from 2004 to 2006, and flatlined from 2006 to 2017 and immensely declined from 2017 at APC of 56.9* (95% CI, -62.9 to -49.8, P <0.001) (Figure 8).

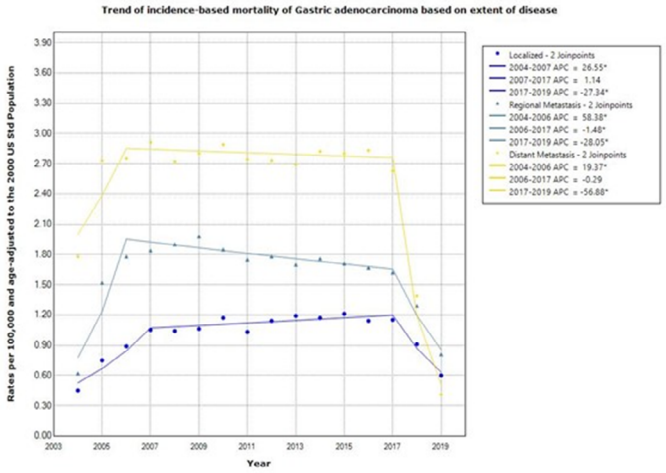

Figure 8: Trend of incidence-based mortality of gastric adenocarcinoma based on the extent of the disease.

Substantial improvement in 1-year survival rate was noted among advanced gastric carcinoma. Regional metastasis survival rates improved from 2004 to 2017 with an APC of 1.1* (95% CI, 0.9 to 1.4, P <0.001) and with an APC of 3.2* (95% CI, 2.6 to 3.8, P <0.001) among distant metastatic disease (Figure 9).

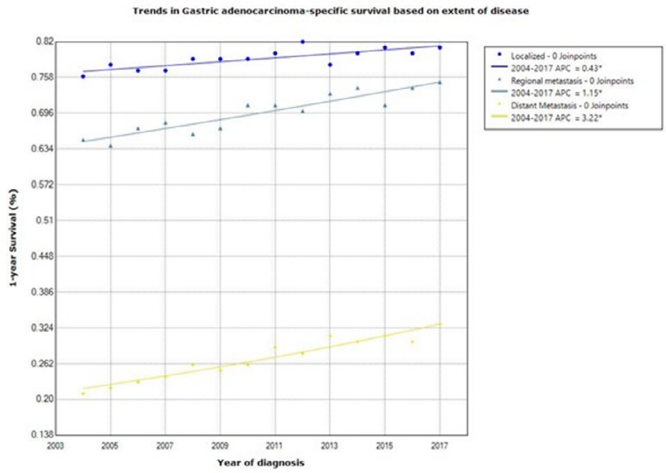

Figure 9: Trend of gastric adenocarcinoma-specific survival based on the extent of the disease.

Discussion

Mortality from gastric cancer were lower in National Center for Health Statistics death-certificate mortality records. A very high incidence rate of gastric carcinoma was found in the male population compared to females. The incidence-based mortality rates are declining, and the two-year survival trend has been improving for both sexes. The highest decline in incidence and the incidence-based mortality rate was found among Asian or Pacific Islanders. Substantial improvement in 2-year survival was noted among the black and white populations. Subgroup analysis of gastric carcinoma showed incidence rate of localized and advanced adenocarcinoma is declining with the highest fall in regional metastatic disease. Incidence-based mortality declined substantially from 2017 to 2019. The survival rate of advanced gastric adenocarcinoma improved significantly.

Gastric cancer is a significant health concern due to its high mortality [14]. Researchers have identified several risk factors and genetic components that contribute to the progression of gastric cancer, leading to increased public awareness and screening programs [15]. Several factors have played role in decreasing mortality trend in all the spectrum, such as the implementation of increased screening with Esophagogastroduodenoscopy (EGD) by the European Council in 2003 has resulted in a lower incidence and mortality rate of gastric cancer [16]. Individual state efforts to increase awareness about the risks of salt, tobacco, and nitro compound food intake have also successfully reduced the incidence of gastric cancer [17]. Consensus statements from American and European countries have recommended national plans for screening and treating H.

pylori, which could also explain the decreasing trend in gastric cancer incidence and mortality [18]. The decline in consumption of salt-preserved foods and nitrites found in preserved meats due to the advent of refrigeration and the increased intake of fresh fruits and vegetables might have also contributed to the declining incidence of gastric cancer [19]. However, access to healthcare and racial disparity remains a significant factor in the higher incidence rate of gastric cancer among Black patients than White patients [19]. Gastric cancer tends to be more predominant in males, and the incidence, mortality, and survival rate are higher in males than females. This might be due to cardia gastric tumors, which are less found in early stages and have higher mortality rates in males [20]. In addition, tobacco use, and the protective effects of sex hormones might also play a role in the incidence of gastric cancer among males and females [21]. The rise in EGD screening and H. pylori eradication has been the main driver of the trend toward early detection of gastric cancer [16].

The treatment modality of gastric carcinoma depends upon the stage of malignancy and functional status of the patient [22]. For stage 1 disease, decreasing trend of surgery alone and increasing trend of surgery and chemotherapy is noted in US population while for stage II/III trend has been shifting from surgery alone to Tri modality therapy of surgery and chemoradiation [23]. For stage IV disease increasing trend of chemotherapy with or without immunotherapy and decline in surgery alone is seen [23]. Finally, targeted therapies such as Trastuzumab and Pembrolizumab for HER2-positive gastric cancer have shown promise in improving survival rates in advanced disease, but we need more extended studies to evaluate these precisely [24]. The improvement in survival rates in all stages of disease can be attributed to advancement in surgical techniques and chemotherapies. Our review noted new emerging immunotherapy looks promising for managing gastric cancer. Artificial Intelligence in medical image-based diagnosis and prognosis prediction models can be the future though limitations exist [24].

Our study is built on a very strong foundation, we used the largest available database from SEER database which is based on high-quality cancer registry database and includes and classifies new cancer diagnosis. This is largely generalizable to US population due to its wide coverage. However, it has its own limitations. It lacks data for modality of treatment and therefore we cannot attribute the results to particular treatment strategy. Migration of patient could be another concern if individuals migrate outside of catchment area, Unrecorded/missing variables, variation in data reporting should also be considered.

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