Title

Epidemiology of Gastric Malignancies 2000—2018 According to Histology: A Population-Based Analysis of Incidence and Temporal Trends

Journal

Clinical Gastroenterology and Hepatology, 21(13)

ISSN

1542-3565

Authors

Rustgi, Sheila D
McKinley, Meg
McBay, Brandon
et al.

Publication Date

2023-12-01

DOI

10.1016/j.cgh.2023.01.037

Peer reviewed

Published in final edited form as:

Clin Gastroenterol Hepatol. 2023 December ; 21(13): 3285–3295.e8. doi:10.1016/j.cgh.2023.01.037.

Epidemiology of Gastric Malignancies 2000–2018 According to Histology: A Population-Based Analysis of Incidence and Temporal Trends

Sheila D. Rustgi[1], **Meg McKinley**[2,3], **Brandon McBay**[4], **Haley M. Zylberberg**[1], **Scarlett L. Gomez**[3,5], **Chin Hur**[1], **Fay Kastrinos**[1], **Samir Gupta**[6,7], **Michelle Kang Kim**[8], **Steven H. Itzkowitz**[8], **Shailja C. Shah**[6,7]

[1]Division of Digestive and Liver Diseases, Columbia University Irving Medical Center, New York, New York

[2]Department of Epidemiology and Biostatistics, University of California San Francisco, San Francisco, California

[3]Greater Bay Area Cancer Registry, University of California San Francisco, San Francisco, California

[4]Department of Public Health, Harvard T. H. Chan School of Public Health, Boston, Massachusetts

[5]Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, California

[6]Gastroenterology Section, VA San Diego Healthcare System, San Diego, California

[7]Division of Gastroenterology, University of California, San Diego, San Diego, California

[8]Dr Henry D. Janowitz Division of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, New York

Correspondence: Address correspondence to: Shailja C. Shah, MD, MPH, 3350 La Jolla Village Drive, GI Section, 3-South (Mail Code: 111D), VA San Diego Healthcare System, San Diego, California 92161. s6shah@health.ucsd.edu.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2023.01.037.

CRediT Authorship Contributions

Sheila D. Rustgi, MD (Conceptualization: Equal; Data curation: Equal; Formal analysis: Equal; Visualization: Equal; Writing – original draft: Equal; Writing – review & editing: Equal)
Meg McKinley, MPH (Data curation: Equal; Formal analysis: Equal; Methodology: Equal; Visualization: Equal; Writing – review & editing: Equal)
Brandon McBay, BS (Visualization: Equal; Writing – review & editing: Equal) Hayley Zylberberg, MD (Visualization: Equal; Writing – review & editing: Equal)
Scarlett Gomez, PhD (Writing – review & editing: Equal)
Chin Hur, MD, MPH (Writing – review & editing: Equal)
Fay Kastrinos, MD, MPH (Writing – review & editing: Equal)
Samir Gupta, MD, MS (Writing – review & editing: Equal)
Michelle K. Kim, MD, PhD (Writing – review & editing: Equal)
Steven H. Itzkowitz, MD (Writing – review & editing: Equal)
Shailja C. Shah, MD, MPH (Conceptualization: Lead; Data curation: Equal; Formal analysis: Equal; Writing – original draft: Equal; Writing – review & editing: Equal)

Conflicts of interest

The authors disclose no conflicts.

Abstract

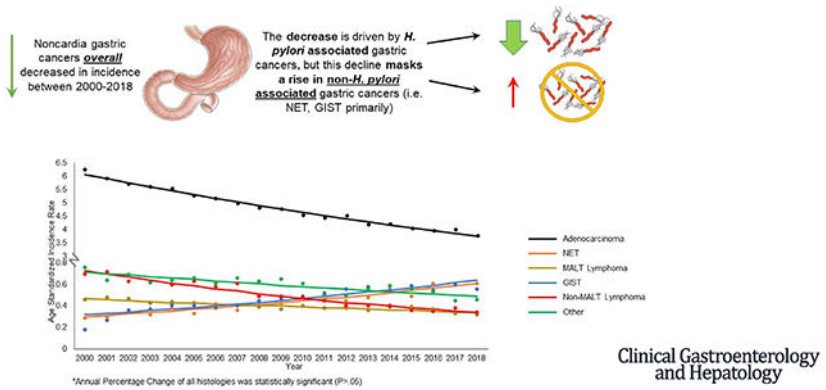
BACKGROUND & AIMS: Gastric cancer (GC) remains a leading cause of cancer and cancer-related mortality. Recent reports suggest noncardia GC is increasing in certain U.S. populations. However, whether these trends are driven by gastric adenocarcinoma (GA) or other histologies, including neuroendocrine tumors (NETs), lymphoma, or gastrointestinal stromal tumors (GISTs), is unclear.

METHODS: We analyzed the Surveillance, Epidemiology and End Results-18 cancer registry (2000–2018) to determine age-standardized incidence rates (ASIR) and annual percentage change (APC) trends for histologically-confirmed GCs, stratified by anatomic location (noncardia vs cardia), age group (20–49 vs 50+ years), sex, race, and ethnicity. Joinpoint regression modeling estimated the statistical significance of trend comparisons.

RESULTS: Of 74,520 individuals with noncardia GC, most (66.2%) were GA, with the next largest categories being non–mucosa-associated lymphoid tissue (non-MALT) lymphomas (6.9%), GIST (6.7%), NET (6.4%), and MALT lymphoma (5.6%). Noncardia GA ASIR was significantly higher than other histologies and demonstrated the greatest differences by race and ethnicity. APCs for GA and MALT, both *Helicobacter pylori*–associated cancers, declined significantly over time, which was driven primarily by trends among individuals ≥50 years-old. NET and GIST APCs significantly increased irrespective of age group, with the highest APCs observed among non-Hispanic white individuals. Cardia GC was rarer than noncardia GC and comprised primarily by GA (87.9%). Cardia GC incidence fell during the study period, which was primarily driven by decline in cardia GA.

CONCLUSIONS: GA was the most common histology. On the basis of our findings, the rise in noncardia GC among certain U.S. populations appears predominantly driven by NET and GIST, not GA. Further studies are needed to clarify underlying etiologies for these findings.

Graphical Abstract



Keywords

Gastric Neoplasm; Adenocarcinoma; Carcinoid; *Helicobacter pylori* ; Ethnic and Racial Minorities

Worldwide, gastric cancer (GC) is the fifth most commonly diagnosed cancer and the fourth most common cause of cancer-related mortality.[1] There is considerable global and

intra-country variation in GC incidence, particularly in the United States where population risks differ by race, ethnicity, sex, and age.[1,2] Although the United States is generally considered a low-intermediate risk country for GC, this still translates to more than 26,000 incident cases and more than 11,000 related deaths annually.[3] Because GC screening is not routine in the United States, only a minority of GCs are diagnosed in an early, potentially curable stage. The high proportion of late-stage diagnoses is reflected in the dismal <32% 5-year overall survival for GC. Besides stage and anatomic location, cancer histology (eg, adenocarcinoma, lymphoma, neuroendocrine tumors [NETs]) is another major determinant of prognosis and treatment approach. Furthermore, the carcinogenic pathways underlying different histologic types of GC differ. Most distinctly, *Helicobacter pylori* infection is a causal risk factor for gastric adenocarcinoma (GA) and mucosa-associated lymphoid tissue (MALT) lymphoma, but not NET and gastrointestinal stromal tumors (GIST).

Describing GC epidemiology trends without regard to histologic classifications overlooks potentially important observations that are relevant for improving resource allocation, targeted cancer attenuation efforts, and stimulation of hypothesis-driven research defining etiologies for observed differences based on demographic factors. Although racial and ethnic differences for GA and trends over time are well-described,[2,4,5] few studies have reported on non-adenocarcinoma GC epidemiology. One recent study of the Surveillance, Epidemiology and End Results (SEER) cancer registry suggested an increase in NET and GIST tumors in the stomach between 1992 and 2016, especially in non-white populations[6]; however, that study did not include other histologic types, did not analyze according to age group, and covered a time period where histologic coding for GIST changed.[7]

Thus, the primary objective of the present study was to conduct a population-based analysis of the SEER cancer registry to evaluate GC trends for the most common GC histologies.[8–11] The secondary objective was to evaluate differences in trends by histology based on race, ethnicity, sex, and age group.

Methods

SEER is a National Cancer Institute–supported program that collects cancer incidence data from population-based cancer registries. For this analysis, we used the publicly available SEER-18 registry (2000–2018).[12] This time period is preferred because it includes updated histology coding. SEER-18 covers approximately 27.8% of the U.S. population, with enrichment for non-white racial and ethnic groups who may be otherwise underrepresented.[13]

We restricted our analysis to tumors with malignant behavior where GC was the first primary cancer (Supplementary Figure 1). We stratified GCs as cardia vs noncardia location based on the International Classification of Disease for Oncology, 3rd edition (ICD-O-3). We then classified GCs on the basis of ICD-O-3 histologic codes as adenocarcinomas, NETs, GISTs, MALT lymphoma, non-MALT lymphoma, or other histologies[2,8,14]; detailed codes are provided in Supplementary Table 1.

Age at GC diagnosis, sex, race, and ethnicity were recorded for each case. Race and ethnicity for each individual were categorized as follows: Hispanic, non-Hispanic white (NHW), non-Hispanic black (NHB), non-Hispanic Asian/Pacific Islander (NHAPI), and non-Hispanic American Indian/Alaska Native (NHAIAN). SEER frequently only includes cases of NHAIAN individuals from counties with purchased/referred care delivery areas where the Indian Health Service contracts health care to an identified Indian community to limit misclassification.[15,16] We included only individuals aged 20 years or older at GC diagnosis. Individuals of unknown race or ethnicity comprised 1.1% of the total cohort and were excluded (Supplementary Figure 1).

To characterize the burden of each tumor subtype, we reported both incidence and age-standardized incidence (defined as a weighted average of the age-specific incidence per 100,000 persons, where the weights are informed by the proportion of persons in corresponding age groups for the U.S. population). The SEER program age-adjusts using the 2000 U.S. Standard population based on single years of age from the Census.[17] When possible, we also computed the annual percentage change (APC) to quantify the change in incidence over time. This measure calculates the change in incidence as a percentage of the previous year's rate in a linear fashion.[18] These measures along with 95% confidence intervals (95% CIs) were calculated using SEER*Stat version 8.3.9 and Joinpoint Regression Program version 4.8.01.[19–22] Joinpoint is a statistical software used for National Cancer Institute publications, which analyzes trends using joinpoint models. Population estimates were created using linear interpolation and extrapolation of decennial U.S. Census data. APC was considered significantly different from 0 (null value) at alpha level 0.05 (*P* value).

We performed analyses separately by anatomic location (cardia vs noncardia), histology, sex (male vs female), age group (overall and 20–49 years [referred to as early-onset] vs 50 years and older), and race or ethnicity (NHW, NHB, NHAPI, Hispanic, and NHAIAN). For the primary analysis we combined C16.8 (over-lapping) and C16.9 (NOS) with noncardia GC (C16.1–C16.6) because of similarities in observed adenocarcinoma trends for these anatomic locations and to allow for increased sample size; herein, this group is referred to as noncardia.[2,6] We also conducted a sensitivity analysis analyzing only C16.1–C16.6 as noncardia GC; there were insufficient case counts to analyze C16.8 and C16.9 as a separate subgroup and make meaningful conclusions.

Results

Overall Gastric Cancers

Between 2000 and 2018, 83,874 cases of primary noncardia GC and 28,199 cardia GC were registered in SEER-18 (Figure 1A and B). Most noncardia (n = 55,563; 66.2%) and cardia (n = 24,792; 87.9%) were histologically confirmed GA. Among the remaining noncardia GCs, 5786 (6.9%) were non-MALT lymphoma, 5601 (6.7%) GIST, 5345 (6.4%) NET, and 4688 (5.6%) MALT lymphoma (Figure 1A). Fewer than 9% of all primary noncardia GCs were histologies other than those listed herein. For cardia GCs, lymphomas (both MALT and non-MALT), GISTs, and NETs comprised less than 5% of diagnoses, and 7% (n = 2027) were other histologies (Figure 1B).

Noncardia GC

The overall age-standardized incidence rate (ASIR) per 100,000 persons for GA was 4.73 (95% CI, 4.69–4.77; Table 1). In contrast, the overall ASIR was less than 1.0 for all non-GA histologies (Table 1). Most noncardia GCs were diagnosed in men (53.7%), adults aged 50 and older (86.4%), and NHW individuals (45.4%) (Figure 1A). We repeated the initial demographic analysis with site location limited to confirmed noncardia anatomic location (C16.1–C16.6) and removing overlapping (C16.8) and not otherwise specified (NOS, C16.9) anatomic sites. Overall patterns were similar (Supplementary Table 2).

Trends Over Time of Noncardia GC Incidence

Although noncardia GC overall declined significantly between the beginning and end of the study interval from 2000–2002 to 2016–2018 (Table 2), there were significant differences when analyzing trends according to age and GC histology. ASIRs for GA, MALT, and non-MALT lymphomas significantly decreased between 2000–2002 vs 2016–2018 (Table 2 and Figure 2), whereas the ASIRs for NET and GIST significantly increased (Table 2 and Figure 2). Additional time trend evaluations by age, sex, race, and ethnicity for each of the histologies are presented in Supplementary Table 3, although small case counts in some subgroups were limiting.

Where possible, we conducted additional analyses to determine APCs based on histology as well as race, ethnicity, and age group. Overall, GC incidence significantly declined among individuals aged 50 years and older (APC, −2.23; $P < .05$; Supplementary Table 4) but significantly increased among those younger than age 50 (APC, +0.53; $P < .05$). GA and MALT lymphoma incidence declined significantly in the age group >50 years (APC, −3.09 and −2.03, respectively; $P < .05$; Supplementary Table 4). Similarly, the incidence of early-onset GA declined significantly among NHAPI, NHB, and NHW individuals (APC, −2.95, −1.93, and −1.19, respectively; all $P < .05$). Although noncardia GA incidence was highest among NHAPI compared with other racial and ethnic groups, the gap narrowed over the study period; all non-white racial and ethnic groups had higher GA ASIR compared with NHW individuals (Figure 3A). In contrast, NET incidence increased in both age groups over time (APC, 5.54 for 20- to 49-year-olds, 3.57 for ≥50; all $P < .05$). Of note, ICD coding for GISTs changed in 2000,[7] which was reflected in the very high APC (49.8) for 2000–2002. Nevertheless, the APC steadily increased in each consecutive observed interval (APC, 2.1 for 2002–2007, 6.5 for 2007–2012; $P < .05$) with a plateau after 2012 (APC, 0.2 2012–2018; $P > .05$). The observed patterns were generally consistent on the basis of sex, race, and ethnicity, although the magnitude of change and statistical significance varied (Figures 3 and 4).

Cardia GC

We repeated all analyses for cardia GC (Table 2 and Supplementary Table 5). GA was the most common histology, comprising 87.9% of all cardia GCs (Figure 1B).

Irrespective of histology, all cardia GC ASIRs were significantly and markedly lower than noncardia GC ASIRs (Supplementary Table 5). All cardia GCs were more common in men than women and in individuals age ≥50 vs 20–49 years. NHW (ASIR, 2.33; 95% CI, 2.30–

2.36) and NHAIAN individuals (ASIR, 2.02; 95% CI, 1.70–2.38) had the highest cardia GA ASIRs. In contrast, other histologic subtypes were extremely rare.

Trends Over Time for Cardia GC

Overall, cardia GC incidence decreased from the beginning (ASIR 2000–2002, 2.50; 95% CI, 2.42–2.57; Table 2) to the end (ASIR 2016–2018, 2.21; 95% CI, 2.15–2.27) of the study period, driven mostly by the small decline in cardia GA (ASIR 2000–2002, 2.18; 95% CI, 2.11–2.26 to ASIR 2016–2018, 1.93; 95% CI, 1.87–1.99) and non-MALT lymphoma (ASIR 2000–2002, 0.04; 95% CI, 0.03–0.05 to ASIR 2016–2018, 0.01; 95% CI, 0.01–0.02). The incidence declined significantly in those 50 and older but not in those ages 20–49 (Supplementary Table 4). There were no significant changes in incidence between the beginning and end of the study period for GISTs, NETs, and MALT lymphoma.

Similarly, the APCs for cardia GC stratified by individuals' age, race, and ethnicity were calculated. Small counts limited most analyses, but among those 50 and older, NHW, NHB, and NHAPI individuals had significant decrease in total cardia GC APC during the study period (Supplementary Table 4). Hispanic individuals aged 20–49 years demonstrated a significant increase in cardia GC overall over time (APC, 2.48), although small counts preclude further analysis by histology.

Discussion

In this contemporary U.S. population-based cancer registry analysis, between 2000 and 2018 the incidence of noncardia GA and MALT lymphoma (both *H pylori*–associated cancers) declined significantly, as did non-MALT lymphoma; in contrast, rates of noncardia NET have steadily increased. Although the incidence of noncardia GIST also demonstrated a steady increase after a coding change in 2000, GIST rates have recently plateaued. Notably, in the younger age group, all histologies either increased (GIST, NET) or remained unchanged (GA, MALT lymphoma); only non-MALT lymphoma rates declined over time. These observed patterns were generally consistent irrespective of race, ethnicity, and sex, with some differences in the magnitude of change. These findings have clinical, epidemiologic, and scientific implications because of the differences between these histologies with respect to treatment, tumor behavior and prognosis, risk factor profiles, and pathogenesis. By presenting a detailed analysis of trends based on primary histology, we significantly extend findings from previous analyses reporting a rise in noncardia GC among certain U.S. populations[4,5] and add additional knowledge about cardia GC histology trends.

The absolute burden of noncardia GA, which comprise the majority of primary GCs, is greater than 10-fold that of NET, GIST, or lymphomas. Non-white racial and ethnic groups, in particular NHAPI individuals, shoulder a disproportionate burden of noncardia GA compared with NHW individuals. To this end, despite mostly favorable trends of noncardia GA over time, we observed a differential rate of decline across several subgroups. The decreasing incidence of noncardia GA over time has in large part been attributed to the lower prevalence of *H pylori* infection with each generation, changes in diet, and decreased tobacco use.[23–25] The decline in *H pylori* prevalence also underlies the observed decline in MALT lymphoma. To our knowledge, no prior studies report trends for MALT lymphoma,

a cancer that is unique in the fact that *H pylori* eradication is often curative and thus considered first-line management. Yet, despite the declining prevalence of *H pylori* in the United States and clear birth cohort effect, with younger individuals having lower *H pylori* prevalence than older individuals, there is a discrepancy in the rate of expected decline in noncardia GA and MALT lymphoma for the younger age group compared with the older age group. This lack of decline in the younger age group suggests non–*H pylori*–associated factors are involved, requiring further research to clarify the role of and interaction between other environmental, micro-biome, and (epi)genomic factors. The number of cases were small, which may limit strong conclusions. Our findings for noncardia GA are similar to a previous study suggesting a rise in noncardia GA in younger groups using North American Association of Central Cancer Registries data.[24] However, that study used different age groupings, which might explain why our findings did not show statistically significant rises.

The rise in gastric NET and GIST is an important finding, because staging, treatment, and prognosis are distinct from GA and other histologies. Detection bias related to increased use of endoscopy might explain part of this increase[25] but is unlikely to account for the total magnitude of observed increase because of the decline in other histologies including non-MALT lymphoma. Although ICD coding for GIST changed in 2000,[7] as reflected by the outlier APC (+49.8), the ongoing rise after the change had time to take effect suggests this represents a true increase. Although changes in terminology and definitions of NET[26] might be relevant to a small extent, the increase likely also represents a true increase. Autoimmune gastritis, which is present in approximately 0.5%–2% of the population and appears to be increasing, is associated with the most common subtype of gastric NET, type 1.[27,28] The widespread use of proton pump inhibitors starting in the early 2000s may further contribute to the observed increase in NET diagnoses.[29] Reassuringly, the prognosis of type 1 gastric NETs is significantly better than GA.[30] Autoimmune gastritis is also associated with increased risk of noncardia GA, and continued vigilance is necessary for providers caring for these patients.[31,32]

Our findings are consistent with and extend knowledge regarding the alarming trend in the rise of early-onset cancer in other digestive organs, including colorectum[11] and pancreas,[10] which is driven to some extent by non-adenocarcinoma histologies. Notably, a recent analysis of cancer registry data demonstrated that up to 20% of early-onset colorectal and up to 34% of early-onset rectal only cancers were histologic NET; like our study, these trends have important prognostic implications.[9] Another cancer registry-based analysis of gastroenteropancreatic NET reported a consistent rise in these tumors starting from the early 1980s through 2012.[8] A recent study by Anderson et al[5] suggested that although overall rates of noncardia GC are declining, rates are rising for those aged <50 years, particularly Hispanic white individuals, but did not specify detailed histology trends. On the basis of our study, we suspect these findings are primarily driven by an increase in NET (and possibly GIST), coupled with a slower (or even lack of) decline in GA. This appears to be the case particularly in younger age groups, especially younger Hispanic individuals. In support of this hypothesis, we demonstrated a steady increase in NET over time, with a greater increase in the 20- to 49-year-old group vs ≥50-year-old group, and an increase in GIST through 2012. Although noncardia GA and MALT lymphoma ASIRs declined overall, these respective ASIRs did not decline among 20-to 49-year-olds between 2000 and 2018.

We noted a small decline in cardia GC, but this was largely driven by the small decline in age group>50 years, because there was a slight increase in cardia GC among the age group 20–49 years. These findings are consistent with a prior nationwide study from 1999 to 2013, which analyzed cardia GC overall, but irrespective of histology.[33]

Our study has important strengths and limitations. We used a high-quality large, nationally representative registry and restricted the analysis to histologically confirmed primary gastric malignancies. This study specifically analyzes GC trends by detailed histology, with additional stratification by anatomic location, age, sex, race, and ethnicity. We used both ASIRs and APCs to describe trends over time and accounted for ICD histology code changes for GIST. One limitation of this study is the lack of access to certain individual-level data, such as tobacco use, *H pylori* infection and eradication treatment status, and concurrent diagnoses such as autoimmune gastritis. On the basis of the observational design, we are unable to comment on mechanisms contributing to the changing incidence. However, these trends are important for informing future research. The small sample size for some strata, particularly younger age groups, rarer histologies, and less populous racial and ethnic groups (eg, NHAIAN) limited our ability to provide robust interpretations of some trends.

In conclusion, by comprehensively evaluating changes in GC by histology over time, this study suggests important nuances in trends by histology and detailed demographic factors. The histology of GC has important implications on prognosis and treatment. Although the overall decrease in GA and gastric lymphoma is a positive development, further studies are needed to understand why some histologies have slower rates of decline and, of more concern, why some have increasing rates over time and in certain populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding

Supported by American Gastroenterological Association Research Scholar Award and Veterans Affairs Career Development Award (ICX002027A) (SCS); the National Institutes of Health (U01CA265729, U24CA272897) (CH), and P30CA013696) (CH and SDR). This work was also supported by the Specialized Cancer Center Support Grant to the University of California San Diego Moores Cancer Center (CA023100-29). The content is solely the responsibility of the listed authors and does not necessarily represent the official views of the funding agencies listed.

Abbreviations:

APC	annual percentage change
ASIR	age-standardized incidence rate
CI	confidence interval
GA	gastric adenocarcinoma
GC	gastric cancer
GIST	gastrointestinal stromal tumor

ICD-O-3	International Classification of Disease for Oncology, Third Edition
MALT	mucosa-associated lymphoid tissue
NET	neuroendocrine tumor
NHAIAN	non-Hispanic American Indian/Alaska Native
NHAPI	non-Hispanic Asian/Pacific Islander
NHB	non-Hispanic black
NHW	non-Hispanic white
SEER	Surveillance, Epidemiology and End Results

References

1. Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021;71:209–249. [PubMed: 33538338]
2. Shah SC, McKinley M, Gupta S, et al. Population-based analysis of differences in gastric cancer incidence among races and ethnicities in individuals age 50 years and older. Gastroenterology 2020;159:1705–1714.e1702. [PubMed: 32771406]
3. Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2021. CA Cancer J Clin 2021;71:7–33. [PubMed: 33433946]
4. Anderson WF, Camargo MC, Fraumeni JF Jr, et al. Age-specific trends in incidence of noncardia gastric cancer in US adults. JAMA 2010;303:1723–1728. [PubMed: 20442388]
5. Anderson WF, Rabkin CS, Turner N, et al. The changing face of noncardia gastric cancer incidence among US non-Hispanic whites. J Natl Cancer Inst 2018;110:608–615. [PubMed: 29361173]
6. Zhu X, Pigazzi A, Zell J, et al. Changing disparity of gastric cancer incidence by histological types in US race-specific populations. Cancer Control 2020;27:1073274820977152.
7. Ma GL, Murphy JD, Martinez ME, et al. Epidemiology of gastrointestinal stromal tumors in the era of histology codes: results of a population-based study. Cancer Epidemiol Biomarkers Prev 2015;24:298–302. [PubMed: 25277795]
8. Lee MR, Harris C, Baeg KJ, et al. Incidence trends of gastroenteropancreatic neuroendocrine tumors in the United States. Clin Gastroenterol Hepatol 2019;17:2212–2217.e2211. [PubMed: 30580091]
9. Montminy EM, Zhou M, Maniscalco L, et al. Contributions of adenocarcinoma and carcinoid tumors to early-onset colorectal cancer incidence rates in the United States. Ann Intern Med 2021;174:157–166. [PubMed: 33315473]
10. Ramai D, Lanke G, Lai J, et al. Early- and late-onset pancreatic adenocarcinoma: a population-based comparative study. Pancreatology 2021;21:124–129. [PubMed: 33334692]
11. Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal cancer incidence patterns in the United States, 1974–2013. JNCI 2017;109.
12. SEER*Explorer: an interactive website for SEER cancer statistics. Surveillance Research Program, National Cancer Institute. Available at: https://seer.cancer.gov/explorer/. Accessed 2021.
13. SEER*Stat Databases: November 2018 submission. National Cancer Institute. Available at: https://seer.cancer.gov/data-software/documentation/seerstat/nov2018/. Accessed March 20, 2021.
14. Morton LM, Wang SS, Devesa SS, et al. Lymphoma incidence patterns by WHO subtype in the United States, 1992–2001. Blood 2006;107:265–276. [PubMed: 16150940]
15. Division of Cancer Prevention and Control CfDCaP. U.S. cancer statistics American Indian and Alaska Native incidence data. United States cancer statistics Web site. https://www.cdc.gov/cancer/uscs/about/tools/AIAN-incidence-analytic-db.htm. Published 2022. Updated June 6, 2022. Accessed September 12, 2022.

16. National Cancer Institute S, Epidemiology and End Results Program. Static county attributes. Available at: https://seer.cancer.gov/seerstat/variables/countyattribs/static.html#chsda. Accessed September 12, 2022.
17. National Cancer Institute S, Epidemiology and End Results Program. Standard populations (millions) for age-adjustment. Available at: https://seer.cancer.gov/stdpopulations/. Accessed September 12, 2022.
18. Annual percent change (APC) and confidence interval. Available at: https://surveillance.cancer.gov/help/joinpoint/setting-parameters/method-and-parameters-tab/apc-aapc-tau-confidence-intervals/estimate-average-percent-change-apc-and-confidence-interval. Accessed October 3, 2022.
19. Tiwari RC, Zou Z. Efficient interval estimation for age-adjusted cancer rates. Stat Methods Med Res 2006;15:547–569. [PubMed: 17260923]
20. JoinPoint trend analysis software. Surveillance Research Program, National Cancer Institute. Available at: https://surveillance.cancer.gov/joinpoint/. Accessed May 1, 2021.
21. Branch SMaA. Joinpoint regression program, version 4.8.01. Surveillance Research Program, National Cancer Institute. Accessed May 1, 2021.
22. Kim HJ, Fay MP, Feuer EJ, et al. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med 2000; 19:335–351. [PubMed: 10649300]
23. Grad YH, Lipsitch M, Aiello AE. Secular trends in Helicobacter pylori seroprevalence in adults in the United States: evidence for sustained race/ethnic disparities. Am J Epidemiol 2011; 175:54–59. [PubMed: 22085628]
24. Islami F, DeSantis CE, Jemal A. Incidence trends of esophageal and gastric cancer subtypes by race, ethnicity, and age in the United States, 1997–2014. Clin Gastroenterol Hepatol 2019;17:429–439. [PubMed: 29902641]
25. Peery AF, Dellon ES, Lund J, et al. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology 2012;143:1179–1187.e1173. [PubMed: 22885331]
26. Rindi G, Klimstra DS, Abedi-Ardekani B, et al. A common classification framework for neuroendocrine neoplasms: an International Agency for Research on Cancer (IARC) and World Health Organization (WHO) expert consensus proposal. Modern Pathology 2018;31:1770–1786. [PubMed: 30140036]
27. Lenti MV, Rugge M, Lahner E, et al. Autoimmune gastritis. Nat Rev Dis Primers 2020;6:56. [PubMed: 32647173]
28. Mahmud N, Stashek K, Katona BW, et al. The incidence of neoplasia in patients with autoimmune metaplastic atrophic gastritis: a renewed call for surveillance. Ann Gastroenterol 2019;32:67–72. [PubMed: 30598594]
29. McCarthy DM. Proton pump inhibitor use, hypergastrinemia, and gastric carcinoids: what is the relationship? Int J Mol Sci 2020;21.
30. Chi W, Warner RRP, Chan DL, et al. Long-term outcomes of gastroenteropancreatic neuroendocrine tumors. Pancreas 2018; 47:321–325. [PubMed: 29401168]
31. Rustgi SD, Bijlani P, Shah SC. Autoimmune gastritis, with or without pernicious anemia: epidemiology, risk factors, and clinical management. Therap Adv Gastroenterol 2021;14: 17562848211038771.
32. Shah SC, Piazuelo MB, Kuipers EJ, et al. AGA clinical practice update on the diagnosis and management of atrophic gastritis: expert review. Gastroenterology 2021;161:1325–1332. e1327. [PubMed: 34454714]
33. Wang Z, Graham DY, Khan A, et al. Incidence of gastric cancer in the USA during 1999 to 2013: a 50-state analysis. Int J Epidemiol 2018;47:966–975. [PubMed: 29672681]

What You Need to Know

Background

Previous studies suggest a rise in gastric cancer incidence in certain subgroups by age and race and ethnicity, but these studies have not been stratified by cancer histology.

Findings

In this study, we found that the incidence of malignant neuroendocrine and gastrointestinal stromal tumors increased between 2000 and 2018, whereas the incidence of noncardia gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma, both *Helicobacter pylori*–associated cancers, decreased over this time.

Implications for patient care

This comprehensive study suggests important nuances in gastric cancer trends by histology and detailed demographic factors. Furthermore, these trends have relevant prognostic and therapeutic implications. Although the overall decrease in noncardia gastric adenocarcinoma and lymphoma is a positive development, further studies are needed to understand why the incidence rates of some histologies are increasing over time and in certain populations.

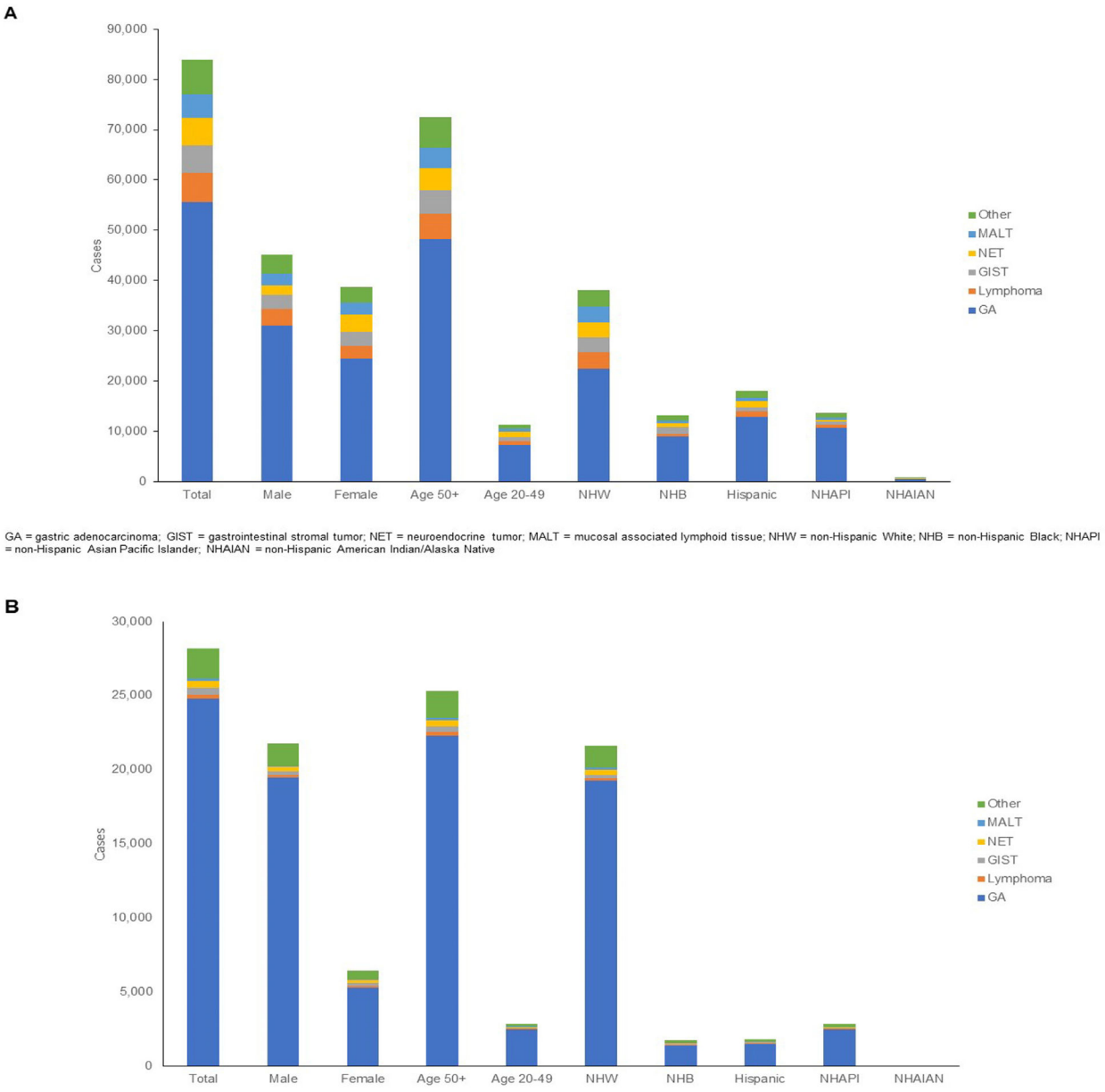


Figure 1.

(*A* and *B*) Noncardia and cardia gastric cancer cases by histology and demographic characteristics, SEER-18 (2000–2018). This figure demonstrates gastric cancer incidence by histology and demographic characteristics.

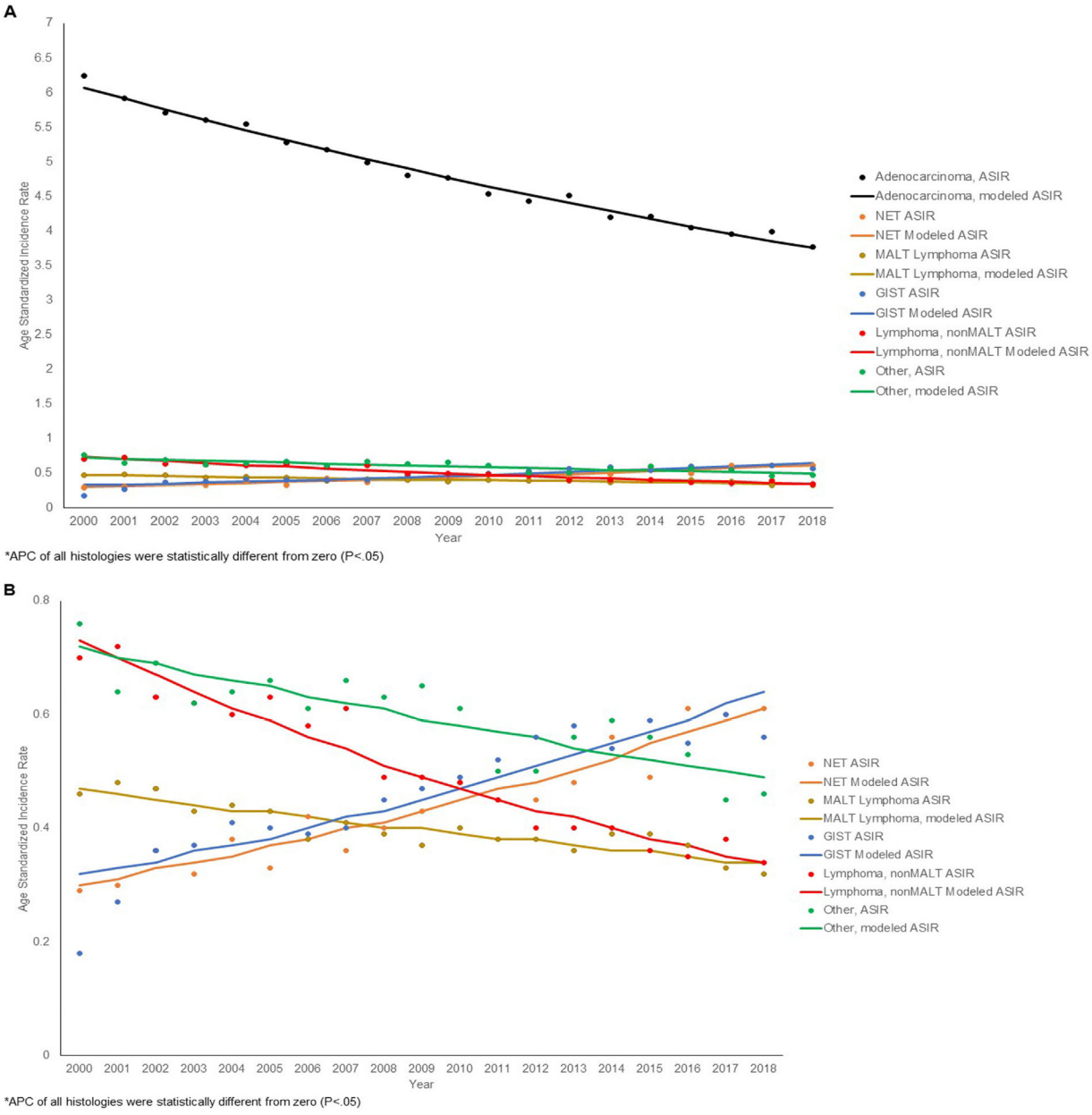


Figure 2.

(*A*) Noncardia gastric cancer time trends by histology, SEER-18 (2000–2018). (*B*) Noncardia gastric cancer time trends for non-adenocarcinoma histologies, SEER-18 (2000–2018). This figure illustrates the ASIRs and modeled ASIRs for noncardia gastric cancer histologies, for combined races, ethnicities, and sexes, among individuals aged 20 years or older. The annual percent change (APC) represents the change in incidence as a percentage of the previous year's rate in a linear fashion. For GA and MALT and non-MALT lymphomas, ASIRs and APCs decreased significantly over the time period, whereas for NET and GIST, ASIRs and APCs increased significantly over time. (*B*) Illustrates the same information, but GA is removed to allow re-scaling of the y-axis and better visualization of the time trends for the rarer non-GA histologies.

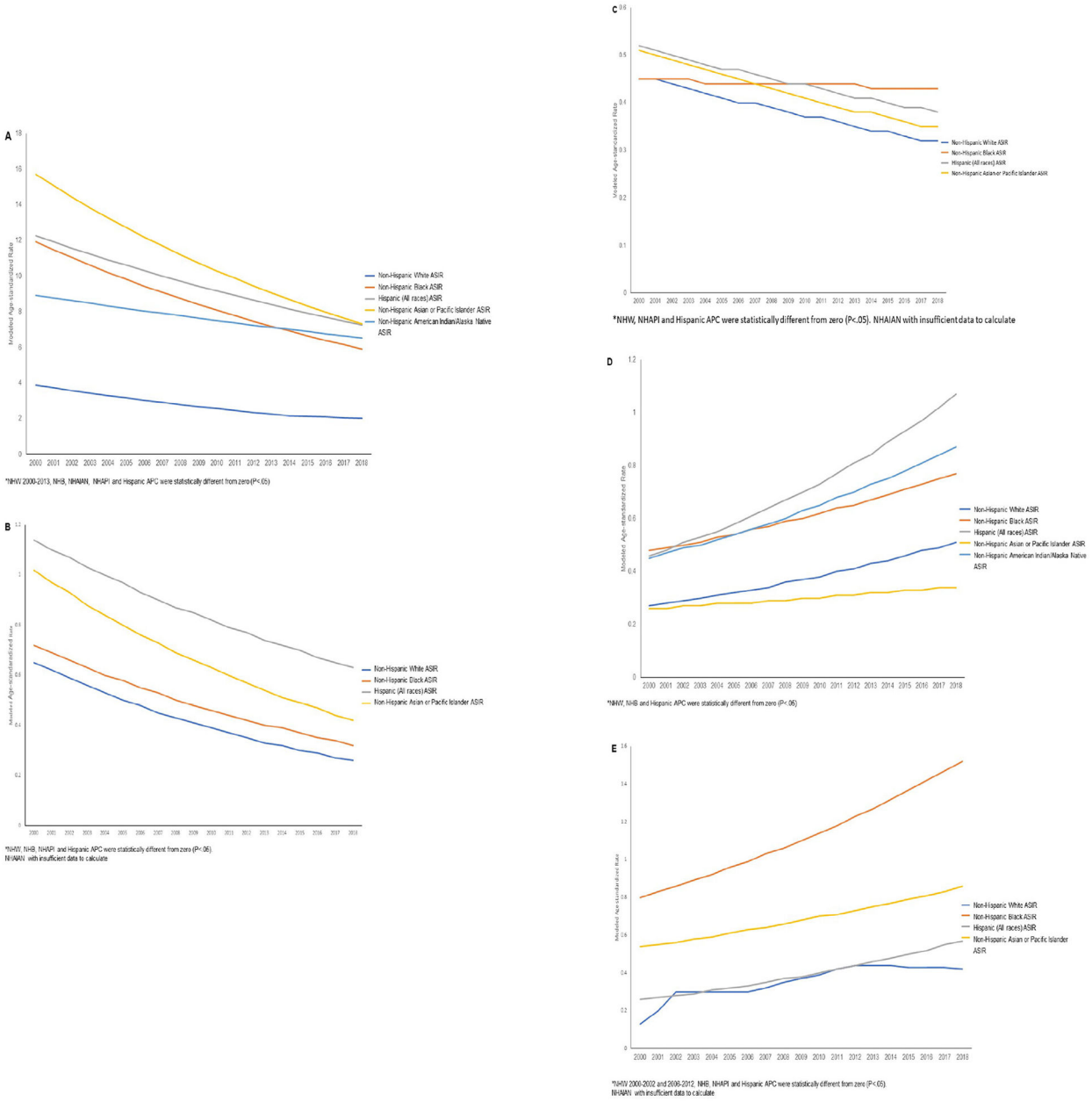


Figure 3.

(*A–E*) Modeled noncardia gastric cancer age-standardized incidence rate (ASIR) trends by race and ethnicity for each histology type, ages 20 and older, SEER-18 (2000–2018): (*A*) adenocarcinoma, (*B*) non-MALT lymphoma, (*C*) MALT lymphoma, (*D*) NETs, and (*E*) GISTs. This figure illustrates the modeled ASIRs for each histology stratified by race and ethnicity, with each race and ethnicity represented by a different *solid-colored line* (men and women combined). *Asterisk* is used to denote groups with statistically significant APC during the time period.

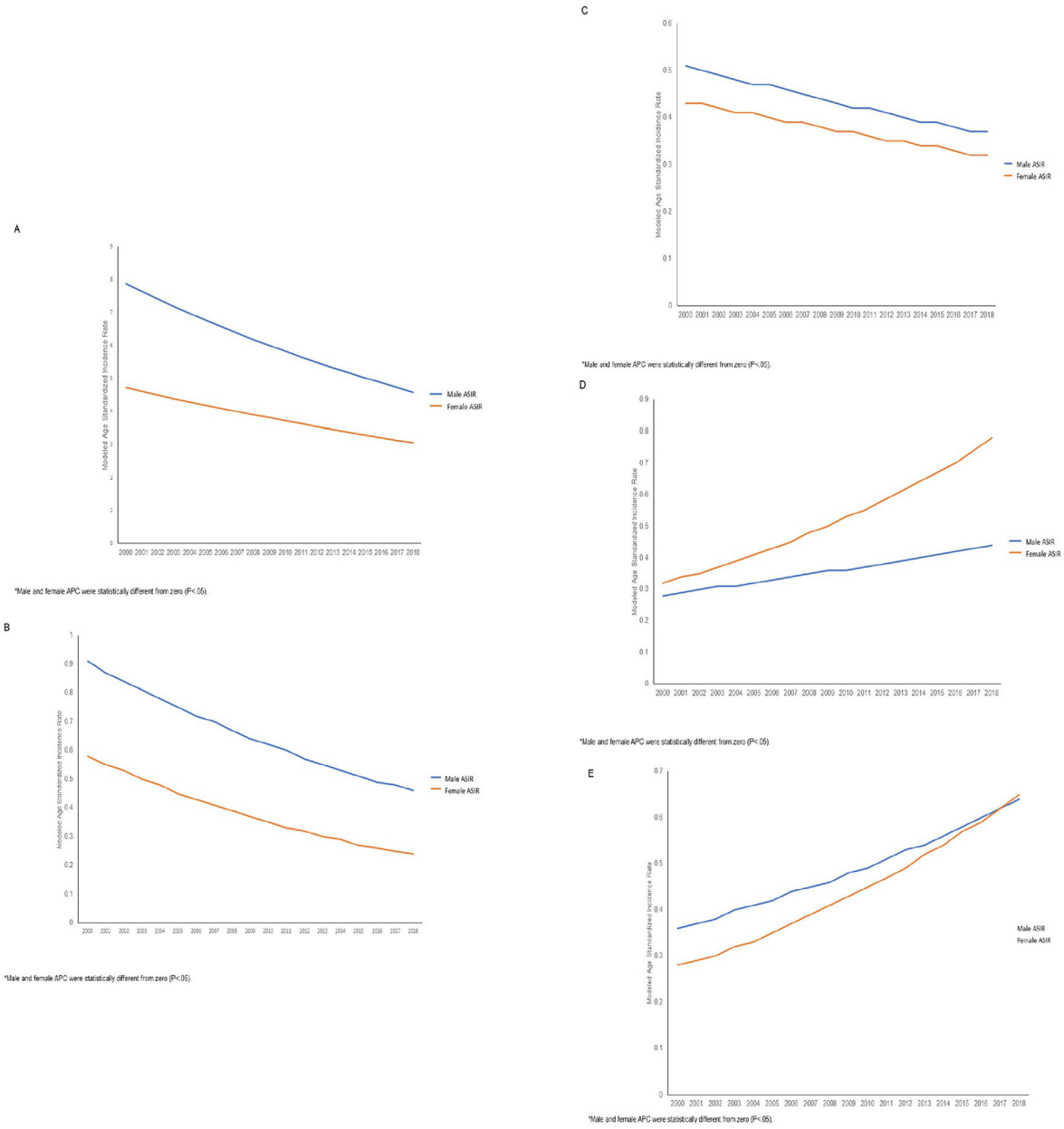


Figure 4.

(*A*–*E*) Modeled noncardia gastric cancer age-standardized incidence rate (ASIR) trends by sex for each histology type, ages 20 and older, SEER-18 (2000–2018): (*A*) adenocarcinoma, (*B*) non-MALT lymphoma, (*C*) MALT lymphoma, (*D*) NETs, and (*E*) GISTs. This figure illustrates the modeled ASIRs for each histology for men versus women. For all histologies, except for NET, men had significantly higher ASIRs compared with women. The largest differences in ASIR between men and women were observed for GA and MALT lymphoma and NET. The ASIR for NET noticeably diverged for men and women, with women demonstrating a sharper increase, whereas the ASIR noticeably converged for GIST.

Table 1.

Age-Standardized Incidence Rates by Histology and Demographic Characteristics, Noncardia Gastric Cancer (C16.1–16.9)

	Total (n = 83,874) ASIR [95% CI]	Adenocarcinoma (n = 55,563) ASIR [95% CI]	Lymphoma (excluding MALT) (n = 5786) ASIR [95% CI]	GIST (5601) ASIR [95% CI]	NET (n = 5345) ASIR [95% CI]	MALT lymphoma (n = 4688) ASIR [95% CI]	Other (n = 6891) ASIR [95% CI]
Sex (combined)	7.12 [7.07–7.17]	4.73 [4.69–4.77]	0.49 [0.48–0.51]	0.47 [0.46–0.48]	0.45 [0.44–0.46]	0.39 [0.38–0.40]	0.59 [0.57–0.60]
Male	8.58 [8.50–8.67]	5.94 [5.87–6.01]	0.64 [0.62–0.66]	0.49 [0.47–0.51]	0.36 [0.35–0.38]	0.43 [0.41–0.45]	0.72 [0.70–0.75]
Female	5.97 [5.91–6.03]	3.78 [3.73–3.83]	0.37 [0.36–0.39]	0.45 [0.43–0.46]	0.53 [0.51–0.55]	0.37 [0.35–0.38]	0.47 [0.46–0.49]
Age (*y*)							
50+	15.7 [15.54–15.77]	10.48 [10.38–10.57]	1.09 [1.06–1.12]	0.99 [0.97,1.02]	0.90 [0.87–0.92]	0.86 [0.84–0.89]	1.34 [1.30–1.37]
20–49	1.72 [1.69–1.75]	1.09 [1.07–1.12]	0.12 [0.11–0.13]	0.13 [0.13–0.14]	0.16 [0.16–0.17]	0.10 [0.09–0.10]	0.11 [0.11–0.12]
Race and ethnicity							
Non-Hispanic white	4.65 [4.61–4.70]	2.73 [2.69–2.77]	0.42 [0.40–0.43]	0.36 [0.34–0.37]	0.38 [0.37–0.39]	0.38 [0.37–0.39]	0.39 [0.38–0.41]
Non-Hispanic black	12.0 [11.84–12.26]	8.32 [8.14–8.50]	0.47 [0.43–0.52]	1.14 [1.08–1.21]	0.61 [0.57–0.66]	0.43 [0.39–0.47]	1.07 [1.01–1.14]
Hispanic	12.60 [12.41–12.80	9.14 [8.98–9.31]	0.81 [0.76–0.86]	0.42 [0.38–0.45]	0.76 [0.72–0.81]	0.43 [0.40–0.47]	1.04 [0.98–1.10]
Non-Hispanic Asian and Pacific Islander	13.42 [13.19–13.64]	10.36 [10.16–10.56]	0.63 [0.58–0.68]	0.69 [0.64–0.74]	0.29 [0.26–0.32]	0.40 [0.36–0.44]	1.05 [0.98–1.11]
Non-Hispanic American Indian/ Alaska Native	9.93 [9.21–10.70]	7.40 [6.77–8.07]	0.40 [0.27–0.58]	0.22 [0.12–0.35]	0.57 [0.41–0.77]	0.36 [0.23–0.52]	0.99 [0.76–1.25]

ASIR, age-standardized incidence rate, per 100,000; GIST, gastrointestinal stromal tumor; MALT, mucosal-associated lymphoid tumor; NET, neuroendocrine tumor.

Table 2.

Comparison of Noncardia and Cardia Gastric Cancer Incidence Rates in the First (2000–2002) and Last (2016–2018) Study Interval by Histology

	2000–2002		2016–2018	
	N (%)	**ASIR [95% CI]**	**N (%)**	**ASIR [95% CI]**
Noncardia				
Total	13,241	8.38 [8.24–8.53]	13,572	6.24 [6.14–6.35]
Adenocarcinoma	9377 (70.8)	5.95 [5.83–6.07]	8454 (62.3)	3.90 [3.81–3.98]
Lymphoma, excluding MALT	1077 (8.1)	0.68 [0.64–0.72]	773 (5.7)	0.36 [0.33–0.38]
GIST	436 (3.3)	0.27 [0.26–0.30]	1252 (9.2)	0.57 [0.54–0.60]
NET	510 (3.9)	0.32 [0.29–0.35]	1311 (9.7)	0.61 [0.57–0.64]
MALT lymphoma	745 (5.6)	0.47 [0.44–0.50]	746 (5.5)	0.34 [0.31,0.36]
Other	1096 (8.3)	0.70 [0.66–0.74]	1036 (7.6)	0.48 [0.45–0.51]
Cardia				
Total	3962	2.49 [2.42–2.57]	4944	2.21 [2.15–2.27]
Adenocarcinoma	3468 (87.5)	2.18 [2.11–2.26]	4322 (87.4)	1.93 [1.87–1.99]
Lymphoma (excluding MALT)	57 (1.4)	0.04 [0.03–0.05]	30 (0.6)	0.01 [0.01–0.02]
GIST	48 (1.2)	0.03 [0.02–0.04]	102 (2.1)	0.05 [0.04–0.06]
NET	44 (1.1)	0.03 [0.02–0.04]	118 (2.4)	0.05 [0.04–0.06]
MALT lymphoma	28 (0.7)	0.02 [0.01–0.03]	28 (0.6)	0.01 [0.01–0.02]
Other	317 (8.0)	0.20 [0.18–0.22]	344 (7.0)	0.15 [0.14–0.17]

ASIR, age-standardized incidence rate, per 100,000; GIST, gastrointestinal stromal tumor; MALT, mucosal-associated lymphoid tumor; N/A, not available; statistics not shown for n <11; NET, neuroendocrine tumor.