

SHORT COMMUNICATION

Case count patterns and survival of
gastrointestinal neuroendocrine tumors in
a large healthcare network: A retrospective
analysis (2012–2024)Fan Cao^{1*}, Michael Tseng², Jiling Chou³, and Priyanka Kanth²¹Georgetown University Medical Center, Washington, D.C., United States of America²Department of Gastroenterology, MedStar University of Georgetown Hospital, Washington, D.C., United States of America³MedStar Research Health Institute, Columbia, Maryland, United States of America

Abstract

Introduction: Gastrointestinal neuroendocrine tumors (GI NETs) represent 1–2% of malignancies arising in the digestive tract, and the incidence has increased in recent years due to greater use of diagnostic tools. However, institution-level patterns in GI NET case counts and survival remain undercharacterized.

Objective: This study aims to evaluate demographic and site-specific case count patterns and survival outcomes across a large multi-hospital healthcare system.

Methods: We conducted a retrospective cohort study of 1,813 patients diagnosed with GI NETs across MedStar Health from November 2012 to September 2024. Cases were identified using the International Classification of Diseases (ICD) codes. Tumors were categorized as benign, malignant, or mixed coding history based on ICD patterns. Case counts were stratified by sex, race, age, and tumor site. Survival analyses used unadjusted Kaplan–Meier curves and log-rank tests to compare tumor categories and six anatomical sites (appendix, large intestine, pancreas, rectum, small intestine, stomach).

Results: GI NET case counts increased over the study period, with higher counts observed among women and individuals aged 51–74 years. Most diagnoses occurred in White (45.8%) and Black (40.7%) patients. Small-intestinal and rectal NETs were the most frequently identified. Survival patterns showed that female sex, White race, younger age, and benign tumors were associated with the most favorable outcomes. Among all anatomical sites, rectal NETs demonstrated the highest long-term survival.

Conclusion: This large institutional study highlights meaningful demographic and site-specific variation in GI NET case counts and descriptive survival patterns. These findings underscore the need for future research addressing access-related and sociodemographic contributors to GI NET outcomes.

Keywords: Gastrointestinal neuroendocrine tumors; Survival outcomes; Case patterns; Retrospective analysis

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1. Introduction

Neuroendocrine tumors (NETs) are a heterogeneous group of neoplasms that can arise in nearly any organ system.¹ These tumors may secrete peptide hormones and produce a wide range of symptoms depending on the specific hormone involved.² Neuroendocrine cells have both endocrine and paracrine functions, releasing hormones that act on distant targets and exerting local regulatory effects, such as in the acid–gastrin–histamine axis.³ Reflecting this distribution, NETs can originate in endocrine organs, neural structures, or organs with scattered neuroendocrine cells.³

First described by Oberndorfer in 1907 as “carcinoid” tumors, NETs were initially recognized for their indolent growth, limited invasiveness, and relatively favorable prognosis.⁴ NETs may present with non-specific symptoms or remain clinically silent.⁵ The gastrointestinal (GI) tract contains the highest concentration of neuroendocrine cells, making it, along with the pulmonary system, a common site for NET development.⁶ Although NETs comprise only approximately 2% of all malignant GI tumors,⁷ their incidence has increased in recent decades, as demonstrated by large national registry studies.^{8,9}

We hypothesized that hospital-based studies reveal local epidemiologic patterns and differences in tumor case counts over time and demographic distributions that are not captured in national datasets, thereby providing institution-specific insights that can inform patient care.

2. Methods

This retrospective study included patients diagnosed with GI and lung NETs between November 2012 and September 2024 across a large health system comprising 10 hospitals in Maryland and Washington, D.C. Lung NETs were included only to describe the overall cohort; all case-count and survival analyses were restricted to GI NETs to avoid mixing biologically distinct disease groups (Figure A1).

2.1. Tumor classification

Tumors were categorized into benign, malignant, and mixed coding-history groups. Because the study period spanned the United States transition from the International Classification of Diseases (ICD)-9 to ICD-10 in 2015, both ICD-9 and ICD-10 codes were used for case identification. Due to reliance on diagnostic codes alone, we were unable to distinguish well-differentiated NET grades (G1–G3) from poorly differentiated neuroendocrine carcinomas. Therefore, ICD-based categories (benign, benign-to-malignant transition, malignant) served as a proxy for malignant potential, reflecting coding patterns rather than World Health Organization (WHO)/European NET Society (ENETS) pathology-based terminology.

Malignant tumors were identified using ICD-9 codes 209.x (e.g., 209, 209.01–209.17, 209.21, and 209.23) and ICD-10 codes C7A.x (e.g., C7A.01–C7A.029, C7A.090, and C7A.092), along with diagnosis descriptions containing terms, such as “malignant” or “neuroendocrine carcinoma.” Benign tumors were identified using ICD-9 codes 209.x (209.4–209.63) and ICD-10 codes D3A.x (D3A.01–D3A.029, D3A.09, D3A.092). Mixed histology was defined as patients who initially carried benign codes but later had malignant codes during follow-up. If both benign and malignant codes appeared at the time of diagnosis, patients were classified as malignant (Tables S1 and S2).

2.2. Case count analyses

GI NET case counts were stratified by sex, race, and age group. Because the case counts in 2012 and 2024 were partially captured, counts from those years were interpreted with caution.

2.3. Survival analyses

Overall survival was estimated using Kaplan–Meier curves from 2012 to 2024, stratified by sex, race, age group, tumor type, and tumor site. The event of interest was death. Because structured last-follow-up dates were unavailable, patients without a documented death were assumed alive through the end of the study period and administratively censored in September 2024. Survival distributions were compared using the log-rank test. All survival analyses were unadjusted. Because key covariates (tumor grade, Ki-67 index, stage, comorbidities, treatment modality, and follow-up timing) were incompletely available, multivariable Cox modeling could not be performed, and proportional hazards assumptions could not be tested. As a result, survival differences should be interpreted as descriptive and likely confounded.

3. Results

A total of 2,128 unique patients were identified, corresponding to 2,294 GI and lung NET diagnoses during the study period (November 2012–September 2024). The 2,294 GI and lung NET represented unique NET site (appendix, large intestine, lung, pancreas, rectum, small intestine, and stomach) based on diagnosis. One thousand nine hundred and seventy-one patients only had one unique site, 150 patients had two, 5 patients had three, and 2 patients had four unique sites. Of these, 1,813 (79%) were classified as GI NETs. Demographic data, including age, sex, race, ethnicity, education level, and mortality status, are summarized in Table 1. About half of the patients (1,174; 55.2%) were aged 51–74 years. The cohort was 60.2% female (1,282) and 40.7% Black (867).

Table 1. Demographics of patients with GI and lung NETs from 2012 to 2024

Characteristic	n=2,128* (%)
Age	
Under 51	321 (15.1)
51–74	1,174 (55.2)
Over 74	633 (29.7)
Sex	
Female	1,282 (60.2)
Male	846 (39.8)
Race	
Asian	48 (2.3)
Biracial/multiracial	6 (0.3)
Black	867 (40.7)
Other	125 (5.9)
Pacific Islander	1 (<0.1)
White	975 (45.8)
Unknown	106 (5.0)
Ethnicity	
Hispanic	51 (2.4)
Non-Hispanic	1,920 (90.2)
Unknown	157 (7.4)
Education (percentage calculated on n=149 known)	
Elementary level	7 (4.7)
High school/GED	53 (35.6)
Some college	33 (22.1)
University degree (s)	29 (19.5)
Post-graduate degree (s)	27 (18.1)
Unknown	1,979
Death	219 (10.3)
Follow-up time (years)	4.8 (2.1, 7.8)

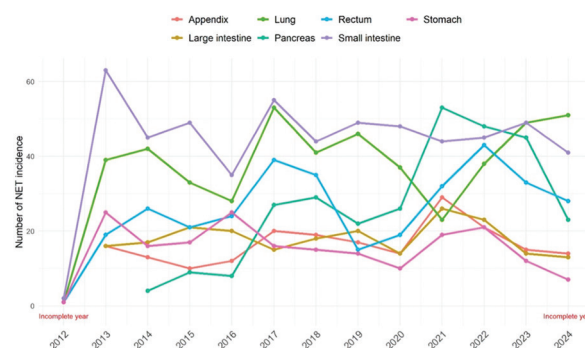
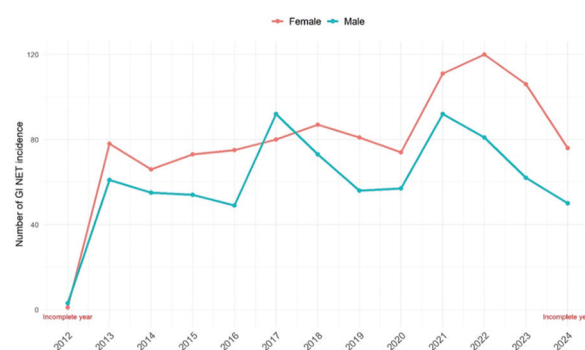
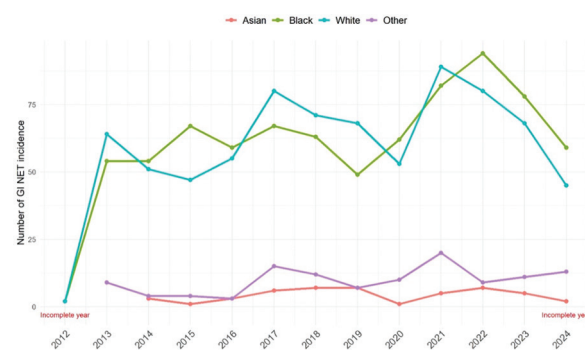
Notes: *Data expressed as n (%) or median (interquartile range).

Abbreviation: GED: General education development;

GI: Gastrointestinal; NET: Neuroendocrine tumor.

3.1. Case count over time

The NET case counts over time were stratified by tumor site (appendix, large intestine, pancreas, rectum, small intestine, stomach, and lung) from 2012 to 2024, as shown in Figure 1 and Table 2. The lung case count was included for comparison. GI NET case count was generally higher in females than in males, except in 2017 when the male case count briefly exceeded the female case count (Figure 2). The majority of GI NETs occurred in Black and White patients (Figure 3) and were most common in patients aged 51–74 years (Figure 4).

**Figure 1.** Case counts of neuroendocrine tumors by site**Figure 2.** Case counts of gastrointestinal neuroendocrine tumors by sex**Figure 3.** Case counts of gastrointestinal neuroendocrine tumors by race

3.2. Survival outcomes

Kaplan–Meier analyses demonstrated significantly higher 12-year survival among females compared with males ($p<0.012$; Figure 5) and among white patients compared to other racial groups ($p<0.018$; Figure 6). Younger patients (<51 years) had superior survival outcomes compared to older age groups ($p<0.012$; Figure 7). Benign GI NETs were associated with the most favorable survival, whereas tumors classified as benign-to-malignant or malignant showed significantly worse outcomes ($p=0.0074$; Figure A2).

Table 2. Case counts of gastrointestinal neuroendocrine tumors from 2012 to 2024

Year	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
Subject number	4	139	121	127	124	172	160	137	131	203	201	168	126

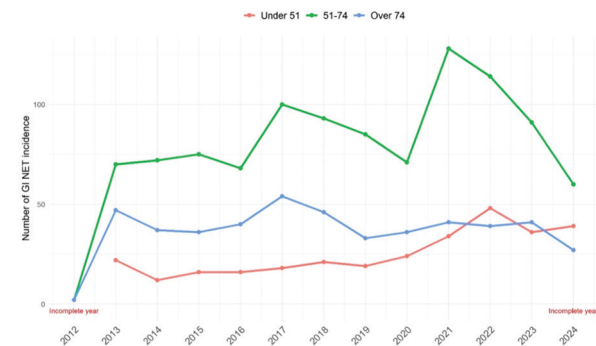


Figure 4. Case counts of gastrointestinal neuroendocrine tumors by age

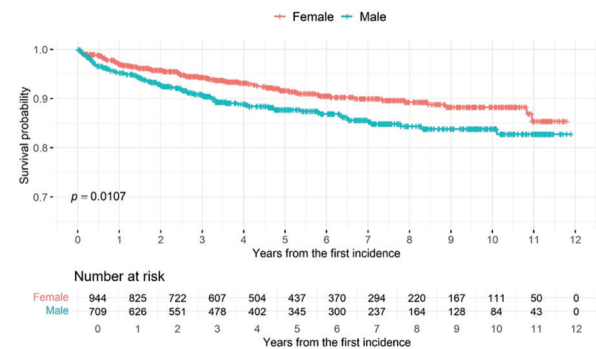


Figure 5. Overall survival of patients with gastrointestinal neuroendocrine tumors stratified by sex

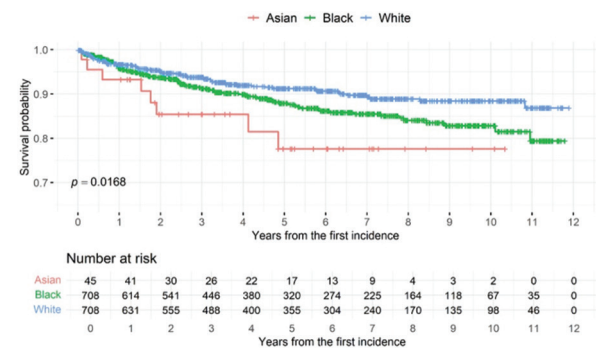


Figure 6. Overall survival of patients with gastrointestinal neuroendocrine tumors stratified by race

Among GI NET subtypes, rectal tumors demonstrated the highest 12-year survival, while pancreatic and large intestinal NETs showed an early decline in survival within the first 5 years, followed by a plateau (Figure A3). Overall, all GI NET subtypes achieved 12-year survival rates

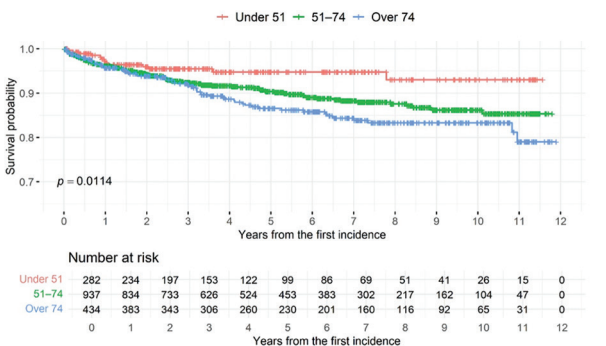


Figure 7. Overall survival of patients with gastrointestinal neuroendocrine tumors stratified by age

exceeding 70%. All survival analyses were unadjusted and should be interpreted as descriptive only.

4. Discussion

In this retrospective cohort study of 2,128 patients with GI and lung NETs across a large, multi-hospital healthcare system from 2012 to 2024, we provide updated insights into institution-level case count patterns and descriptive survival outcomes across demographic and tumor groups. Previous single-center studies have offered limited perspectives. For example, one study analyzed 155 gastro-entero-pancreatic neuroendocrine neoplasms (GEP-NENs) over 11 years and reported an increasing incidence trend, with the pancreas as the most common primary site and non-functional tumors predominating; surgical resection was the most frequent and effective treatment modality.¹⁰ Another retrospective analysis of 52 patients with gastroduodenal NETs emphasized the prognostic importance of tumor grade and size in guiding management.¹¹ Similarly, a 10-year single-center study of 63 GI NETs reported that most tumors originating in the midgut were grade 1 by histology, and frequently presented with non-specific symptoms, such as abdominal pain.¹²

Compared to these prior single-center studies, our study leveraged a substantially larger and more diverse patient population across 10 hospitals, allowing for robust characterization of local epidemiologic patterns and survival outcomes. By including both GI and lung NETs over a 12-year period, we provide a broader perspective on case count patterns for multiple tumor sites and demographic subgroups. Furthermore, our analysis highlights clinically relevant survival differences by age, sex, race, and tumor

classification (benign, benign-to-malignant, malignant) that are not commonly addressed in smaller institutional studies. Because these categories reflect coding-based distinctions rather than WHO/ENETS biological classification, the findings should be interpreted as descriptive patterns rather than mechanistic differences. These findings not only complement national registry data but also offer institution-specific insights that may inform future strategies for early detection, risk stratification, and management of NETs.

Our survival analyses are based solely on unadjusted Kaplan–Meier curves and log-rank tests. Therefore, they are highly susceptible to confounding by age, sex, race/ethnicity, tumor site, comorbidities, treatment, and other unmeasured factors. As such, the observed survival differences between tumor categories should be interpreted as descriptive rather than causal.

4.1. Case count over time

The majority of NET diagnoses in our cohort occurred in females (60.2%) and in patients aged 51–74 years (55.2%), with a disproportionately high representation of Black patients (40.7%). These findings align with prior studies demonstrating an increasing case count of NETs, particularly among older adults and women.¹³ The similar case counts observed between Black and White patients may reflect differences in local population demographics, diagnostic practices, or healthcare access, though these patterns cannot be interpreted without population-level denominators. Notably, while national data have shown a temporary decline in NET incidence during the COVID-19 pandemic,¹⁴ our study did not observe a decrease in case counts.

Consistent with national surveillance, epidemiology, and end results data, the appendix, small intestine, and rectum remain the most common sites for GI NETs, with a particularly notable increase in rectal NETs, especially among younger patients and women.¹⁵ We also observed an increase in pancreatic NET case counts between 2014 and 2021, followed by a modest decline from 2022 to 2024, a pattern similar to that reported in prior single-center GEP-NEN studies.¹⁰ In addition, although benign-to-malignant NETs were less frequent, they demonstrated the worst prognosis, underscoring the importance of early detection and accurate tumor grade characterization. Because ICD codes cannot reliably determine grade, differentiation, or Ki-67 index, it is unclear whether these differences represent true biological behavior or coding-based misclassification.

4.2. Survival outcomes

In general, survival in GI NETs varies significantly by tumor location, grade, and stage.¹⁶ Although our study did

not stratify survival by tumor grade or stage, we observed an overall favorable 12-year survival rate exceeding 70% across all GI NET subtypes, with rectal NETs demonstrating the most favorable outcomes. This aligns with prior population-based studies reporting 10-year survival rates of up to 90.3% for non-metastatic rectal NETs and 89.6% for well-differentiated appendiceal NETs.^{16,17} In contrast, pancreatic and large intestinal NETs exhibited an early survival decline within the first 5 years, followed by a plateau, suggesting either a more aggressive disease course or delays in diagnosis. Without stage or treatment information, these patterns may reflect differences in stage at diagnosis, tumor biology, or treatment access rather than inherent site-based differences.

Demographic factors also influenced survival. Female sex, younger age (<51 years), and White race were each significantly associated with improved outcomes, consistent with prior population-level analyses.¹⁷ These associations likely reflect a combination of earlier detection, comorbidity differences, healthcare access, treatment patterns, and other social determinants of health. Interpretation of racial survival differences is particularly limited without socioeconomic, insurance, comorbidity, and treatment data.

4.3. Clinical and public health implications

These findings underscore the importance of site-specific surveillance strategies, particularly for pancreatic and large intestinal NETs, where early mortality is more pronounced. Moreover, the survival advantage in younger, White, and female patients suggests potential disparities in diagnosis timing, access to specialized care, or treatment adherence. The observed demographic survival patterns highlight the need to investigate structural factors, including early diagnostic access, specialty referral patterns, and treatment availability, that may contribute to inequities in NET outcomes.

4.4. Limitations

This study has several important limitations. Its retrospective design and reliance on ICD-9/10 diagnostic coding introduced the potential for misclassification and under-ascertainment of certain NET subtypes. The study period spanned from November 2012 to September 2024. However, incidence estimates for the calendar years 2012 and 2024 are limited due to incomplete case capture in those years. Because population-at-risk data and age-standardization were unavailable, we cannot conclude true incidence rates or temporal trends.

Our tumor classification framework does not align with contemporary WHO (2019/2022) or ENETS guidelines,

which differentiate NETs by grade and differentiation rather than a benign versus malignant paradigm. ICD-9/10 codes cannot reliably determine tumor grade, Ki-67 index, mitotic count, or differentiation status, making misclassification possible. This limitation may bias survival analyses, particularly if indolent NETs were miscoded as malignant or vice versa. As a result, the survival estimates by tumor category should be interpreted with caution.

The absence of key clinical covariates—including stage at diagnosis, tumor grade, and treatment details (e.g., surgery, systemic therapy, somatostatin analogs, peptide receptor radionuclide therapy, and radiation)—limits the ability to account for important prognostic factors. Patients without an observed event (death) were censored at the end of the study date. These missing variables represent a significant limitation. The next iteration of this work should link pathology data (Ki-67, mitotic count), imaging-based staging, operative reports, and oncology treatment records to enable proper tumor classification and confounding control.

Calendar-related factors may also influence the observed patterns in case counts. The study period spans major structural transitions, specifically the ICD-9 to ICD-10 coding change in 2015, which may affect case capture independent of true disease burden. Although a formal sensitivity analysis was not performed, the potential impact of coding should be recognized as an additional source of bias when interpreting temporal patterns in NET case counts. A future iteration of this work should incorporate sensitivity analyses that evaluate trend stability across coding eras to better distinguish true epidemiologic changes from artifacts of administrative transitions.

The survival analyses are also limited by methodological constraints. Specifically, the analytic approach did not account for left truncation, which may occur if patients entered the MedStar system after their initial diagnosis. In addition, competing risks were not assessed, which may bias cause-specific survival estimates, particularly in an older population where non-cancer mortality is common. Proportional hazards assumptions were not tested, and violations could further limit the validity of hazard ratios or survival comparisons across tumor categories. These methodological gaps should be recognized as significant limitations, and the interpretation of survival outcomes, especially cause-specific estimates, should be viewed with caution. Future iterations of this work should incorporate competing-risks models and test proportional hazards to ensure more robust and interpretable survival estimates.

The presentation of the analytic cohort is limited by an inconsistent distinction between GI and lung NETs. Although the cohort description references both GI and

lung NETs, the primary analyses focus only on GI tumor sites. Without a clearly defined analytic cohort in Section 2 and separate flow diagrams outlining case identification and exclusions for each group, there is a risk of confusion and potential selection bias. This discrepancy should be acknowledged as a limitation. Future iterations of the study should explicitly define the analytic cohort at the outset, separate GI and lung NET case-capture pathways, and provide distinct flowcharts to ensure clarity and avoid inadvertent inclusion or exclusion bias.

Survival differences likely reflect confounding by age, race, sex, tumor site, comorbidities, treatment, and other unmeasured factors. Subgroup Kaplan–Meier analyses (sex-, race-, age-, subtype-specific) are exploratory and may be subject to inflated type I error due to multiple comparisons.

5. Conclusion

Our study reinforces the generally favorable prognosis of GI NETs while highlighting clinically relevant differences in case count and survival by tumor site and patient demographics. Rectal NETs demonstrated the most favorable long-term outcomes, whereas pancreatic and large intestinal NETs showed early survival decline. The observed survival advantage in younger, female, and White patients raises questions about potential biological influences, healthcare access disparities, and the timing of diagnosis.

Future research should integrate tumor grade, stage, treatment modalities, and molecular characteristics to refine risk stratification and guide personalized management. Multi-institutional or prospective studies are warranted to validate these findings and to explore the underlying mechanisms driving the demographic survival differences. Incorporating social determinants of health and genetic data will be critical to improving equity in NET outcomes and informing targeted screening strategies.

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Conflict of interest

The authors declare that they have no competing interests.

Author contributions

Conceptualization: Fan Cao and Priyanka Kanth

Formal analysis: Fan Cao and Jiling Chou

Investigation: Priyanka Kanth

Methodology: Fan Cao and Priyanka Kanth

Writing – original draft: Fan Cao

Writing – review & editing: Fan Cao, Priyanka Kanth,
Michael Tseng

Ethics approval and consent to participate

This study was reviewed and approved by Institution Review Board of MedStar Health Research Institute (Approval ID. STUDY00008275). Informed consent was obtained from all individual participants included in the study.

Consent for publication

All participants provided informed consent for the publication of the findings derived from this study. Where applicable, participants gave explicit permission for the publication of any data, images, or information that could potentially reveal their identity. The authors affirm that all relevant consent forms have been obtained and are available upon request.

Availability of data

Data are available upon request from corresponding author.

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Appendix

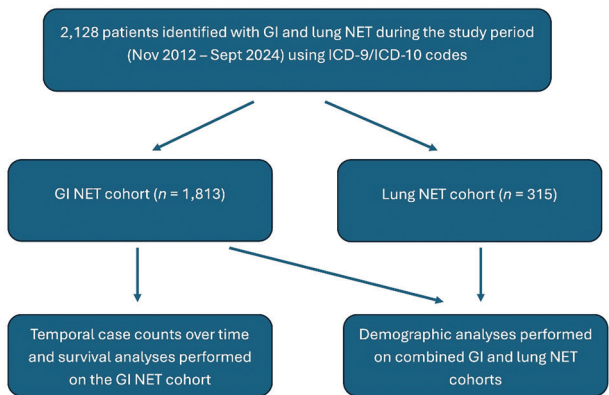


Figure A1. Study flow chart
Abbreviations: GI NET: Gastrointestinal neuroendocrine tumor;
ICD: International classification of diseases.

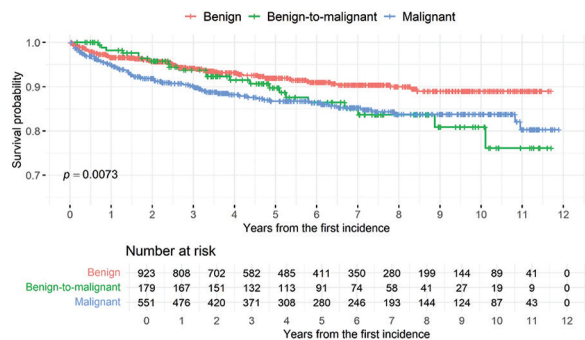


Figure A2. Overall survival of patients with gastrointestinal neuroendocrine tumors stratified by tumor type

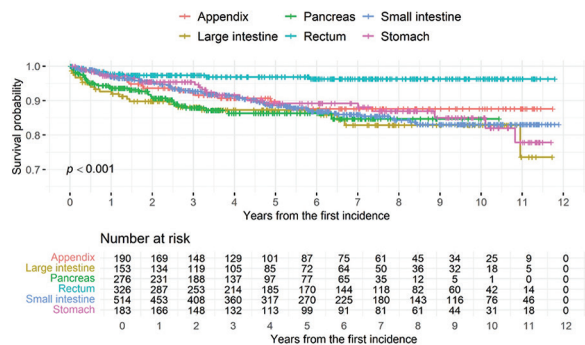


Figure A3. Overall survival of patients with gastrointestinal neuroendocrine tumors stratified by tumor site