Patterns of care amongst older adults diagnosed with locally advanced esophageal cancer: A cohort study

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ABSTRACT

Introduction: Since the early 2010s, neoadjuvant chemoradiation followed by esophagectomy (trimodal therapy) has been a recommended treatment for patients diagnosed with locally advanced esophageal cancer. However, it may also add treatment-related toxicity, particularly for older adults with significant comorbidity and frailty burdens. We examined contemporary patterns of care in older adults, which have not been well characterized.
Materials and Methods: We used the Surveillance Epidemiology and End Results-Medicare database to identify a cohort of US adults aged 66 years and older diagnosed with incident locally advanced esophageal cancer between 2004 and 2017. Calendar year age-standardized percentages of treatment receipt were calculated. Joinpoint regression was used to detect temporal trends in treatment receipt. Descriptive associations between patient factors and treatment were assessed. Trend analyses quantified how the percentage of trimodal and definitive chemoradiation (no surgery) patients receiving cisplatin-based, carboplatin-based, and other chemotherapy regimens evolved over time.
Results: In total, 4332 adults aged ≥66 years with locally advanced esophageal cancer were included. The age-standardized percentage of patients receiving trimodal therapy increased from 16.7% in 2004 to 26.1% in 2017 (annual percent change = 3.5%; 95% confidence interval [CI], 0.7%–6.4%) in adenocarcinomas and from 7.3% in 2004 to 9.1% in 2017 (annual percent change = 0.4%; 95% CI, −4.1%–5.1%) in squamous cell carcinomas. By 2017, definitive chemoradiation became the most frequently used treatment modality for adenocarcinomas (49.8%; 95% CI, 43.5–56.0) and squamous cell carcinomas (59.5%; 95% CI, 50.8–68.2). Patients with higher comorbidity and frailty burdens were less likely to be treated with trimodal therapy. Amongst patients receiving chemoradiation as part of their treatment, a large and swift channeling away from cisplatin and towards carboplatin-based regimens was observed.
Discussion: In practice, definitive chemoradiation is the most commonly received treatment by older adults with locally advanced esophageal cancer. Four out of five older adults do not receive trimodal therapy, some of whom are potentially undertreated.

1. Introduction

Esophageal cancer is an aggressive malignancy with a five-year survival rate of 20% [1]. Over 15,000 deaths are attributed to esophageal cancer in the United States annually [2]. The incidence of esophageal adenocarcinoma has risen dramatically over time, potentially attributable to an increase in obesity and gastroesophageal reflux disease [3,4]. Similar to most malignancies, esophageal cancer incidence increases precipitously with advancing age, reaching a peak of 26.2 new cases per 100,000 amongst individuals 80–84 years of age [5]. As the U. S. population ages, the burden of esophageal cancer will continue to increase [6,7].

At the time of diagnosis, most patients with esophageal cancer present with locally advanced disease. Treatments for locally advanced cancers recommended by clinical guidelines from the National Comprehensive Cancer Network (NCCN) and the American Society of

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Clinical Oncology (ASCO) include definitive chemoradiation and neoadjuvant chemoradiation followed by surgery (trimodal therapy) [8,9]. Trimodal therapy is widely accepted as conferring the longest survival benefit due to the results of the Chemoradiotherapy for Esophageal Cancer Followed by Surgery Study (CROSS) randomized trial, which demonstrated superior overall survival (24.6 months longer median survival) in patients receiving trimodal therapy compared to surgery alone [10–12]. However, definitive chemoradiation is also considered an acceptable alternative based on studies showing about 20–30% of patients receiving trimodal therapy experience pathologic complete response [11,13].

Uptake of trimodal therapy may be limited for older adults, a clinically complex population that was underrepresented in the CROSS trial. The median age of CROSS participants was 60 years, whereas the median age at diagnosis of esophageal cancer in the United States is 68 years. This limits the generalizability of CROSS to older adults, a frequent limitation of randomized trials [14,15]. On average, older patients with cancer have higher comorbidity burdens, increased frailty, and decreased life expectancy compared to younger patients with cancer; in totality these may dampen the potential beneficial effect of trimodal therapy and inflate adverse events, concerns which may influence treatment selection [16]. In light of the morbidity and mortality of esophagectomy, many older adults may instead receive definitive chemoradiation.

Treatment trends over time and factors influencing treatment selection in older adults in the decade after the publication of the CROSS trial results have not been well-characterized. Understanding the treatment landscape is critical for assessing care quality and identifying populations that may be receiving undertreatment and overtreatment. The objective of this study was to describe patterns of initial cancer-directed therapy amongst a population of older adults with locally advanced esophageal cancer.

2. Materials and Methods

2.1. Data Source

This cohort study leveraged data from the Surveillance Epidemiology and End Results (SEER)-Medicare linkage to identify a population of older adults diagnosed with esophageal cancer between 2004 and 2017. SEER is a system of population-based cancer registries supported by the National Cancer Institute (NCI) that capture incident cancers from select state and regional registries that collectively cover 28% of the U.S. population [17]. Medicare is the federally-funded governmental program administered by the Center for Medicare and Medicaid Services that provides health insurance to adults 65 years of age and older, as well as individuals with end-stage-renal-disease and disabilities. Over 97% of adults 65 years of age and older are enrolled in Medicare, though our study uses data only from SEER cases with fee-for-service Medicare [18]. Administrative data from Medicare used in this study include beneficiary enrollment information and medical claims (Medicare Parts A and B).

2.2. Study Population

We focused on a population of older adults (defined as 66 years of age and older) with locally advanced esophageal cancer for which trimodal therapy is a recommended treatment option per current NCCN and ASCO guidelines [8,9]. Incident cases diagnosed between 2004 and 2017 were identified using the SEER-Medicare database. We included individuals 66 years of age or older at the time of diagnosis who had a histologically-confirmed incident diagnosis of adenocarcinoma or squamous cell carcinoma not originating in the cervical esophagus (ICD Oncology-3 site codes C15.1-C15.9). Cases diagnosed via death certificate or autopsy were excluded. We used the NCCN and ASCO clinical guidelines coupled with the American Joint Committee on Cancer 7th edition staging manual to identify cancers of interest based on the tumor (T), node (N), and metastasis (M) case data supplied by the registry. All locally advanced cancers were required to be non-metastatic (M0). There were two T and N combination groups eligible amongst the non-metastatic cases: (1) any resectable tumor (T1-T4a) with positive nodes (N1−N3) and (2) more advanced resectable tumors (T2-T4a) with any nodal status (N0−N3). Eligible cases were required to have at least twelve months of continuous fee-for-service Medicare insurance and no managed care enrollment prior to the cancer diagnosis. We further excluded patients who were diagnosed with other cancers (e.g., lung) in the year before their first esophageal cancer diagnosis to assure that cancer-directed treatments observed in the claims data were for treatment of esophageal cancer.

2.3. Patient Characteristics

We assigned the date of diagnosis as the first of the month in which the cancer was diagnosed. The following patient-level characteristics were identified at the date of diagnosis: age, sex, race and ethnicity, tumor site (location), histologic subtype, tumor stage group, tumor grade, number of previous cancers in the registry (first diagnosed more than a year before incident esophageal cancer), geographic region of the reporting registry, percentage of population living below the federal poverty line in the census tract, and county-level urbanicity. We calculated the NCI adaption of the Charlson comorbidity score [19,20] and the Kim frailty index [21] using medical claims data from the year prior to cancer diagnosis. These claims-based indices serve as proxies of patient comorbidity and frailty, respectively [21–24]. As imperfect proxies, they may not fully capture the extent and severity of comorbidities and frailty; for instance, two individuals with the same Charlson score may have different conditions leading to the score or the same conditions but varying severity. The Kim frailty index uses International Classification of Disease (ICD) diagnosis codes, Current Procedural Terminology (CPT) codes, and Healthcare Common Procedure Coding System (HCPCS) level II codes for frailty-related variables (e.g., walking aid) to predict frailty based on a deficit accumulation approach. The index has been externally validated using data from the Health and Retirement Study [21]. In categorizing levels of the frailty index, we used cutoffs supplied previously implemented by the index developers (Robust: <0.15, Prefrail: 0.15–0.24, Mildly Frail: 0.25–0.34, Moderately-to-severely frail: ≥ 0.35).

2.4. Outcome Assessment: Initial Treatment Received

We were primarily interested in five categories of treatment: trimodal therapy (neoadjuvant chemoradiation followed by surgery), definitive chemoradiation, surgery alone or other surgery-based multimodal therapy (e.g., chemotherapy followed by surgery), palliative therapy (chemotherapy or radiation alone), and no treatment. A nine-month treatment window extending from the date of diagnosis was used to assess the treatments received based on the occurrence and sequence of medical claims corresponding to treatments of interest. Given the lethality of esophageal cancer, a substantial number of cases were anticipated to die prior to completion of the nine-month assessment window. Thus, we did not require nine months of survival. If an individual received any treatment prior to death within nine months, this treatment information was used to classify the individual into a treatment group using all therapies received prior to death. However, individuals were excluded from the analysis if they lost their fee-for-service insurance coverage within nine months of diagnosis and prior to death, an uncommon occurrence (Fig. 1).

Surgery consisted of resection (esophagectomy) and was identified using ICD-9 and 10 procedure codes, as well as CPT codes. Chemotherapy consisted of any intravenous chemotherapy with a corresponding HCPCS code. All chemotherapy agents received within 28 days of the first delivery of chemotherapy were used in characterizing

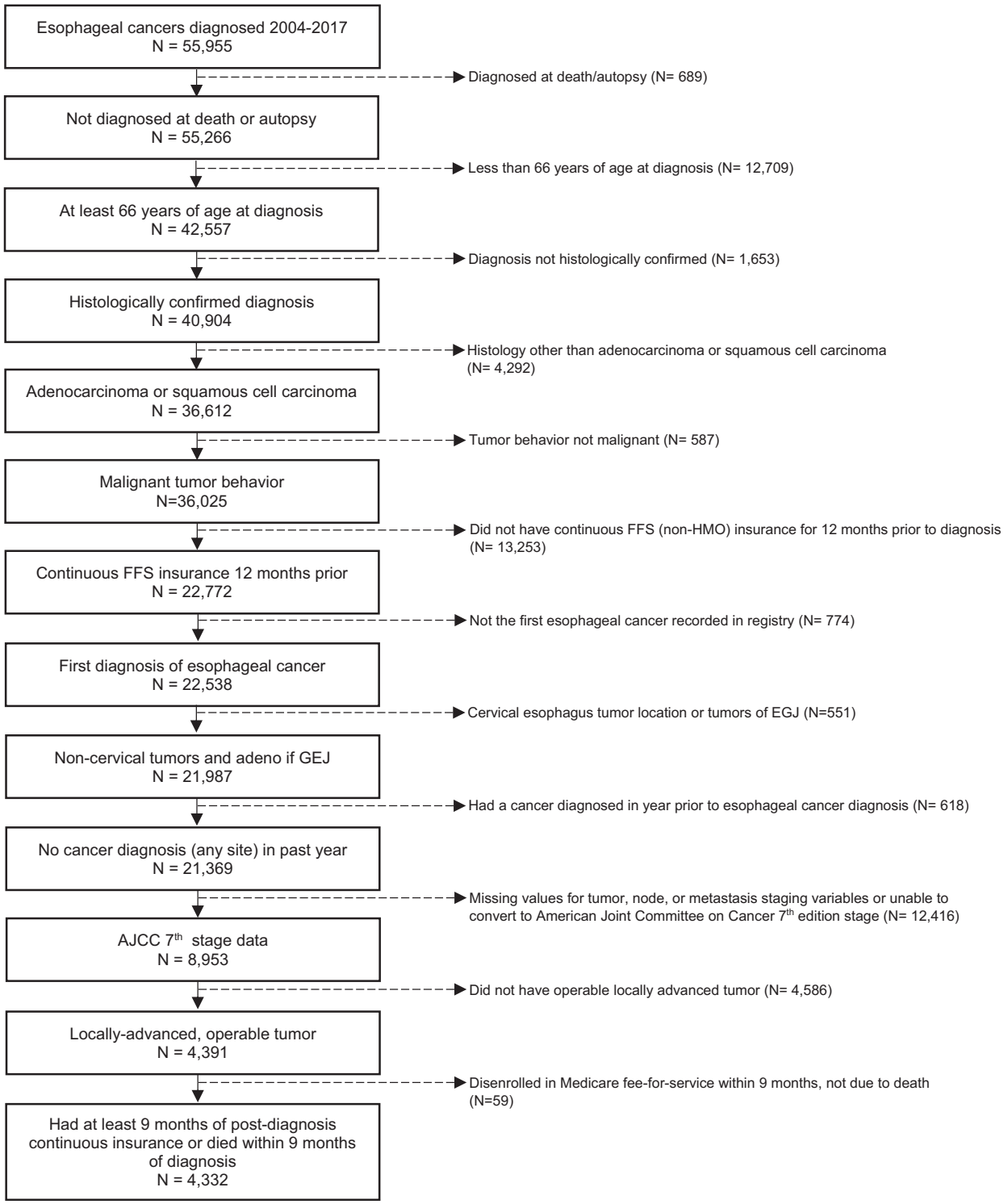

Fig. 1. Flowchart Depicting Selection of Study Population Through Application of Eligibility Criteria.

different regimens. Radiation consisted of external beam radiation and was identified with radiation treatment delivery CPT codes. Individuals who received chemotherapy and radiation before surgical resection were classified as trimodal therapy patients. Individuals who received chemotherapy and radiation, but no surgery, were categorized as belonging to the definitive chemoradiation treatment group. Individuals receiving only resection or who received either chemotherapy or radiation (but not both before surgery) with surgery were classified in the "surgery or other multimodal" group. Cases receiving only chemotherapy or only radiation were classified in the palliative care group. Lastly, cases not receiving any one of these modalities were classified as no treatment. All codes used to identify treatments are provided in Supplemental Table 1.

2.5. Statistical Analysis

Given the differences in etiology, pathogenesis, treatment, and prognosis between adenocarcinomas and squamous cell carcinomas, all

analyses were stratified by histologic subtype. Descriptive characteristics were calculated for the study population. The age-standardized annual percentage of individuals in each treatment group was reported across study years of diagnosis (2004–2017). Direct standardization was used to provide age-standardized percentages using the age distribution of individuals diagnosed in 2017 as the standard population [25].

Joinpoint regression software was used to detect and quantify significant trends in age-standardized percentages for each treatment over calendar time. A maximum of two join points (three trends) was considered, and the permutation statistical test was used to select the final model. Joinpoint regression is a data-adaptive trend analysis method that allows for non-linearities in data by allowing for separate trend "segments" with distinct slopes across the time being considered in trend analysis. Within each segment, the relationship between year of diagnosis and percentage receiving a given treatment is assumed to be linear on the log scale [26].

Descriptive statistics of treatment receipt were calculated and represented with bar charts. These graphics presented the proportion of individuals in each treatment category according to values of each respective clinical and demographic characteristic under consideration. Descriptive (non-causal) risk ratios [27] comparing the probability of receiving trimodal therapy versus all other treatment modalities across levels within each variable were calculated using univariable modified Poisson regression models and presented in the supplementary materials [28].

To evaluate temporal trends in receipt of specific chemotherapy regimens across the study years, joinpoint regression analysis was performed within the subset of the cohort treated with definitive chemoradiation or trimodal therapy.

This study was approved by the University of North Carolina at Chapel Hill Institutional Review Board (21–1217). All analyses were performed using SAS 9.4 (Cary, NC).

3. Results

3.1. Study Population

After applying study eligibility criteria, the final study population consisted of 4332 individuals 66 years of age and older with incident locally-advanced esophageal cancer diagnosed between 2004 and 2017 (Fig. 1). Study population descriptive statistics for demographic and clinical variables are reported in Table 1, stratified by histologic subtype. There were 2801 adenocarcinomas and 1531 squamous cell carcinomas. The median ages of individuals with adenocarcinomas and squamous cell carcinomas were 74 and 75 years, respectively. Over 93% of individuals with adenocarcinomas were non-Hispanic White, compared to only 71.8% of squamous cell carcinomas. In both histologic subtypes, less than half of the population were classified in the robust (healthiest) frailty index category.

3.2. Temporal Trends in Treatment Received

Age-standardized percentages of the cohort corresponding to each treatment group are presented in Fig. 2. Accompanying estimates are presented in Table 2. The age-standardized rates are plotted with a trend line produced via joinpoint regression models.

For adenocarcinomas, the age-standardized percentage of adenocarcinomas receiving trimodal therapy increased from 16.7% (95% confidence interval [CI], 10.7–22.7%) in 2004 to 26.1% (95% CI, 20.8%–31.5%) in 2017. The joinpoint regression of these rates found one (increasing) trend for trimodal therapy, with an annual percent change from 2004 to 2017 of 3.5% (95% CI, 0.7%–6.4%). The age-standardized percentage of cases receiving definitive chemoradiation increased from 17.7% (95% CI, 11.6%–23.7%) in 2004 to 49.8% (95% CI, 43.5%–56.0%) in 2017, the largest increasing percentage change of any of the therapeutic groups. The corresponding joinpoint regression of these definitive chemoradiation rates found two increasing trends, with annual percent changes from 2004 to 2010 and 2010–2017 of 14.6% (95% CI, 6.4%–23.3%) and 3.0% (95% CI, 0.3%–5.8%), respectively. In contrast to these increases, the percentage of cases receiving surgery or

Table 1
Study population descriptive statistics stratified by histologic subtype, SEER-Medicare 2004–2017.

	Adenocarcinomas (N = 2801)	Squamous cell carcinomas (N = 1531)
Age, median (IQR)	74 (70–80)	75 (70–80)
Sex		
Male	2412 (86.1)	855 (55.9)
Female	389 (13.9)	676 (44.2)
Race		
Non-Hispanic White	2609 (93.2)	1099 (71.8)
Hispanic White	97 (3.5)	83 (5.4)
Black	54 (1.9)	231 (15.1)
Another race and ethnicity or missing	41 (1.5)	118 (7.7)
Year of diagnosis		
2004–2008	646 (23.1)	381 (24.9)
2009–2013	1054 (37.6)	631 (41.2)
2014–2017	1101 (39.3)	519 (33.9)
Registry region[a]		
Northeast	641 (22.9)	348 (22.7)
Midwest	420 (15.0)	165 (10.8)
South	615 (22.0)	350 (22.9)
West	1125 (40.2)	668 (43.6)
Tumor grade		
Grade I	117 (4.2)	83 (5.4)
Grade II	1040 (37.1)	630 (41.2)
Grade III	1238 (44.2)	540 (35.3)
Undetermined differentiation	406 (14.5)	278 (18.2)
Tumor location		
Upper and middle	201 (7.2)	950 (62.0)
Lower	2394 (85.5)	436 (28.5)
Overlapping or NOS	206 (7.4)	145 (9.5)
Stage group		
IB	286 (10.2)	54 (3.5)
IIA	149 (5.3)	290 (18.9)
IIB	1095 (39.1)	601 (39.3)
IIIA	936 (33.4)	459 (30.0)
IIIB	207 (7.4)	77 (5.0)
IIIC	128 (4.6)	50 (3.3)
Number of prior non-esophageal cancers		
0	2313 (82.6)	1119 (78.3)
1	415 (14.8)	266 (17.4)
≥2	73 (2.6)	66 (4.3)
Charlson comorbidity score		
0	1218 (43.5)	692 (45.2)
1–2	1099 (39.2)	591 (38.6)
3–4	326 (11.6)	167 (10.9)
≥5	158 (5.6)	81 (5.3)
Kim Frailty Index		
Robust, <0.15	1368 (48.8)	692 (45.2)
Prefrail, 0.15–0.24	1156 (41.3)	674 (44.0)
Mildly frail, 0.25–0.34	224 (8.0)	135 (8.8)
Moderate-to-severely frail, 0.35	53 (1.9)	30 (2.0)
Census tract poverty percent		
0%–<5%	694 (26.8)	330 (22.6)
5%–< 10%	782 (30.2)	413 (28.3)
10%–<20%	728 (28.1)	385 (26.4)
20%–100%	384 (14.8)	333 (22.8)
Missing	213	70
Level of urbanization		
Metropolitan	2350 (83.9)	1335 (87.2)
Urban	315 (11.3)	151 (9.9)
Rural	136 (4.9)	45 (2.9)

[a] West consisted of: California, Hawaii, New Mexico, Utah and Seattle. Northeast consisted of Connecticut and New Jersey. Midwest consisted of Iowa and Detroit. South consisted of Georgia, Kentucky, and Louisiana.

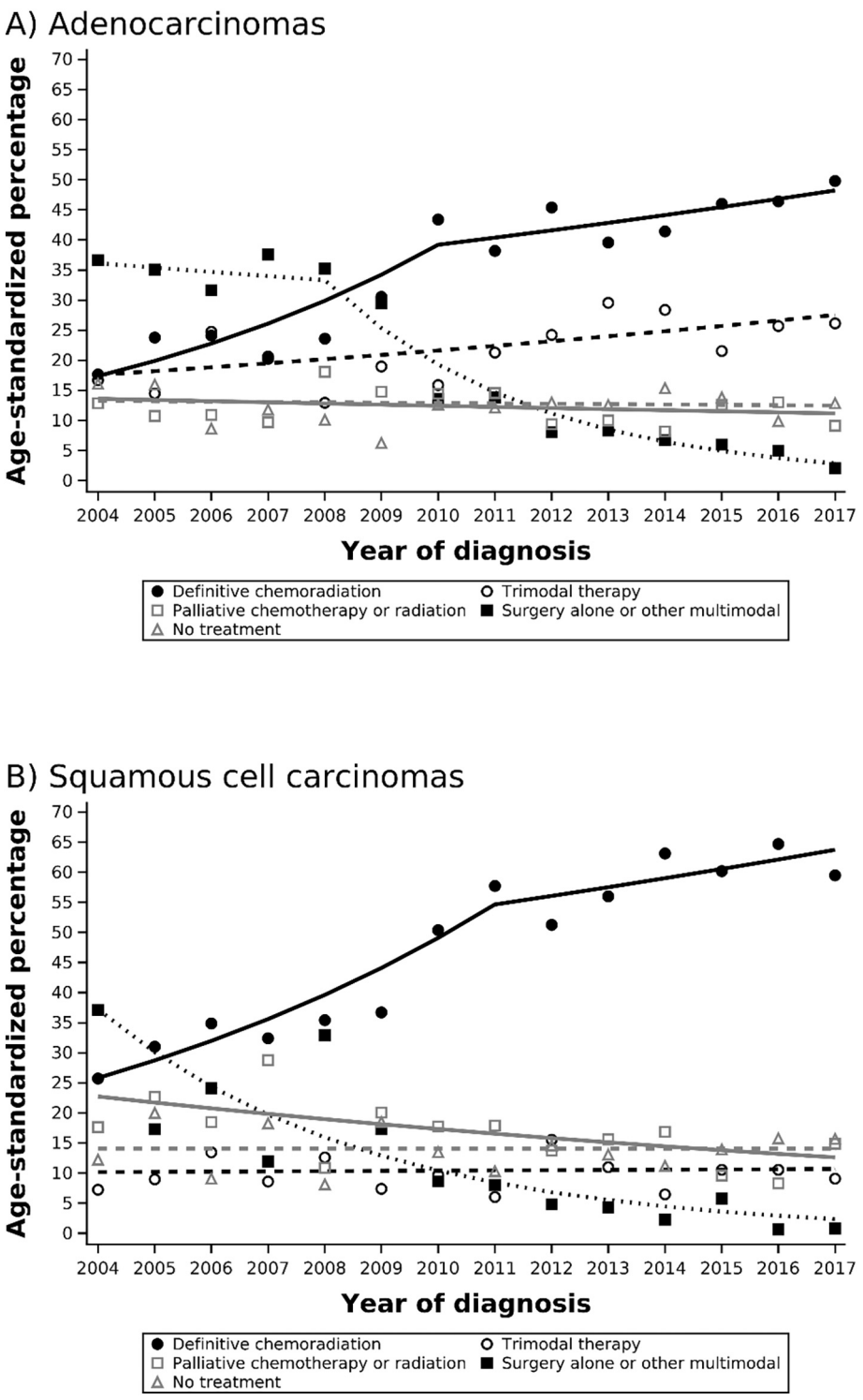

Fig. 2. Modelled Temporal Trends in the Age-Standardized Percentage of Individuals Receiving Each Treatment for A) Adenocarcinomas and B) Squamous Cell Carcinomas, in a Medicare-Enrolled Population of Adults 66 Years of Age and Older Diagnosed With Locally Advanced Esophageal Cancer in a SEER Registry Region Between 2004 and 2017.

other multimodal therapy decreased over the study period. The percentages of patients receiving palliative treatment and none of these treatments were stable.

For squamous cell carcinomas, the age-standardized percentage of adenocarcinomas receiving trimodal therapy increased from 7.3% (95% CI, 2.5–12.0%) in 2004 to 9.1% (95% CI: 4.1%–14.1%) in 2017. The joinpoint regression of these percentages detected no change over time. The age-standardized percentage of cases receiving definitive chemoradiation increased from 25.7% (95% CI, 17.7%–33.8%) in 2004 to 59.5% (95% CI, 50.8%–68.2%) in 2017, constituting the largest increasing percentage change of any of the therapeutic groups. The corresponding joinpoint regression of these definitive chemoradiation rates found two increasing trends, with annual percent changes from 2004 to 2011 and 2011–2017 of 11.3% (95% CI, 6.4%–16.5%) and 2.6% (95% CI, −0.8%–6.1%), respectively. Regarding the other treatment groups, receipt of palliative treatment and surgery or other multimodal

Table 2
Temporal Trends in Treatment Received Stratified by Histologic Subtype, SEER-Medicare 2004–2017.

Treatment group	Age-standardized percentage in 2004 (95% CI)	Age-standardized percentage in 2017 (95% CI)	Temporal trend segment	Annual percent change during segment, %	Average annual percent change across all segments, 2004–2017
Adenocarcinomas					
Definitive chemoradiation	17.7 (11.6–23.7)	49.8 (43.5–56.0)	2004–2010 2010–2017	14.6 (6.4–23.3) 3.0 (0.3–5.8)	8.2 (4.8–11.7)
Trimodal therapy	16.7 (10.7–22.7)	26.1 (20.8–31.5)	2004–2017	3.5 (0.7–6.4)	3.5 (0.7–6.4)
Surgery alone or other multimodal	36.7 (28.8–44.5)	2.1 (0.9–3.9)	2004–2008 2008–2017	−2.0 (−13.4–10.9) −29.1 (−18.4 to −8.9)	−17.8 (−22.0 to −13.3)
Palliative chemotherapy or radiation	12.9 (7.5–18.3)	9.1 (5.6–12.7)	2004–2017	−1.5 (−4.7–1.8)	−1.5 (−4.7–1.8)
No treatment	16.1 (10.5–21.7)	12.9 (8.6–17.1)	2004–2017	−0.5 (−3.3–2.4)	−0.5 (−3.3–2.4)
Squamous cell carcinomas					
Definitive chemoradiation	25.7 (17.7–33.8)	59.5 (50.8–68.2)	2004–2011 2011–2017	11.3 (6.4–16.5) 2.6 (−0.8–6.1)	7.2 (4.5–10.0)
Trimodal therapy	7.3 (2.5–12.0)	9.1 (4.1–14.1)	2004–2017	0.4 (−4.1–5.1)	0.4 (−4.1–5.1)
Surgery alone or other multimodal	37.1 (27.6–46.7)	0.8 (0.0–2.4)	2004–2017	−19.1 (−24.8 to −13.0)	−19.1 (−24.8 to −13.0)
Palliative chemotherapy or radiation	17.7 (10.1–25.2)	14.9 (8.7–21.1)	2004–2017	−4.4 (−7.7 to −1.0)	−4.4 (−7.7 to −1.0)
No treatment	12.2 (5.7–18.8)	15.7 (9.3–22.1)	2004–2017	0.0 (−3.4–3.4)	0.0 (−3.4–3.4)

therapy decreased over time. The percentage of patients receiving none of these treatments was stable.

3.3. Relationships between Patient Characteristics and Treatment Received

The relationships between select demographic and clinical characteristics and treatment received are represented in Fig. 3. The plots and estimates for all variables considered can be found in Supplemental Figs. 1–4 and Supplemental Tables 2–5. As seen in Fig. 3, the probability of receiving trimodal therapy decreased with increasing age and increasing comorbidity burden for both histologic subtypes. With increasing frailty, the probability of receiving trimodal therapy also decreased (Supplemental Figs. 2 and 4). For instance, amongst adenocarcinomas, 37.7% of individuals aged 66–70 received trimodal therapy compared to only 27.0% of those aged 71–75 (RR = 0.72; 95% CI, 0.62–0.83) and 11.7% of those 76 years of age and older (RR = 0.31; 95% CI, 0.26–0.40). Treatment with trimodal therapy was highest in stage IIIB tumors for adenocarcinomas and stage IIIA for squamous cell carcinomas. A comprehensive reporting of the probabilities of receiving trimodal therapy and corresponding descriptive (unadjusted, non-causal) risk ratios are presented in Supplementary Tables 6 and 7.

3.4. Temporal Trends in Chemotherapeutic Regimens

Temporal trends in the age-standardized percentage of individuals who received cisplatin-based, carboplatin-based, and other chemotherapeutic regimens amongst those treated with definitive chemoradiation or trimodal therapy are presented in Fig. 4 and Table 3. The age-standardized percentage of individuals with adenocarcinomas and squamous cell carcinomas receiving cisplatin-based therapies decreased at an average annual percent change of −18.0% (95% CI, −24.9% – -10.5%) and − 13.7% (95% CI: −19.6% – -7.5%), respectively. This decrease coincided with an increase in the use of carboplatin-based therapies; for instance, amongst individuals with adenocarcinomas there was a 17.8% (95% CI: 7.1–29.7) annual percent increase in carboplatin-based therapy between 2008 and 2014. As expected, approximately 90% of those initiating carboplatin also had a claim for paclitaxel within 28 days of initiating chemotherapy.

4. Discussion

Our study empirically documented patterns of care in older adults with locally advanced esophageal cancer between 2004 and 2017 using data from SEER-Medicare. Although the use of trimodal therapy increased over time, treatment with definitive chemoradiation increased at a faster rate and remains the dominant treatment paradigm for older adults in practice. We have shown that receipt of trimodal therapy varies across levels of demographic and clinical characteristics. Amongst patients receiving definitive chemoradiation or trimodal therapy, we found a strong substitution of cisplatin with carboplatin. This suggests that the chemotherapy regimen used in CROSS (carboplatin and paclitaxel) has become favored even in non-surgical populations.

The results of our study add to the existing literature. Molena et al. examined esophageal cancer treatment trends in older adults using SEER-Medicare data from 2001 to 2009 and similarly found that definitive chemoradiation was the dominant treatment strategy (48.5%, using a denominator of patients who received any chemotherapy, radiation, or surgery), though the study ended eight years prior to ours and before the final results of CROSS were disseminated [29]. Our findings that the use of trimodal therapy and definitive chemoradiation have both increased suggests that the CROSS regimen has been adopted by oncologists treating older adults, though many individuals may not be fit to receive esophagectomy, may not be offered surgery, or may not elect to receive offered surgery. No prior research has documented the trends in use of different chemotherapy regimens in this population, though our finding of a channeling away from cisplatin and towards carboplatin is reflective of studies that document higher rates of grade 3 toxicities in patients receiving cisplatin and 5-fluorouracil compared to carboplatin and paclitaxel [30].

Our study has numerous strengths. We described contemporary trends in treatment including calendar years after publication of the results from the CROSS trial. Our incorporation of a novel frailty index was germane to the older adult population, providing insight into how treatment is distributed according to levels of frailty. Detailed understanding of potential confounding factors is a prerequisite for producing a methodologically rigorous comparative effectiveness study. This work provides a detailed, quantitative depiction of factors that may influence treatment selection and prognosis, thereby serving as a roadmap for future studies seeking to compare outcomes across these modalities.

Limitations of the study include the reliance on claims-based proxies for comorbidity and frailty in place of clinical measurement. Without data on patient preference and the results of geriatric assessment—cornerstones of shared decision making [31–33]—our study does not determine the appropriateness of treatment received. Future work describing the distribution of treatment according to levels of

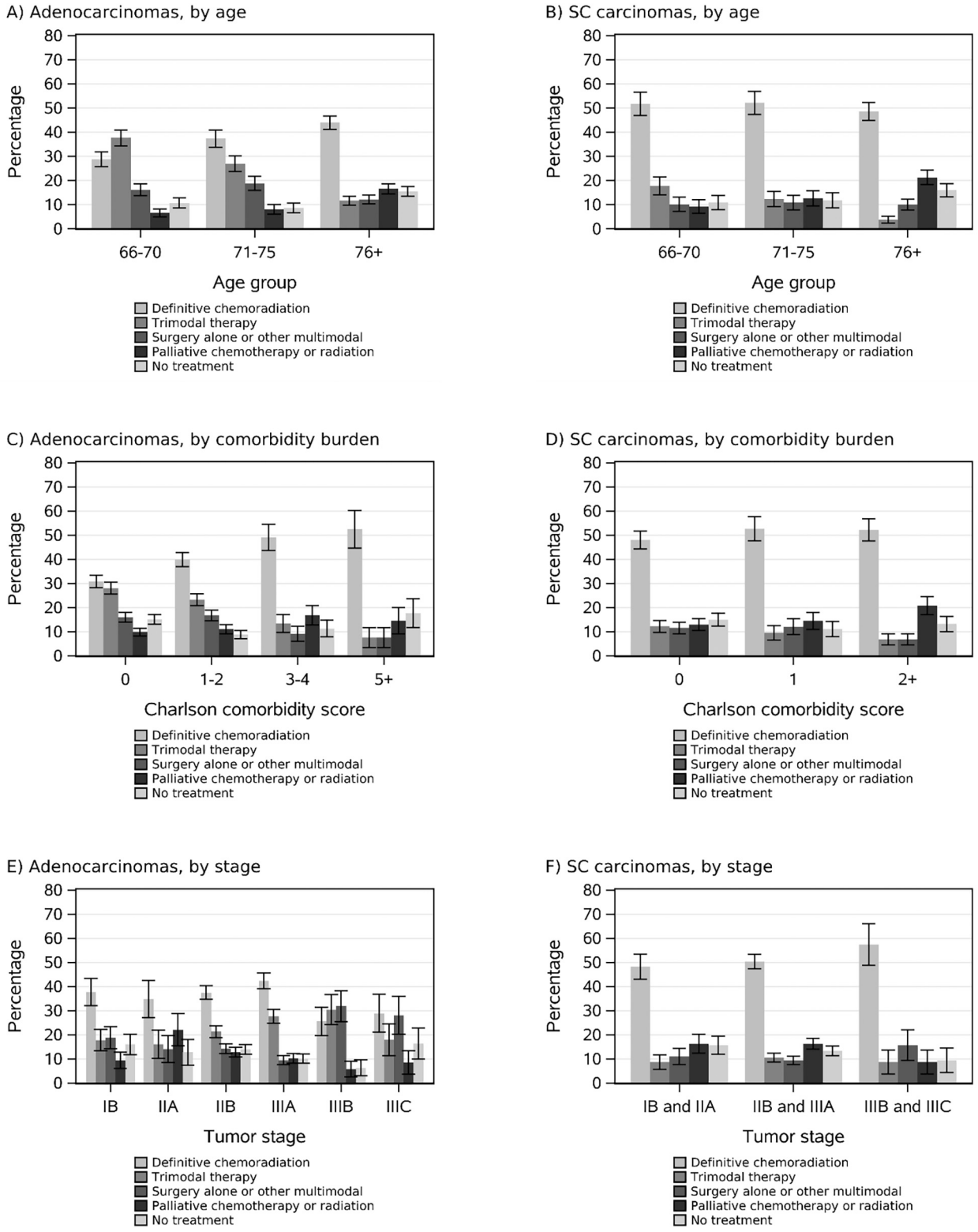

Fig. 3. Distribution of Treatment Receipt by Age (Panels A and B), Comorbidity Score (Panels C and D), and Tumor Stage (Panels E and F) Amongst Older Adults Diagnosed with Locally Advanced Esophageal Adenocarcinomas or Squamous Cell Carcinomas, SEER-Medicare 2004–2017.
Abbreviations: SC, squamous cell.
Categories used when presenting data may vary across histologic subtypes in order to be in accordance with data confidentiality requirements.

clinically-assessed frailty and functional status would better illuminate quality-of-care gaps. The generalizability of our findings is also restricted to those with Medicare fee-for-service. Medicare Advantage beneficiaries tend to have a higher health status [34], potentially impacting treatment patterns.

Given the possibility of complete response and the significant morbidity and mortality associated with resection, definitive chemoradiation may be appropriate treatment for some older adults. However,

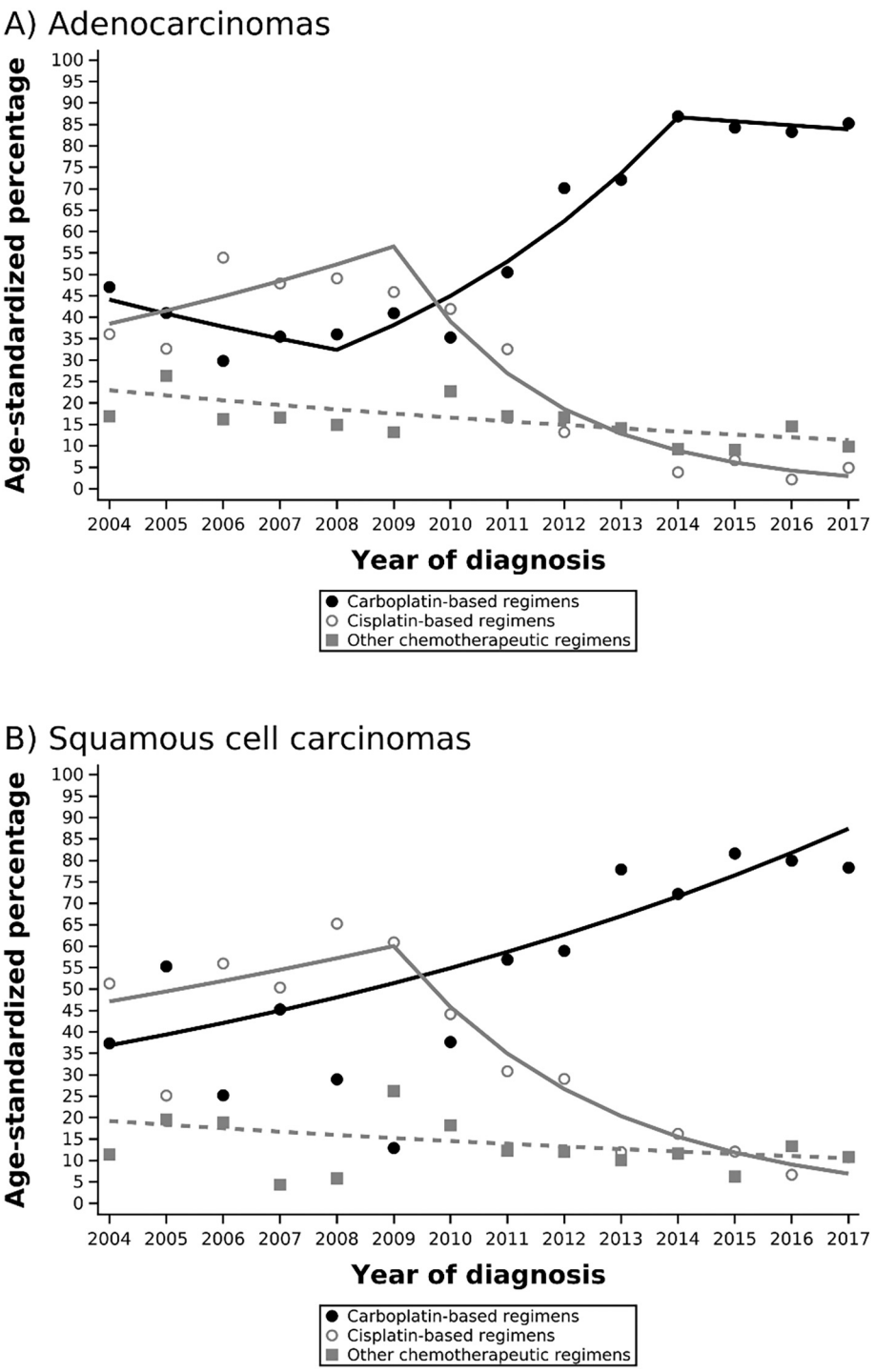

Fig. 4. Modelled Temporal Trends in the Age-Standardized Percentage of Cases Receiving Each Chemotherapy Regimen Amongst a Population of Adults 66 Years of Age and Older Diagnosed with Locally Advanced Esophageal Cancer Who Received Definitive Chemoradiation or Trimodal Therapy, SEER-Medicare 2004–2017.

despite its prognostic importance, pathologic complete response is notoriously difficult to predict based on clinical parameters [35,36]. Additionally, adenocarcinomas have been demonstrated to have lower rates of pathologic complete response than squamous cell carcinomas [11,37], suggesting a role for additional resection. Even in our most recent year of data (2017), less than a third of older adults diagnosed with adenocarcinomas received trimodal therapy, signaling potential undertreatment in the subset of these patients that are candidates for surgery. Ultimately, whether older adults with locally advanced esophageal cancer are overtreated or undertreated cannot be determined from this study alone. Central to the appropriateness of care are the comparative effectiveness of the treatments and patient preferences. Though beyond the scope of this work, future research using the SEER-Medicare database could examine the association between treatment and patient outcomes such as survival, treatment-related functional adverse events, and home time. Patient preferences were unavailable in the retrospective database, a limitation of our work. However, primary data collection could be undertaken to document the treatment preferences of older adults with esophageal cancer and examine how factors such as prognosis, quality of life, and frailty impact

Table 3
Temporal trends in chemotherapy regimen received amongst study population individuals treated with either definitive chemoradiation or trimodal therapy, SEER-Medicare 2004–2017.

Treatment group	Age-standardized percentage in 2004 (95% CI)	Age-standardized percentage in 2017 (95% CI)	Segment	Annual percent change during segment, %	Average annual percent change across all segments, 2004–2017
Adenocarcinomas					
Carboplatin-based regimens	47.0 (33.2–60.8)	85.3 (80.1–90.3)	2004–2008 2008–2014 2014–2017	−7.4 (−28.0–18.9) 17.8 (7.1–29.7) −1.1 (−8.0–6.3)	5.1 (−2.3–13.0)
Cisplatin-based regimens	36.1 (23.0–49.2)	4.9 (1.8–8.0)	2004–2009 2009–2017	8.0 (−10.5–30.3) −31.0 (−38.4 to −22.6)	−18.0 (−24.9 to −10.5)
Other chemotherapy regimens	16.9 (6.9–26.9)	9.8 (5.5–14.1)	2004–2017	−5.3 (−8.9 to −1.6)	−5.3 (−8.9 to −1.6)
Squamous cell carcinomas					
Carboplatin-based regimens	37.3 (16.3–58.3)	78.3 (69.5–87.2)	2004–2017	6.9 (3.3–10.6)	6.9 (3.3–10.6)
Cisplatin-based regimens	51.3 (29.7–72.9)	10.8 (4.3–17.4)	2004–2009 2009–2017	5.0 (−9.8–22.2) −23.7 (−30.3 to −16.4)	−13.7 (−19.6 to −7.5)
Other chemotherapy regimens	11.4 (2.3–20.5)	10.8 (4.3–17.4)	2004–2017	−4.5 (−9.4–0.6)	−4.5 (−9.4–0.6)

Abbreviations: CI, confidence interval.

treatment selection.

In conclusion, the treatment of older adults with locally advanced esophageal cancer has evolved over time. The percentage of individuals receiving definitive chemoradiation and trimodal therapy have both increased since 2004. The larger increase has been in definitive chemoradiation, which remains the dominant form of treatment for older adults in practice.

Ethics Approval and Consent to Participate

This study of secondary data was approved by the University of North Carolina at Chapel Hill Institutional Review Board (21–1217).

Consent for Publication

All authors consent to publication.

Availability of Data and Materials

The SEER-Medicare data can be obtained through an application and data use agreement with the National Cancer Institute.

Author Contributions

Study conception and design (CEG, NJS, RSS, JKE, HBN, HKS, JLL); data collection (CEG, JLL); analysis and interpretation of data (CEG, NJS, RSS, JKE, HBN, HKS, JLL); wrote or critically revised paper (CEG, NJS, RSS, JKE, HBN, HKS, JLL).

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Declaration of Competing Interest

Dr. Lund's spouse was employed by GlaxoSmithKline (within the last 12 months) and owned stock in the company (within the last 12 months). In addition, Dr. Lund receives research support to UNC from AbbVie and F. Hoffmann-La Roche AG.

Appendix A. Supplementary Data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jgo.2022.08.009.

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