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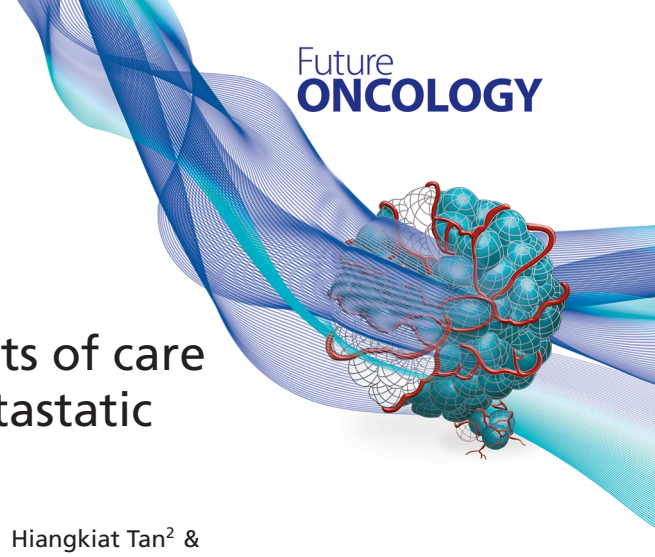

Healthcare utilization and total costs of care among patients with advanced metastatic gastric and esophageal cancer

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Aim: Study first-line (1L) treatment patterns and economic outcomes among patients with advanced metastatic gastric cancer (GC) and esophageal cancer (EC). **Materials & methods:** Newly diagnosed patients with systemic GC and EC treatments were identified between 1 January 2011 and 31 July 2017; costs were presented as per patient per month (PPPM) basis. **Results:** Study included 392 GC and 436 EC patients. Most frequently used 1L regimens were: 5-fluorouracil (5-FU) + oxaliplatin (22.5%) and epirubicin + cisplatin + 5-FU (ECF)/ECF modifications (21.9%) in patients with GC; and carboplatin + paclitaxel (29.6%) and 5-FU + oxaliplatin (11.5%) in EC patients. Mean all-cause costs were US$16,242 PPPM for GC, and $18,384 PPPM for EC during 1L treatment. **Conclusion:** GC and EC were resource intensive and costly. High costs and short treatment durations underscored a gap in care in 1L treatment.

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Keywords: esophageal cancer • first-line systemic treatment • gastric cancer • second-line systemic treatment • treatment pattern

Surgery is considered as the best curative option for medically fit patients when gastric cancer (GC) and esophageal cancer (EC) are detected early. However, unresectable locally recurrent, advanced or metastatic (adv/met) GC/EC are associated with poor clinical outcomes and substantial economic burden [1–4] and in the USA, systemic therapy is typically prescribed [5–9].

National Comprehensive Cancer Network (NCCN) guidelines recommend first-line (1L) systemic treatment for adv/met GC/EC, which includes a platinum-based chemotherapeutic agent (oxaliplatin [OXA] or cisplatin [CIS]) plus a fluoropyrimidine such as 5-fluorouracil (5-FU) or its oral prodrug capecitabine [4,10]. Despite treatment, adv/met GC/EC progress over time, and prognosis is poor for most later-stage patients [11]. Options for managing disease progression expanded in 2014 when updated NCCN guidelines included preferential use of ramucirumab in combination with paclitaxel (PAC) into the existing recommendations for single-agent treatments such as PAC, docetaxel, and irinotecan [12].

Existing adv/met GC/EC treatments had been associated with low patient adherence, high discontinuation rates, poor survival rates and high costs [1,2,10,13,14]. Casamayor *et al.* reported mean annual costs of $46,501 for patients with adv/met GC between 1998 and 2003 [1]. Hess *et al.*, using a combination of electronic medical records and claims data, showed that the mean total cost of care was $40,811 for individuals receiving 1L therapy for adv/met GC [2]. In a case–control study, Knopf *et al.* reported mean monthly costs of $10,653 for patients with adv/met GC [15].

Unfortunately, the few real-world studies available in the literature, are either specific to the US Medicare population or are too dated to reflect the most recent, evolving treatment regimens and guideline recommendations [2,3,15,16]. This study aimed to understand current real-world treatment patterns, healthcare resource utilization (HCRU) and costs for 1L systemic therapy among patients with adv/met GC/EC.

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Materials & methods

Study design & data source

This retrospective cohort study utilized medical and pharmacy claims from the HealthCore Integrated Research Database (HIRD®), a large, geographically-dispersed US-based administrative claims repository, to identify separate cohorts of patients with diagnoses of GC (ICD-9-CM: 151.x; ICD-10-CM: C16.%) or EC (ICD-9-CM: 150.x; ICD-10-CM: C15.%) for which systemic therapy was required between 10 January 2011 and 31 July 2017. The index date was defined as the first observed medical or pharmacy claim for systemic treatment during the intake period, 01 January 2012–30 June 2017. The baseline period was the 3-months prior to the index date. The follow-up period was from the index date to the first of health plan disenrollment, death or the end of the study period. This observational study was exempt from informed consent requirements, as researchers accessed a limited dataset devoid of individual enrollee identifiers and only reported summary statistics. The study complied with applicable provisions of the Health Insurance Portability and Accountability Act.

Study population

Inclusion/exclusion criteria

To be included in the study, patients in both cohorts were required to have ≥1 medical or pharmacy claim(s) for systemic therapy of adv/met GC/EC from 01 January 2012 through 30 June 2017. Patients aged 18 years and older as of the index date, and who had at least 3-months pre-index continuous medical and pharmacy coverage, at least 1 month of postindex continuous medical and pharmacy coverage were included. Excluded from the study were patients with a diagnosis of gastrointestinal stromal tumor during the 3-year period prior to the index date (excluding index date), as well as those receiving gastrointestinal stromal tumor-related systemic therapy (e.g., imatinib) during the study period. Patients who had prior systemic cancer therapy or gastrectomy, esophagostomy or a pregnancy in the 3-month period before the index date were excluded. Also excluded were patients with two or more diagnoses of the same cancer type, apart from GC and EC, on different service dates during the study period.

Study measures

This study examined demographic characteristics (at index date) including age, gender, health plan type, indicator for Medicare Advantage coverage and geographic region of patients' residence. Clinical characteristics assessed at baseline included location of the primary tumor, diagnosis of metastasis and time from the first diagnosis to index date. Treatment pattern assessments included duration of therapy and the top five most frequent systemic treatment regimens during 1L of therapy. The initial therapy received after the first evidence of adv/met GC/EC diagnosis was defined as the 1L of therapy. The end of a line of therapy was defined as complete discontinuation of the systemic regimen for >45 days or addition to the systemic regimen of a new drug, excluding the addition of biologic or targeted agent. Initiation of the next line of therapy was defined as the start date of the revised systemic regimen. NCCN Clinical Practice Guidelines was used to define the guideline-based therapy [4,10]. All-cause HCRU was measured during the follow-up periods. Cancer-related HCRU was defined for any medical encounter associated with diagnosis codes for GC/EC, and any chemotherapy/immunotherapy-related outpatient pharmacy dispensing.

All-cause & cancer-related healthcare costs

During the follow-up periods, all-cause and cancer-related costs for the HCRU encounters were reported and calculated on per patient per month (PPPM) basis with categorization as medical (all places of service combined: inpatient visits, emergency department visits and outpatient services), outpatient pharmacy and total costs. Costs represented the sum of plan paid, patient paid and third party paid amounts. Cancer-related HCRU during follow-up were based on medical encounters associated with the diagnosis codes for GC or EC, and chemotherapy and immunotherapy-related outpatient pharmacy dispensing. All costs were adjusted for inflation to 2017 US dollars using the medical care Consumer Price Index provided by the US Department of Labor, Bureau of Labor Statistics [17].

Statistical analyses

Descriptive statistics, including means (standard deviation [SD]) and absolute/relative frequencies for continuous and categorical data, respectively, were reported. Given the descriptive nature of the study, no hypothesis testing was performed. Kaplan–Meier analysis was used to estimate the median duration of 1L treatment. Statistical analyses were performed using SAS Enterprise Guide 7.1 (SAS Institute, Inc., NC, USA).

Table 1. Patient identification table.

Steps	Criteria	GC	EC
1	Patients with either ≥1 medical claim(s) of gastric cancer only (GC cohort), esophageal cancer (EC cohort) only	8932	6225
2	Patients with ≥1 medical or pharmacy claims of systemic cancer therapy during intake period; earliest fill of advanced chemotherapy agent was assigned as an index date	2983	1888
3	Patients ≥18 years and older as of index date and with at least 3 months pre-index continuous medical and pharmacy coverage	2591	1654
4	Patients without ≥2 medical claims of same cancer type on different service dates during 3-year prior to index date	850	611
5	Patients with no claim for GIST during 3-year prior to index date and no claim for GIST-related systematic therapy (rituximab/imatinib) during study period	697	601
6	Patients with no claim for chemotherapy 3-month prior to index date (excluding index date)	631	544
7	Patients with at least 1 month of postindex eligibility or until death	620	520
8	Patients with no medical claim for pregnancy/gastrectomy/esophagostomy during 3-month prior to index date (adjuvant chemotherapy)	503	517
9	Patients without ≥2 medical claims of same cancer type diagnosis codes other than GC or EC on different dates on/during postindex period	392	436

EC: Esophageal cancer; GC: Gastric cancer; GIST: Gastrointestinal stromal tumor.

Results

Patient selection

Two separate cohorts of patients with adv/met GC (n = 392) and adv/met EC (n = 436) were identified and included in the analysis Table 1.

Baseline patient demographic & clinical characteristics

Adv/met GC

The mean (SD) age of patients with adv/met GC was 62.4 years (12.92); 61.0% were men Table 2. About a third (32.9%) of patients were with Medicare Advantage, and 57.9% had Preferred Provider Organization health plan type. The three most common sites of GC primary tumor location were pyloric antrum (11%), body of stomach (11%) and gastroesophageal junction cancer (part of GC)/cardia (9.7%).

Adv/met EC

The mean (SD) age of patients with adv/met EC was 65.2 years (10.53); 77.1% were men; more than a third had Medicare Advantage health plans (38.5%) and more than a half were covered under Preferred Provider Organization plans (62.2%). The majority resided in the Midwest (38.8%) and South (28.7%) US regions. The primary location of the tumor in 25.5% of the patients with adv/met EC was the lower third of the esophagus.

Treatment patterns

Adv/met GC

The mean (SD) treatment duration of 1L therapy was 3.8 (2.64) months Table 3. Overall, 17.6% of the patients died after 1L treatment, without starting second-line (2L) therapy. About 41.6% of patients started 2L treatment during the available follow-up period, after their 1L regimens. The most frequently used adv/met GC regimens were 5-FU + OXA (22.5%), epirubicin + CIS + FU/epirubicin + CIS + FU modifications (21.9%), and trastuzumab containing therapies (8.4%) during 1L therapy (Epirubicin (EPI) + cisplatin (CIS) + fluorouracil (FU)/EPI + CIS + FU modifications included the following regimens: EPI + CIS + 5-FU, EPI + oxaliplatin (OXA) + 5-FU, EPI + CIS + capecitabine (CAP), EPI + OXA + CAP, CAP + EPI + 5-FU + OXA).

Adv/met EC

The mean (SD) treatment duration of 1L therapy in the adv/met EC cohort was 3.0 (1.97) months. A fifth (20.6%) of the patients died after 1L treatment, prior to possibility of 2L therapy initiation. About a quarter (25.5%) of patients started 2L therapy in the available follow-up period after 1L discontinuation. The most frequently used adv/met EC regimens were carboplatin + PAC (29.6%), 5-FU + OXA (11.5%) and trastuzumab containing therapies (7.6%) during 1L therapy.

Table 2. Baseline patient characteristics.

Characteristics	Adv/met GC	
	n (%)/mean (SD)	n (%)/mean (SD)
Patients, n (%)	392 (100)	436 (100)
Age at index date, years (mean, SD)	62.4 (12.92)	65.2 (10.53)
Age group, years (%)		
– 18–49	63 (16.1)	25 (5.7)
– 50–64	163 (41.6)	197 (45.2)
– 65–74	166 (42.3)	214 (49.1)
Gender, n (%)		
– Male	239 (61.0)	336 (77.1)
Baseline patient characteristics		
Site of cancer–primary cancer location		
– Gastroesophageal junction cancer (part of gastric cancer)/cardia	38 (9.7)	–
– Pyloric antrum	43 (11.0)	–
– Body of stomach	43 (11.0)	–
– Lower third of esophagus	–	111 (25.5)
– Esophagus, unspecified	–	230 (52.8)
Geographic region, n (%)		
– Northeast	80 (20.4)	71 (16.3)
– South	110 (28.1)	125 (28.7)
– Midwest	102 (26.0)	169 (38.8)
– West	100 (25.5)	71 (16.3)
Health plan type at index date, n (%)		
– HMO	117 (29.8)	115 (26.4)
– PPO	227 (57.9)	271 (62.2)
– CDHP	46 (11.7)	50 (11.5)
– Others	2 (0.5)	0 (0.0)
Medicare advantage n, (%)	129 (32.9)	168 (38.5)
Deyo–Charlson comorbidity index score, (mean, SD, median)	6.6 (3.21)	6.2 (3.40)

adv/met: Advanced or metastatic; CDHP: Consumer driven health plans; EC: Esophageal cancer; GC: Gastric cancer; HMO: Health Maintenance Organization; PPO: Preferred Provider Organization; SD: standard deviation.

Table 3. Summary of first-line treatment.

Adv/met GC (n = 3920)		Adv/met EC (n = 436)	
Duration of therapy, mean (SD), (months)	3.8 (2.64)	**Duration of therapy, mean (SD), months**	3.0 (1.97)
Regimen classes in 1L	**n (%)**	**Regimen classes in 1L**	**n (%)**
– 5-FU + OXA	88 (22.5)	CARB + PAC	129 (29.6)
– ECF/ECF modifications†	86 (21.9)	5-FU + OXA	50 (11.5)
– TRA containing regimen	33 (8.4)	TRA containing regimen	33 (7.6)
– DCF/DCF modification‡	18 (4.6)	CIS + 5-FU	25 (5.7)
– CARB + PAC	17 (4.3)	ECF/ECF modifications†	14 (3.2)

†ECF modifications include the following regimens: EPI + CIS + 5-FU, EPI + OXA + 5-FU, EPI + CIS + CAP, EPI + OXA + CAP, CAP + EPI + 5-FU + OXA.
‡DCF modifications include the following regimens: DOC + CIS + 5-FU, DOC + OXA + 5-FU, DOC + CARB + 5-FU, CARB + CIS + DOC + 5-FU, CARB + DOC + 5-FU + OXA.
1L: First line; 5-FU: 5-Fluorouracil; adv/met: Advanced or metastatic; CAP: Capecitabine; CARB: Carboplatin; CIS: Cisplatin; DOC: Docetaxel; DCF: Docetaxel + cisplatin + 5-fluorouracil; EC: Esophageal cancer; ECF: Epirubicin + CIS + FU; EPI: Epirubicin; GC: Gastric cancer; OXA: Oxaliplatin; PAC: Paclitaxel; SD: Standard deviation; TRA: Trastuzumab.

Healthcare utilization & costs in the follow-up period

Adv/met GC

Overall, about 68.9 and 64.8% of adv/met GC patients had at least one all-cause and cancer-related hospitalization, respectively, during the entire follow-up period (average of 12.4 months) Table 4. The average lengths of stay were from 14.3 to 14.4 days. About 39.5 and 22.7% of adv/met GC patients had at least one all-cause and cancer-related

Table 4. All-cause healthcare resource utilization during follow-up for advanced or metastatic gastric cancer and esophageal cancer patients.

Characteristics	Adv/met GC total n (%)/mean (SD)	Adv/met EC total n (%)/mean (SD)	Adv/met GC 1L n (%)/mean (SD)	Adv/met EC 1L n (%)/mean (SD)
Sample size (n)	392	436	392	436
Duration of follow-up (months)	12.4 (13.19)	9.8 (10.62)	3.8 (2.64)	3.0 (1.97)
All-cause healthcare utilization				
– Hospitalizations (n ≥1, %)	270 (68.9%)	277 (63.5%)	181 (46.2%)	175 (40.1%)
– Hospitalizations per patient with ≥1 hospitalization, n (mean, SD)	2.3 (1.73)	2.0 (1.50)	1.6 (0.90)	1.5 (0.86)
– Length of stay per patient with ≥1 hospitalization (mean, SD)	14.4 (13.94)	15.1 (16.61)	8.6 (7.23)	7.0 (7.03)
– 30-day readmission, n (%)	115 (29.3%)	100 (22.9%)	63 (16.1%)	52 (11.9%)
– ER visits, n (%)	155 (39.5%)	168 (38.5%)	99 (25.3%)	88 (20.2%)
– ER per patient, n (mean, SD)	0.70 (1.25)	0.75 (1.58)	0.33 (0.63)	0.28 (0.66)
– Physician office visits, n (%)	383 (97.7%)	432 (99.1%)	382 (97.4%)	429 (98.4%)
– Pharmacy prescriptions, n (%)	355 (90.6%)	386 (88.5%)	355 (90.6%)	380 (87.2%)
– Fills per patient, n (mean, SD)	24.5 (31.88)	21.0 (27.27)	9.7 (9.61)	8.3 (9.35)
Cancer-related healthcare utilization				
– Inpatient admissions, n (%)	254 (64.8%)	262 (60.1%)	173 (44.1%)	166 (38.1%)
– Hospitalizations per patient with ≥1 hospitalization, n (mean, SD)	2.2 (1.59)	2.0 (1.44)	1.5 (0.88)	1.4 (0.82)
– Length of stay per patient with ≥1 hospitalization (mean, SD)	14.3 (13.51)	15.5 (16.87)	8.7 (7.31)	7.1 (7.06)
– 30-day readmission, n (%)	101 (25.8%)	93 (21.3%)	55 (14.0%)	47 (10.8%)
– ER visits (number of patients, %)	89 (22.7%)	111 (25.5%)	63 (16.1%)	66 (15.1%)
– ER visits per patient ≥1 ER visit, n (mean, SD)	1.6 (1.12)	1.5 (1.33)	1.2 (0.45)	1.2 (0.57)
– Physician office visits, n (%)	357 (91.1%)	422 (96.8%)	350 (89.3%)	416 (95.4%)
– Systemic therapy pharmacy prescriptions, n (%)	126 (32.1%)	52 (11.9%)	114 (29.1%)	36 (8.3%)

1L: First line; adv/met: Advanced or metastatic; EC: Esophageal cancer; ER: Emergency room; GC: Gastric cancer; SD: Standard deviation.

emergency room (ER) visits during the entire follow-up time, correspondingly. While receiving 1L therapy, 46.2% of the adv/met GC cohort had inpatient hospitalizations. The average length of all-cause stay was 8.6 days, and cancer-related inpatient stay was 8.6 days, and 16.1% of patients with adv/met GC had a 30-day readmission. During 1L, 25.3 and 16.1% of the patients had all-cause and cancer-related ER visits, respectively. While the mean total all-cause healthcare costs were $9717 during the entire follow-up, the mean total all-cause healthcare costs during 1L were $16,242 PPPM. The mean systemic therapy-related costs were $6738 PPPM in 1L Table 5.

Adv/met EC

Overall, about 63.5% and 60.1% of adv/met EC patients had at least one all-cause and cancer-related hospitalization, respectively, during the entire follow-up period (average of 9.8 months). The average lengths of stay were from 15.1 to 15.5 days. About 38.5 and 25.5% of adv/met EC patients had at least one all-cause and cancer-related ER visits during the entire follow-up time, correspondingly. About 40.1% of the adv/met EC cohort had all-cause inpatient services while on 1L treatment. The average length of all-cause and cancer-related inpatient stay was 7.04 and 7.06 days, respectively. Overall, 11.9% of patients with adv/met EC had a 30-day readmission while receiving 1L therapy. During 1L therapy, 20.2 and 15.1% of the patients had all-cause and cancer-related ER visits, respectively. The mean total all-cause healthcare cost at follow-up was $11,433 PPPM. The total all-cause healthcare costs PPPM were $18,384 during 1L treatment. The mean systemic therapy-related costs were $2589 PPPM.

Discussion

This study examined treatment patterns, HCRU and cost outcomes for 1L systemic treatment of patients with adv/met GC/EC. A large majority (80%) of the patients with adv/met GC received NCCN guideline-based therapy. In the adv/met EC cohort, 70% of the patients received guideline-based 1L treatment.

Table 5. Per patient per month healthcare costs during follow-up for advanced or metastatic gastric cancer and esophageal cancer patients.

Characteristics	Adv/met GC total mean (SD)	Adv/met EC total mean (SD)	Adv/met GC 1L* mean (SD)	Adv/met EC 1L* mean (SD)
Sample size (n)	392	436	392	436
All-cause healthcare costs				
– Inpatient admissions	$3482 ($8004)	$3948 ($11,836)	$4884 ($12,942)	$3313 ($10,076)
Emergency room visits	$142 ($497)	$175 ($612)	$243 ($910)	$207 ($1006)
– Outpatient services	$5559 ($6235)	$6902 ($8399)	$10,027 ($8609)	$14,248 ($14,357)
– Physician office visits	$202 ($158)	$213 ($171)	$313 ($212)	$335 ($230)
– Other outpatient services	$5358 ($6158)	$6689 ($8319)	$9714 ($8558)	$13,913 ($14,285)
– Physician other services	$40 ($78)	$41 ($98)	$62 ($162)	$54 ($137)
– Procedures	$562 ($860)	$1545 ($2904)	$764 ($1629)	$3512 ($7058)
– Imaging	$598 ($709)	$806 ($1017)	$855 ($1001)	$1344 ($2227)
– Tests – lab	$211 ($570)	$160 ($291)	$362 ($936)	$260 ($464)
– Tests – other	$11 ($24)	$20 ($53)	$14 ($45)	$28 ($136)
– Durable medical equipment	$66 ($166)	$84 ($249)	$107 ($242)	$89 ($183)
– Medication and related services	$3118 ($4665)	$2701 ($4749)	$6612 ($7280)	$5972 ($7416)
– Other	$731 ($2599)	$1304 ($3583)	$919 ($3882)	$2627 ($6890)
– PT/OT/speech	$19 ($64)	$29 ($104)	$18 ($70)	$26 ($122)
– Pharmacy prescriptions	$534 ($858)	$407 ($840)	$1088 ($1690)	$616 ($1214)
– Total medical costs	$9183 ($11,490)	$11,026 ($15,153)	$15,154 ($16,663)	$17,768 ($18,089)
– Total costs (sum of medical and pharmacy cost)	$9717 ($11,640)	$11,433 ($15,283)	$16,242 ($16,718)	$18,384 ($18,195)
Systemic therapy and related services				
– Total medical costs related to systematic therapy	$2905 ($4701)	$2488 ($5171)	$6021 ($7321)	$5152 ($7740)
– Total pharmacy cost related to prescription of systematic therapy	$267 ($725)	$101 ($429)	$717 ($1540)	$191 ($692)
– Total costs related to systematic therapy	$3172 ($4774)	$2589 ($5216)	$6738 ($7332)	$5343 ($7787)
Cancer-related healthcare costs				
– Total medical costs	$8038 ($11,254)	$9868 ($14,884)	$13,465 ($16,648)	$16,313 ($17,713)
– Total costs (sum of medical and pharmacy cost)	$8305 ($11,315)	$9969 ($14,916)	$14,182 ($16, 619)	$16,504 ($17,730)

1L: First line; adv/met: Advanced or metastatic; EC: Esophageal cancer; GC: Gastric cancer; OT: Occupational therapy; PT: Physical therapy; SD: Standard deviation.

While the majority of the patients in both adv/met GC and adv/met EC cohorts initiated NCCN guideline-based 1L treatment, the median duration of 1L therapy was only 3.5 and 2.7 months for patients with adv/met GC and adv/met EC, respectively. The data do not provide reasons for 1L treatment discontinuation, which might include physician decision or patient preference, treatment failure, inability to tolerate further treatment because of comorbid conditions or declining performance status, or death [18,19].

In our study, 17.6% of the patients with adv/met GC died after 1L therapy and only 41.6% initiated 2L treatment. Whereas for patients with adv/met EC, 20.6% died after 1L therapy and only 25.5% initiated 2L treatment. Progression to 2L therapy in our study was lower than in the Barzi *et al.* study, which reported that 59–62% of adv/met GC/EC patients received 2L [19], somewhat lower than the approximately 50% progression to 2L therapy found in other recent observational studies, [2,3,19,20] but higher than historic studies that reported approximately 20% of patients progressing to 2L therapy [21,22].

Across both cohorts, patients required a range of healthcare services. The total costs were mainly driven by outpatient services (over 50%), followed by inpatient admissions (over 33%). The trends were consistent across both cohorts. The costs in these treatment settings were also identified as the main drivers by Hess *et al.*, whose study specifically identified chemotherapy infusion in the hospital setting, inpatient costs and chemotherapy in nonhospital settings as high-cost drivers. During 1L, almost a half of the patients with adv/met GC needed inpatient hospitalization, with stays exceeding a week (average 8.6 days), and about one patient in five had a 30-day readmission. A study with patients with GC on 1L treatment by Hess *et al.* reported a lower hospitalization rate of 13.4%, but the study included a considerable subset of non-metastatic patients with GC [2]. Our results showed that about one in six patients with adv/met GC cancer had cancer-related ER visits during 1L, and that more than

a half of the study patients had outpatient visits. These observations were consistent with findings of the Hess *et al.* study [2].

Similarly, a substantial proportion (40.1%) of the adv/met EC cohort received cancer-related inpatient services while on 1L treatment, with stays averaging 7 days. Consistent with data from prior studies, [14,23] substantial proportions of patients with adv/met EC required ER visits (20.2%) and pharmacy services (87.2%), while all received outpatient care (100.0%) during their 1L treatment periods.

The PPPM healthcare costs were higher during 1L therapy than those during the entire follow-up period for both adv/met GC and EC patients. The trends were consistent across all settings, including inpatient, ER, outpatient, pharmacy, etc. This could be driven by multiple factors, such as poor response to treatment, initial frequent visits/tests, active treatment, prolonged prognosis, high costs incurred before the end of life (nearly one-fifth of patients died after 1L treatment). The actual causes could not be determined due to the limitations of data source. Nonetheless, the high economic burden during the 1L therapy appeared to be significant.

The findings of this study provide novel data and insights, to bolster the current, limited body of knowledge on treatment patterns, HCRU and costs for patients with adv/met GC or adv/met EC receiving guideline-based 1L systemic therapy [1,2,14,15]. Compared with the estimated mean annual costs of $141,345–169,862 for elderly patients with adv/met GC (age >65) [1], our study's estimated costs would appear lower ($9717 PPPM), noting the difference in per unit estimation between annual and monthly costs. This could be driven by the predominance of the relatively younger managed care population in our data source, and hence, the overall study cohort. We found that systemic therapy-related costs alone during 1L treatment of patients with adv/met GC were $6738 PPPM. Similarly, high costs were reported in a study by Hess *et al.*, with mean total cost of care of $40,811 during 1L therapy for patients with adv/met GC for an average duration of 53.5 days [2]. A case–control study by Knopf *et al.* reported mean monthly costs of $10,653 for patients with adv/met GC, three-quarters of whom required inpatient care [15].

This study offers an important addition to the relatively small body of data on HCRU and costs of 1L therapy for adv/met GC and adv/met EC in the US. With the expectation that about 28,000 patients with adv/met GC and 18,000 patients with adv/met EC would be diagnosed in 2019 [13], this study provides insights of value to a range of decisions on the allocation of resources and management of patients with adv/met GC and adv/met EC in the US.

In addition, the cancer-related costs accounted for about 86 and 87% of the all-cause healthcare costs among patients with adv/met GC and adv/met EC, respectively. This was also supported by low Deyo–Charlson comorbidity index (DCI) scores, an indicator of comorbidity burden. Given patients with metastatic solid tumor would have a minimum DCI score of 6 by definition, the observed means DCI of 6.6 and 6.2 (for adv/met GC and adv/met EC patients, respectively, Table 2) indicated that the study population in general did not have many other severe comorbidities. Or more importantly, cancer care was the dominant focus for these adv/met GC and EC patients.

Limitations

Notable limitations in this study include the inherent shortcomings of administrative claims data, the primary data source, which were repurposed to understand treatment patterns. Cancer stage may have been misclassified for some patients in the analysis, because stage information is not available in ICD-9 and ICD-10 diagnoses requiring application of data interpretation and assumptions in an effort to include only patients with adv/met GC/EC, using the most relevant advanced treatment and metastasis diagnosis codes. Also, histology information was not available in claims. Therefore, stratification of outcomes by histology types was not feasible. The lines of therapy were approximated using administrative data with observed treatment continuity/gap, the actual treatment lines and reasons of discontinuation and change of therapy were not available to confirm. The study sample was identified from claims in one large US administrative claims database and consisted of patients with commercial and Medicare Advantage health insurance plans. As a result, these results might not be generalizable to patients covered by other plan types or to populations that were underinsured or uninsured.

Conclusion

The complex disease progression of GC and EC require detailed management and interventions in a variety of service settings, including inpatient and outpatient care and pharmacy services. This study demonstrated that these conditions were both resource and cost intensive. While treatment approaches in this study population were shown

to align with NCCN guidelines, the durations of 1L treatment were short. These findings suggested a possible unmet need for more effective treatments in 1L, in order to help mitigate the resource use and economic burden in the management of adv/met GC/EC. Additional research would help to improve the base of information required for key patient management decisions.

Summary points

- The complex disease progression of gastric cancer and esophageal cancer require detailed management and interventions in a variety of service settings, including inpatient and outpatient care and pharmacy services.
- This study demonstrated that these conditions were both resource and cost intensive.
- While treatment approaches in this study population were shown to align with National Comprehensive Cancer Network guidelines, the durations of first-line treatment were short.
- These findings suggested a possible unmet need for more effective treatments in first line, in order to help mitigate the resource use and economic burden in the management of adv/met gastric cancer/esophageal cancer.
- Additional research would help to improve the base of information required for key patient management decisions.

Author contributions

P Abraham, J Gricar and R Kelly were responsible for study conception and design. L Wang, Z Jiang and H Tan were responsible for acquisition of data and analysis. All authors were responsible for interpretation of data/results and drafting and revision of the manuscript.

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Ethical conduct of research

This observational study was conducted under the research exception provisions of the Privacy Rule, 45 CFR 164.514(e), and was exempted from Investigational Review Board (IRB) informed consent requirements.

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