Clinical Epidemiology

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ORIGINAL RESEARCH

Esophageal and Gastric Cancer Incidence and Mortality Trends in Norway, 1993–2022: A Registry-Based Study

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Introduction: Esophageal and gastric cancers account for nearly 1.5 million new cases and 1.1 million deaths annually worldwide. In western countries, the incidence of esophageal cancer is rising while that of gastric cancer has decreased, although the pattern varies between the morphological types and subsites. We aim to describe the burden of esophageal and gastric cancers in Norway by providing national trends in incidence and mortality, separately for esophageal squamous cell carcinoma (SCC) and adenocarcinoma (AC), and for gastric ACs by gastric subsites.

Methods: We extracted information about all esophageal (ICD10 C15) and gastric cancer (ICD10 C16) patients diagnosed 1993–2022 from the Cancer Registry of Norway. Age-standardized (European standard population) rates and performed joinpoint regression analyses were calculated to examine trends in incidence and mortality over time, for esophageal cancer SCC and AC and by subsite for gastric AC (cardia: ICD10 C16.0 and non-cardia: ICD10 C16.1–9). We used annual percent change (APC) and weighted average APC (AAPC), stratified by sex, age group, and stage at diagnosis.

Results: During 1993–2022, 6,433 esophageal cancers (2,616 SCC, 3,817 AC) and 14,453 gastric AC were diagnosed, and 4,683 esophageal and 10,421 gastric AC deaths occurred. The incidence and mortality of esophageal ACs increased whereas the rates for esophageal SCC declined in men and were stable in women. The highest AC incidence and mortality increases were seen in men (incidence AAPC = 2.8) and ages ≥70 years (incidence AAPC = 5.9). In contrast, the incidence and mortality of gastric cancer decreased over time, most pronounced for non-cardia gastric AC (incidence AAPC men =−5.3, women =−3.9).

Conclusion: The incidence and mortality of esophageal AC has increased in Norway during the last decades, most pronounced in men, ages ≥70 years. The rates of SCCs decreased, although trends differed between sex and age groups. The incidence and mortality of gastric AC decreased in all age-groups for both sexes, especially for non-cardia gastric cancer.

Plain Language Summary: Over recent decades, the incidence of esophageal adenocarcinoma has increased in North America and parts of Europe, while in other regions, including East Asia, the trend varies by subtype and country. In this study, we observed that the incidence and mortality rates of esophageal ACs have risen in Norway over the last two decades, particularly among elderly men, while for esophageal SCCs the incidence and mortality rates have decreased. Also the rates for gastric (AC) cancer have decreased across age-groups and sex, especially for non-cardia gastric cancer. Our trend analysis contributes as a valuable reference to guide clinical awareness, and surveillance strategies in similar high-risk populations.

Keywords: esophageal, gastric, cancer incidence, cancer mortality, registry data, nationwide

Received: 30 October 2024
Accepted: 10 September 2025
Published: 7 November 2025

Introduction

Worldwide, esophageal cancer ranks 11th and gastric cancer ranks 5th in terms of incidence.[1] The diagnosis of these cancers occurs primarily in advanced stages, resulting in poor survival.[2,3] Gastric and esophageal cancers are the 7th and 5th leading neoplasms respectively in terms of mortality.[1] In Norway, however, these are rare cancers with age-standardized incidence rates of three per 100,000 for esophageal cancer and 42.2 per 100,000 for gastric cancer.[1,4]

The two main morphological types of esophageal cancer include adenocarcinoma (AC) and squamous cell carcinoma (SCC).[5] In Europe and North America, the incidence of esophageal cancer overall has been low, however over the last decades observations have shown an increasing incidence for AC, whereas for the SCC the incidence has decreased.[6,7] Esophageal AC typically arises in the distal third of the esophagus and is strongly associated with chronic gastro-esophageal reflux and Barrett's esophagus, while SCC more commonly affects the mid to upper esophagus and is linked to alcohol and tobacco use.[8–10]

In most populations worldwide, the incidence of gastric cancer has shown decreasing trends due to the declining prevalence of *Helicobacter pylori* infection.[11] However, other risk factors also include dietary exposures (eg, high-salt, high-nitrogen diets), family history, genetic predisposition, and smoking.[12] AC comprises 95% of all gastric cancer and is frequently subdivided into two main subsites, cardia and non-cardia.[13,14]

Men are at higher risk for both esophageal and gastric cancers compared to women.[15] In many developed countries, there has been an increasing trend in esophageal AC, with a male-to-female ratio of up to 9:1.[15,16] A better understanding of recent trends in incidence and mortality, stratified by cancer subtype, can highlight the contribution of modifiable risk factors and help guide prevention, early detection, and surveillance efforts.[16] Our aim was to report the Norwegian trends in incidence and mortality for esophageal SCC and AC, and for cardia and non-cardia gastric ACs during the period 1993–2022, stratified by sex, age, and stage of disease.

Methods

Study Design and Data

The Cancer Registry of Norway (CRN) has since 1953 registered all malignancies in Norway (except basal cell carcinoma of the skin), according to the International Classification system for Diseases (ICD), using revision 10 since 1996,[17] and then using the ICD for Oncology (ICD-O) version 3 since 2007.[18] Mandatory reporting from several independent sources ensures complete and high-quality data.[4] The CRN is regularly linked to the Norwegian Cause of Death Registry and the Central Population Registry about underlying causes of death and the vital status (death or emigrated) with dates, respectively.[4] Data on esophageal SCC and AC and cardia and non-cardia ACs were obtained from the Cancer Registry of Norway (CRN) for the years1993–2022. Although the CRN has data available since 1953, complete and consistent subtype and subsite classification data were available from 1993 only. Annual counts of all first primary esophageal (ICD-10 C15) SCC and AC, and gastric (ICD-10 C16) AC cases were collected, along with corresponding annual death counts (Supplementary Table S1). Gastric ACs were classified by location as cardia (ICD-10 C16.0) and non-cardia (ICD-10 C16.1–C16.9). Esophageal cancers were classified into squamous cell carcinoma (SCC) and adenocarcinoma (AC) using ICD-O morphology codes (SCC: 8050–8089; AC: 8140–8576). Esophageal adenocarcinomas (ACs) arising in the lower third of the esophagus or extending from the gastroesophageal junction (GEJ) were included as esophageal ACs based on ICD-O topography (ICD-10 C15.5–C15.9) and morphology codes. Gastric cardia cancers were separately classified under C16.0. We also obtained annual numbers of esophageal cancers and gastric AC by stage at diagnosis, classified as localized stage (invasive cancer without any metastases), regional/distant stage (any infiltration into surrounding areas, regional metastases or distant metastases), and unknown stage (excluded from stage-specific analyses).[19] Year of diagnosis was grouped into 5-years intervals (1993–1997, 1998–2002, 2003–2007, 2008–2012, 2013–2017, 2018–2022). The annual population counts were obtained from Statistics Norway. We excluded cases with unknown or unspecified morphology (n = 7), benign morphology (n = 110) and gastric cancers with SCC morphology (n = 40). The study included a total of 6433 cases and 4683 deaths of esophageal cancer and 14453 cases and 10421 deaths of gastric AC cancer.

Statistical Analysis

According to our intention, we did not directly compare the cancer subsites and types, but rather present and interpret the temporal trends for each histological and anatomical subtype individually. We reported frequencies and proportions for categorical variables. The age-standardized incidence and mortality rates were calculated by dividing the annual number of cases and deaths by the annual population for Norway by sex and five-year age groups from age 20 to ≥85 years. Rates were then directly age-standardized using the European standard population.[20] In age-specific analyses, we used the two age groups 50–69 years and ≥70 years at diagnosis. We excluded <50 years from age-specific analyses due to few cases and deaths.

Our analysis involved two steps. Firstly, we examined the temporal trends for esophageal SCC and AC and non-cardia and cardia gastric ACs by sex, age and stage at diagnosis, using the lowess smoother weighted function (LOWESS) in Stata software version 18.0 (StataCorp LLC, College Station, Texas, USA), with 95% confidence intervals.[21] LOWESS smoothing curves were generated using STATA's default bandwidth of 0.8 to describe trends over time. Secondly, we analyzed the change in incidence and mortality trends as the annual percent change (APC) and the average annual percent change (AAPC). The maximum number of joinpoints was set to 6, and the optimal number was determined using the permutation test method at a significance level of a = 0.05, as implemented in Joinpoint software (version 4.5.0.1).[22]

Results

Descriptive Results: Proportions and Counts of Incidence and Mortality

During the period 1993–2022, 6,433 patients were diagnosed with esophageal cancer, of whom 2,616 were SCC, and 3,817 were AC (Table 1). Among the incident cases, 73% were men, 51.5% were aged ≥70 years, and 53.9%, and 16.6% were diagnosed in a regional/distant, and localized stage with around 29.5% unknown stage. The age-adjusted incidence rate of esophageal AC increased from 2.9/100,000 in 1993 to 10.1/100,000 in 2022 in men and from 0.3/100,000 to 1.8/100,000 in women, while the incidence rates for SCC decreased from 5.5/100,000 to 3.1/100,000 in men and from 1.9/100,000 to 1.5/100,000 in women (Table 2).

During this 30-year time-period, 4,683 deaths occurred due to esophageal cancer, whereof 73% in men, 52.8% at ages ≥70 years, and 57%, and 13.1% following a regional/distant, and localized stage diagnosis with 30% unknown stage (Table 1). The age-adjusted mortality rate of esophageal AC increased from 2.9/100,000 to 6.3/100,000 in men and from 0.4/100,000 to 1.1/100,000 in women, while the mortality rates for SCC decreased from 4.1/100,000 to 2.2/100,000 in men and from 1.2/100,000 to 0.8/100,000 in women (Table 2).

In the same time period, 14,453 patients were diagnosed with gastric AC and 10,421 died from the disease. Cardia gastric AC accounted for 24.4% of cases and 25.2% of the deaths, while non-cardia gastric AC accounted for 75.5% of cases and 74.7% of the deaths. The age-adjusted incidence rate of cardia gastric AC decreased from 6.8/100,000 in 1993 to 5.3/100,000 in 2022 in men and from 1.7/100,000 to 1.1/100,000 in women, while the rates for non-cardia gastric AC decreased from 28.2/100,000 to 5.8/100,000 in men and from 13.4/100,000 to 4.2/100,000 in women. The age-adjusted mortality rate of cardia gastric AC increased slightly, from 2.7/100,000 to 3.9/100,000 in men and from 0.6/100,000 to 0.7/100,000 in women, while the rates for non-cardia gastric AC decreased from 26.2/100,000 to 4.6/100,000 in men, and from 10.3/100,000 to 3.2/100,000 in women (Table 2). A larger proportion of gastric AC diagnosis (62%) and deaths (61.5%) were seen in men, at ages ≥70 years (63.1%, 64.1%), and after a regional/distant stage diagnosis (64.2%, 70.8%), compared to women.

Trends in Incidence and Mortality (1993–2022): Joinpoint and LOWESS Analyses

Esophageal SCC

For esophageal SCC, the age-adjusted incidence and mortality rates declined in men and were stable in women (Figure 1). The joinpoint analysis revealed a non-significant declining trend in incidence aged 50–69, while no trend was observed for those aged ≥70 years, in both sexes (Figure 2 and Table 3). The results by stage at diagnosis showed a non-significant trend of decline in incidence of localized disease, while for regional/distant

Table 1 Numbers (n) and Proportions (%) Incident Cases and Deaths for Esophageal and Gastric Cancer in Norway 1993–2022, by Sex, Morphology and Topography, and Stratified by Age and Stage at Diagnosis

			Esophageal (C15)					Gastric (AC) (C16)				
			Overall C15 N (%)	Sex		Morphology		Overall C16 N (%)	Sex		Topography	
				Men N (%)	Women N (%)	SCC N (%)	AC N (%)		Men N (%)	Women N (%)	Cardia C16.0 N (%)	Non-Cardia C16.1–9 N (%)
Incidence	**Total**		**6433 (100.0)**	**4775 (100.0)**	**1658 (100.0)**	**2616 (100.0)**	**3817 (100.0)**	**14,453 (100.0)**	**8963 (100.0)**	**5490 (100.0)**	**3540 (100.0)**	**10,913 (100.0)**
	Age	**<50 years**	318 (4.9)	257 (5.4)	61 (3.7)	122 (4.7)	196 (5.1)	792 (5.5)	423 (4.7)	369 (6.7)	234 (6.6)	558 (5.1)
		50-69 years	2799 (43.5)	2218 (46.5)	581 (35.0)	1169 (44.7)	1630 (42.7)	4541 (31.4)	3064 (34.2)	1477 (26.9)	1390 (39.3)	3151 (28.9)
		70+ years	3316 (51.5)	2300 (48.2)	1016 (61.3)	1325 (50.6)	1991 (52.2)	9120 (63.1)	5476 (61.1)	3644 (66.4)	1916 (54.1)	7204 (66.0)
	Stage	**Localized**	1065 (16.6)	727 (15.2)	338 (20.4)	449 (17.2)	616 (16.1)	2383 (16.5)	1451 (16.2)	932 (17.0)	480 (13.6)	1903 (17.4)
		Regional/Distant	3468 (53.9)	2724 (57.0)	744 (44.9)	1266 (48.4)	2202 (57.7)	9275 (64.2)	5842 (65.2)	3433 (62.5)	2338 (66.0)	6937 (63.6)
		Unknown stage	1900 (29.5)	1324 (27.7)	576 (34.7)	901 (34.4)	999 (26.2)	2795 (19.3)	1670 (18.6)	1125 (20.5)	722 (20.4)	2073 (19.0)
Mortality	**Total**		**4683 (100.0)**	**3488 (100.0)**	**1195 (100.0)**	**1976 (100.0)**	**2707 (100.0)**	**10,421 (100.0)**	**6408 (100.0)**	**4013 (100.0)**	**2632 (100.0)**	**7789 (100.0)**
	Age	**<50 years**	206 (4.4)	168 (4.8)	38 (3.2)	77 (3.9)	129 (4.8)	575 (5.5)	320 (5.0)	255 (6.4)	180 (6.8)	395 (5.1)
		50-69 years	2004 (42.8)	1614 (46.3)	390 (32.6)	874 (44.2)	1130 (41.7)	3162 (30.3)	2126 (33.2)	1036 (25.8)	1007 (38.3)	2155 (27.7)
		70+ years	2473 (52.8)	1706 (48.9)	767 (64.2)	1025 (51.9)	1448 (53.5)	6684 (64.1)	3962 (61.8)	2722 (67.8)	1445 (54.9)	5239 (67.3)
	Stage	**Localized**	613 (13.1)	405 (11.6)	208 (17.4)	313 (15.8)	300 (11.1)	970 (9.3)	576 (9.0)	394 (9.8)	225 (8.5)	745 (9.6)
		Regional/Distant	2667 (57.0)	2100 (60.2)	567 (47.4)	999 (50.6)	1668 (61.6)	7382 (70.8)	4622 (72.1)	2760 (68.8)	1858 (70.6)	5524 (70.9)
		Unknown stage	1403 (30.0)	983 (28.2)	420 (35.1)	664 (33.6)	739 (27.3)	2069 (19.9)	1210 (18.9)	859 (21.4)	549 (20.9)	1520 (19.5)

Abbreviations: SCC, Squamous cell carcinoma, AC, Adenocarcinoma.

https://doi.org/10.2147/CLEP.S503847

Table 2 Age-Standardized (European Standard Population) Incidence and Mortality Rates per 100,000 for Esophageal and Gastric Cancer in Norway 1993–2022, by Sex, Morphology and Topography

Year	Incidence								Mortality							
	Esophageal (C15)				Gastric (AC) (C16)				Esophageal (C15)				Gastric (AC) (C16)			
	SCC		AC		Cardia C16.0		Non-Cardia C16.1-9		SCC		AC		Cardia C16.0		Non-Cardia C16.1-9	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
1993	1.91	5.51	0.28	2.88	1.72	6.82	13.36	28.25	1.22	4.05	0.39	2.93	0.64	2.75	10.35	26.16
1994	2.08	2.87	0.81	2.85	1.93	6.61	14.65	26.23	1.76	4.06	0.55	2.56	1.21	4.64	11.87	23.40
1995	1.39	4.93	0.72	4.21	1.99	5.84	13.82	25.13	1.16	4.70	0.46	3.26	1.48	5.38	12.23	22.52
1996	1.57	4.73	0.23	3.10	1.71	7.56	12.64	26.49	1.27	3.76	0.37	2.52	1.61	4.85	9.82	20.80
1997	1.73	4.76	0.66	4.11	1.71	5.62	11.18	24.82	1.90	4.46	0.38	3.08	1.64	6.34	9.26	20.21
1998	2.21	4.94	0.80	4.07	1.86	6.83	11.13	21.79	1.59	4.38	0.60	3.16	1.25	5.07	8.66	17.67
1999	1.71	4.23	0.72	5.14	1.68	6.51	10.06	20.35	1.74	4.24	0.60	4.13	1.62	6.29	9.52	18.70
2000	1.74	3.80	1.28	3.85	2.17	7.40	9.66	19.48	1.12	3.28	0.97	3.77	1.04	5.33	8.16	13.92
2001	1.49	4.53	1.25	4.28	1.81	6.17	8.91	21.29	1.66	3.03	0.89	3.34	1.39	5.91	7.89	16.43
2002	1.05	4.07	1.43	4.28	1.49	5.00	10.57	18.31	1.04	3.48	0.99	3.99	1.51	4.33	7.21	13.80
2003	1.85	3.90	1.15	5.91	1.89	6.42	8.64	17.97	1.21	3.57	1.11	3.70	1.48	5.28	6.92	14.92
2004	1.32	3.60	1.53	6.80	1.55	6.34	9.26	18.01	1.27	3.00	1.19	5.46	1.13	4.57	6.96	13.34
2005	1.38	2.92	1.81	5.71	1.45	4.22	9.24	16.97	1.08	2.93	1.50	5.22	1.72	4.12	8.04	13.11
2006	1.62	4.04	0.61	5.75	1.39	5.67	8.76	14.50	1.17	3.05	0.87	4.33	0.86	4.13	6.64	9.19
2007	1.53	3.02	1.20	5.65	1.63	8.08	8.37	13.72	0.89	3.02	0.75	5.08	1.16	5.13	6.18	10.49
2008	1.83	4.16	1.24	6.33	1.26	4.27	8.22	13.86	1.32	3.41	0.98	4.03	1.29	4.03	6.26	9.21
2009	1.38	2.65	1.37	6.68	1.04	4.35	8.73	11.37	1.51	1.83	1.07	4.55	1.00	3.03	5.81	7.80
2010	1.36	4.11	1.54	7.10	1.40	5.39	6.17	12.60	1.21	2.90	1.43	5.60	1.07	3.37	5.32	9.14
2011	1.58	3.58	1.31	7.23	1.65	5.98	7.38	13.22	0.80	3.04	0.70	5.19	1.11	4.12	5.60	8.78

(*Continued*)

https://doi.org/10.2147/CLEP.S503847

Table 2 (Continued).

Year	Incidence								Mortality							
	Esophageal (C15)				Gastric (AC) (C16)				Esophageal (C15)				Gastric (AC) (C16)			
	SCC		AC		Cardia C16.0		Non-Cardia C16.1-9		SCC		AC		Cardia C16.0		Non-Cardia C16.1-9	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
2012	1.44	3.51	1.81	6.88	1.61	5.31	6.51	10.96	0.84	3.30	0.99	4.43	0.90	4.04	4.75	8.12
2013	1.55	3.35	1.18	7.73	1.50	5.53	5.52	11.63	1.19	2.26	0.73	5.91	1.15	3.50	5.26	8.16
2014	1.72	3.50	1.39	8.82	1.93	6.53	5.90	9.79	1.14	2.82	1.03	5.23	1.44	3.85	3.64	7.01
2015	1.79	3.15	1.64	7.90	1.40	6.42	4.65	8.30	0.90	1.55	1.52	5.67	1.30	4.37	3.24	6.42
2016	1.57	3.20	1.77	7.76	0.81	5.50	5.11	9.81	1.25	2.32	1.19	5.34	0.45	4.41	3.94	6.33
2017	1.85	3.08	1.54	8.00	1.22	7.19	5.99	7.36	0.82	1.80	0.94	4.78	0.89	4.17	4.09	5.10
2018	2.05	3.38	1.11	8.46	1.26	3.79	4.82	7.48	1.04	2.64	0.95	5.75	0.97	4.07	3.81	4.95
2019	1.90	2.96	1.65	8.14	1.46	5.70	4.72	8.49	0.99	2.30	1.05	5.91	0.85	3.23	3.22	5.41
2020	1.77	3.16	1.99	10.68	1.13	5.09	5.07	7.32	1.17	2.79	1.58	6.21	0.69	3.62	3.56	4.89
2021	1.84	3.15	1.92	8.60	1.28	3.69	4.58	6.33	1.13	1.89	1.24	6.18	0.93	2.84	3.08	4.30
2022	1.52	3.08	1.85	10.12	1.06	5.26	4.24	5.83	0.83	2.24	1.09	6.28	0.74	3.98	3.18	4.64

https://doi.org/10.2147/CLEP.S503847

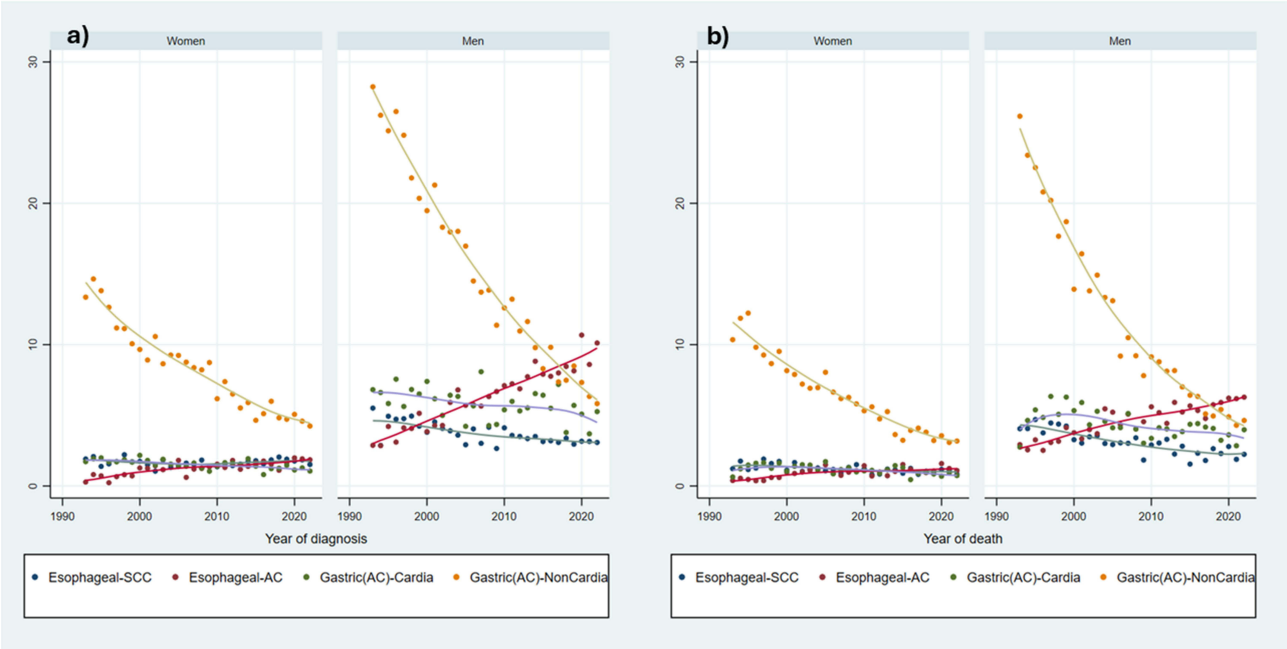

Figure 1 Age-standardized (European standard population) incidence (**a**) and mortality (**b**) rates, per 100,000 persons for esophageal cancer and gastric adenocarcinoma in Norway 1993–2022, stratified by sex.

disease the incidence was stable in men and increasing in women (Figure 3, Table 3 and supplementary Table S2). The mortality rates showed a consistent decreasing trend overall, by sex, age and stage, although with occasional variations between time periods (supplementary Table S3, S2, and S4).

Esophageal AC

Between 1993 and 2022, there was a non-significant increase in the incidence and mortality rates of esophageal AC in men (incidence: AAPC = 4.3; mortality: AAPC = 3) and women (incidence: AAPC = 4.3; mortality: AAPC = 3.5) (Figure 1, Table 3). The highest increase in incidence (APC 5.9) was seen in men ≥70 years (Figure 2, Table 3), and the largest increase was seen from 2010 (AAPC = 2.8) in men (supplementary Table S3). In women, the steepest increase in incidence was seen in the period 1993–1996 (AAPC = 12.9) (supplementary Table S3). Furthermore, the results showed non-significant increasing trends for localized disease in men and for regional/distant stage in both sexes (Figure 3, Table 3, supplementary Table S2).

Gastric AC

In general, the incidence rate for gastric AC has decreased in the time-period 1993–2010 (Figure 1, Table 3), although occasionally variations were observed (supplementary Table S3). The decrease was seen for both sexes, age groups and stage categories (Figure 2 and 3, Table 3). Overall, the mortality rates were stable, with a non-significant increasing trend for both age groups and stage categories in men, while a decreasing trend was seen for both stage categories in women (Figure 2 and 3, Table 3). For non-cardia gastric AC overall, a significant decrease in incidence was seen both in men (AAPC=−5.3) and women (AAPC=−3.9) (Figure 1, Table 3). A similar decreasing trend was observed for mortality (AAPC men=−5.9, and AAPC women=−4.2) (Figure 1, Table 3). In men, the decline in incidence and mortality was significant for both age groups (Figure 2, Table 3). A significant decrease in incidence was seen for localized stage in women (AAPC = 6.5) and for regional/distant stage in men (APC = 5.2), while for mortality the decrease was not significant (Figure 3, Table 3, supplementary Table S2).

https://doi.org/10.2147/CLEP.S503847

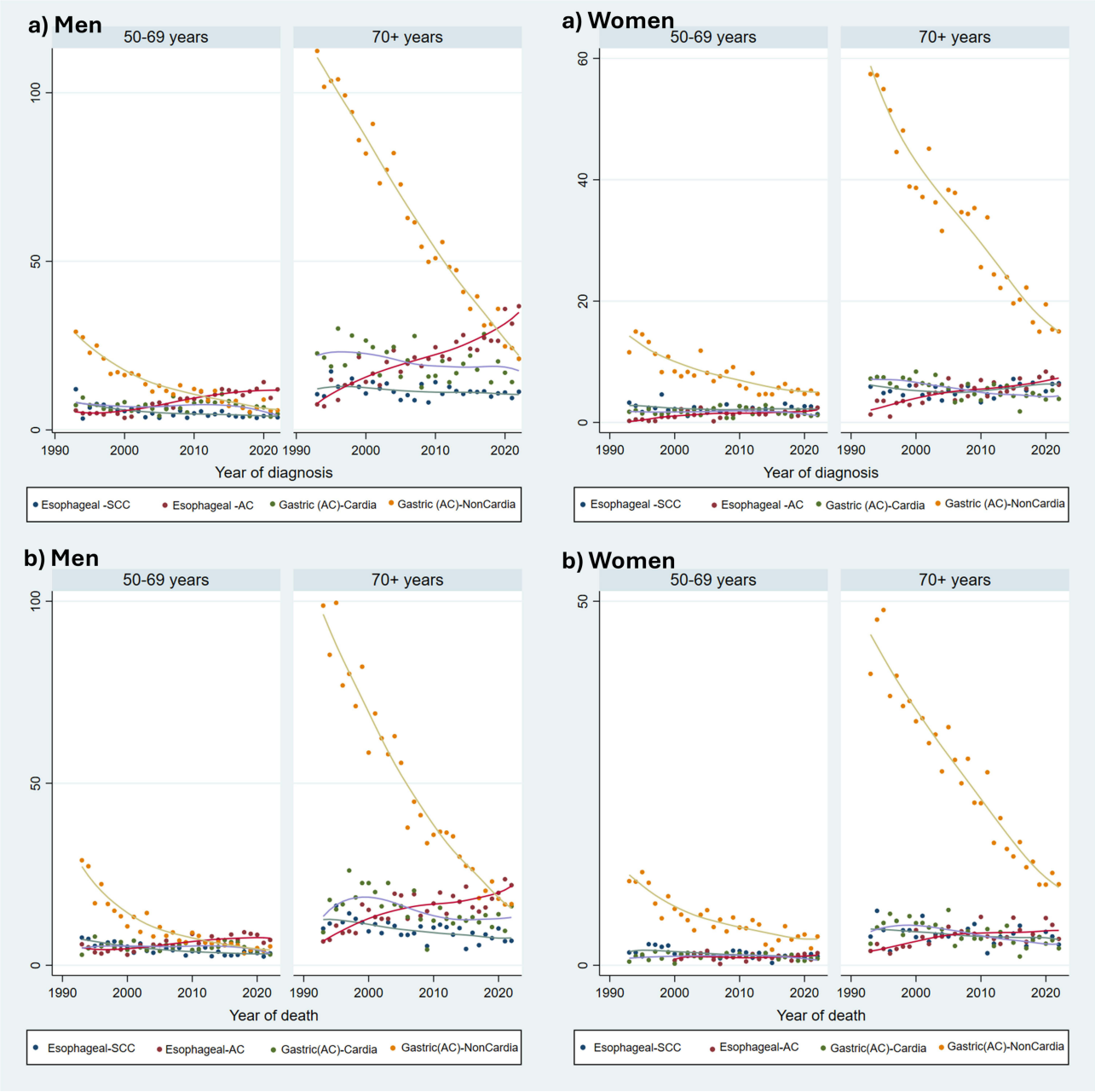

Figure 2 Age-standardized (European standard population) incidence (**a**) and mortality (**b**) rates, per 100,000 persons, for esophageal cancer and gastric adenocarcinoma in Norway 1993–2022, stratified by sex and age category.
Abbreviations: EC, esophageal cancer (C15), GC, gastric cancer (C16); SCC, squamous cell carcinoma; AC, adenocarcinoma; Cardia: C16.0, Non-cardia: C16.1–9.

Discussion

Our results showed increasing incidence and mortality rates for esophageal AC during 1993–2022, and mostly in men, at ages ≥70 years and for regional/distant stage, while the incidence and mortality rates for esophageal SCC declined in men and were stable in women. For gastric AC, the incidence and mortality rates have declined since 1993, with the steepest decline for non-cardia gastric AC. Our paper is the first to report esophageal and gastric cancer trends in Norway, focusing on histology, age, sex, and stage at diagnosis.

Esophageal and gastric cancers are most prevalent in less developed regions, particularly in East and Central Asia, Latin America, and Africa, where SCC is the predominant subtype of esophageal cancer.[23,24] However, in recent years,

Table 3 Average Annual Percent Change (AAPC), with 95% Confidence Intervals (CI) and P-values for Incidence and Mortality Rates of Esophageal Cancer and Gastric Adenocarcinoma in Norway from 1993–2022 by Sex, Age, Morphology, Topography, and Stage at Diagnosis

Outcome	Stage at Diagnosis	Topography	Morphology	Age Category	Sex	AAPC	Lower CI	Upper CI	Test Statistic~	P-value~
Incidence	Overall	Esophageal, C15	SCC	Total	Women	−0.9	−7.3	6	−0.3	0.796
					Men	−1.6	−5.7	2.7	−0.7	0.467
				50-69	Women	−2.6	−14.8	11.3	−0.4	0.697
					Men	−2.4	−10.8	6.7	−0.5	0.591
				>70	Women	0.1	−7.7	8.6	0	0.982
					Men	0.2	−6.3	7.2	0.1	0.943
		Esophageal, C15	AC	Total	Women	4.3	−5.7	15.3	0.8	0.411
					Men	4.3	−3.5	12.6	1.1	0.289
				50-69	Women	7.1	−6.4	22.5	1	0.319
					Men	2.4	−2.6	7.7	0.9	0.345
				>70	Women	3.7	−6	14.3	0.7	0.466
					Men	5.9*	0.7	11.4	2.2	0.025
		Gastric (Cardia), C16.0		Total	Women	−1.7	−6.2	3	−0.7	0.474
					Men	−1.2	−10.2	8.6	−0.3	0.802
				50-69	Women	−1.3	−12.8	11.8	−0.2	0.841
					Men	−2	−9.4	6.1	−0.5	0.62
				>70	Women	−1.8	−10.9	8.2	−0.4	0.715
					Men	−0.4	−9.1	9.2	−0.1	0.938
		Gastric (Non-cardia), C16.1-9		Total	Women	−3.9*	−7	−0.7	−2.4	0.016
					Men	−5.3*	−9.3	−1.2	−2.5	0.012
				50-69	Women	−3.2	−11.1	5.4	−0.8	0.451
					Men	−5.7*	−10.6	−0.4	−2.1	0.034
				>70	Women	−4.4	−8.8	0.1	−1.9	0.054
					Men	−5.6*	−8.2	−2.9	−4	< 0.001

(*Continued*)

Table 3 (Continued).

Outcome	Stage at Diagnosis	Topography	Morphology	Age Category	Sex	AAPC	Lower CI	Upper CI	Test Statistic~	P-value~
	Localized	Esophageal, C15	SCC		Women	−2.6	−23.7	24.3	−0.2	0.831
					Men	−5.3	−20.1	12.4	−0.6	0.536
		Esophageal, C15	AC		Women	0.4	−20.9	27.4	0	0.974
					Men	3.4	−6	13.7	0.7	0.496
		Gastric (Cardia), C16.0			Women	−1.6	−41.1	64.3	−0.1	0.95
					Men	−2.5	−14.6	11.3	−0.4	0.708
		Gastric (Non-cardia),C16.1-9			Women	−6.5*	−10	−2.8	−3.4	0.001
					Men	−5.7	−15.4	5.1	−1.1	0.286
	Regional/Distant	Esophageal, C15	SCC		Women	1.7	−10.4	15.4	0.3	0.796
					Men	−0.5	−7.9	7.5	−0.1	0.895
		Esophageal, C15	AC		Women	4.4	−13.6	26.2	0.4	0.656
					Men	4.5	−4.9	14.8	0.9	0.36
		Gastric (Cardia), C16.0			Women	−1	−6.8	5.1	−0.3	0.736
					Men	−0.6	−9.6	9.3	−0.1	0.9
		Gastric (Non-cardia),C16.1-9			Women	−3.8	−8.8	1.4	−1.4	0.151
					Men	−5.2*	−9	−1.3	−2.6	0.01

https://doi.org/10.2147/CLEP.S503847

Mortality	Overall	Esophageal, C15	SCC	Total	Women	−1.3	−9.9	8.2	−0.3	0.78
					Men	−2.2	−8.3	4.2	−0.7	0.489
				50-69	Women	−0.6	−12.2	12.4	−0.1	0.92
					Men	−3.1	−12.2	7	−0.6	0.534
				>70	Women	−1.7	−14.2	12.7	−0.2	0.809
					Men	−1.5	−9.3	6.9	−0.4	0.711
		Esophageal, C15	AC	Total	Women	3.5	−7.7	16.2	0.6	0.555
					Men	3	−1.4	7.6	1.3	0.188
				50-69	Women	3.5	−14.8	25.7	0.3	0.728
					Men	0.3	−7.8	9.2	0.1	0.944
				>70	Women	1.7	−6.6	10.6	0.4	0.699
					Men	4.4	−3	12.4	1.2	0.248
		Gastric (Cardia), C16.0		Total	Women	0.4	−8.2	9.7	0.1	0.938
					Men	0.6	−5	6.6	0.2	0.835
				50-69	Women	1.3	−13.2	18.1	0.2	0.874
					Men	0.2	−7.4	8.3	0	0.966
				>70	Women	−0.8	−13.5	13.8	−0.1	0.907
					Men	0.8	−7.4	9.8	0.2	0.855
		Gastric (Non-cardia),C16.1-9		Total	Women	−4.2*	−8.1	−0.2	−2.1	0.039
					Men	−5.9*	−8.9	−2.7	−3.6	< 0.001
				50-69	Women	−4.3	−14.3	6.9	−0.8	0.433
					Men	−6.0*	−11.2	−0.5	−2.1	0.033
				>70	Women	−4.3	−8.4	0	−1.9	0.052
					Men	−5.9*	−10.3	−1.3	−2.5	0.012

(*Continued*)

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Table 3 (Continued).

Outcome	Stage at Diagnosis	Topography	Morphology	Age Category	Sex	AAPC	Lower CI	Upper CI	Test Statistic~	P-value~
	Localized	Esophageal, C15	SCC		Women	−7.3	−22.5	10.9	−0.8	0.409
					Men	1.1	−10.7	14.3	0.2	0.865
		Esophageal, C15	AC		Women	1.9	−25.9	40	0.1	0.909
					Men	3	−20.3	33.1	0.2	0.82
		Gastric (Cardia), C16.0			Women	−2.8	−27.5	30.4	−0.2	0.851
					Men	1.3	−9.9	13.9	0.2	0.827
		Gastric (Non-cardia),C16.1-9			Women	−9.5	−19.2	1.3	−1.7	0.083
					Men	−3.8	−7.6	0.1	−1.9	0.057
	Regional/Distant	Esophageal, C15	SCC		Women	−7.4	−21.1	8.8	−0.9	0.352
					Men	−0.8	−9	8	−0.2	0.848
		Esophageal, C15	AC		Women	−0.7	−13.1	13.4	−0.1	0.914
					Men	3.6	−1.3	8.7	1.4	0.157
		Gastric (Cardia), C16.0			Women	−3.6	−18.3	13.7	−0.4	0.66
					Men	0.6	−7.4	9.4	0.1	0.886
		Gastric (Non-cardia),C16.1-9			Women	−8.8	−18	1.4	−1.7	0.09
					Men	−5.9	−12	0.5	−1.8	0.071

Notes: * Indicates that the average annual percent change (AAPC) is significantly different from zero at the $\alpha = 0.05$ level. If the AAPC is within one segment, the t-distribution is used. Otherwise, the normal (z) distribution is used.

https://doi.org/10.2147/CLEP.S503847

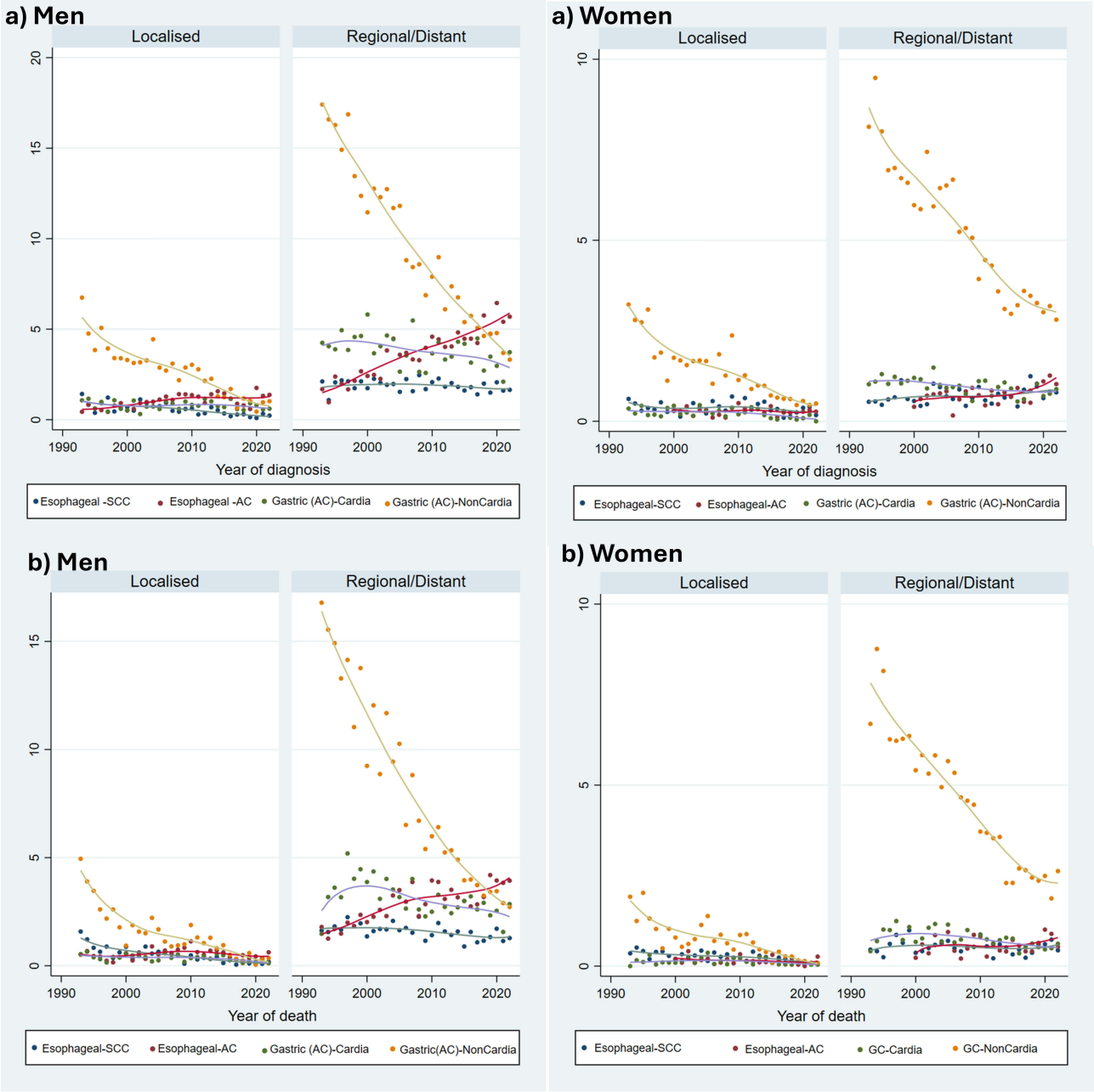

Figure 3 Age-standardized (European standard population) incidence (**a**) and mortality (**b**) rates, per 100,000 persons, for esophageal cancer and gastric adenocarcinoma in Norway 1993–2022, stratified by sex and stage at diagnosis.
Abbreviations: EC, esophageal cancer (C15); GC, gastric cancer (C16); SCC, squamous cell carcinoma, AC, adenocarcinoma Cardia; C16.0, Non-cardia, C16.1–9.

despite global declines in overall incidence, these cancers have shown increasing occurrence in more developed countries, with esophageal AC now being the most common subtype.[6,7]

Incidence

The decrease we observed in the incidence of esophageal SCC is in line with previous studies[23,25] and might result from awareness and prevention efforts that have been implemented to reduce exposure to common cancer risk factors. Exposure to risk factors such as smoking, excessive alcohol consumption, inadequate intake of fruits and vegetables, and poor oral hygiene have been linked to risk of several cancers, including esophageal SCC, especially in high-income countries.[26,27]

https://doi.org/10.2147/CLEP.S503847

A previous study, based on data from all Nordic countries, reported an increase in esophageal AC incidence in men during 1971–2000, but in women, the rates were lower with an incidence increase in Denmark only.[28] The present study shows that this trend and the sex difference persists. Also, the transition from esophageal SCC to AC has been previously noted in Europe, North America and Asian countries.[26,29,30] The increasing incidence of esophageal AC is largely attributed to rising rates of obesity, gastroesophageal reflux disease (GERD), and Barrett's esophagus, which are distinct risk factors for AC but not SCC.[31,32] Population-data shows a steep increase in the prevalence of overweight and obesity 1990–2022, most pronounced in men,[33] also in Norway,[34] and its prevalence is suggested to continue to rise.[33,35]

The sex disparity in the incidence of esophageal and gastric cancer may be related to the protective effect of sex hormones, such as estrogen in women or the potential contrasting effect of androgens in men. However, these mechanisms are not yet fully understood.[36,37] Recent research has suggested that although the decrease in infection by H. *pylori* have reduced the risk of esophageal SCC and gastric AC, it may be partly responsible for the increasing rates of esophageal AC. The bacteria can regulate the secretion of gastric acid, and after the bacterium is eradicated, there is an increased risk of reflux.[38,39] HP eradication next to the other factors including diet, and lack of physical activity, which in combination with genetics may lead to an increase in obesity, which is one of the major factors responsible for the increased trend of esophageal AC.[40,41]

Several studies highlighted the importance of mass eradication of *H. pylori* to reduce gastric cancer but noted that the long-term effects on other cancers remain unclear.[42] Over the last decade, the global prevalence of *H. pylori* infection has decreased in adults, dropping from 52.6% to 43.9% between 1990 and 2022.[7] In Norway, the infection rate was 32.9% among adults and 20.1% among children/adolescents between 2016 and 2019.[43] We observed a decrease in the incidence of both the cardia and non-cardia gastric AC, with a greater magnitude for the latter. Other than a decrease in the prevalence of *H. pylori* infection, which is the most likely cause for decrease in gastric AC.[7,44] Also, other preventive measures may have contributed to this trend, such as regulations of tobacco smoking and alcohol consumption.[45] Thus, these time-trends in incidence may reflect how changes in population-level exposure to modifiable etiological factors can contribute to disease burden over time.

Mortality

The mortality trends mirrored the incidence trends, both for esophageal cancer, particularly among older people and for non-cardia gastric AC, which emphasizes the fatality of these diseases. Factors of most importance for mortality include age and stage of the disease at the time of diagnosis.[46] Furthermore, raising awareness about signs and risk factors, ensuring prompt diagnosis, and providing timely treatment are crucial strategies in managing esophageal cancer and reducing associated death rates.[46,47] In general, some studies have suggested that the use of certain nutrients, such as selenium, vitamin E, and beta-carotene, in people under 55 years of age, might help to reduce mortality.[48–50]

For esophageal SCC, the decrease in mortality across both age groups and stages was slightly stronger than the decline in incidence, however, with overlapping CIs. The decrease was most pronounced in men. Recent reports indicate that gastric cancer mortality has decreased almost equally in both men and women globally, with some exceptions such as Denmark, Greece, and Norway, with a more pronounced decline in women.[51] The stronger decline seen in men may result from cessation of tobacco smoking and reduction in H. pylori infection in men, who historically have had higher prevalences of both these exposures than women.[52]

Although the incidence of esophageal AC has been increasing overall, when we examined the stage at diagnosis, we found a greater change for regional/distant stage cases compared to localized stage cases in terms of both incidence and mortality. This could be due to the fact that AC histological groups have a worse prognosis and are usually diagnosed in the late stage, which might result in a lower likelihood of pursuing surgical treatment and higher treatment-related mortality. Another possibility could be improvements in diagnosis methods and imaging processes, which may explain the rising proportion of late-stage cases over time.[50,53,54]

Strengths and Limitations

The main strength of this study is the use of data from complete and high-quality national registries, with a 30-year period for incidence and mortality trends. Due to alterations in the coding system for the location of tumors located at the

gastro-esophageal junction, we restricted our analysis to the period after 1993 to avoid misclassification. A weakness is the high proportion of cases without information on stage at diagnosis.

To our knowledge, this report provides the first comprehensive analysis of the incidence and mortality trends of esophageal and gastric cancer, by morphology types, subsites, sex, age groups, and stage at diagnosis in the Norwegian population between 1993 and 2022.

In conclusion, our results show increasing incidence and mortality rates in esophageal AC during the last decades, most pronounced in men, at ages ≥70 years at diagnoses, and for regional/distant stage at diagnoses. Since 2018, the mortality of esophageal AC in older men has been higher than for gastric AC. The rates for esophageal SCC have declined, although trends differed between sex and age groups. For gastric AC, the incidence and mortality rates have declined since 1993, most pronounced for non-cardia gastric AC. Our trend analysis contributes as a valuable reference for future research on EC, supporting increased clinical awareness and the identification of high-risk populations for targeted prevention efforts.

Abbrevations

AAPC, The average annual percent change; APC, The annual percent change; CRN, Cancer Registry of Norway; EBV, Epstein–Barr virus; GERD, Gastroesophageal reflux disease; GE, Gastro-esophageal; H. pylori, Helicobacter pylori.

Data Sharing Statement

Data used in this study is available by application to helsedata.no. Access will be conditional to adherence to local ethical and security policy. Further information is available from the corresponding author upon request.

Ethics Approval and Informed Consent

Our study is exempt from approval based on national legislation guidelines. The use of de-identified data and the analyses presented in this manuscript fall under the purview of the Cancer Registry of Norway's mandate and approval to provide delivery of statistics covered under the Health Registry act § 19.

Author Contributions

All authors (MSS, PB, CTN, HL and TER) made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Consent for Publication

All authors have agreed with this publication in its current form.

Funding

This work was supported by the Marco Polo Program, funded by the University of Bologna (Provvedimento Dirigenziale Rep. n. 154 Prot. n. 4102 del 26/05/2023).

Disclosure

The authors declare no conflicts of interest in this work.

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