

Updated incidence trends in cardia and non-cardia gastric adenocarcinoma in Sweden

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ABSTRACT

Background: The aim of this study was to provide an update of the recent incidence trends of cardia and non-cardia gastric adenocarcinoma in Sweden.

Methods: Temporal trends in the age-standardised incidence were assessed separately for cardia and non-cardia gastric adenocarcinoma in 1970–2014 among all people in Sweden aged ≥ 50 years. Data were retrieved from the Swedish Cancer Registry. The log-linear joinpoint regression method was used to identify change points in the incidence trends. The annual percent changes with 95% confidence intervals (CI) were calculated for each segment before and after change points.

Results: The overall incidence of cardia adenocarcinoma increased during the earlier period of 1970–1988, but was stable during the later period of 1989–2014 (annual percent change: -0.3% , 95% CI: -0.7 to 0.2%). In contrast, in women aged 50–69 years the incidence of cardia adenocarcinoma increased by 6.6% annually (95% CI: 1.9 to 11.5%) during the period 2005 to 2014. The incidence of non-cardia gastric adenocarcinoma decreased by 4.4% per year (95% CI: -4.6 to -4.2%) in 1984–2014 and the decrease was stronger in men aged 70 years or older compared to other groups.

Conclusion: The incidence of cardia adenocarcinoma is seemingly rapidly increasing in younger women, while it has been stable in other groups during recent years in Sweden. The incidence of non-cardia gastric adenocarcinoma continues to decrease, particularly in older men.

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Introduction

Gastric cancer is the fifth most common cancer and the third most common cause of cancer death globally [1]. The incidence trends in this cancer have changed substantially during the last few decades, with rapidly increasing trends in cardia cancer and strongly decreasing trends in non-cardia gastric cancer [2]. Because the vast majority ($>90\%$) of malignant gastric tumours are of the histological type adenocarcinoma and these have a distinct aetiology and treatment compared to other histological types [3], it is important to evaluate the incidence trends for adenocarcinoma separately. In addition, due to the divergent incidence patterns for cardia and non-cardia gastric adenocarcinoma, these sub-locations need to be analysed separately in studies evaluating the incidence trends of this tumour. We have previously reported on the incidence trends in gastric adenocarcinoma in Sweden up to the year 2008 [4], showing that the cardia adenocarcinoma incidence had decreased after 1990 (annual percentage decrease: -1.0 , 95% confidence interval (CI): -1.6 to -0.3%), whereas the decreasing incidence of non-cardia gastric adenocarcinoma has continued (annual percentage decrease: -4.9 , 95% CI: -5.2 to -4.7%). By using updated data until the year 2014 with valid nationwide incidence data, this study aimed to assess the incidence trends

separately for cardia and non-cardia gastric adenocarcinoma in Sweden with sub-group analyses for sex and age groups.

Methods

Study design

This was a population-based study assessing the incidence of cardia and non-cardia gastric adenocarcinoma diagnosed between 1 January 1970 and 31 December 2014 in the entire Swedish population.

Data source

Data were obtained from the Swedish Cancer Registry, which provides high-quality and complete information about all tumour sites and histological types as well as year of diagnosis, sex and age at diagnosis. The start year of the study as 1970 was prompted by the fact that this was when the Cancer Registry began registering cardia adenocarcinoma using a separate code apart from non-cardia adenocarcinoma. The diagnosis codes representing cardia cancer (151.1) and non-cardia gastric cancer (151.0, 151.8 and 151.9) were defined using the seventh edition of the International Classification of Diseases (ICD-7). The histology classification

WHO/HS/CANC/24.1 defined adenocarcinoma (code 096). The Swedish Cancer Registry has 98% national coverage of cardia and non-cardia gastric cancer and the rate of histological confirmation is 100% [5,6].

Statistical analysis

The annual age-standardised incidence rates were calculated using the direct method, with the age distribution of the Swedish population in five-year age groups in year 1989 as the standard population. Due to the small number of gastric adenocarcinoma patients diagnosed at an age below 50 years ($n = 2723$ out of 45,641, 5.1%), the incidence rates were calculated among individuals aged at least 50 years. Log-linear joinpoint regression was used to identify change points in incidence trends and to estimate the annual percent change with 95% CI for each time segment before and after the change point [7]. The joinpoint regression enables testing if an apparent change over time from visual inspection if the potential trend is statistically significant. The joinpoint regression was used on the assumption that the rates change at a constant percentage per year on a log scale in each time segment. A maximum of four change points were pre-defined. The analyses were stratified into males and females and into the age groups 50–69 years and 70 years or older. All statistical analyses were performed according to a pre-defined study protocol and executed by an experienced biostatistician (FM). The statistical software SAS version 9.4 (SAS Institute, Cary, NC) and Joinpoint Regression Program version 4.3.1.0 (Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute, the United States) were used.

Results

Patients

The study included 6918 patients diagnosed with cardia adenocarcinoma and 43,345 patients with non-cardia gastric adenocarcinoma. In both tumour groups, the majority of patients were male and at least 70 years of age (Table 1).

Table 1. The distribution of patients diagnosed with cardia or non-cardia gastric adenocarcinoma in Sweden from 1970 to 2014.

	Gastric adenocarcinoma	
	Cardia Number (%)	Non-cardia Number (%)
All	6918 (100)	43,345 (100)
Sex		
Men	5288 (76)	26,011 (60)
Women	1630 (24)	17,334 (40)
Age (years)		
50–69	3087 (45)	15,142 (35)
≥70	3831 (55)	28,203 (65)
Sex and age (years)		
Men aged 50–69	2503 (36)	9588 (22)
Men aged ≥70	2785 (40)	16,423 (38)
Women aged 50–69	584 (8)	5554 (13)
Women aged ≥70	1046 (15)	11,780 (27)

Table 2. Overall and sex-specific change points in the incidence time trends of cardia and non-cardia gastric adenocarcinoma in Sweden with annual percent changes and 95% confidence intervals (CI) before and after change points.

Gastric site	Patients (n)	Calendar period	Annual percent change (95% CI)	Men			Women		
				Patients (n)	Calendar period	Annual percent change (95% CI)	Patients (n)	Calendar period	Annual percent change (95% CI)
Cardia	6918	1970–1989	4.1 (3.2 to 4.9)	5288	1970–1990	4.1 (3.3 to 5.0)	1630	1970–1988	3.9 (1.9 to 6.0)
		1989–2014	–0.3 (–0.7 to 0.2)		1990–2014	–0.7 (–1.2 to –0.2)		1988–2014	0.2 (0.7 to 1.0)
Non-cardia	43,345	1970–1973	1.1 (–3.1 to 5.4)	26,011	1970–1989	–2.6 (–3.0 to –2.2)	17,334	1970–1980	–3.9 (–4.9 to –2.8)
		1973–1976	–7.6 (–15.5 to 1.0)		1989–2014	–5.0 (–5.4 to –4.7)		1980–1984	–0.1 (–7.6 to 8.0)
		1976–1984	–1.3 (–2.5 to 0.0)					1984–2014	–4.1 (–4.4 to –3.7)
		1984–2014	–4.4 (–4.6 to –4.2)						

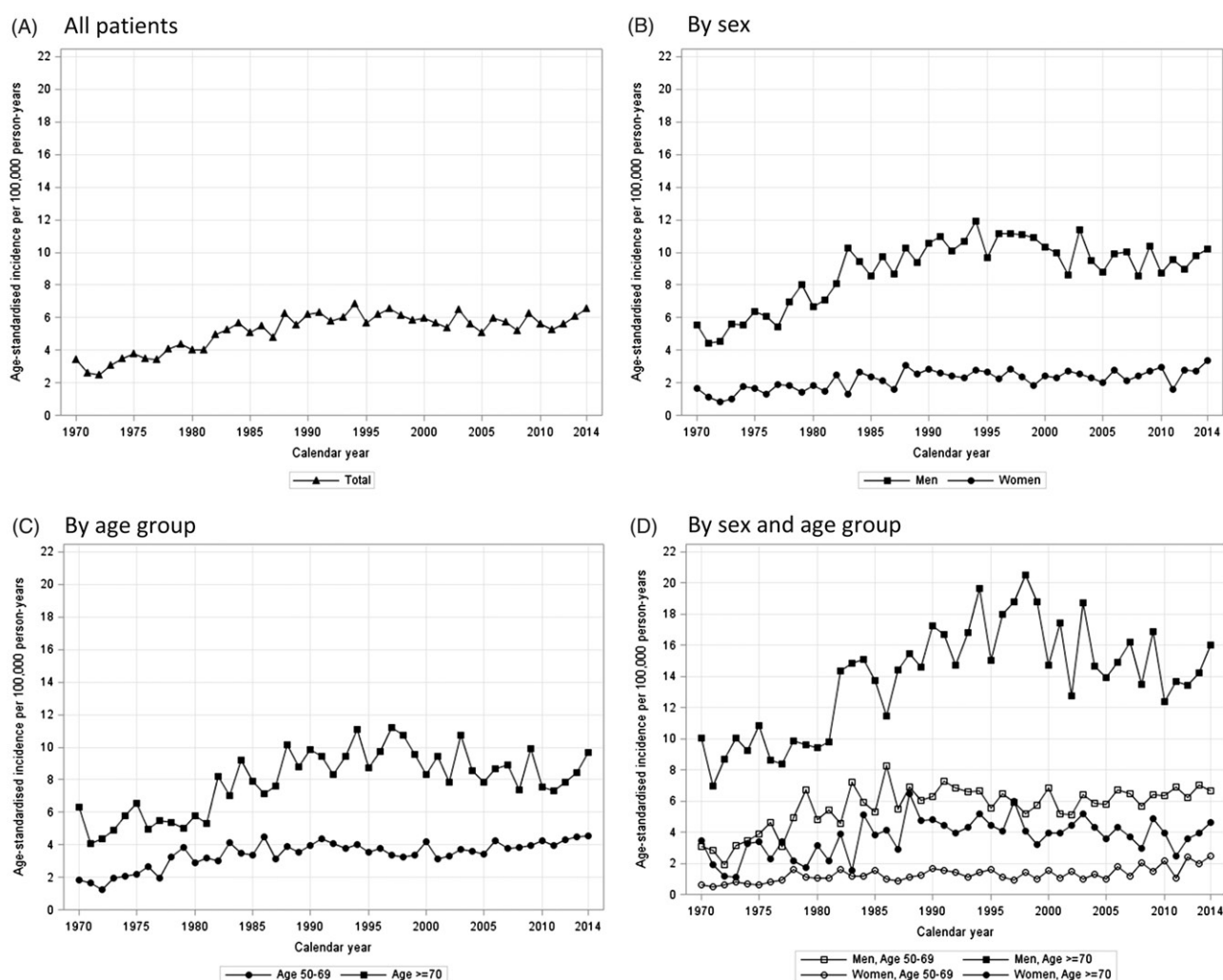


Figure 1. Age-standardised incidence in gastric cardia adenocarcinoma in 1970–2014 in Sweden.

Table 3. Age-group specific change points in the incidence time trends of cardia and non-cardia gastric adenocarcinoma in Sweden with annual percent changes and 95% confidence intervals (CI) before and after change points.

Gastric site	Age 50–69 years			Age ≥ 70 years		
	Patients (n)	Calendar period	Annual percent change (95% CI)	Patients (n)	Calendar period	Annual percent change (95% CI)
Cardia	3087	1970–1979	10.1 (5.8 to 14.6)	3831	1970–1994	3.3 (2.4 to 4.1)
		1979–2014	0.5 (0.1 to 0.9)		1994–2014	–1.2 (–2.1 to –0.2)
Non-cardia	15,142	1970–1989	–2.4 (–2.8 to –2.0)	28,203	1970–1973	1.8 (–3.2 to 7.1)
		1989–1997	–8.1 (–10.3 to –5.8)		1973–1976	–8.9 (–18.2 to 1.4)
		1997–2014	–3.1 (–4.0 to –2.2)		1976–1985	–0.8 (–2.1 to 0.4)
					1985–2014	–4.2 (–4.5 to –4.0)

Gastric cardia adenocarcinoma

The overall (both sexes) incidence of cardia adenocarcinoma increased during the period 1970 to 1988, but was stable in 1989 to 2014 with an annual percent change of -0.3% (95% CI: -0.7 to 0.2% ; Table 2, Figure 1(A)). Similar patterns were revealed in men and women (Table 2, Figure 1(B)). The stable incidence started earlier (in 1979) in individuals aged 50–69 years and later (in 1994) in the older age group (Table 3, Figure 1(C)). In analyses stratified for both sex and age, women aged 50–69 years had an increasing incidence with an annual increase at a rate of 6.6% (95% CI: 1.9 to 11.5%) during the period 2005 to 2014, which was in sharp contrast

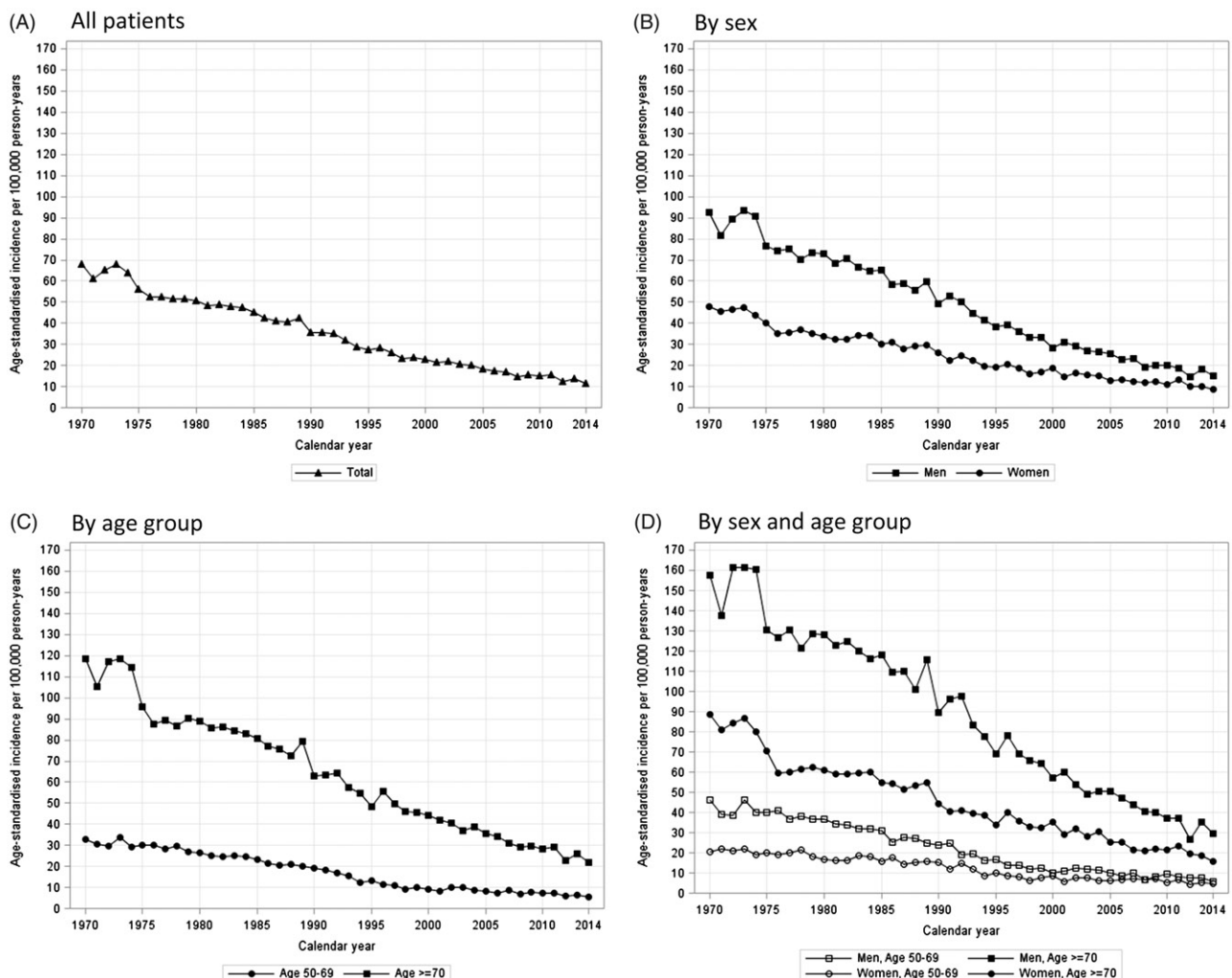
to the stable incidence rates in the other age and sex groups (Table 4, Figure 1(D)).

Non-cardia gastric adenocarcinoma

The overall incidence of non-cardia gastric adenocarcinoma decreased from 1973 onwards at a varying rate (Table 2, Figure 2(A)). In the recent period from 1984 to 2014, the annual decrease was 4.4% (95% CI: -4.6 to -4.2%). The annual percent decrease was more pronounced in men than in women (Table 2, Figure 2(B)). The decrease was seemingly slightly faster in older individuals compared to younger

Table 4. Sex and age-group specific change points in the incidence time trends of cardia and non-cardia gastric adenocarcinoma in Sweden with annual percent changes and 95% confidence intervals (CI) before and after change points.

Gastric site	Men aged 50–69 years			Men aged ≥ 70 years		
	Patients (n)	Calendar period	Annual percent change (95% CI)	Patients (n)	Calendar period	Annual percent change (95% CI)
Cardia	2503	1970–1983	6.8 (4.1 to 9.6)	2785	1970–1994	3.4 (2.6 to 4.3)
		1983–2014	−0.1 (−0.6 to 0.5)		1994–2014	−1.4 (−2.3 to −0.4)
Non-cardia	9588	1970–1988	−2.7 (−3.2 to −2.1)	16,423	1970–1989	−2.1 (−2.6 to −1.7)
		1988–1998	−7.6 (−9.7 to −5.4)		1989–2014	−4.8 (−5.2 to −4.4)
		1998–2014	−3.5 (−4.8 to −2.1)			
Gastric site	Women aged 50–69 years			Women aged ≥ 70 years		
	Patients (n)	Calendar period	Annual percent change (95% CI)	Patients (n)	Calendar period	Annual percent change (95% CI)
Cardia	584	1970–1978	12.3 (2.8 to 22.6)	1046	1970–1989	4.3 (1.9 to 6.7)
		1978–2005	0.3 (−0.9 to 1.4)		1989–2014	−0.9 (−2.2 to 0.4)
		2005–2014	6.6 (1.9 to 11.5)			
Non-cardia	5554	1970–1990	−1.9 (−2.5 to −1.2)	11,780	1970–1973	0.5 (−5.5 to 6.8)
		1990–1997	−8.9 (−13.4 to −3.7)		1973–1976	−10.6 (−21.6 to 2.0)
		1997–2014	−2.2 (−3.7 to −0.8)		1976–1984	−0.6 (−2.5 to 1.4)
					1984–2014	−3.8 (−4.1 to −3.5)

**Figure 2.** Age-standardised incidence in gastric non-cardia adenocarcinoma in 1970–2014 in Sweden.

during the last few years (Table 3, Figure 2(C)). The analysis stratified by both sex and age showed a decreasing incidence in all groups, but during the last years the decrease was more pronounced in men aged at least 70 years compared to the other groups (Table 4, Figure 2(D)).

Discussion

Although this study indicates a stable overall incidence rate of gastric cardia adenocarcinoma during recent years in Sweden, a rapidly increasing incidence was noted in women aged below 70 years during the last decade. The incidence

rate of non-cardia gastric adenocarcinoma has also continued to decrease during the last few years, with a more pronounced decrease in men aged at least 70 years.

Strengths of this study include the nationwide and highly complete registration of all gastric cancers and the accurate information about the sub-site and histological type of the tumours. The study included data until the year 2014, which is recent from an international perspective. A limitation is that the study included only one country, which limits generalisability. However, historically the incidence trends in cardia and non-cardia gastric cancer in Sweden have well mirrored the changes in incidence trends in most other countries; at least in Western populations [4,8–10]. Additionally, there is always a level of uncertainty regarding the exact change points in joinpoint regression analysis and the change points must therefore be interpreted with some caution.

The available studies reporting on the incidence trends in gastric cancer have not contained data from the more recent years, which is because of long latency in registration. Additionally, few studies have evaluated cardia and non-cardia gastric adenocarcinoma separately. Yet, most studies assessing the incidence from earlier periods have found similar results as in the present study, i.e., a stable incidence in gastric cardia cancer, whereas the incidence of non-cardia gastric cancer has declined [11–14]. A recent comprehensive review of European countries showed a mean annual reduction in the incidence of gastric cancer of 2.1% in Europe from 1993 to 2007 with little variation between countries [15]. Globally, a study using data from Cancer Incidence in five continents from 2003 to 2007 reported an annual decrease of approximately 3% in Europe, Japan and Korea and 2% in North and Latin America [14].

The finding of an increased incidence of gastric cardia adenocarcinoma in younger women during the last decade is interesting, because this, to the best of our knowledge, has not been reported earlier. It is not possible to rule out chance as the explanation for this finding, but we may also speculate about potential biological mechanisms behind this finding. Gastro-oesophageal reflux disease is a main risk factor for cardia adenocarcinoma [16], but the prevalence of this disease is similar in the sexes and higher in older age groups. Tobacco smoking is an established risk factor for cardia adenocarcinoma [17]. The overall tobacco smoking prevalence has decreased substantially in Sweden during several decades, but the smoking prevalence has seen to be increased in younger women [18]. However, if this were the only factor involved, the incidence of non-cardia gastric adenocarcinoma should also increase because smoking also increases the risk of this cancer [19], but this is not the case according to the present study. Obesity is another well-known risk factor for cardia adenocarcinoma [20], which is potentially more relevant because it does not increase the risk of non-cardia gastric adenocarcinoma [21] and the prevalence of obesity is increasing in younger women in Sweden [22]. Yet, more research is obviously needed to confirm whether this changing pattern in women is true and if so, which mechanisms are actually responsible.

The main reasons for the decreasing incidence of non-cardia gastric cancer are likely to be the improvements in

dietary intake of e.g., fresh fruit and vegetables combined with the declining prevalence of gastric colonisation with *Helicobacter pylori* [15]. Additionally, the increased use of effective eradication in the treatment of this bacterium further decreases the risk of non-cardia gastric adenocarcinoma [23,24].

In conclusion, this nationwide Swedish study with data available up to and including the year 2014 shows a seemingly rapidly increasing incidence of gastric cardia adenocarcinoma in women aged below 70 years, while the incidence has been stable in other groups during recent years. The incidence rate of non-cardia gastric adenocarcinoma has continued to decrease during the last few years, with a faster decrease in older men.

Disclosure statement

The authors declare that they have no conflict of interest.

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