

## Does immigration play a role in the risk of gastric cancer by site and by histological type? A study of first-generation immigrants in Sweden

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**Abstract** The observed increased risks of gastric cancer among first-generation immigrants compared to those in Swedes suggest the role of childhood environmental exposure in the risk of this disease.

**Keywords** Adenocarcinoma · Cardia · Gastric cancer · Immigrants · Risk · Sweden

### Introduction

The distribution of gastric cancer is characterized by wide geographical variations [1]. The highest rates (about 20/100,000) have been reported from Japan, China, and some Latin American countries. The lowest rates, of less than 6/100,000, are reported from North America, Northern and Western Europe, most African countries, the Indian

subcontinent, and Australia [2]. The gastric cancer rate in men (5.7/100,000) is about two times higher than that in women (3.1/100,000) in Sweden [2].

Worldwide, a decreased rate of gastric cancer has been reported for several decades. However, the incidence rate of cancer of the cardia, the proximal part of the stomach, has been showing an increased rate in some developed countries [1]. Similarly, the incidence of esophageal adenocarcinoma has been increasing in those countries since the 1970s [3], which suggests the presence of the same risk factors, such as obesity or gastroesophageal reflux [4]. *Helicobacter pylori* infection is a known risk factor for non-cardia gastric cancer. A diet poor in fresh fruits and vegetables and a high salt intake are other associated factors. However, studies have also suggested that genetic susceptibility, familial aggregation, and blood group (A) have an influence on gastric cancer risk [1].

Previous studies have not shown uniform patterns of gastric cancer risk among immigrants. For example, a sharply decreased risk of gastric cancer was reported among Korean-Americans compared with their native counterparts, and even compared with the white United States population [5]. Such a difference was also reported among Japanese immigrants in Brazil [6]. In contrast, Chinese male immigrants to the United States were reported to have a rate similar to that of white Americans, whereas the rate in female Chinese immigrants was twice that of white Americans [7].

To our knowledge no study has explored whether the gastric cancer risk in immigrants varies by different site and histology. In the present report, we studied the risk of gastric cancer by site, histological type, and length of stay in first-generation immigrants to Sweden in order to search for etiological clues.

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**Table 1** Standardized incidence ratios (SIRs) for gastric cancer among immigrants to Sweden by site and histological type from 1958 to 2008

Birth region	Site																	
	All						Cardia						Non cardia					
	Male		Female		Male		Female		Male		Female		Male		Female			
	N	SIR <sup>a</sup>	95% CI	N	SIR	95% CI	N	SIR	95% CI	N	SIR	95% CI	N	SIR	95% CI	N	SIR	95% CI
Sweden	23,579	1.00		12,484	1.00		11,016	1.00		6,339	1.00		12,563	1.00		6,145	1.00	
Finland	512	<b>1.60</b>	1.46 1.74	439	<b>1.47</b>	1.33 1.61	233	<b>1.76</b>	1.54 2.00	216	<b>1.49</b>	1.29 1.70	279	<b>1.48</b>	1.31 1.67	223	<b>1.45</b>	1.27 1.66
Denmark	121	0.96	0.79 1.14	50	0.81	0.60 1.07	46	0.84	0.61 1.12	22	0.73	0.46 1.10	75	1.05	0.82 1.31	28	0.89	0.59 1.28
Norway	136	1.08	0.90 1.27	126	1.13	0.94 1.34	63	1.11	0.85 1.42	66	1.19	0.92 1.52	73	1.05	0.82 1.32	60	1.06	0.81 1.36
Baltic countries	149	<b>1.58</b>	1.34 1.85	66	<b>1.31</b>	1.02 1.67	76	<b>1.62</b>	1.28 2.03	33	1.26	0.86 1.76	73	<b>1.54</b>	1.20 1.93	33	1.38	0.95 1.93
Germany	145	1.07	0.91 1.26	118	<b>1.32</b>	1.09 1.58	66	1.11	0.86 1.41	53	1.20	0.90 1.57	79	1.05	0.83 1.31	65	<b>1.43</b>	1.11 1.83
Poland	67	<b>1.52</b>	1.17 1.93	53	<b>1.61</b>	1.21 2.11	29	<b>1.50</b>	1.01 2.16	20	1.35	0.82 2.08	38	<b>1.53</b>	1.08 2.10	33	<b>1.83</b>	1.26 2.57
Russia	57	<b>1.68</b>	1.27 2.17	33	<b>1.66</b>	1.14 2.33	26	<b>1.59</b>	1.04 2.33	17	1.71	0.99 2.73	31	<b>1.76</b>	1.20 2.50	16	1.61	0.92 2.62
Former Yugoslavia	93	<b>1.33</b>	1.07 1.63	48	<b>1.49</b>	1.10 1.98	42	<b>1.45</b>	1.05 1.96	18	1.20	0.71 1.89	51	1.24	0.92 1.63	30	<b>1.75</b>	1.18 2.49
Other Eastern European <sup>b</sup>	174	<b>2.29</b>	1.96 2.65	87	<b>2.19</b>	1.75 2.70	62	<b>2.51</b>	1.92 3.22	33	<b>2.00</b>	1.38 2.81	112	<b>2.18</b>	1.80 2.62	54	<b>2.32</b>	1.74 3.02
Greece	37	<b>1.73</b>	1.22 2.38	11	1.40	0.70 2.51	16	<b>2.03</b>	1.16 3.29	8	2.11	0.91 4.16	21	1.55	0.96 2.38	3	0.74	0.15 2.17
Other Southern European <sup>c</sup>	44	1.21	0.88 1.63	21	<b>1.71</b>	1.06 2.62	22	1.51	0.94 2.28	9	1.53	0.70 2.90	22	1.01	0.64 1.53	12	1.89	0.98 3.30
Other European <sup>d</sup>	38	0.85	0.60 1.16	12	0.59	0.31 1.03	14	0.82	0.45 1.37	8	0.84	0.36 1.66	24	0.86	0.55 1.29	4	<b>0.37</b>	0.10 0.95
Turkey	36	<b>1.75</b>	1.22 2.42	14	1.48	0.81 2.49	16	<b>2.20</b>	1.26 3.58	5	1.26	0.41 2.93	20	1.50	0.92 2.31	9	1.65	0.75 3.12
Iran	18	0.99	0.59 1.57	10	1.17	0.56 2.15	10	<b>2.20</b>	1.05 4.04	3	1.02	0.21 2.99	8	0.59	0.25 1.16	7	1.25	0.50 2.57
Asian Arab countries	32	1.26	0.86 1.77	23	<b>2.09</b>	1.32 3.13	13	<b>1.96</b>	1.04 3.35	16	<b>4.08</b>	2.33 6.63	19	1.01	0.61 1.57	7	0.98	0.40 2.03
Indian Subcontinent	8	1.07	0.46 2.11	3	0.97	0.20 2.84	2	0.82	0.10 2.98	0			6	1.19	0.44 2.59	3	1.60	0.33 4.68
Southeast Asia	5	0.77	0.25 1.80	19	<b>2.96</b>	1.78 4.62	0			9	<b>3.83</b>	1.75 7.27	5	1.11	0.36 2.58	10	<b>2.46</b>	1.18 4.52
East Asia	21	<b>1.82</b>	1.13 2.78	21	<b>3.19</b>	1.98 4.88	6	1.48	0.54 3.23	11	<b>4.18</b>	2.09 7.48	15	<b>2.00</b>	1.12 3.30	10	<b>2.53</b>	1.22 4.66
North America	35	<b>0.69</b>	0.48 0.96	27	0.94	0.62 1.36	16	0.67	0.39 1.09	10	0.67	0.32 1.23	19	0.70	0.42 1.10	17	1.22	0.71 1.96
South America	52	<b>2.33</b>	1.74 3.06	31	<b>2.26</b>	1.54 3.21	27	<b>3.95</b>	2.60 5.75	18	<b>3.32</b>	1.97 5.25	25	<b>1.62</b>	1.05 2.38	13	1.57	0.83 2.68
Africa	26	1.27	0.83 1.86	5	0.75	0.25 1.76	11	1.79	0.89 3.21	3	1.21	0.25 3.53	15	1.05	0.59 1.72	2	0.48	0.06 1.75
All immigrants	1,806	<b>1.38</b>	1.31 1.44	1,217	<b>1.40</b>	1.32 1.48	796	<b>1.46</b>	1.36 1.57	578	<b>1.39</b>	1.28 1.50	1,010	<b>1.31</b>	1.23 1.40	639	<b>1.40</b>	1.30 1.52

Table 1 continued

Birth region	Histology		Adenocarcinoma						Signet-ring cell carcinoma					
	Male			Female			Male			Female				
	N	SIR	95% CI	N	SIR	95% CI	N	SIR	95% CI	N	SIR	95% CI		
Sweden	5,137	1.00		2,985	1.00		526	1.00		509	1.00			
Finland	193	<b>1.57</b>	1.35 1.80	138	<b>1.39</b>	1.17 1.64	20	1.44	0.88 2.22	42	<b>2.22</b>	1.60 3.00		
Denmark	37	0.88	0.62 1.21	17	0.90	0.52 1.43	5	1.13	0.37 2.63	2	0.61	0.07 2.21		
Norway	37	0.98	0.69 1.35	26	0.82	0.54 1.20	2	0.52	0.06 1.87	6	1.15	0.42 2.50		
Baltic countries	43	<b>2.50</b>	1.81 3.37	16	1.47	0.84 2.38	3	1.94	0.40 5.66	3	1.99	0.41 5.83		
Germany	54	1.31	0.99 1.72	38	1.39	0.98 1.91	8	1.83	0.79 3.61	11	<b>2.34</b>	1.17 4.19		
Poland	25	<b>1.64</b>	1.06 2.42	24	<b>1.92</b>	1.23 2.85	5	3.03	0.98 7.06	6	2.19	0.80 4.77		
Russia	18	<b>2.61</b>	1.54 4.12	7	1.35	0.54 2.78	0			1	1.08	0.03 6.00		
Former Yugoslavia	34	1.27	0.88 1.78	21	<b>1.82</b>	1.13 2.79	6	2.04	0.75 4.44	3	1.33	0.27 3.89		
Other Eastern European <sup>b</sup>	116	<b>2.72</b>	2.25 3.26	40	<b>2.07</b>	1.48 2.81	18	<b>3.58</b>	2.12 5.65	17	<b>3.82</b>	2.22 6.11		
Greece	18	<b>1.70</b>	1.01 2.69	4	1.30	0.35 3.34	1	0.81	0.02 4.50	3	4.47	0.92 13.05		
Other Southern European <sup>c</sup>	19	1.33	0.80 2.07	5	1.23	0.40 2.88	5	<b>3.10</b>	1.01 7.24	1	1.31	0.03 7.30		
Other European <sup>d</sup>	16	0.82	0.47 1.34	3	0.43	0.09 1.25	3	1.32	0.27 3.87	2	1.34	0.16 4.84		
Turkey	14	1.35	0.74 2.26	9	2.09	0.96 3.98	5	<b>4.13</b>	1.34 9.63	1	1.03	0.03 5.75		
Iran	13	1.12	0.60 1.91	6	1.31	0.48 2.86	3	2.06	0.43 6.03	2	1.61	0.20 5.82		
Asian Arab countries	21	1.27	0.79 1.94	16	<b>2.63</b>	1.50 4.27	5	2.43	0.79 5.68	2	1.25	0.15 4.53		
Indian Subcontinent	5	1.28	0.41 2.98	2	1.45	0.18 5.24	1	2.01	0.05 11.20	1	2.67	0.07 14.90		
Southeast Asia	4	1.12	0.31 2.87	9	<b>2.91</b>	1.33 5.52	0			6	<b>6.71</b>	2.46 14.61		
East Asia	13	<b>2.28</b>	1.22 3.91	10	<b>3.30</b>	1.58 6.07	2	2.98	0.36 10.77	3	3.90	0.81 11.41		
North America	9	0.79	0.36 1.50	3	0.48	0.10 1.40	0			1	0.96	0.02 5.32		
South America	26	<b>2.08</b>	1.36 3.05	19	<b>2.97</b>	1.79 4.63	7	<b>4.50</b>	1.81 9.27	1	0.60	0.02 3.34		
Africa	14	1.22	0.67 2.05	2	0.63	0.08 2.27	3	2.06	0.42 6.01	2	2.26	0.27 8.17		
All immigrants	729	<b>1.51</b>	1.40 1.62	415	<b>1.43</b>	1.30 1.58	102	<b>1.89</b>	1.54 2.29	116	<b>2.06</b>	1.70 2.47		

<sup>a</sup> Bold type: 95% confidence interval (CI) does not include 1.00

<sup>b</sup> Other Eastern European: Romania, Slovakia, Czechoslovakia, Czech Republic, Hungary, and Bulgaria

<sup>c</sup> Other Southern European: France, Italy, and Spain

<sup>d</sup> Other European: Iceland, The Netherlands, UK, Ireland, Belgium, Liechtenstein, Luxembourg, Switzerland, Andorra, Cyprus, Israel, Malta, Monaco, Portugal, San Marino, State of the Vatican City, Albania, Macedonia, Moldova, and Slovenia

## Subjects, materials, and methods

We used the 2010 update of the Swedish Family-Cancer Database (FCD) for the present study [8]. Data on cancers in the FCD have a 4-digit diagnostic code according to the 7th revision of the ICD (<http://www.wolfbane.com/icd>): cardia (ICD = 1510). From 1993 onwards, the Systematized Nomenclature of Medicine (SNOMED) has been used: adenocarcinoma (SNOMED = 8140) and signet-ring cell carcinoma (8490) [9]. All gastric cancers (100%) reported to the Cancer Registry are histologically and anatomically verified. First-generation immigrants were defined as those born outside Sweden without identified parents in the Database. The start of follow-up was defined as the birth year, the date of immigration, or January 1, 1958, whichever came latest. For the histology-specific standardized incidence ratio (SIR), the start of follow-up was January 1, 1993. If the date of immigration was missing (about 134,000 immigrants), follow-up was started on the first year in which the immigrant was present in a census. The end of follow-up was defined as the date of cancer diagnosis, death, or emigration, or the end of the last year of presence in the census, or the closing date of our study, December 31, 2008, whichever came earliest.

Standardized incidence ratios (SIRs) were calculated as the ratio of the observed to expected numbers of cases. The expected numbers were calculated from 5-year age groups, sex and time periods (10-year bands from 1958 to 2008) in native Swedes as the reference population. Additionally, the effect of residential time was tested for two groups: time since immigration <20 years and  $\geq 20$  years. Confidence intervals (95% CI) were calculated assuming a Poisson distribution. SAS software ver.9.2 was used for the data analysis (SAS Institute, Cary, NC, USA).

## Results

The FCD included 23,579 male and 12,484 female cases of gastric cancer in native Swedes, and 1,806 and 1,217 cases in immigrants, respectively (Table 1). As compared to the native Swedes, the risk of gastric cancer was increased in all immigrants (SIR: men = 1.38, women = 1.40), except for North American men (0.69). The highest risk of cardia gastric cancer was seen among South American men (3.95) and some Asian (3.83–4.18) and South American (3.32) women. The highest risk of non-cardia gastric cancer was seen among “other East Europeans” (see Table 1 for definitions of the regional categories) (men = 2.18, women = 2.32), and Southeast Asian and East Asian women (2.46–2.53). Only “other European” women had a decreased risk (0.37). The highest risk of adenocarcinoma was seen among some Eastern European men (2.61–2.72) and some Asian (2.63–3.30) and South American (2.97)

women. However, Finnish, German, and Southeast Asian women; and “other Eastern European”, “other Southern European”, Turkish, and South American men had the highest risk of signet-ring cell carcinoma (2.22–6.71).

No trend was observed for the risks in immigrants according to the length of stay. For example, increased risks were observed for immigrant men ( $N = 687$ , SIR = 1.44, 95% CI = 1.34–1.56) and women ( $N = 470$ , SIR = 1.63, 95% CI = 1.49–1.79) who had resided in Sweden for less than 20 years. However, the risks remained high among immigrant men ( $N = 1,119$ , SIR = 1.34, 95% CI = 1.26–1.42) and women ( $N = 747$ , SIR = 1.28, 95% CI = 1.19–1.38) who had resided in Sweden for more than 20 years (data not shown).

## Discussion

Increased risks of gastric cancer among immigrants were observed in both anatomical sites noted in the present study: cardia and non-cardia. Also, these increased risks were mostly attributable to the increased risks of adenocarcinoma, which had a higher frequency than other histological types. Our findings reflect the incidence rates in the immigrants’ countries of origin [9]. For example, Finns showed an increased risk of gastric cancer, which was higher in Finland compared with Sweden [10–12].

Risk factors for gastric cancer, such as diet and *Helicobacter pylori* infection, may have been retained upon migration [13, 14]. We found that the observed increased risks among immigrants were independent of the length of stay. Our results, in line with the GLOBOCAN-2008 report [2] and the geographical spread of *Helicobacter pylori* [15], may show a major role for childhood environmental exposure in the etiology of gastric cancer.

The number of gastric cancer cases among second-generation immigrants was too small ( $N = 123$ ) for further consideration. However, the study of second-generation immigrants may show the role of gene-environmental interaction in the etiology of this cancer.

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