Does the risk of stomach cancer remain among second-generation immigrants in Sweden?

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Abstract The observed increased risks of noncardia stomach cancer among foreign-born second-generation immigrants compared to the Swedes suggest that these immigrants were infected by *Helicobacter pylori* before immigration.

Keywords Cancer · *Helicobacter pylori* · Infection · Risk · Second-generation immigrants · Stomach · Sweden

Previous descriptive epidemiological studies have shown that the risk of stomach cancer is influenced by environmental factors, in particular by *Helicobacter pylori* infection and diet [1]. However, the interaction between genetic susceptibility and environmental factors is suggested to play an important role in the etiology of stomach cancer [2, 3]. Several observations indicate that stomach cancer in the cardia region is etiologically different from that in the noncardia region [4, 5]. For example, the association of *H. pylori* infection with the risk of stomach cancer is restricted to the noncardia region, while the cardia region shares the same risk factors as the distal part of esophagus, for which an inverse association of *H. pylori* infection with

esophageal adenocarcinoma has been reported [4, 6–8]. It has been found that diet and smoking is associated with the risk of cancer in both stomach regions [4, 9, 10].

Although there are controversies regarding the influence of migration on the risk of stomach cancer [11–13], our previous study showed an increased risk of stomach cancer risk among first-generation immigrants in Sweden. It was suggested that childhood infection with *H. pylori* would be a possible cause [14, 15]. The prevalence of *H. pylori* varies from more than 80% among middle-aged adults in developing countries to less than 20% in developed countries [15, 16]. A change in the seroprevalence of *H. pylori* to the rate of that in host country has been reported among second-generation immigrants whose parents moved from high-risk countries [17, 18]. However, the effect of migration on the risk of stomach cancer through the next generations is still unclear and there is no study in the current literature, to our knowledge, exploring the risk of stomach cancer by site among second-generation immigrants [19–21]. In this report, as a subpopulation of our previous publication, we studied the risk of stomach cancer among second-generation immigrants by tumor site, in 304 stomach cancer cases, which is some 7 times the number of cases in previous publications on the same topic [14, 19–21].

We used the updated version of the Swedish Family-Cancer Database (FCD) [22]. Data on cancers in the FCD are coded based on the 7th revision of the International Classification of Disease (ICD), with stomach cancer coded as 151. The FCD has used the ICD-9 classification from 1987 onward, which codes cardia as 1510 and noncardia as 1511–1516, 1518, and 1519. The second-generation immigrants were defined as Swedish-born or foreign-born with identified mothers in the database. As in our previous studies, the expected number of cases and the standardized incidence ratios (SIRs) were calculated [23–25]. We used

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the native Swedes as the reference population. To capture the maximum number of cases, the second-generation immigrants were classified based on the risk of stomach

Table 1 Standardized incidence ratios (SIRs) for stomach cancer among second-generation immigrants to Sweden from 1958 to 2008

Birth region of mother	Birth region of second generation	Stomach cancer		
		N	SIR	95% CI
Sweden	Sweden	3,345	1.00	
High-risk countries	Sweden	92	1.22	0.98 1.49
	High-risk countries	133	2.06	1.73 2.44
Other countries	Sweden	55	1.16	0.88 1.52
	Other countries	21	1.77	1.09 2.70
All immigrants	Sweden	149	1.20	1.02 1.41
	All immigrants	155	1.99	1.69 2.33

Bold non-underlined SIRs values: 95% CI does not include 1.00. Bold underlined SIRs: higher than 1.00 at the 1% confidence level

High-risk countries: Finland, Baltic countries, Germany, Poland, Eastern Europe, Russia, former Yugoslavia, Greece, Southern Europe, Turkey, Iraq, Southeast Asia, East Asia, Chile, and Latin America. Other countries: Denmark, Norway, United Kingdom, Iran, Asian Arab countries: Lebanon, Syria, United Arab Emirates, Bahrain, Brunei, Gaza, Strip, Jordan, Kuwait, Oman, Palestine, Qatar, Saudi Arabia, South Yemen and Yemen. Indian Subcontinent, North America, and Africa

cancer observed in the first-generation immigrants in our previous report (“high-risk” countries: SIR was significantly increased and “other” countries: SIR was not significant) and based on the birth region of the mothers [14]. As the sex-specific analysis showed no differences in the risk of stomach cancer, the data were analyzed together for both sexes. The histology-specific risk of esophageal cancer, WHO/HS/CANC/24.1 Histology Code, “PAD”: adenocarcinoma (PAD = 96) and squamous-cell carcinoma (PAD=146) was also calculated to examine the effect of *H. pylori* infection from 1958 [4, 6]. Confidence intervals (95% CI) were calculated assuming a Poisson distribution, and a *P* value of less than 0.05 was considered as statistically significant. A *P* value of 0.01 was also used to minimize chance findings [26]. SAS software version 9.2 was used for the data analysis (SAS Institute, Cary, NC, USA).

Our data showed that the risk of stomach cancer was increased among foreign-born second-generation immigrants whose mothers had moved from “high-risk” countries (SIR = 2.06) or from “other” countries (1.77) (Table 1). The total number of stomach cancer cases with a defined site in the FCD was 3,446, and 282 of them were diagnosed in second-generation immigrants (Table 2).

Table 2 Standardized incidence ratios (SIRs) for stomach cancer by site and esophageal cancer by histology among second-generation immigrants to Sweden

Birth region of mother	Birth region of second generation	Stomach cancer ^a				Esophageal cancer ^b			
		<i>N</i>	SIR	95% CI		<i>N</i>	SIR	95% CI	
		Cardia				Squamous-cell carcinoma			
Sweden	Sweden	928	1.00			754	1.00		
High-risk countries	Sweden	25	1.14	0.74	1.69	14	1.04	0.57	1.74
	High-risk countries	23	1.26	0.80	1.89	18	1.37	0.81	2.17
Other countries	Sweden	14	1.05	0.57	1.76	5	0.51	0.16	1.18
	Other countries	3	0.89	0.18	2.61	3	1.26	0.26	3.69
All immigrants	Sweden	40	1.13	0.80	1.53	20	0.85	0.52	1.31
	All immigrants	26	1.18	0.77	1.72	21	1.33	0.82	2.03
		Noncardia				Adenocarcinoma			
Sweden	Sweden	2,236	1.00			704	1.00		
High-risk countries	Sweden	62	1.24	0.95	1.59	23	1.50	0.95	2.25
	High-risk countries	100	<u>2.33</u>	1.90	2.83	9	0.68	0.31	1.28
Other countries	Sweden	36	1.15	0.80	1.59	9	0.91	0.42	1.72
	Other countries	17	<u>2.15</u>	1.25	3.44	6	2.45	0.90	5.34
All immigrants	Sweden	99	1.21	0.98	1.47	32	1.26	0.86	1.78
	All immigrants	117	<u>2.25</u>	1.86	2.70	15	0.93	0.52	1.53

Significant SIRs: 95% CI does not include 1.00, and bold underlined SIRs were higher than 1.00 at the 1% confidence level

^a Based on ICD-9 classification from 1987 to 2008

^b Based on PAD classification from 1958 to 2008

High-risk countries: Finland, Baltic countries, Germany, Poland, Eastern Europe, Russia, former Yugoslavia, Greece, Southern Europe, Turkey, Iraq, Southeast Asia, East Asia, Chile, and Latin America. Other countries: Denmark, Norway, United Kingdom, Iran, Asian Arab countries: Lebanon, Syria, United Arab Emirates, Bahrain, Brunei, Gaza, Strip, Jordan, Kuwait, Oman, Palestine, Qatar, Saudi Arabia, South Yemen and Yemen. Indian Subcontinent, North America, and Africa

An increased risk of noncardia cancer was observed among foreign-born second-generation immigrants whose mothers had moved from “high-risk” countries (2.33) or from “other” countries (2.15). No increased risk of cardia cancer was observed in the second-generation immigrants. A non-significant decreased risk of esophageal adenocarcinoma was observed among foreign-born second-generation immigrants whose mothers had moved from “high-risk” countries (SIR = 0.68, 95% CI = 0.31–1.28).

In conclusion, the present data showed that the risk of noncardia stomach cancer was increased only among foreign-born second-generation immigrants. A likely explanation is that these immigrants were infected by *H. pylori* before immigration.

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