



Epidemiology note

Gastric cancer in Iceland

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Gastric cancer incidence varies substantially within Europe [1,2]. Incidences within the highest risk populations (>30 per 100000 age-adjusted [world population] in males from Eastern Europe) are similar to those seen in Japan. Low-risk populations (<10 per 100000) have incidences similar to those for Caucasians in the United States. Consistent with the general worldwide pattern, the overall incidence in nearly all European countries, including Iceland, has been declining for several decades, and this is thought to be due to the combination of an improved diet and a reduced prevalence of *Helicobacter pylori* infection [1–3]. The mortality from this disease is generally high. About half the cases seen in the Western world [4] and Iceland are resectable [5,6], where the chance of cure for those resected is approximately 35% [6]. The mortality is related to the stage of the disease, and, in Japan, a high-incidence

country, screening programs have yielded more patients in early stages, leading to improved results after surgery [7].

The people in Iceland used to be at high risk of gastric cancer [1,5,8,9], but the incidence has declined steadily during the past five decades. Gastric cancer ranked first and second in the group of most frequent cancer types in Icelandic males and females, respectively [10], but a steady decrease in incidence for both sexes has been seen during the past 50 years. The incidence for males has declined from 77 to 15 cases per 100000 between 1955 and 1999, whereas the incidence has declined from 32 to 6 per 100000 for females during the same time period (Fig. 1). Information on cancer cases in Iceland is obtained from the Icelandic Cancer Registry, which has been in operation since 1954; the information on cancer incidence in Iceland is, therefore, likely to be nearly complete for 1955 and onwards for cancer at all sites. When compared with other common cancer types (Fig. 1), the reduction in gastric cancer incidence is unique, as a reciprocal trend is found for other common cancer types, in both males (i.e., prostate, lung, and colon; Fig. 1a) and females (i.e., breast, lung, and colon; Fig. 1b). While the reasons for this decline in gastric cancer incidence are not clear, the world-wide geographic differences (Table 1) [2]; the coincidence of the decline with socioeconomic improvement and changes in diet and food preservation; and the role of *H. pylori* infection [2] all suggest that environmental factors underlie these trends. Gastric cancer incidence in Iceland is compared with rates in countries in South and North America, Europe, and Asia in Table 1. In this context, Iceland is now a country of intermediate incidence, but it was clearly a high-risk nation in the 1950s. The reduction in incidence probably represents a combination of lower incidence and better healthcare during the past 50 years.

Earlier studies showed considerable geographic variation in gastric cancer incidence within Iceland

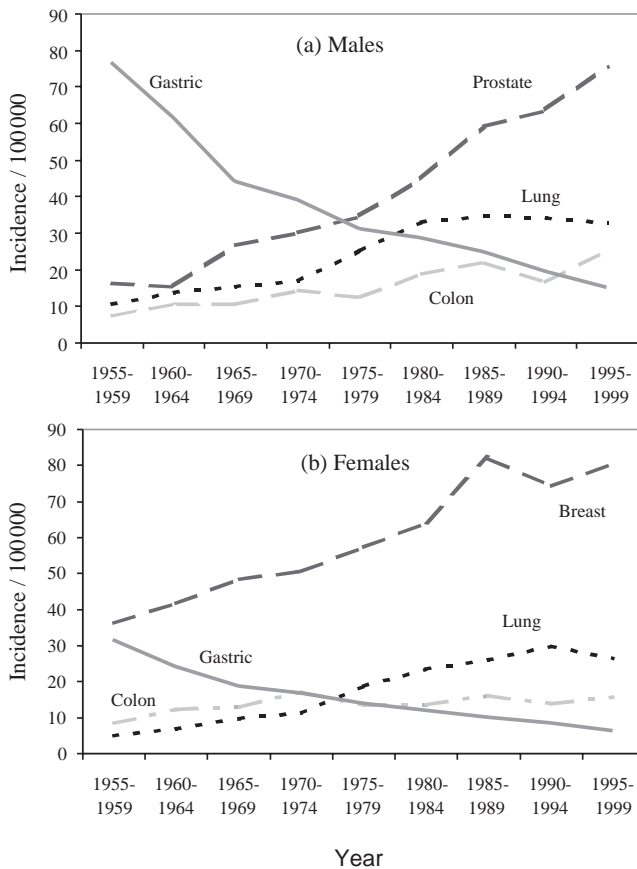
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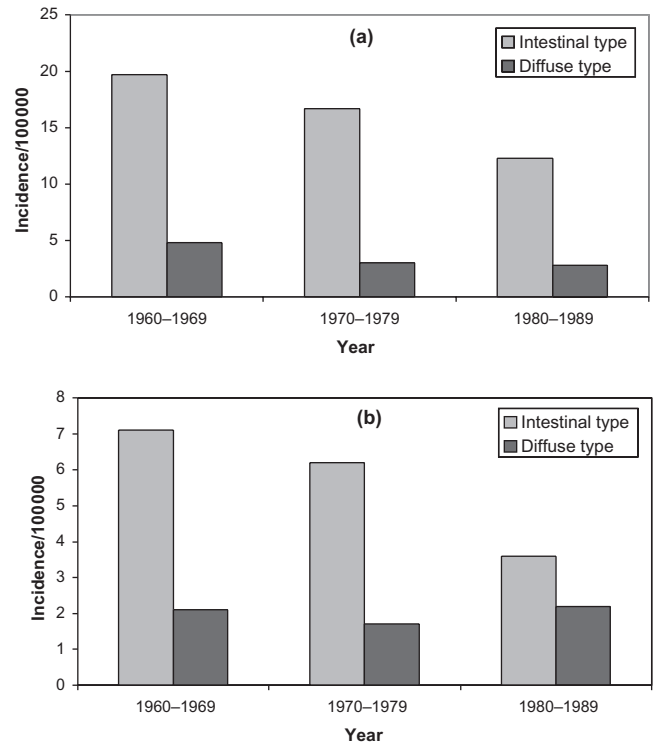
Table 1. Age-adjusted (world population) gastric cancer mortality rates in Iceland and in selected countries by sex (rates per/100000 population)

	Argentina 1996	United States 1996	Japan 1996	United Kingdom 1996	Norway 1996	Iceland 1957	Iceland 1996
Men	11.6	5.2	30.5	9.3	9.0	77.1	9.6
Women	4.9	2.3	12.2	3.6	4.1	24.0	5.5

Source: WHO Cancer mortality database, 2001 [25]

**Fig. 1a,b.** Changes in the incidence of common cancers in Icelandic **a** males and **b** females during the period 1955–1999; data from the Icelandic Cancer Registry

[10,11], and this led to the belief that the high incidence was related to a diet rich in pickle-salted, smoked, and singed food. An excess of gastric cancer was found among farmers and was found to correlate well with the consumption of home-smoked and home-grilled food in rural areas. In many of these homemade products, the content of nitrites and nitrates was higher than that considered safe for human consumption [10]. The dietary habits of Icelanders have changed considerably during the past 50 years, and the smoked and salted food is now more a traditional delicacy consumed on special occasions, and it has largely been replaced by

**Fig. 2a,b.** Changes in the incidence of intestinal-type and diffuse-type gastric cancer in Icelandic **a** males and **b** females in the period 1960–1989

fresh and frozen products. This change in dietary habits is probably another of the factors that can help to explain the decrease in the incidence of gastric cancer in Iceland.

In Icelandic males during the period 1955–1984, 78.1% of all gastric cancers were intestinal type, and 16.5% were diffuse type; in Icelandic females, 73.1% were intestinal type and 20.7% were diffuse type [10]. There has been a more pronounced change in incidence of the intestinal type (Laurèn), as the decline during the past five decades (i.e., 1955–1999) in gastric cancer in Icelanders has mostly affected the intestinal type of tumor, whereas diffuse-type tumors have declined only slightly in both sexes (Fig. 2) [5,10]. Based on this pattern, it has been suggested that the major determinants of the intestinal gastric cancer type are environmental rather than genetic [10]. This pattern is also found in

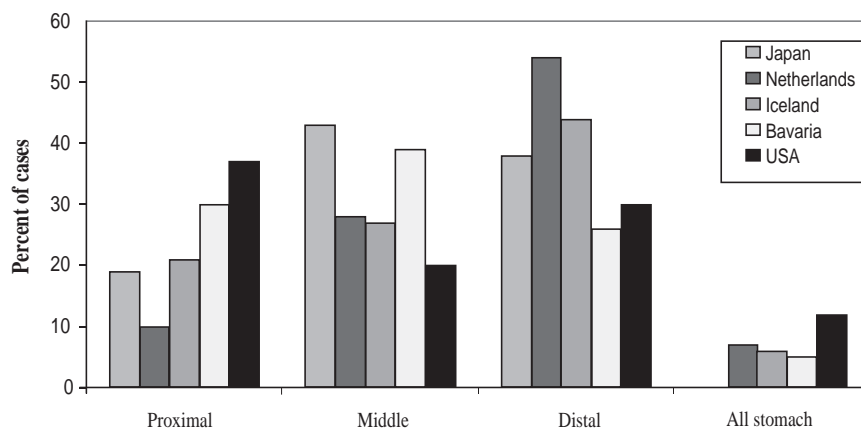


Fig. 3. Location of gastric cancer tumors in Iceland and four other countries/regions during the period 1980–1990 [26–29]

other high-risk countries [3,12]. Diet and infection with *H. pylori* are probably the prominent environmental risk factors for gastric cancer, but familial aggregation, in a variable but significant proportion of cases, suggests the importance of genetic predisposition [3,13,14]. This has been supported by reports of a dominantly inherited predisposition to gastric cancer [3,15–18] and, subsequently, the description of germline mutation in the *E-cadherin/CDH1* gene in Maori kindreds with hereditary, early onset, diffuse-type gastric cancer [19]. In a recent study [20], the genetic epidemiological aspects of gastric cancer in Iceland were investigated. It was found that first-degree relatives of gastric cancer patients have a two- to three fold increased risk of developing gastric cancer compared with the general population. The risk is elevated for both sexes, although the elevation is greater for males. Signs of a histological specific risk were found, as relatives of those probands diagnosed with the diffuse type were at higher risk compared with relatives of those probands diagnosed with the intestinal type. Overall, it was suggested that genealogical and familial aggregation information might have important prospective value for the relatives of gastric cancer patients.

In Iceland, most gastric cancers are located in the distal stomach (antrum/pylorus), followed by the middle and the proximal stomach (cardia/fundus) (Fig. 3). A similar pattern is found in the Netherlands, but in Japan and Bavaria (Germany), tumors are most common in the middle stomach, and in the United States they are most common in the proximal stomach. The different location patterns may have relevance for gastric cancer patients, as the prevalence of *H. pylori* infection is higher in patients with the cancer located distally than in those with the cancer located proximally [21]. Also, a study from Japan [22] indicates that the familial gastric cancers are frequently located in the cardiac region (proximal) and that they appear to be more aggressive than sporadic gastric cancers (in general, proximal can-

cers have a worse prognosis). In Iceland, *H. pylori* was detected in 80% of patients with gastric cancer, and there was significant decrease in IgG antibody levels over a period of several years before the diagnosis [23]. In a recent review [24], a weak association was found between *H. pylori* and gastric cancer, but the association was much lower than that needed to account for the sharp variations in gastric cancer mortality between different populations (e.g., 20-fold higher in certain parts of China than in the United States [24]) or between past and present (e.g., eight fold decrease in Iceland between 1957 and 1996; Table 1). This observation implies that important cause(s) of gastric cancer still await discovery.

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