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# The epidemiology of gastric cancer

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**Abstract**
**Gastric cancer mortality has declined markedly around the world. In South Australia, the reduction approximated 40% over the last 20 years. Possible reasons include: better refrigeration; reduced consumption of salted, smoked, and chemically preserved foods; increased intake of fruit and vegetables; and improved living standards and a greater use of antibiotics, which may have reduced *Helicobacter pylori* infection. Reductions generally have been greater for intestinal than diffuse histopathologies. Gastric cancer remains the second leading cause of cancer death worldwide, probably accounting for about 10% of newly diagnosed cancers. High rates apply to Japan, China, Central and South America, Eastern Europe, and parts of the Middle East, and low rates to North America, Australia and New Zealand, Northern Europe, and India. Rates usually are higher in lower socioeconomic groups. Five-year relative survivals of around 20% or less are frequently reported. A figure of 50% or more has been cited for Japan, where there has been radiological screening, although this exceptional figure could have been affected artificially by lead-time and related effects. Male-to-female incidence ratios generally are in the 1.5–2.5 range, with higher ratios for intestinal than diffuse cancers and higher-risk populations. In South Australia, the ratio has been *1.8 to one*, although higher at *4.6 to one* for cardia lesions. Recent increases in cardia cancers, especially in males in populations of European extraction, often are accompanied by increases for esophageal adenocarcinoma. It is estimated that the global burden of gastric cancer could be reduced by up to 50% by dietary changes that included an increased intake of fruit and vegetables.**

**Key words** Gastric cancer · Incidence · Mortality · Survival · Cardia lesions

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## Introduction

There have been widespread reductions in gastric-cancer incidence and mortality around the world in the last 50 years, which have been described by some authorities as an "unplanned triumph" [1–3]. Nonetheless, gastric cancer is still estimated to account for about 10% of invasive cancers worldwide (excluding non-melanocytic skin cancers) and probably is the second leading cause of cancer death [2,4]. Even in South Australia, where incidence and mortality rates are relatively low, gastric cancer was the sixth leading cause of cancer death in 1997–1999, exceeded only by cancers of the lung, colon/rectum, female breast, prostate, and pancreas [5–7].

The incidence of gastric cancer varies greatly across populations [8]. In this report, regional and time trends are described, and explanations for these and other trends are suggested.

## Regional trends

### *Incidence*

Incidence data from volume VII of *Cancer incidence in five continents* [8] point to an almost eight-fold variation in incidence of gastric cancer around the world circa 1990 (Table 1). By far the highest incidence applied to Japan, but elevated rates also were indicated for China, Central and South America, Eastern Europe, and (less so) Southern Europe. By comparison, low rates applied to North America, India, Australia and New Zealand, and Northern Europe. The high rates in Japan often are attributed to a high intake of salt, although ecological studies have not shown a consistent association [4,9,10].

Data for South Australia confirm that the Australian-born have a low risk of gastric cancer, with migrants from other countries having an age-sex standardized

**Table 1.** Mean annual age-standardized (world population) incidence of gastric cancer per 100 000 residents by region of the world: diagnostic period, circa 1990[a]

| Region | Incidence (95% confidence limits) | |
|---|---|---|
| | Males | Females |
| Africa | 15.0 (13.8, 16.2) | 8.5 (7.6, 9.4) |
| Central and South America | 29.5 (28.8, 30.2) | 14.6 (14.2, 15.0) |
| North America | 9.6 (9.4, 9.8) | 4.0 (3.9, 4.1) |
| China | 34.0 (33.5, 34.5) | 15.3 (15.0, 15.6) |
| India | 9.7 (9.3, 10.1) | 4.7 (4.4, 5.0) |
| Japan | 72.1 (71.4, 72.8) | 30.2 (29.8, 30.6) |
| Other Asia | 14.1 (13.6, 14.6) | 7.3 (7.0, 7.6) |
| United Kingdom and Ireland | 16.3 (16.0, 16.6) | 6.5 (6.4, 6.6) |
| Northern Europe | 13.4 (13.2, 13.6) | 6.2 (6.1, 6.3) |
| Eastern Europe | 27.9 (27.6, 28.2) | 12.4 (12.3, 12.5) |
| Southern Europe | 21.4 (21.0, 21.8) | 9.9 (9.7, 10.1) |
| Australia and New Zealand | 11.2 (10.9, 11.5) | 4.6 (4.4, 4.8) |

[a] Data source: *Cancer incidence in five continents (volume VII)* [8]

incidence approximately 60% higher [11]. The elevation was 65% for British-Irish migrants and 70% for migrants from Southern Europe. This is broadly consistent with differences expected from cancer rates for their countries of origin (Table 1) [8].

There has been widespread population screening by radiological means in Japan since the late 1960s, which could have inflated incidence figures through increased detection [3,4,9,12,13]. Nonetheless, it is relevant to observe that age-sex standardized (world population) mortality rates circa 1993 also showed a marked elevation, with the rate being approximately five to six times higher in Japan than for the United States and Canada, and four to five times higher than for Australia and New Zealand [14].

### *Age and sex distribution*

The global age-standardized incidence of gastric cancer for males was about 2.2 times higher than for females circa 1990 [8,9]. Males had higher rates in all regions, with the male-to-female ratio ranging from *1.8 to one* for Africa to *2.5 to one* for the United Kingdom/Ireland (Fig. 1). A tendency is suggested for the ratio to be higher for higher-than lower-risk areas of the world, although exceptions apply. Generally, the ratio has been close to 1.00 in age groups under 40–50 years, but higher in the older age groups [4]. Generally, higher male-to-female ratios have been reported for the intestinal than diffuse histopathologies [4,9,15]. Gastric cancer is largely a disease of the older age groups in most countries [8]. In South Australia, 54.8% were diagnosed in people aged 70 years or more during 1977–1999, whereas the corresponding proportion in this age range for all cancers registered on the State registry was lower, at 43.4% [5–7]. Conversely, the proportion diagnosed in people under 40 years of age was lower, at 2.1% for stomach cancer, compared with 7.2% for all registered cancers.

### *Subsite distribution*

The percentage of gastric cancers sited in the cardia, as opposed to more distal specified subsites, was 31.7% for males and 18.8% for females, with higher percentages applying to males than females in each region (Fig. 2) [8]. The percentage in the cardia varied markedly by region, with the highest percentages applying to the United Kingdom/Ireland, Australia and New Zealand, China, North America, and Northern Europe, and the lowest to Africa, Japan, and Southern Europe. Lesions of the cardia vary in prevalence within populations [9]. In the United States, they reportedly occur disproportionately in young white males [16].

In South Australia, the male-to-female ratio in 1997–1999 was *1.8 to one* for all gastric cancers, *4.6 to one* for cardia lesions, and *1.6 to one* for cancers of the more distal subsites. Around the world, the male-to-female ratio for cardia lesions was relatively high for North America, Southern Europe, Australia and New Zealand, and the United Kingdom/Ireland, but low for Japan, Africa, and Eastern Europe (Fig. 3).

## Time trends

### *All subsites (in total)*

There has been a worldwide decline in stomach cancer mortality over the last 50 years, with many researchers citing changes in diet as likely causes, including a greater consumption of fruit and vegetables, and a reduced intake of salted, pickled, and preserved foods; and improvements in refrigeration [3,4,17–20].

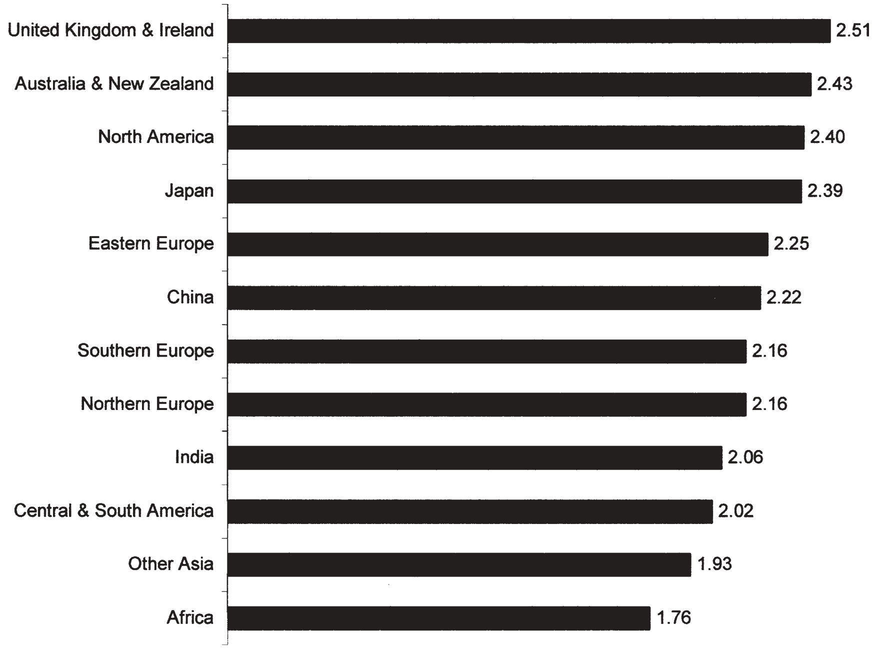


**Fig. 1.** Male-to-female ratio of age-standardized (world population) incidence rates for gastric cancer by region of the world: diagnostic period, circa 1990. Data source: *Cancer incidence in five continents (volume VII)* [8]

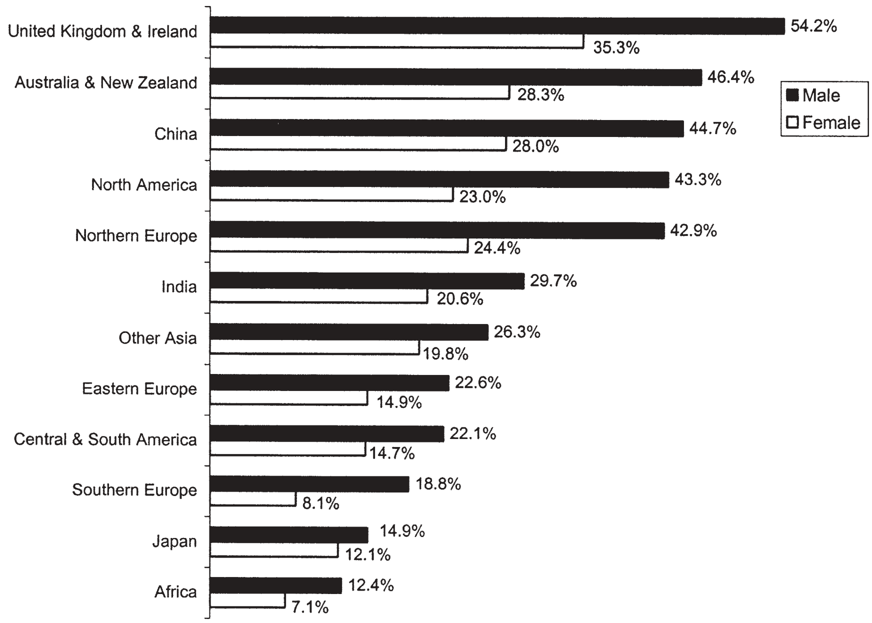


**Fig. 2.** Percentage of annual age-standardized (world population) incidence rates applying to the gastric cardia, as opposed to other specified gastric subsites, by region of the world: diagnostic period, circa 1990. Data source: *Cancer incidence in five continents (volume VII)* [8]

These tumors have been broadly classified histologically as intestinal or diffuse, with the intestinal type generally being more common in high-risk areas of the world, in males and in older age groups [21]. Data for Norway and for Hawaiian Japanese indicate that the decline in gastric cancer has applied mostly to intestinal lesions [22,23].

South Australian data show a larger decline in age-sex standardized mortality rate, of about 40%, between 1977–1981 and 1997–1999 than the corresponding 33% decline in incidence (Table 2). This scale of decline is similar to that seen in many populations [3]. In South Australia, declines were similar in magnitude between males and females, whereas in France and some other parts of Europe, the decline reportedly has been greater in females [3].

In many countries, including the United Kingdom, Spain, Japan, New Zealand, and the United States (males), the decline in incidence and mortality appears to be decelerating, with smaller reductions apparent for the younger age groups [3,16,24]. South Australian mortality data suggest a similar pattern, with the age-sex

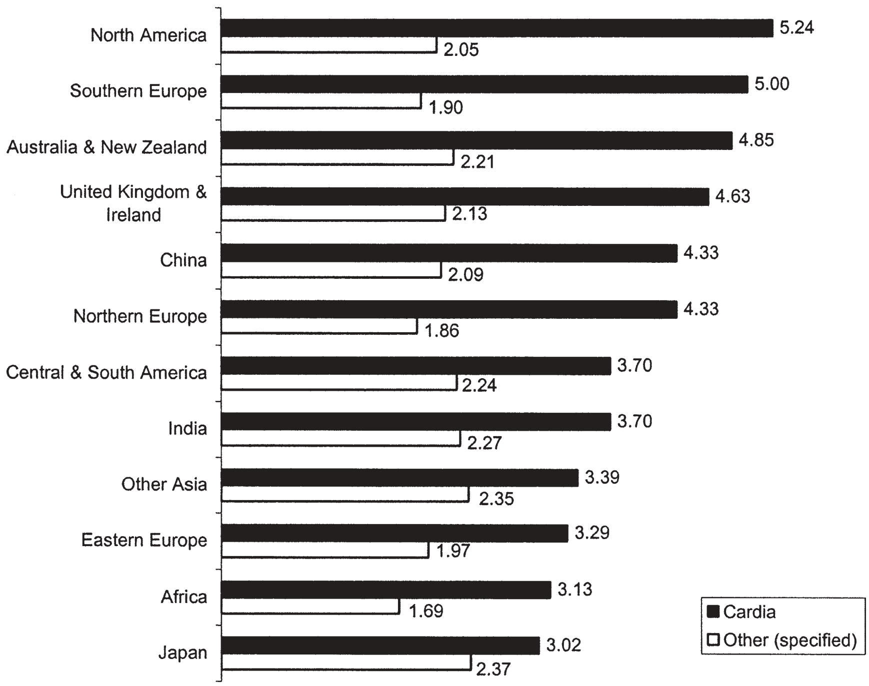


**Fig. 3.** Male-to-female ratio of age-standardized (world population) incidence rates for gastric cancer by subsite and region of the world: diagnostic period, circa 1990. Data source: *Cancer incidence in five continents (volume VII)* [8]

**Table 2.** Mean annual age-standardized (world population) incidence and mortality rates for gastric cancer: South Australia, 1977–1999[a]

| | Period | Rates (95% confidence limits) |
|---|---|---|
| Incidence | 1977–1981 | 1.00 |
| | 1982–1986 | 0.90 (0.84, 0.97) |
| | 1987–1991 | 0.75 (0.70, 0.80) |
| | 1992–1996 | 0.72 (0.67, 0.77) |
| | 1997–1999 | 0.67 (0.61, 0.73) |
| Mortality | 1977–1981 | 1.00 |
| | 1982–1986 | 0.86 (0.79, 0.93) |
| | 1987–1991 | 0.72 (0.66, 0.77) |
| | 1992–1996 | 0.66 (0.61, 0.71) |
| | 1997–1999 | 0.60 (0.54, 0.66) |

1977–1981 Baseline rates set to "1.00"
[a] Data source: *SA Cancer Registry* [7]

standardized (world population) rate reducing between 1977–1981 and 1997–1999 by 31% for people under 50 years of age, as compared with larger reductions, of 35%, for 50 to 69-year-olds, and 44% for those aged 70 years or more. In general, the decline in gastric-cancer rates around the world appears to be lower in cohorts born since the 1930s [3].

Most of the global decline in gastric-cancer mortality can be attributed to the reduction in incidence. There is also the indication, however, of small secular gains in case survival [3,7,25]. In South Australia, 5-year relative survivals increased from 18.9% for the 1977–1983 diagnostic period to 20.9% for 1984–1990 and 22.1% for 1991–1998 [7]. United States Surveillance, Epidemiology, and End Results (SEER) data show similar gains in 5-year survivals, from 16.5% for the 1977–1979 diagnostic period to 21.8% for 1992–1997 [25]. Because few deaths occur after 5 years from diagnosis [7,25], these figures are probably a good approximation of longterm outcomes.

Gains in case survival have been attributed by some researchers to earlier detection from a greater use of gastroscopy [9]. While 5-year survivals from this cancer have approximated 20% or less for most populations, figures of about 50% or more have been reported for Japan [4,26]. This reflects the history in Japan of population-based radiological screening since the late 1960s. It is still uncertain, however, how much of this gain is real and how much reflects an increased diagnosis of more benign lesions (potentially including a proportion of intra-epithelial lesions), together with lead-time and related artificial influences [3].

There is speculation whether the smaller secular reduction in recorded cancer incidence in Japan, when compared with most other countries, has been due to an "offsetting" increase in detection through screening of more benign lesions [3]. By comparison, percentage reductions in mortality in Japan have been equivalent in scale to reductions seen in Europe [3]. This has led some researchers to consider that the reduction in mortality in Japan may not have resulted from screening [3]. An alternative explanation could be that the scale of the reported incidence reduction is valid and that the larger mortality reduction reflects an additional contribution from screening effects.

While a number of case-control and other observational studies suggest an effect of screening on gastric-cancer mortality of around 50%, the effects cannot be assessed with certainty without a randomized trial [12,27–30]. Such a trial reportedly is underway, with Japanese municipalities being used as the unit of random allocation [13].

*Individual subsites*

In contrast with the general decline in incidence, an increase has been observed for cardia lesions in many regions [3,9,16,31]. Comparatively high rates are evident for the United Kingdom/Ireland, Northern Europe, Australia and New Zealand, China, and North America [3]. The increase in incidence of cardia lesions has been associated with parallel increases for adenocarcinomas of the lower esophagus, where hyperacidity, reflux esophagitis, Barrett's esophagus, and obesity have been proposed as likely risk factors [16].

## Other trends

*Race*

South Australian data indicate a higher incidence of gastric cancer in Aboriginal than in Caucasian and other non-Asian residents, with the relative risk (95% confidence limits) for Aboriginal residents being 2.21 (1.24, 3.64) circa 1977–1996, after age-sex adjustment [32]. By comparison, Asian residents had an incidence similar to that for other non-Aboriginal residents [5]. The elevated incidence for the Aboriginal population likely reflects their living standards, with a poorer access to good-quality refrigeration, and diets characterized by a low content of fresh fruit and vegetables [32].

United States data indicate that the black population has an incidence approximately twice that reported for white residents [9]. For example, United States SEER data circa 1990 pointed to an elevated relative risk for the black as compared with the white population, after age-sex adjustment, of 1.93 (1.82, 2.04) [8]. Again, this may reflect differences in diet and broader environmental influences [9].

More detailed data by race are available for Los Angeles [8], where, compared with the white population, age-sex adjusted relative risks (95% confidence limits) varied by race as follows:

- Blacks — 1.84 (1.68, 2.00)
- Chinese — 1.87 (1.56, 2.21)
- Japanese and Korean — 3.84 (3.45, 4.26).

Again, it is likely that these differences would reflect dietary and broader environmental effects [9].

*Socioeconomic status*

United States data reportedly show an incidence of gastric cancer up to two times higher in the poorer than in the more affluent sectors of the population [9]. Other populations also show an excess in lower socioeconomic groups [33–35]. In South Australia, the mean annual age-sex standardized (world population) incidence per 100 000 (95% confidence limits) was 7.9 (7.3, 8.5) during 1977–1996 for the upper socioeconomic postcodes of the State capital, compared with 8.6 (8.2, 9.1) for the middle and 10.4 (9.5, 11.4) for the lower socioeconomic postcodes [5]. This gradient has been attributed to differences in diet and living standards.

Occupational differences in age-sex standardized incidence generally are thought to reflect socioeconomic differences, rather than occupational effects per se, although there is some indication of an association between gastric cancer and exposures to asbestos, polycyclic aromatic hydrocarbons, and N-nitroso compounds [9,36,37]. In South Australia, the relative risk (95% confidence limits) of gastric cancer for specified occupational groups circa 1977–1999 (compared with all occupational groups combined) varied as follows:

- Labourers, cleaners and related workers — 1.58 (1.12, 2.16)
- Metal workers — 2.25 (1.33, 3.56)
- Carpenters — 1.91 (1.11, 3.06)
- Welders — 2.44 (1.17, 4.49)
- Bricklayers and concrete workers — 2.54 (1.42, 4.19)
- Chefs, waiters, and waitresses — 3.03 (1.45, 5.57)
- Tertiary qualified teachers — 0.36 (0.13, 0.78)
- Medical practitioners — 0.23 (0.03, 0.82).

Again, these results are consistent with a low socioeconomic gradient of this cancer.

## Risk factors and control procedures

*Environmental factors*

Diet. A high consumption of fruit and vegetables is negatively related to risk of gastric cancer [9,18,20,38]. These food items are thought to have a protective antioxidant effect and to inhibit endogenous nitrosation through their vitamin C content and possibly through other micronutrients [4,9,38]. A high intake of salted foods, and potentially of smoked, cured, and pickled foods, is thought to be a risk factor [4,9,18,39]. These foods may include elevated levels of N-nitroso compounds, or their precursors, which have been shown to be potent carcinogens in animal experiments, including experiments on non-human primates [40]. Salted foods also may have abrasive qualities that may predispose to degeneration of the gastric mucosa [9,36]. There is also additional preliminary evidence that high-nitrate and high-starch diets may be risk factors, whereas allium (e.g., garlic and onions) and green tea may have protective qualities [4,9,36].

Ionizing radiation. This is an established cause of gastric cancer, based on evidence from populations exposed to A-bombs and patients with ankylosing spondylitis who were therapeutically exposed [41,42].

Alcohol and tobacco. Alcohol consumption has shown only a weak association with gastric cancer, generally without evidence of a dose response [4,9]. There is some indication, however, that very high consumption levels for red wine and vodka may be a risk factor [4]. While smokers generally have an elevated risk, dose-response relationships have not been demonstrated consistently and the association is uncertain [4,9].

*Helicobacter pylori.* Infection with these organisms is strongly implicated as a risk factor [4]. It is thought to predispose to gastritis, which may progress through metaplastic and dysplastic change to the development of a cancer [4,43]. Infection levels have been found to correlate, albeit weakly, with risk of gastric cancer in ecological and other observational studies [4,31].

### *Host factors*

Gastric morbidity. Adenomatous polyps, environmental and autoimmune chronic atrophic gastritis, and intestinal metaplasia are thought to be antecedent conditions for gastric cancer [9,18,44]. A history of a gastric ulcer also may signify an increased risk, although the evidence is uncertain [4,9,45].

Familial susceptibility. Familial risk is known to occur [9,18,46]. Blood type A is thought to be a risk factor for diffuse cancers [9,23].

Other factors. Pernicious anemia also is associated with an increased risk of gastric adenocarcinomas, particularly papillary lesions [16,18]. Meanwhile, the risk of proximal cancers may be associated with obesity and reflux esophagitis [16].

## Cancer control

It has been estimated that the global burden of gastric cancer could be reduced by up to 50% if there were dietary modification that led to a high intake of fresh fruit and vegetables [47]. While population screening, theoretically, could have a comparable effect, this is uncertain [3]. Moreover, the cost-effectiveness of screening would be questionable, unless restricted to high-risk groups [3].

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