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Gastric cancer incidence in the Romagna Region of Italy: A spatial and temporal analysis

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ABSTRACT

Background: The worldwide decrease in gastric cancer incidence is due to a birth-cohort-dependent decrease in exposure to major risk factors.

Methods: In an area of northern Italy with a historically strong internal geographical gradient in gastric cancer incidence, variations in rates by municipality and age group between 1987 and 2008 were evaluated. The study period was divided into three nonadjacent periods. End points included: age- and sex-standardised incidence rates; incidence rate ratio between age- and sex-standardised incidence rates; smoothed relative risks of gastric cancer incidence, and posterior probabilities of the relative risk being >1.

Results: In 1987–1990, the estimate of posterior probabilities of relative risk being >1 showed a higher incidence in hilly/mountainous areas. Between 1987–1990 and 2005–2008, a uniform decrease of more than 50% was observed (incidence rate ratio: plain, 0.45 (95% confidence interval 0.40–0.51); hill, 0.44 (0.34–0.58); mountain, 0.48 (0.22–1.02)). The decrease in the mountainous area was weak in the middle time period, with an incidence rate ratio of 0.92 (0.46–1.84), and intensified afterwards. The decrease occurred earlier and was more pronounced among younger people. In 2005–2008, gastric cancer risk was uniform across ages and municipalities.

Conclusions: The observed changes in gastric cancer incidence is the epilogue of a birth-cohort-dependent decrease in exposure to major risk factors.

1. Introduction

The worldwide decrease in gastric cancer (GC) incidence and mortality that has been observed for decades suggests that exogenous (environmental and lifestyle) factors are major contributors to the aetiology of the disease. The main risk factors are *Helicobacter pylori* (*H. pylori*) infection and a dietary pattern that includes a low intake of leafy vegetables and fresh fruit and a high intake of complex carbohydrates, hard grains, salt, salt-preserved foods, and nitrites [1,2].

Both *H. pylori* infection and dietary risk factors are characterised by two key features. First, they are associated with a low socioeconomic status [2] and, second, they operate mainly before adulthood [3]. These features account for most of the descriptive epidemiology of the disease.

In particular, the socioeconomic correlates of exposure to gastric carcinogens largely explain the geographic pattern of GC incidence on a global scale a well as the long-term incidence trend. On the one hand, nearly two-thirds of GC cases occur in developing countries [2,4] and, on the other, the favourable time trend observed in these countries and in limited high-risk areas of more developed parts of the world is linked to continuing improvements in socioeconomic status. This includes increased income and education, better food and nutrition policies, and improved living conditions during childhood with respect to overcrowding and poor sanitation [5–8].

However, since gastric carcinogens act mainly before adulthood, a decreased exposure has a greater impact on the risk of disease if it occurs early in life. For this reason, the long-term decrease in incidence that has been caused by the above socioeconomic changes qualifies as a birth-cohort-dependent phenomenon [9,10]. The decrease has taken place starting from young people, and each new generation entering the population has had a lower risk of getting GC than the preceding one.

The Romagna Region of Italy still has one of the highest incidence rates of GC in the Western world [11]. The area, however,

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Table 1
Italian National Statistics Bureau official code number and terrain classification of the 24 municipalities in the study area.

ISTAT official code number	Municipality name	Current health care district	ISTAT official terrain classification	Average population[a]
039004	Brisighella	Ravenna	Hill	7735
039005	Casola Valsenio	Ravenna	Hill	2850
039006	Castel Bolognese	Ravenna	Plain	8218
039007	Cervia	Ravenna	Plain	25,931
039010	Faenza	Ravenna	Plain	54,447
039014	Ravenna	Ravenna	Plain	141,451
039015	Riolo Terme	Ravenna	Hill	5154
039016	Russi	Ravenna	Plain	10,788
039018	Solarolo	Ravenna	Plain	4114
040003	Bertinoro	Forlì	Plain	9025
040005	Castrocaro Terme/Terra del Sole	Forlì	Hill	5818
040009	Civitella di Romagna	Forlì	Hill	3762
040011	Dovadola	Forlì	Hill	1578
040012	Forlì	Forlì	Plain	110,448
040013	Forlimpopoli	Forlì	Plain	11,640
040014	Galeata	Forlì	Hill	2303
040019	Meldola	Forlì	Hill	9320
040022	Modigliana	Forlì	Hill	4786
040031	Portico/San Benedetto	Forlì	Mountain	871
040032	Predappio	Forlì	Hill	6127
040033	Premilcuore	Forlì	Mountain	883
040036	Rocca San Casciano	Forlì	Hill	2110
040043	Santa Sofia	Forlì	Mountain	4230
040049	Tredozio	Forlì	Hill	1366

ISTAT, Italian National Statistics Bureau.
[a] Average annual population (both sexes combined) in the years 1987–1990, 1996–1999, and 2005–2008.

has been historically characterised by a much higher risk of disease in its southern part, which has a hilly and mountainous terrain and a lower population density. In the 1960s–1970s, the rural municipalities, particularly the southernmost ones, had a twofold greater mortality from GC than the urban municipalities [12]. Local studies [13,14] confirmed the etiological role of dietary risk factors and of exposure to these in the first two decades of life.

After World War II, the local economy experienced an impressive economic growth [15,16]. Since 1951, the proportion of active agricultural workers out of the total male population has dropped from 42% to less than 5% [17]. The level of income and the employment rate have increased, especially in the southern part of the area [15]. Since 1980s, the excess mortality previously reported from rural municipalities has no longer been observed [12,15,16].

The present study evaluated the impact of the new socioeconomic scenario on GC incidence rates by municipality and age group between 1987 and 2008.

2. Methods

2.1. Study design and objectives

Based on the above general and local epidemiologic background, the purpose of the present study was to demonstrate: first, that the decrease in GC incidence – as expected – was larger in the high-risk municipalities, *i.e.*, in the most exposed ones at the beginning of cancer registration; second, that the decrease – by implication – was associated with an attenuation of differences between municipalities, resulting in a more uniform incidence and reflecting the more regular prevalence of non-exogenous risk factors; and third, that the incidence decrease and attenuation of differences were more pronounced among younger people.

2.2. Incidence data

We obtained the individual case records of registered GC patients from the Romagna Cancer Registry, a general, population-based cancer registry accredited by the International Agency for Research on Cancer. Major information sources include archives of histology and cytology reports, hospital discharge records, oncology department outpatient records, private clinical records, and death certificates from local public health departments. Additional details, including the indices of data quality, are reported elsewhere [11].

The registry was established in 1986 in the former health care districts of Forlì, Ravenna, and Faenza, which includes 24 municipalities and accounts for approximately half of the region. The remaining part, gradually covered by cancer registration in later years, was excluded from the study. Data for the first year of registration were not used because of concerns about their completeness. All cases of invasive cancer, including death certificate only (DCO) cases, were eligible.

Municipalities were identified with the Italian National Statistics Bureau (ISTAT) official code number. Their terrain classification (plain, hill, mountain) was based on the ISTAT criteria. Table 1 shows the ISTAT official code number and the terrain classification of the municipalities in the study area.

2.3. Statistical methods

We divided the study period into three nonadjacent time periods (1987–1990, 1996–1999, and 2005–2008). All estimates were for both sexes combined.

Directly age- and sex-standardised incidence rates (hereby briefly referred to as standardised incidence rates) were calculated using the world standard population [18]. A change in incidence was calculated as the ratio, with 95% confidence interval (CI), between the observed standardised incidence rates in the years 1996–1999 and 2005–2008 and that expected based on rates observed in 1987–1990 (incidence rate ratio, IRR).

The standardised incidence ratio (SIR) (observed/expected number of cases standardised for age and sex) for each municipality versus the entire study area (both sexes combined) was also computed. The entire population of the 24 study municipalities was used as the standard population. Indirect standardisation by age