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Different trends in stomach and pancreatic cancer mortality rates

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The research on stomach and pancreatic cancer mortality trends in Spain, recently published in The Spanish Journal of Gastroenterology by Lucía Cayuela and colleagues, analyzes, using different approaches, the recent cancer mortality changes undergone by these two digestive tumours in the country (1,2).

In their manuscript on gastric cancer (1), Cayuela et al. describe gastric cancer mortality trends in Spain over the period 1980-2021 using joinpoint analysis, and evaluate the independent age, period of death and birth, cohort effects on this trend. Globally, age-standardized gastric cancer mortality rates decreased from 48.7 deaths per 100,000 in 1980 to 13.4 in 2021 for males, and from 25.5 deaths in 1980 to 6.3 in 2021 for females. Also, the joinpoint analysis estimated an average annual percentage decline in death rates of 3.3 % and 3.1 % in females and males, respectively. The use of age-period-cohort models separately in men and women helped Cayuela and colleagues to further deepen into the importance of each factor in the risk of dying from gastric cancer. As with most cancers, gastric cancer mortality risk increased with age in both sexes. On the other hand, they also showed that gastric cancer mortality risk decreased in men and women with calendar time and in successive birth cohorts.

In agreement with the stabilizing decline in risk registered for cohorts born since the 1970s, stable trends were also observed among the men and women younger than 35
years of age. Stomach cancer is the only tumor for which there has been a significant and constant decrease in incidence and mortality figures since the past century in most countries of the world, without an organized preventive strategy intervention. For this reason, in 1986 Howson et al. defined the decline in gastric cancer as the epidemiology of an unplanned triumph (3), and suggested that gastric cancer, like most other malignancies, was the result of environmental causes. In the early 1980s, while research on the etiology of stomach cancer was aiming to understand the role of different risk factors, mainly diet-related factors, the publications by Warren and Marshall on bacterial colonization of the stomach caused a major revision of the etiopathology of gastric cancer (4,5). Subsequently, Helicobacter pylori (H. pylori) was identified as a cause of gastritis, peptic ulcer disease and gastric cancer, and in 1994 the IARC published an assessment stating that there was sufficient evidence to categorize this bacterium as carcinogenic to humans (group 1) (6).

Forty years after the discovery of H. pylori the decline in gastric cancer incidence and mortality rates described by Howson and the role of environmental exposures in the etiology of gastric cancer are easier to interpret. Overall, the decreasing trend in gastric cancer incidence rates has been similar worldwide, being described in high and low risk areas, both in men and women, and is parallel to the decrease in the prevalence of H. pylori infection. However, it is also known that gastric cancer incidence trends are different according to anatomical location and morphological subtype. Even though mortality data do not allow to separately study trends by subtype, population-based cancer registries have shown that the decrease in gastric cancer incidence over the last few decades has been mainly due to a decrease in the non-cardia and intestinal subtypes, more directly related to severe atrophic gastritis due to chronic infection with H. pylori, and inversely related to lower socioeconomic status (7). In contrast, cardia cancers have registered increasing incidence rates in different populations, and present similar epidemiological characteristics to esophageal cancers, being directly associated to obesity and reflux (7). Since the proportion of these two subtypes has been changing over time, a surveillance of gastric cancer trends by subtype is required to explain incidence and mortality trends
over time, especially among the young.

Another singularity of gastric cancer epidemiology is the fact that men register rates twice as high as those of women across age groups, regions and periods of time. Although *H. pylori* infection is the main risk factor for stomach cancer, numerous factors modulate the risk of developing this tumor, including *H. pylori* virulence factors, host factors (family history), and environmental exposures such as smoking, alcohol consumption, dietary factors and obesity. Whereas no clear explanation exists for the higher stomach cancer mortality rate in men, differences in exposure to these factors could probably explain the different rates observed by sex.

Taking all this information into account, it is currently accepted that the decrease in gastric cancer is mainly due to improvements in nutrition, sanitation and hygiene (7,8), and that the most promising public health strategy to prevent gastric cancer is *H. pylori* eradication, although optimal implementation strategies need to be established at the local level (7,9).

As regards the paper on pancreatic cancer (2), Cayuela et al. analyzed the risk of dying from pancreatic cancer in Spain by sex and region between 1980 and 2021. Overall, pancreatic mortality increased over the study period by 1.5 % per year in men and 1.8 % in women. The joinpoint analysis showed that the trend increase was not consistent over the study period, and detected a change in trend in 1988 in males and 1987 in females. During the first period, pancreatic cancer rates had increased by 3.6 % per annum in both sexes, while thereafter the rate of increase slowed down (0.9 % per annum in men and 1.4 % in women). When studying these trends by sex and autonomous community, they had also increased in all regions and in both sexes between 1980 and 2021, although a deceleration in increase rate had occurred since around 2000 among males in Galicia, Madrid and Navarre, and among women in Madrid in 1992.

When the analysis was restricted to the 30-64 years of age group, the increase in rates over the study period was slightly lower (1 % per year in males and 1.7 % in females) than in the whole population. In males, a change in trend was identified in 2001, with a 1.8 % increase per year between 1980 and 2001, and a 0.1 % increase from 2001 to 2021, while in females there was a constant rise over the whole period in this age
group.
These results, as Cayuela and colleagues suggest, might indicate that the increase in pancreatic cancer mortality could have started to level off in Spain, at least in men. There are several established risk factors for pancreatic cancer, including tobacco consumption, diabetes, chronic pancreatitis and body mass index, and some authors have suggested that nearly two-thirds of the known causes of this deadly cancer are potentially avoidable (10). Tobacco smoking is one of the best-established risk factors for pancreatic cancer. Consequently, the increase in pancreatic cancer rates during the early years of the study period might be due to the high smoking prevalence rates described in Spain in the 1980s (11). Also, the levelling-off of the increasing trend of pancreatic cancer mortality in men could be reflecting differences in the evolution of tobacco use prevalence rates between men and women. A recent analysis of the Spanish National Health Survey and the European Health Survey in Spain found that the prevalence of tobacco consumption decreased by 29 percentage points in men and 4.5 in women between 1987 and 2020 (12). Changes in the prevalence of other risk factors for pancreatic cancer, such as overweight, obesity or diabetes, may certainly be playing an increasingly important role in the trends of pancreatic cancer incidence and mortality. Epidemiological, basic and clinical research is essential to better understand the etiology of pancreatic cancer and improve early detection and prevention for this cancer.

Nowadays, regarding incidence, the estimation of cancer figures for 2024 in Spain resulted in 9,986 new cases for pancreatic cancer and 6,868 new cases for gastric cancer, ranking eighth and thirteenth in incidence, respectively (13). However, since both gastric and pancreatic cancer present low survival rates, pancreatic cancer was the fourth most common cause of cancer-related death in 2022 in both males and females, while gastric cancer ranked seventh and eighth in females and males, respectively (14).

To conclude, pancreatic and gastric cancer mortality rates displayed different trends throughout the study period. Gastric cancer mortality declined in both sexes, likely due to decreased exposure to gastric cancer risk factors, in particular chronic H. pylori infection. In contrast, pancreatic cancer mortality rates increased in all Spanish regions, although the magnitude of this increase slowed down in men, likely reflecting
the decreasing prevalence of tobacco use since 1980. Continuous monitoring of cancer mortality trends and surveillance of cancer risk factors is needed to enable adequate primary and secondary prevention programs, particularly in the younger age groups.

References


