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Shifting global patterns of early-onset gastrointestinal cancers: lessons from the Spanish trends

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Dear Editor,

We read with great interest the analysis of gastrointestinal cancer (GIC) incidence trends in Spain (1999–2023) by *Cayuela L et al.* [1], which compellingly illustrates an epidemiologic transition: sustained declines in infection- and tobacco-related malignancies (gastric and oesophageal cancers) alongside steady rises in metabolic-related cancers (pancreatic and liver) and an emerging plateau in early-onset colorectal cancer after 2016–2017. Authors' national, sex-stratified Joinpoint approach provides timely granularity for policy action and, importantly, frames early-onset trends as sentinel signals rather than statistical curiosities.

We wish to contextualize the recent findings from Spain on early-onset gastrointestinal cancers (EOGICs) within the broader global trends, particularly in relation to early-onset stomach cancer

(EOSC) and early-onset esophageal cancer (EOEC). Our population-based analysis using data from GLOBOCAN 2022 [2], has highlighted some key global patterns that may provide additional context to the Spanish data. We extracted estimates of incidence and case counts EOEC and EOSC cancers in individuals aged 0–49 years were from the International Agency for Research on Cancer (IARC) GLOBOCAN 2022 database, and projections to 2045 using the IARC Cancer Tomorrow platform. Age-standardized incidence rates (ASRs, world standard population) and absolute case numbers were retrieved by country and aggregated according to the Human Development Index (HDI) classification published by the United Nations Development Programme for the corresponding year. Projected case counts represent the direct outputs of the Cancer Tomorrow tool under its standard demographic scenario, which assumes constant age-specific incidence rates with future changes driven by United Nations population forecasts.

In 2022, globally, there were 82,121 new cases of EOSC among individuals aged 0–49 years, with the highest incidence rates observed in high-HDI countries (ASR 1.5) and very-high-HDI regions (ASR 1.3). However, projections to 2045 suggest a significant shift in the global burden of EOSC, with the largest proportional increases expected in low- and medium-HDI countries, where cases are predicted to double, predominantly reflecting demographic change under the constant-rate projection scenario. In contrast, high- and very-high-HDI countries are projected to experience a decline in EOSC cases, with a decrease of 6.8% and 7.3%, respectively. (Figure 1) Similarly, for early-onset esophageal cancer (EOEC), an estimated 45,399 new cases occurred globally in 2022, with the highest incidence observed in medium-HDI regions (ASR 1.3) and the lowest in very-high-HDI countries (ASR 0.32). Mortality rates mirrored the incidence, with the greatest burden observed in medium- and low-HDI regions. Projections indicate that by 2045, EOEC incidence will more than double in low-HDI countries (increases of 100.9% in both sexes) and grow by 40.2% in medium-HDI countries. In contrast, very-high-HDI countries are projected to see a decrease in EOEC cases, with a reduction of 6.7%. These patterns highlight the widening disparity in EOEC burden between high- and low-resource settings, with significant increases in lower-HDI countries due to demographic expansion rather than risk escalation.

This global divergence, marked by stabilizing or declining incidence rates in higher-HDI settings and a redistribution of absolute case burden toward lower-HDI regions, has direct relevance for Spain. First, the decline in late-onset gastric and esophageal cancers should not be interpreted as closure of the prevention agenda but as an opportunity to recalibrate efforts toward early-onset phenotypes increasingly linked to obesity, insulin resistance, metabolic dysfunction–associated steatotic liver disease, and gastroesophageal reflux–related pathways [3–5]. Second, Spain should prioritize enhanced surveillance of early-onset gastrointestinal cancers through registry reporting stratified by age, histology, and anatomic subsite. Such monitoring would permit early detection of cohort effects and support integration of cancer prevention within broader cardiometabolic risk-reduction strategies.

In conclusion, the central message is clear. Early onset gastrointestinal cancers serve as indicators of future population burden. Spain has demonstrated effective control of infection related malignancies. The next priority is systematic monitoring and prevention of metabolically associated disease within an integrated public health framework. This focused approach, grounded in registry data and risk factor control, will determine whether current favorable trends are sustained.

Author Contributions

- Conceptualization: MP,
- Data acquisition: MP
- Analysis and interpretation: MP
- Drafting of manuscript: MP
- Critical revision: MP
- Final approval: MP

All authors meet the four ICMJE criteria for authorship.

Statement of Interests

The authors declare no conflicts of interest

STATEMENT OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS:

Grammarly AI solely for grammar and fluency enhancement. The tool did not generate scientific content, data interpretation, or references. All analyses, interpretations, and final editorial decisions were made by the author, who takes full responsibility for the accuracy and integrity of the manuscript.

Sex- and Gender-Based Analysis:

This study reports incidence estimates stratified by sex (male and female) as provided by the GLOBOCAN 2022 database. Analyses reflect sex-disaggregated epidemiologic data but do not incorporate gender identity variables, as such data are not available within the source databases. The interpretation of findings considers known biological differences in gastrointestinal cancer epidemiology between males and females; however, no additional sex-specific modeling was performed beyond database-reported estimates.

Data Availability Statement

The data supporting the findings of this study are available in a public repository. All incidence estimates and projections were obtained from the International Agency for Research on Cancer GLOBOCAN 2022 database and the IARC Cancer Tomorrow platform, accessible at <https://gco.iarc.fr/today>. These data are publicly available and can be reproduced using the same age group (0–49 years), cancer sites, and Human Development Index stratifications described in the Methods section.

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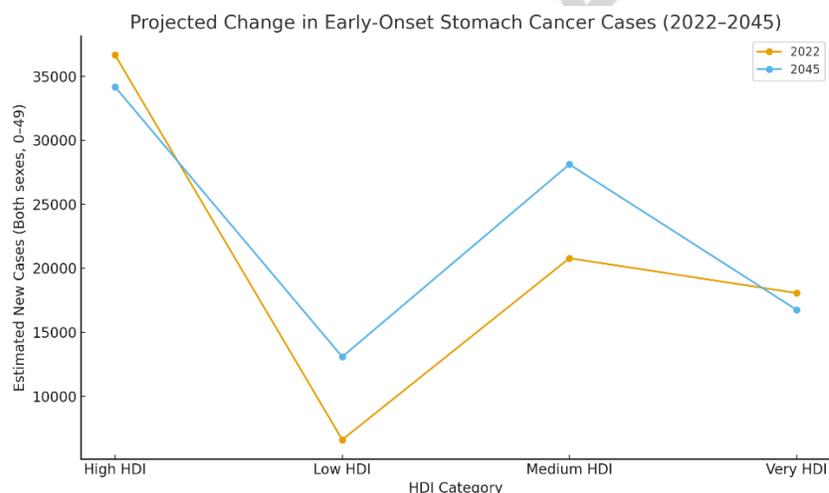


Figure 1. Projected percentage change in early-onset stomach cancer (ages 0–49 years) case counts from 2022 to 2045 by Human Development Index (HDI) category. Data derived from GLOBOCAN 2022 and the IARC Cancer Tomorrow platform. Projections reflect the standard demographic scenario assuming constant age-specific incidence rates; the figure represents a reconstructed visualization based on tabulated outputs from the database.