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## Research Letter

# Global Burden and Trends of Cervical Cancer in Spain Based on GBD 2023

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Cervical cancer is the fourth most common cancer in the world, with approximately 662,000 new cases and 348,000 deaths in 2022.[1] It has been observed that in less affluent areas, mortality could be 18 times higher than in high-income countries.[1] The relationship between this disease and human papillomavirus (HPV) is well documented.[2–5] The most common type is squamous, accounting for 70% of cases.[6]

This study aimed to supplement long-term data on combined cervical cancer prevention and control in high-middle sociodemographic index (SDI) countries. Based on data from the Global Burden of Disease (GBD) Study spanning 1990–2023, we present changes in incidence, mortality, and disability-adjusted life years (DALYs) following the implementation of HPV vaccination and stratified screening programs in Spain, providing references for optimizing prevention and control strategies in similar countries. The latest 2024 report on the status of cervical cancer screening in Spain (SEOM, 2024) indicates a lack of long-term effectiveness data following the integration of HPV testing, and the 2023 outcome data provided in this study fill this gap. In conjunction with the European Union's 2025 Initiative for Promoting Cancer Screening (European Union, 2025), the findings of this study provide empirical support for the implementation of this initiative in high-middle SDI countries.

The GBD aims to analyze mortality and disability rates for different diseases and risk factors worldwide. The data provided in the latest update covers the period from 1990 to 2023. It includes 204 countries, which are divided into regions or according to sociodemographic indices, among other criteria. GBD uses data from scientific literature databases, government data, and other collaborators, based on hospital records, censuses, and surveys, among others, using a program called Global Health Data Exchange. The inclusion criteria used by GBD are mortality, prevalence, or incidence data on diseases or risks from the different countries that have provided such data, classified by age and sex since 1990. In this study, cervical cancer and the year 2023 were used. On the other hand, low-quality studies or poorly classified causes of death are excluded. To calculate the different variables, a Bayesian method is used in cases where the necessary data cannot be provided. The formulas used are as follows:

-age-standardized mortality rate,

age-standardised mortality rate

$$= \frac{\sum_{i=1}^{n}\left(\text{specific age rate}_i \times \text{standard population}\right)}{\sum_{i=1}^{n}\text{standard population}_i}$$

-age-standardized incidence rate (ASIR):

$$\text{ASIR} = \frac{\sum\left(\text{Age specific rate} \times \text{standard population age}\right)}{(\text{Total standard population}) \times 10^{n}}$$

The other formula used for DALYs is *DALY* = years of life lost + years lived with disability.

The estimate has a 95% confidence interval, and up to a thousand calculations are performed for each estimate, mainly using DisMod-MR 2.1 to perform the calculation, with Python and R software used to process large-scale data.[7]

As noted above, GBD obtains information from different sources, so biases are possible in the accurate classification of diseases. Therefore, although various tools are used to improve the estimate, these data should be treated with caution.

In order to enable earlier diagnosis, various strategies have been established. In Spain, the decision was made to implement HPV vaccination and screening programs, with the result that by 2024 it had reached 15th place in terms of frequency of diagnosis, improving mortality figures.[1] Screening was introduced in most of Spain's autonomous communities in 1980–1990, using cytology and on an opportunistic basis. In 2019, HPV testing was incorporated for part of the population.

The screening program is aimed at women aged 25–65 and is organized as follows: 25–34 years old, a smear test every 3 years; 35–65 years old, HPV testing; if negative, repeated every 5 years; if positive, a triage with cytology is performed. If the latter is negative, the HPV test is repeated after one year. In women under 25

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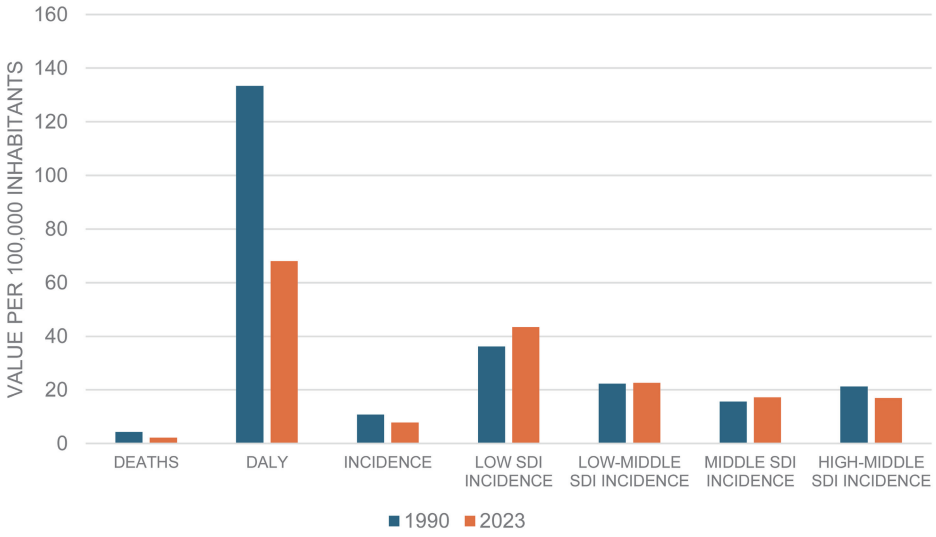


**Fig. 1. Changes in key cervical cancer indicators in Spain (1990–2023) and incidence comparisons across sociodemographic index (SDI) groups.** DALY, disability-adjusted life year.

years oldwith no known history of sexual intercourse, screening would not be indicated, but primary prevention through HPV vaccination would be indicated.[8]

On the other hand, HPV vaccination in Spain is currently recommended at age 12, with two doses administered 5–6 months apart. If vaccination is carried out from age 14 onwards, three doses are administered. Vaccination is also indicated for people with WHIM syndrome, HIV infection, men who have sex with men, sex workers up to the age of 26, and women of any age who have undergone cervical surgery. HPV vaccination has been shown to protect against 63–73% of HPV-related cervical cancer, with protection extending beyond serotypes 16 and 18 to include cross-protection against types such as 31 and 45. It has also been associated with a reduced incidence of cervical intraepithelial neoplasia, particularly high-grade lesions (e.g., CIN3).[9]

In Spain, according to the GBD study, data from 1990 and 2023 were compared, the latter being the most recent year available, as shown in Figure 1 corresponding to the standardized death rate, DALYs, and incidence. In all cases, the rates have improved. In terms of deaths, they decreased from 4.27 (3.88–4.73) per 100,000 inhabitants in 1990 to 2.12 (1.84–2.38) per 100,000 inhabitants in 2023, adjusted for age; DALYs decreased from 133.38 (124.18–143.73) in 1990 to 68.06 (60.85–77.01) in 2023 per 100,000 inhabitants; and incidence decreased from 10.81 (9.31–12.54) in 1990 to 7.85 (6.37–9.38) in 2023 per 100,000 inhabitants.

When analyzing the incidence data for Spain, which corresponds to a high-middle–level country according to the SDI, with low, low-middle, middle, and high-middle SDI groups, the following data were obtained, which are illustrated in Figure 1. In the same group to which Spain belongs, a similar improvement in incidence was observed, in this case from 21.31 (16.36–26.64) in 1990 to 16.96 (13.44–22.5) in 2023. In the other groups, the incidence increased significantly in 2023 in the low SDI group, from 36.21 per 100,000 inhabitants (22.05–56.67) in 1990 to 43.45 per 100,000 inhabitants (29.24–61.88). In the other two groups, middle SDI and low-middle SDI, it remains at similar levels, with practically the same incidence in the low-middle group, remaining consistently higher in 2023.

This study has several limitations. First, the analysis relies on modeled GBD estimates rather than primary patient-level data. Second, causal inferences regarding vaccination and screening cannot be directly established. Third, regional disparities within Spain were not analyzed. Finally, potential misclassification and reporting biases inherent to secondary data sources should be considered when interpreting the findings.

In conclusion, as in Spain and other countries belonging to the high-middle SDI group, a certain improvement has been observed in terms of incidence, with Spain showing a minimal improvement compared to the average for countries in this group. The greatest improvement in DALYs was observed in Spain. All this has been made possible by cervical cancer screening programs and HPV vaccination. In fact, similar recommendations were established in the European Union in 2022, which is why these countries have contributed to the improvement in results.[10] We believe that these programs are essential in order to contain the disease and improve the quality of life of those affected. As we can see, there are still inequalities in the disease burden, and it would be interesting to develop more universal screening and HPV vaccination programs so that countries with lower SDIs could benefit and achieve better results in terms of incidence.

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## Conflict of interest

None.

## Author contributions

Study design (JGC, GMI, CPS), data collection (JII, IEP, CPS), manuscript writing (JGC, GMI), and supervision (JII, GMI). All

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