Revista Española de Enfermedades Digestivas
The Spanish Journal of Gastroenterology

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DOI: 10.17235/reed.2024.10317/2024
Link: PubMed (Epub ahead of print)

Please cite this article as:
Cayuela Lucía, Flox-Benítez Gema, Peiró Villalba Clara, Giráldez Gallego Álvaro, Cayuela Domínguez Aurelio. Investigating temporal patterns of colorectal cancer incidence in Spain: a comprehensive analysis of age, period and cohort effects, 1990-2019. Rev Esp Enferm Dig 2024. doi: 10.17235/reed.2024.10317/2024.

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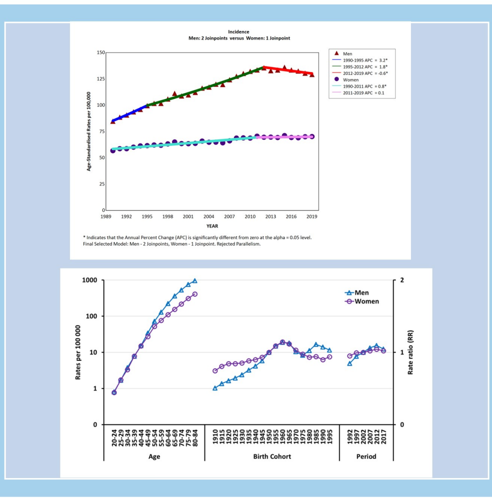
This study examined how age, period and birth cohort influence the incidence of colorectal cancer (CRC) in Spain from 1990 to 2019. Using data from the Global Burden of Disease Study 2019, the researchers identified patterns that showed a steady increase in CRC incidence rates, which were significantly higher in men. Different trends emerged for each sex: men had three phases of increase, slowdown and subsequent decline, while women had a single increase followed by stabilization. The study revealed temporal and age-related changes in CRC risk, which was consistently higher in men. Individuals born since the early 20th century had an increased risk, which peaked in the 1960s and remained stable until the late 1990s. The findings highlight the need for a comprehensive approach to CRC prevention, addressing age, period and cohort factors, and promoting lifestyle changes to reduce incidence and improve public health in Spain.



Cayuela L, et al.

Revista Española de Enfermedades Digestivas (REED)
The Spanish Journal of Gastroenterology

Revista Española de Enfermedades Digestivas
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Investigating temporal patterns of colorectal cancer incidence in Spain: a comprehensive analysis of age, period and cohort effects, 1990-2019

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'What is already known about this topic?'

- Colorectal cancer (CRC) is a global health concern with increasing incidence worldwide, particularly in developed regions like Europe.
- It is the third most common cancer, with an estimated 1.93 million new cases and 9.96 million deaths reported in 2020.

'What does this study add?'

- This research sheds light on the intricate trends of colorectal cancer (CRC) in Spain over the past three decades, employing advanced analytical methods to identify the underlying epidemiological factors.
- Utilizing data from the Global Burden of Disease (GBD) study, the study provides a comprehensive examination of CRC incidence patterns from 1990 to 2019.

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- The study highlights the unique epidemiological characteristics of CRC in Spain, revealing a stabilization of incidence rates in women that lagged behind the European trend by approximately eight years.
- After 2012, the incidence of CRC in men decreased significantly, causing the wide gap between men and women to narrow slightly.
- In Spain, colorectal cancer incidence rates are generally stable in younger individuals (aged <45 years) but tend to rise in older age groups.
- Older groups see increases, influenced by historical trends and cohort-specific vulnerabilities.

How the results will influence clinical practice?

- The outcomes of this study have profound implications for clinical practice. By illuminating the nuanced dynamics of CRC in Spain, the research lays the foundation for developing targeted and personalized prevention strategies.

Lay summary

This study examined how age, period and birth cohort influence the incidence of colorectal cancer (CRC) in Spain from 1990 to 2019. Using data from the Global Burden of Disease Study 2019, the researchers identified patterns that showed a steady increase in CRC incidence rates, which were significantly higher in men. Different trends emerged for each sex: men had three phases of increase, slowdown and subsequent decline, while women had a single increase followed by stabilisation. The study revealed temporal and age-related changes in CRC risk, which was consistently higher in men. Individuals born since the early 20th century had an increased risk, which peaked in the 1960s and remained stable until the late 1990s. The findings highlight the need for a comprehensive approach to CRC prevention, addressing age, period and cohort factors, and promoting lifestyle changes to reduce incidence and improve public health in Spain.

Key points

1. In Spain, the stabilization of colorectal cancer incidence rates in women lagged behind the European trend by approximately eight years.
2. After 2012, the incidence of CRC in men decreased significantly, causing the wide gap between men and women to narrow slightly.
3. In Spain, colorectal cancer incidence rates are generally stable in younger individuals (aged <45 years) but tend to rise in older age groups.
4. Older groups see increases, influenced by historical trends and cohort-specific vulnerabilities.

Abstract

Aim: This study aimed to evaluate how age, period, and cohort (A-P-C) impact colorectal cancer (CRC) incidence in Spain from 1990 to 2019.

Method: Using data from the Global Burden of Disease Study 2019, we used joinpoint analysis to identify long-term trends and A-P-C modelling to quantify net drift, local drift, longitudinal age curves, and rate ratios (RRs) of period and cohort effects.

Results:

CRC incidence increased steadily in Spain from 1990 to 2019, with a more significant rise in men than in women. The age standardised rates rose from 84.9 to 129.3 cases per 100,000 in men and from 56.9 to 70.3 cases per 100,000 in women. Joinpoint analysis revealed distinct patterns for men and women: men's incidence showed three phases--a surge until 1995, a slowdown until 2012, and a subsequent decrease--while women's incidence experienced a single increase until 2011 and then stabilized. Local drifts increased in all age groups over 45, with stability in men under 45 and a decrease in women aged 30-39. The risk of CRC increased with age, with men consistently having a higher risk than women. The risk of CRC increased over time for both men and women but at different rates. The risk for cohorts born in the early to mid-20th century peaked in the 1960s and remained stable until the late 1990s.

Conclusion:

The increasing incidence of CRC in Spain, with distinct patterns by gender and birth cohort, underlines the importance of preventive strategies adapted to temporal and demographic variations to address this public health challenge.

Keywords: Colorectal cancer. Incidence. Age. Period. Cohort. Spain.

Investigando patrones temporales de incidencia de cáncer colorrectal en España: Un análisis exhaustivo de los efectos de edad, periodo y cohorte, 1990-2019

Resumen

Objetivo: Este estudio tuvo como objetivo evaluar cómo la edad, el período y la cohorte (A-P-C) impactan la incidencia de cáncer colorrectal (CCR) en España desde 1990 hasta 2019.

Método: Utilizando datos del Global Burden of Disease Study 2019, se utilizó el análisis joinpoint para identificar las tendencias a largo plazo y el modelado A-P-C para cuantificar la deriva neta, la deriva local, las curvas longitudinales de edad y las razones de tasas (RR) de los efectos de período y cohorte.

Resultados:

La incidencia del CCR aumentó de forma constante en España entre 1990 y 2019, con un incremento más significativo en hombres que en mujeres. Las tasas estandarizadas por edad aumentaron de 84,9 a 129,3 casos por 100.000 en hombres y de 56,9 a 70,3 casos por 100.000 en mujeres. El análisis Joinpoint reveló patrones distintos para hombres y mujeres: la incidencia masculina mostró tres fases -un repunte hasta 1995, una ralentización hasta 2012 y un posterior descenso-, mientras que la incidencia femenina experimentó un único aumento hasta 2011 y luego se estabilizó. Las derivas locales aumentaron en todos los grupos de edad mayores de 45 años, con estabilidad en los hombres menores de 45 años y un descenso en las mujeres de 30 a 39 años. El riesgo de CCR aumentó con la edad, siendo sistemáticamente mayor en los hombres que en las mujeres. El riesgo de CCR aumentó con el tiempo tanto en hombres como en mujeres, pero a ritmos diferentes. El riesgo para las cohortes nacidas entre principios y mediados del siglo XX alcanzó su máximo en la década de 1960 y se mantuvo estable hasta finales de la década de 1990.

Conclusiones: La creciente incidencia del CCR en España, con patrones distintos por sexo y cohortes de nacimiento, subraya la importancia de estrategias preventivas adaptadas a las variaciones temporales y demográficas para abordar este desafío de salud pública.

Palabras clave: Cáncer colorrectal, incidencia, edad, periodo, cohorte, España.

INTRODUCTION

Colorectal cancer (CRC) is a major global health problem. With an estimated 1.9 million new cases and 904,019 deaths in 2022, it is the four most common cancer worldwide[1]. More than half of all CRC cases are diagnosed in regions with a high Human Development Index, particularly in Europe, East Asia, and North America[2,3]. The age-standardised incidence rate (ASIR) of CRC has steadily increased worldwide since 1990[2,4], and this trend is expected to continue[5,6]. While the ASIR of CRC has also increased in Europe, it has stabilised in recent years[7].

The Global Burden of Disease (GBD) study, which provides the most comprehensive data on disease, injury and risk factors worldwide, provides detailed estimates of CRC incidence in 204 countries and territories, including Spain, from 1990 to 2019[2,8,9].

Age-period-cohort (A-P-C) analysis is a valuable tool for understanding the complex interplay of factors that contribute to changing patterns of CRC incidence and mortality[10,11]. It has been widely used in different settings, including Spain and other countries, to disentangle the effects of ageing, period-specific changes in risk factors and cohort-specific exposures on the burden of disease[3,4,6,7,12–14].

Incidence rates of CRC in Spain have traditionally been lower than in other European countries; however, the trend has been increasing over the period 1975-2004. This trend showed a slight decrease in both sexes around 1995, coinciding with a turning point[13,14]. Despite this slight decline, CRC remains an important public health problem[15–17].

To gain a deeper understanding of the factors driving CRC trends in Spain, this study aims to update and evaluate the impact of A-P-C effects on CRC incidence using GBD-2019 data in Spain from 1990 to 2019. The findings will provide valuable insights for developing personalized prevention strategies.

MATERIAL AND METHODS

We conducted an ecological trend study of CRC incidence in Spain during the period 1990-2019.

Data source:

We obtained CRC incidence data for Spain from 1990 to 2019, categorized by sex and age, using the Global Health Data Exchange online query tool. This tool provides access to a comprehensive dataset of health indicators, including CRC incidence, from various sources worldwide. The data for Spain is available at: https://vizhub.healthdata.org/gbd-results/.

This study included all colorectal cancers (CRCs) as defined by the International Classification of Diseases (ICD) coding systems. We employed both ICD-10 codes (C18-C21, D01.0-D01.3) and ICD-9 codes (153-154, 230.3-230.6) to capture the full spectrum of CRCs. This decision aligns with the colorectal continuum model, which recognizes colon and rectal cancers as a single entity arising from a common precursor[18].

In addition, the Data Input Sources Tool provides a detailed overview of the data sources used in the GBD 2019 study, including the specific sources for CRC incidence data in Spain. The main sources of data used for GBD estimation are cancer registries, vital registration systems, sample registration systems, and verbal autopsies[9]. This information is available at: https://ghdx.healthdata.org/gbd-2019/data-input-sources.

These data sources are carefully vetted and documented to ensure the accuracy and transparency of the GBD estimates as suggested in the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER), a statement that promotes best practices in reporting health estimates.

The Spanish National Statistics Institute provided population data for the period 1990 to 2019, disaggregated by age, sex, and year (available at: https://www.ine.es/). The population data was estimated on July 1st of each year.

Statistical analyses

ASIRs were estimated by sex using the direct method and the revised European Standard Population[19]. The Joinpoint regression program, version 4.9.1.0, was used to estimate rates and mortality trends (available at https://surveillance.cancer.gov/joinpoint/). Using the software's default settings, we calculated the turning points in the trend and the annual percentage change (APC) for each identified period. We also estimated the average annual percentage change (AAPC) between 1990 and 2019, which is a geometrically weighted average of the individual APCs. The weights correspond to the duration of each period within a given period. To assess whether the trends are parallel for both sexes, we used the "Pairwise comparison" option of the software. All calculated rates are given per 100,000 persons. The ratio of men to women was also estimated.

To apply the A-P-C model, we structured the dataset into six 5-year periods, spanning from 1990-1994 to 2015-2019. Additionally, we divided the data into 13 5-year age groups, ranging from 20-24 to 80-84 years old. This configuration resulted in a total of 18 birth cohorts, labelled according to the central year of birth, ranging from 1910 to 1995. For each age group and 5-year period, we computed a matrix of age-specific death rates, which served as a key element of the A-P-C model analysis.

The A-P-C effects were assessed using the National Cancer Institute A-P-C tools (available at https://analysistools.nci.nih.gov/apc/). We focused on the following estimable functions: longitudinal age-specific rates, period and cohort rate ratios, and local drifts with net drift. The longitudinal age curve gives the fitted longitudinal age-specific rates in reference cohorts adjusted for period deviations, while the period (or cohort) relative risk (RR) is the period (or cohort) RR adjusted for age and non-linear cohort (or period) effects in a period (or cohort) relative to the reference. The net drift is the overall log-linear trend by calendar period and birth cohort and gives the overall annual percentage change, whereas the local drifts are the log-linear trend by calendar period and birth cohort for each age group and give the annual percentage change for each age group. All A-P-C analyses used the central age, calendar period and birth cohort group as the reference group. Wald's chi-square tests were used to test the significance of estimable functions. Statistical significance was established at $P < .05$.

The data used did not require informed patient consent as it was publicly available. Furthermore, the data used in the GBD study adhered to the Guidelines for Accurate and Transparent Health Estimation Reporting for Population Health Research (GATHER), ensuring the credibility and integrity of the findings.

RESULTS

Over the period 1990-2019, an estimated 1,010,186 cases of CRC were diagnosed in Spain. The average annual growth rate was 3.2%, with a slightly higher increase for men (3.6%) than for women (2.7%).

Figure 1 presents the ASIR of CRC in Spain from 1990 to 2019, stratified by sex and complemented with joinpoint analysis findings. The graph highlights a consistent upward trend in CRC ASIR for both men and women, with a more pronounced rise in men (AAPC: 1.4%) compared to women (AAPC: 0.7%). The incidence rate in men rose from 84.9 cases per 100,000 in 1990 to 129.3 in 2019. For women, the rate increased from 56.9 to 70.3. The male-to-female ratio was 1.8 over the whole period, reflecting a higher CRC incidence rate in men than in women. This ratio increased from 1.5 in 1990 to 1.9 in 2019.

Joinpoint analysis demonstrates distinct patterns in CRC ASIR between men and women, indicating non-parallel trends. In men, the analysis revealed three distinct periods: a significant increase from 1990 to 1995, with an annual per cent change (APC) of 3.2% ($P < 0.05$); a slowing of the upward trend from 1995 to 2012, with an APC of 1.8% ($P < 0.05$), and a subsequent decrease from 2012 to 2019, with an APC of -0.6% ($P < 0.05$). In contrast, the incidence trend for women exhibited a single period of increase from 1990 to 2011, with an APC of 0.8% ($P < 0.05$), followed by a period of stabilization from 2011 to 2019, with an APC of 0.1% that was not statistically significant.

Figure 2 shows the net drift (annual percentage change in overall expected age-adjusted rates) and local drift (age-specific rates over time) of CRC incidence in Spain from 1990 to 2019. The overall net drift per year was 0.9% (95% CI, 0.7% to 1.1%) for men and 0.3% (95% CI, 0.1% to -0.5%) for women. In particular, there was an increase in local drift in all age groups for both sexes from the age of 45. However, for men under 45, there was stability across all age groups. A similar pattern was observed for women, except for a significant decrease in the 30-39 age group, while the other age groups remained stable.

Figure 3 shows the longitudinal age curves, estimated cohort relative risk (RR) trends and estimated period RR trends for CRC incidence rates in Spain by sex. The longitudinal trends (age effect) were generally consistent for both sexes, with a consistently higher incidence risk observed in men. The risk of CRC incidence increased steadily with increasing age in both women and men. The highest incidence rates were found in the 80-84 age group.

In Spain, the RR of CRC incidence showed a steady upward trend over different periods. The RR increased from 0.85 for men and 0.95 for women in 1990-1994 to 1.10 and 1.04, respectively, in 2010-2014. Notably, this upward trend diverged between the sexes, stabilising for women and decreasing for men.

For men and women born between the early 20th century and the mid-20th century, the risk of CRC incidence showed a steady upward trend, peaking in the 1960s. This increased risk remained at a relatively constant level until the late 1990s.

Furthermore, Wald tests revealed that all net drifts, local drifts, cohort effects, and period effects were statistically significant for both sexes (all p-values < 0.001). These findings indicate that the incidence of CRC exhibited a statistically significant difference in local drifts and net drifts, as well as age, period, and cohort deviations. These differences suggest the potential influences of age, cohort, and period on the observed temporal trends in CRC incidence (Table 1).

DISCUSSION

Based on the latest GBD 2019 data, this study examines the trends in CRC incidence in Spain over the last three decades. At the same time, we identify the epidemiological characteristics of CRC in Spain by analysing the age, period and cohort effects of CRC incidence. The results of the study serve as a valuable tool for designing effective CRC prevention strategies.

CRC incidence rates have exhibited distinct patterns across different regions. In developed Western nations, CRC incidence rates have stabilized or even declined, while rapidly developing countries like Shanghai have witnessed an upward trend. Japan, Singapore, and Hong Kong experienced rapid increases in CRC incidence followed by stabilization, mirroring their economic development[20]. Conversely, a study found that CRC incidence rates decreased in Somalia, Eswatini, South Africa, Central African Republic, and Libya from 2010 to 2019, a trend contrary to the overall increase observed in most other African countries[21].

CRC ASIR trends in Spain have followed the overall European trend, increasing from 1990 to 2019[7]. However, since 2003, CRC incidence rates have stabilized across Europe[7]. Notably, in Spain, the stabilization of CRC incidence rates in women lagged behind the European trend by approximately eight years. Conversely, a significant decrease in CRC incidence rates in men was observed from 2012 onwards, widening the gap between male and female incidence rates.

The increasing incidence of CRC in Spain has been linked to changes in diet, reduced physical activity and ageing[13,14]. Economic development has led to changes in dietary habits, with increased consumption of processed foods and reduced intake of fibre and fruit[22,23]. These dietary changes have contributed to obesity, a risk factor for CRC[24]. Ageing also increases the risk of CRC through genetic mutations and exposure to harmful lifestyle factors[25].

Age effects: CRC incidence typically rises with age, but most populations see a slight decline in incidence at advanced ages. The UK, USA, and Australia exhibit a more pronounced decline in CRC incidence compared to Japan, Hong Kong, Shanghai, Singapore, and India [20]. Spain stands apart, with incidence peaking in the 80-84 age group.

In Spain, CRC incidence trends exhibit distinct patterns across age groups. In younger individuals (aged <45 years), CRC incidence rates are generally stable, except for a slight decrease in women aged 30-39 years. This is in contrast to the global trend of increasing CRC rates in younger adults[26]. In older age groups (>45 years), CRC incidence rates tend to rise, with men having slightly higher rates than women (similar to what has been observed in other studies)[27]. This trend is likely due to a combination of factors, such as increased exposure to risk factors over time, a longer time for precancerous lesions to develop into cancer, and a decline in the effectiveness of the immune system in detecting and eliminating abnormal cells[28].

Studies have shown that CRC incidence rates have increased in Spain over time, affecting all age groups simultaneously[14]. This phenomenon, known as period effects, has also been observed in other countries[20]. Our analysis showed a significant increase in CRC incidence rates for both sexes between 1990 and 2014, especially for men. After 2014, however, a clear shift emerged, with CRC rates stabilising in women and even declining in men. Due to the short-term nature of these observations, longer-term monitoring is essential to capture the complex mechanisms driving these shifts.

Western populations, particularly those born in the 1950s and 1960s, exhibit an escalating trend in CRC incidence, reflecting a cohort-specific vulnerability [20]. Asian populations, excluding India, present a converse trend, showcasing a decline in CRC incidence among individuals born in the 1950s. Notably, Japan mirrors Western patterns, experiencing an increasing trend in CRC incidence among those born in the 1960s [3,20]. Hong Kong, Shanghai and Singapore showed signs of an upward trend in their more recent cohorts [29]. In contrast, Spain has maintained a stable CRC risk for individuals born since the 1970s. It is important to note, however, that the confidence intervals for these trends in Spain are wider, indicating some uncertainty in the stability assessment. Despite the potential efficacy of screening strategies and colonoscopic polypectomy in reducing CRC incidence in Western countries, their impact on the current younger age groups is anticipated to be less pronounced compared to older generations. This discrepancy arises from the standard recommendation of CRC screening for individuals aged 50 and above [30].

The study has many strengths. It used a robust statistical methodology including A-P-C modelling to disentangle the complex interaction of A-P-C effects on CRC incidence. The long follow-up of older birth cohorts not only increases the reliability and power of the results but also enhances international comparability. In particular, the study treated CRC as a single entity, recognising the differential impact of risk factors on different subsites (colon vs rectum, left vs right colon).

However, the study had several limitations. First, reliance on routinely collected data is limited by the age-related increase in CRC incidence, which may underestimate cohort effects in younger individuals. Second, the linear dependence between age, period and cohort poses a challenge to model identifiability and requires caution in interpreting the results. Finally, the study couldn't examine temporal variation in risk factors and screening due to a lack of individual-level data.

CONCLUSION

This study provides valuable insights into the complex factors influencing CRC incidence in Spain and offers a roadmap for effective prevention strategies. By addressing the interplay between age, period and cohort effects, as well as lifestyle and dietary changes, Spain can strive to further reduce CRC incidence.

Final declarations

Funding: This research did not receive specific grants from funding agencies in the public, commercial or not-for-profit sectors.

Conflict of interest: The authors declared that they had no conflicts of interest about the contents of this manuscript.

Authors Contributions: All authors contributed to the conception and design of the work; the acquisition, analysis, and interpretation of data; drafting the work and revising it critically for important intellectual content; approved the version to be published; and are responsible for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are properly investigated and resolved.

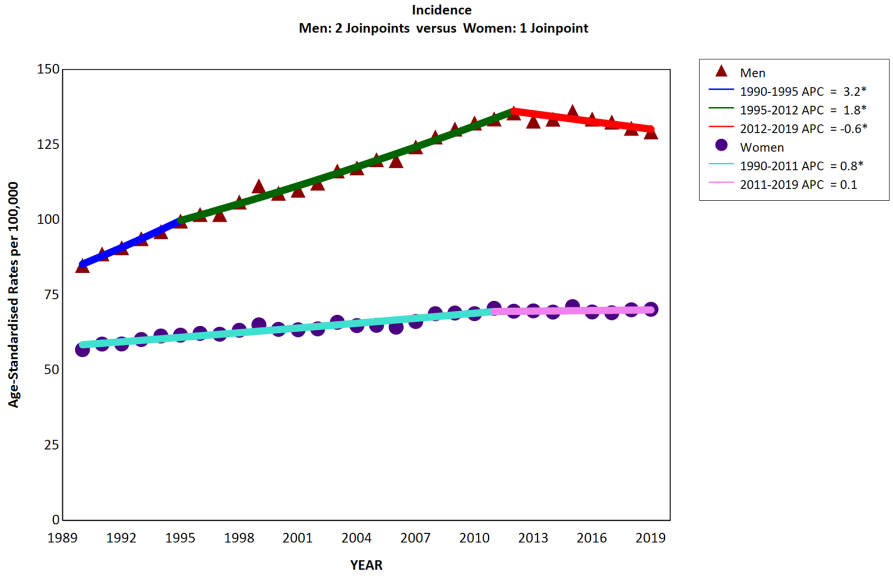
Ethics Statement: As the data extracted from the Global Burden Study were anonymous, following the principles of good clinical practice and the Declaration of Helsinki, no participants were identified and no personal information was accessed, this study did not require patient consent or ethics committee approval.

Data availability statement

The data that support the findings of this study are openly available at: https://vizhub.healthdata.org/gbd-results/ .

Table 1: Wald Chi-square test for estimable parameters in the age-period-cohort model.

Null hypothesis		Men		Women	
	df	Chi-square	P-Value	Chi-square	P-Value
NetDrift = 0	1	61.1	< .001	11.3	< .001
All Age Deviations = 0	11	2067.9	< .001	1580.2	< .001
All Period Deviations = 0	4	119.3	< .001	19.7	< .001
All Cohort Deviations = 0	16	126.5	< .001	137.4	< .001
All Period RR = 1	5	156.3	< .001	27.4	< .001
All Cohort RR = 1	17	1267.9	< .001	391.1	< .001
All Local Drifts = Net Drift	13	125.6	< .001	136.0	< .001



* Indicates that the Annual Percent Change (APC) is significantly different from zero at the alpha = 0.05 level.
Final Selected Model: Men - 2 Joinpoints, Women - 1 Joinpoint. Rejected Parallelism.

Figure 1: Age Standardised Incidence Rates (all ages) and trends estimated by joinpoint analysis for colorectal cancer in Spain over the period 1990-2019 by sex.

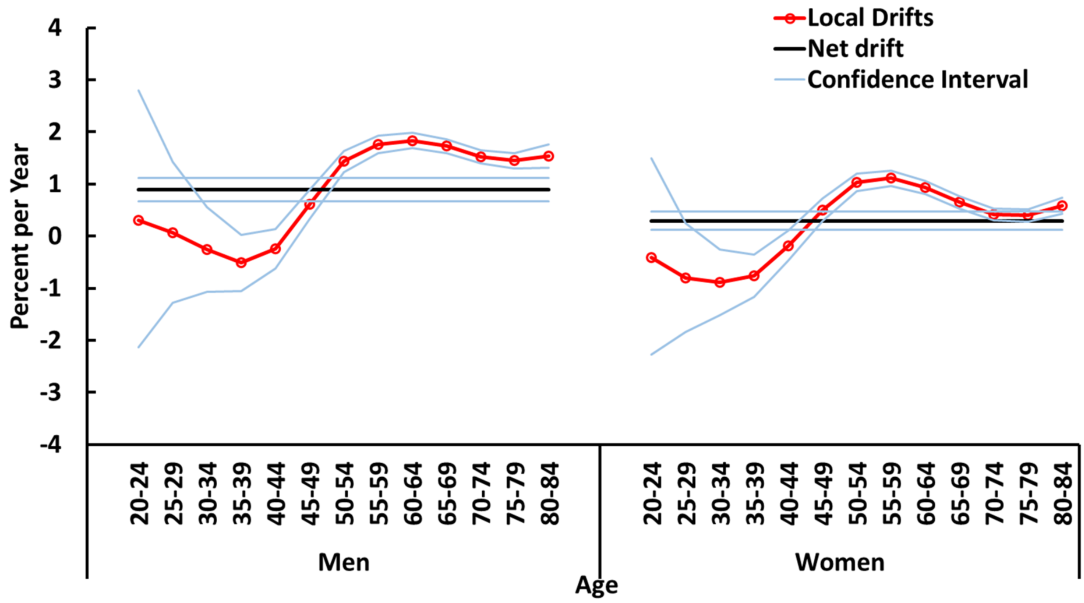


Figure 2: Local and net drift of colorectal cancer incidence in Spain from 1990 to 2019), for men and women.

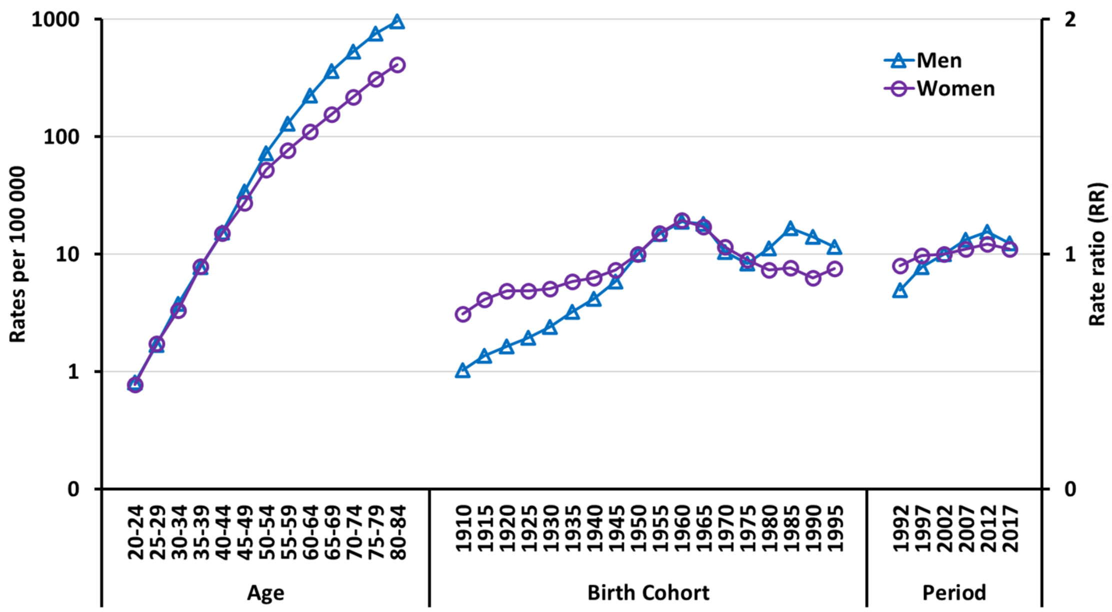


Figure 3: Age-period-cohort (APC) modelling results for colorectal cancer incidence in Spain from 1990 to 2019, for men and women.

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