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Research Article

Joinpoint Analysis and Age–Period–Cohort Effect on Mortality of Colorectal Cancer in Iran From 1990 to 2021

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Background: Colorectal cancer reported the fourth most common cancer in Iran. The aim of this study was to describe the time trends of colorectal cancer mortality from 1990 to 2021, focusing on the effects of age, period, and cohort.
Method: Our data included the number of colorectal cancer deaths and population recorded by the global burden of disease (GBD) and categorized by 5-year age groups from 1990 to 2021. Joinpoint regression and the age–period–cohort (APC) model were used to reflect temporal trend and effects of age, period, and cohort on colorectal cancer mortality, respectively.
Results: The crude mortality rate of colorectal cancer was significantly increased in men, with an average annual percentage change (AAPC) of 1.558% (95% confidence interval [CI]: 1.398%, 1.778%), while the crude mortality rate increased (AAPC = 1.340%; 95% CI: 1.215%, 1.465%) and the age-standardized mortality rate decreased in women (AAPC = −0.307%; 95% CI: −0.460%, −0.152%). APC analysis showed that the risk of death increased with age in both genders ($Coef_{15-19} = -2.823$ vs. $Coef_{>95} = 1.731$ in men and $Coef_{15-19} = -2.628$ vs. $Coef_{>95} = 1.964$ in women) and time ($Coef_{1992-1996} = -0.385$ vs. $Coef_{2017-2021} = 0.438$ in men and $Coef_{1992-1996} = -0.271$ vs. $Coef_{2017-2021} = 0.380$ in women) and was lower in later-born cohort ($Coef_{2002-2006} = -1.590$ in men and $Coef_{2002-2006} = -1.543$ in women) than earlier-born cohort ($Coef_{<1901} = 1.458$ in men and $Coef_{<1901} = 1.208$ in women).
Conclusions: Due to the increasing trend from colorectal cancer mortality and age and period effects, it seems necessary to modify early detection strategies and increase public awareness to reduce the burden of this cancer.

Keywords: age–period–cohort effect; colorectal cancer; Iran; joinpoint regression; mortality

1. Introduction

Cancer is a major public health problem of the 21st century, causing 3 out of 10 premature deaths from non-communicable diseases, causing almost 16.8% of deaths worldwide [1]. Colorectal cancer is the fourth most common cancer in the world, with over 1.9 million cases in 2022 and age-standardized mortality rate (ASMR) of 8.1 per 100,000 [2]. In both genders, there are differences in the incidence and mortality rates of colorectal cancer in various regions around the world. The incidence rate in developed countries is three to four times higher than that in developing countries, while the mortality rate in developing countries is reported more [3]. For example, the incidence rate of this cancer is increasing in Eastern Europe, Southeast, South Asia, and South America [4]. In Iran, colorectal cancer was reported the fourth most common cancer, with 12,899 cases and age-standardized rate of 13.9 per 100,000 and also 6739 deaths and ASMR of 8.2 in men and 6.5 in women per 100,000 in 2022 [2].

Evidence has shown that the risk of colorectal cancer increases gradually from the age of 40 and sharply after the age of 50 [5]. In addition to the age effect, some events occurred during certain periods that may affect throughout the age range (period effect). Similarly, factors can affect a generation as well as promote distinct changes in consecutive age groups and periods (cohort effect). Therefore, age–period–cohort (APC) models allow us to estimate the age, period, and cohort effect and determine which one affects the most in incidence and mortality rates [6].

Among cancer types, colorectal cancer accounts for the largest percentage of global cancer-related economic costs (10.9%). Therefore, investing in effective public health interventions is essential to reduce the burden of cancer [7]. Because advances in screening, early detection, and treatment of colorectal cancer can lead to changes in trends of incidence and mortality rates in different age groups and thus affect patients' survival and quality of life, understanding this trend is important. Therefore, the aim of this study is to estimate the effect of APC on colorectal cancer mortality from 1990 to 2021 in Iran.

2. Method

2.1. Data Sources. The data were collected from the Global Health Data Exchange (GHDx), a project organized by the Institute for Health Measurement and Evaluation at the University of Washington. The latest study estimated the burden of disease from 369 cases and 87 risk factors for different age groups, genders, and causes in 204 countries and regions between 1990 and 2019 based on indicators such as incidence, mortality, years of life lost, years of life with disabilities, and years of life adjusted with disabilities. Complete details of the global burden of disease (GBD) methodology have been reported [8]. Web address for GBD data acquisition: https://ghdx.healthdata.org/gbd-results-tool. Our study data includes age- and year-specific colorectal cancer deaths and population in Iran from 1990 to 2021.

2.2. Joinpoint Regression Analysis. First, we calculated ASMR by direct standardization using standard population for low- and middle-income countries [9]. To identify changes in mortality rate trends, joinpoint regression was estimated by using the Joinpoint Regression Program, Version 5.0.2 from the Surveillance Research Program of the US National Cancer Institute. Briefly, this method uses colorectal cancer mortality rate as input to determine the years in which trend changes occurred, calculates annual percentage change (APC) of the rates between trend change points and also estimates the average annual percentage change (AAPC) over the entire study period. If there is no joinpoint, APC is constant and, therefore, equal to AAPC. Otherwise, the entire period is divided at points of trend change. AAPC is a weighted average of APC, with the length of each segment being considered as the weight. The joinpoint regression model can be expressed as follows:

$$E[y|x] = \beta 0 + \beta 1 x + \sigma 1 (x - \tau_1) + + \ldots + \sigma k (x - \tau_k) +, \tag{1}$$

where y represents the mortality of colorectal cancer, and x represents the year. The constant term in the model is denoted by β. σ, τ, and k represent the regression coefficients of each piecewise function, the unknown turning points, and the number of turning points, respectively. When $(x - \tau_1) > 0$, $(x - \tau_k)^+ = (x - \tau_k)$; otherwise, $(x - \tau_1) = 0$. The Monte Carlo permutation test with Bonferroni modification was used to determine the best suitable combination of line segments and joinpoints [10].

2.3. APC Analysis. In APC analysis, colorectal cancer mortality data were divided into consecutive 5-year age groups (15–19, 20–24, . . ., and ≥ 95 years) and the same 5-year intervals for calendar periods (1992–1996, 1997–2001, . . ., and 2017–2021). As a result, 21 cohorts were created based on the 17 age categories and six period groups, which are categorized as < 1901, 1902–1906, and continuing through 1997–2001.

APC effects were calculated by the corresponding relative risk (RR) and 95% confidence interval (CI) using Poisson regression. The APC effects act multiplicatively on the rate, and its logarithm of the expected rate is a linear function of the effects of age, period, and cohort, known as follows:

$$Y_{ij} = \log(M) = \mu + \alpha\, \text{age}_i + \beta\, \text{period}_j + \gamma\, \text{cohort}_k + \varepsilon_{ijk}, \tag{2}$$

where Y_{ij} is the PC mortality rate for the ith age group at the jth period, μ means the intercept of the regression equation representing the baseline level of risk of onset of disease or death, ε_{ijk} represents the term error, and α, β, and γ are the effects of age group, period group and cohort group i, j, and k, respectively, where i, j, and $k = 1, 2, \ldots$.

Since there is a linear relationship between age, period, and cohort, it is difficult to estimate the unique set for each age, period, and cohort effect. This problem is called the nonidentification problem [11]. To overcome this issue, we used intrinsic estimator (IE) method because of its excellent statistical properties, e.g., it provides unbiased estimates for small time periods and rate tables and does not require the determination of reference categories for age, period, and cohort coefficients [12].

The coefficient is expressed in exponential form $(\exp(\text{coef.}) = e^{\text{coef.}})$ and reflects the RR of incidence and mortality associated with a particular age, period, or birth cohort compared with the average level. RR values greater than one indicate a higher risk of incidence or mortality compared with the average. Conversely, RR values less than one indicate a lower risk of incidence or mortality compared to the average. Besides, smaller values for Akaike's information criterion (AIC) and Bayesian information criterion (BIC) with parameter penalty terms denote a better fit. The findings were considered statistically significant at

Table 1: Crude and age-standardized mortality trend of colorectal cancer among Iranian men and women based on joinpoint regression during 1990–2021.

Variable	Years	APCh (95% CI)	*p* value	AAPC (95% CI)	*p* value
Men					
Crude rate	1990–1993	1.323 (0.630, 2.020)	< 0.001	—	—
	1993–2001	−1.043 (−1.224, −0.862)	< 0.001	—	—
	2001–2012	3.433 (3.322, 3.543)	< 0.001	—	—
	2012–2015	4.761 (3.334, 6.208)	< 0.001	—	—
	2015–2019	2.120 (1.422, 2.823)	< 0.001	—	—
	2019–2021	−3.037 (−4.358, −1.699)	< 0.001	—	—
	1990–2021	—	—	1.588 (1.398, 1.778)	< 0.001
Age-standardized mortality rate	1990–2001	−1.245 (−1.370, −1.120)	< 0.001	—	—
	2001–2007	2.387 (1.959, 2.818)	< 0.001	—	—
	2007–2016	1.552 (1.345, 1.760)	< 0.001	—	—
	2016–2019	−0.444 (−2.293, 1.440)	0.624	—	—
	2019–2021	−4.687 (−6.458, −2.883)	< 0.001	—	—
	1990–2021	—	—	0.106 (−0.121, 0.335)	0.359
Women					
Crude rate	1990–1993	0.376 (−0.018, 0.773)	0.059	—	—
	1993–2001	−1.647 (−1.750, −1.543)	< 0.001	—	—
	2001–2004	1.417 (0.620, 2.220)	0.002	—	—
	2004–2010	3.779 (3.596, 3.962)	< 0.001	—	—
	2010–2016	4.470 (4.286, 4.655)	< 0.001	—	—
	2016–2019	1.716 (0.917, 2.521)	< 0.001	—	—
	2019–2021	−2.173 (−2.941, −1.398)	< 0.001	—	—
	1990–2021	—	—	1.340 (1.215, 1.465)	< 0.001
Age-standardized mortality rate	1990–1993	−0.932 (−1.551, −0.309)	0.005	—	—
	1993–2002	−1.856 (−1.990, −1.721)	< 0.001	—	—
	2002–2016	1.475 (1.408, 1.542)	< 0.001	—	—
	2016–2019	−0.600 (−1.839, 0.653)	0.326	—	—
	2019–2021	−4.186 (−5.380, −2.977)	< 0.001	—	—
	1990–2021	—	—	−0.307 (−0.460, −0.152)	< 0.001

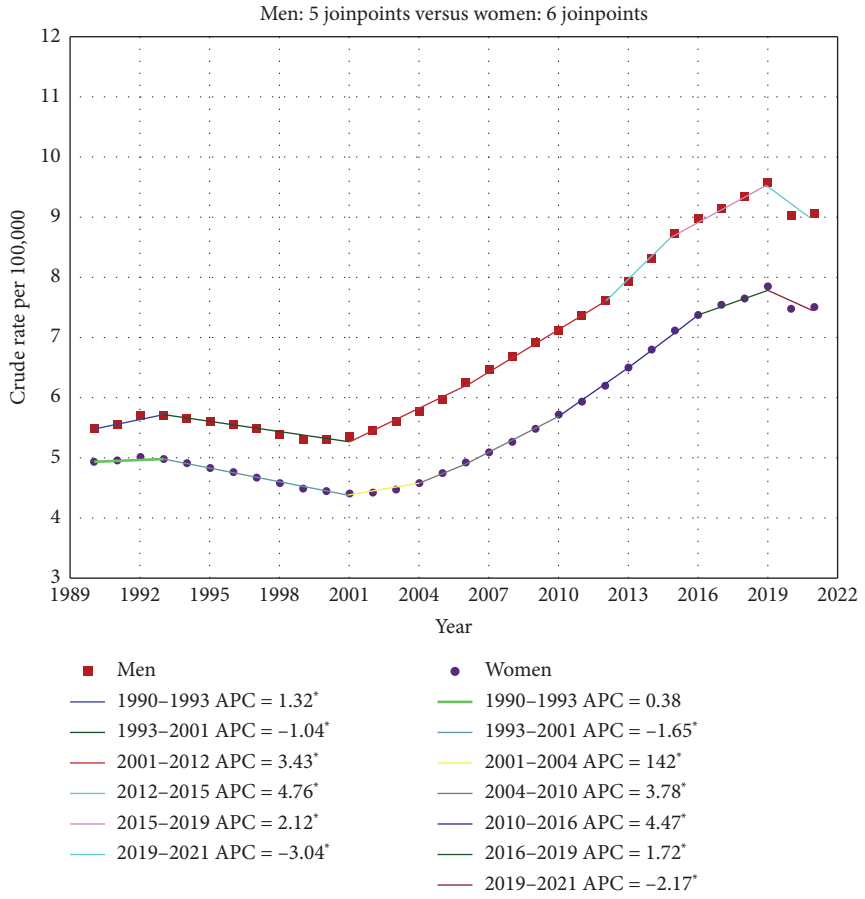
$p < 0.05$. APC analyses were performed the "apc-ie" command using statistical software STATA Version 17.0.

3. Results

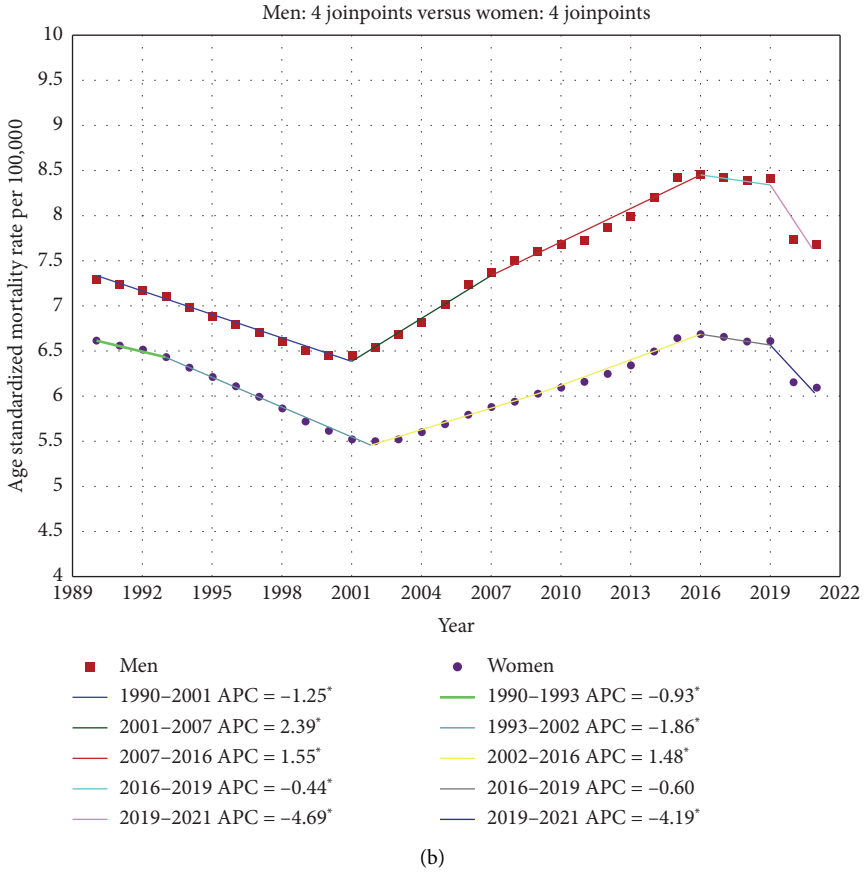
Joinpoint regression analysis indicated that crude mortality rates occurred at five joinpoints in men and six joinpoints in women. Increases in crude mortality rates were observed in both genders in all periods except 1993–2001 and 2019–2021. Over the entire period, crude mortality rates increased on average 1.588% (95% CI: 1.398%, 1.778%; $p < 0.001$) per year in men and 1.340% (95% CI: 1.398%, 1.778%; $p < 0.001$) per year in women. ASMR decreased in men for all periods except 2001–2007 and 2007–2016 and in women for all periods except 2002–2016. The AAPC for ASMR also increased but not significantly (AAPC = 0.106%; 95% CI: −0.121%, 0.335%; and $p = 0.359$) in men but decreased in women (AAPC = −0.307%; 95% CI: −0.460%, −0.152%; and $p < 0.001$) (Table 1 and Figure 1).

Cohort trends in colorectal cancer mortality in various age groups are shown in Figure 2. For both men and women, colorectal cancer mortality is higher in older people than in younger people. The graph is almost constant up to age 70–74, but in the 75–79+ age group, the younger cohorts has a higher mortality rate than the older cohorts, and for men aged 95+, the mortality trend fluctuated.

As mentioned before, we used the APC model with IE method to calculate the coefficients for age, period, and cohort effects. Age effect increased for both genders, with the highest coefficients being 1.731 for men and 1.964 for women aged 95 years. In other words, the mortality rate from colorectal cancer for men and women aged 95 years and older is 95.011 and 98.691 times higher ($e^{\text{coef}(>95)-\text{coef}(15-19)}$), respectively, than for people aged 15–19 years, and this interpretation can be used to compare each both age groups. It is also noteworthy that the RRs are greater than one for men aged 50 years or older and women aged 55 years or older (Table 2 and Figure 3(a)). The risk of colorectal cancer mortality has increased over time, with the RRs increasing from 0.680 (95% CI: 0.661, 0.699) in 1992–1996 to 1.549 (95% CI: 1.517, 1.584) in 2017–2021 for men and from 0.762 (95% CI: 0.740, 0.785) to 1.462 (95% CI: 1.430, 1.496) for women (Table 2 and Figure 3(b)). In addition, the mortality rate from colorectal showed a decreasing trend with the transition of birth cohorts. That is, people born in recent years had a lower mortality rate than those born in previous years. The cohort effect coefficients for men and women decreased from 1.458 (95% CI: 1.077, 1.838) and 1.208 (95% CI: 0.858, 1.558) before 1901 to −1.590 (95% CI: −1.988, −1.193) and −1.543 (95% CI: −1.938, −1.148) in 2002–2006, representing a decrease of 209.05% and 227.73%, respectively (Table 2 and Figure 3(c)). It



(a)



(b)

Figure 1: The joinpoint analysis of crude (a) and age-standardized (b) mortality rates of colorectal cancer among Iranian men and women during 1990–2021.

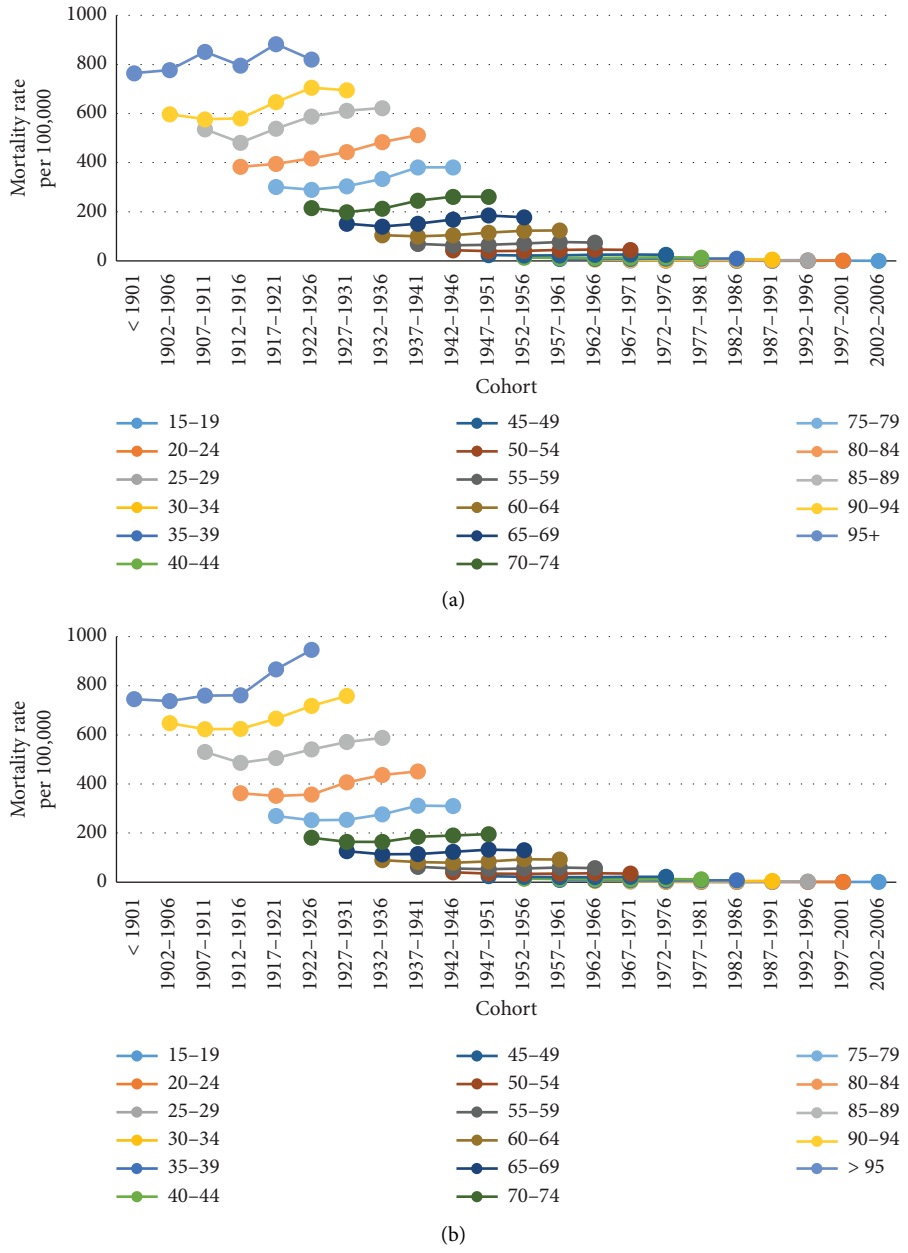


Figure 2: Cohort trends of mortality rate of colorectal cancer among different age groups of Iranian men (a) and women (b).

should be noted that the cohort patterns shown in Figure 2 may appear inconsistent with this reduced trend because the crude cohort curves in Figure 2 reflect the combined effect of age and period. Consequently, visual cohort trends should be interpreted with caution, as they may be partially confounded by age-related mortality increases and period-specific changes.

4. Discussion

In this study, we analyzed trends in colorectal cancer mortality in Iran over the past 30 years using the most recent GBD 2021 data. The joinpoint regression results showed that the crude rate and ASMR of colorectal cancer in men and the crude mortality rate in women have increased steadily each year. Similarly, Ilic and Ilic [13] reported rising colorectal cancer mortality in both genders, a trend also observed in several developing countries such as South American nations, Romania, and Russia [4]. In contrast, this trend appears to be declining in many developed countries [4]. This decrease is largely attributed to improvements in screening techniques and strategies that facilitate early diagnosis and treatment, thereby reducing disease-related mortality and increasing life expectancy [14]. One study found that colonoscopy screening reduced the risk of colorectal cancer incidence and death by 40%–60% [15]. A systematic evaluation conducted in Arab countries demonstrated increasing colorectal cancer incidence and mortality across

Table 2: APC model analysis results of colorectal cancer mortality among Iranian men and women.

Factor	Men				Women			
	Coef.	SE	95% CI	*p* value	Coef.	SE	95% CI	*p* value
Age (*years*)								
15–19	−2.823	0.072	−2.966, −2.680	< 0.001	−2.628	0.071	−2.768, −2.487	< 0.001
20–24	−2.521	0.056	−2.632, −2.410	< 0.001	−2.381	0.056	−2.493, −2.269	< 0.001
25–29	−2.095	0.045	−2.185, −2.005	< 0.001	−1.824	0.043	−1.910, −1.738	< 0.001
30–34	−1.455	0.035	−1.524, −1.385	< 0.001	−1.451	0.036	−1.523, −1.379	< 0.001
35–39	−1.128	0.031	−1.189, −1.067	< 0.001	−1.183	0.032	−1.248, −1.119	< 0.001
40–44	−0.839	0.028	−0.895, −0.784	< 0.001	−0.844	0.029	−0.901, −0.786	< 0.001
45–49	−0.390	0.024	−0.439, −0.341	< 0.001	−0.444	0.026	−0.495, −0.393	< 0.001
50–54	0.037	0.021	−0.005, 0.080	0.087	−0.097	0.023	−0.142, −0.051	< 0.001
55–59	0.371	0.019	0.333, 0.410	< 0.001	0.214	0.020	0.173, 0.255	< 0.001
60–64	0.705	0.017	0.670, 0.740	< 0.001	0.500	0.019	0.463, 0.538	< 0.001
65–69	0.944	0.017	0.911, 0.978	< 0.001	0.720	0.018	0.683, 0.756	< 0.001
70–74	1.168	0.016	1.135, 1.201	< 0.001	0.981	0.018	0.945, 1.016	< 0.001
75–79	1.399	0.017	1.364, 1.434	< 0.001	1.308	0.018	1.271, 1.345	< 0.001
80–84	1.560	0.020	1.521, 1.600	< 0.001	1.554	0.020	1.514, 1.595	< 0.001
85–89	1.676	0.024	1.629, 1.724	< 0.001	1.742	0.024	1.693, 1.790	< 0.001
90–94	1.657	0.033	1.592, 1.722	< 0.001	1.868	0.033	1.803, 1.933	< 0.001
> 95	1.731	0.056	1.620, 1.842	< 0.001	1.964	0.058	1.849, 2.079	< 0.001
Period								
1992–1996	−0.385	0.014	−0.414, −0.357	< 0.001	−0.271	0.015	−0.301, −0.241	< 0.001
1997–2001	−0.321	0.012	−0.345, −0.296	< 0.001	−0.253	0.013	−0.280, −0.227	< 0.001
2002–2006	−0.135	0.010	−0.156, −0.114	< 0.001	−0.151	0.012	−0.174, −0.127	< 0.001
2007–2011	0.096	0.009	0.078, 0.115	< 0.001	0.047	0.010	0.026, 0.068	< 0.001
2012–2016	0.306	0.009	0.287, 0.325	< 0.001	0.248	0.010	0.227, 0.268	< 0.001
2017–2021	0.438	0.011	0.417, 0.460	< 0.001	0.380	0.011	0.358, 0.403	< 0.001
Cohort								
< 1901	1.458	0.194	1.077, 1.838	< 0.001	1.208	0.178	0.858, 1.558	< 0.001
1902–1906	1.317	0.102	1.116, 1.518	< 0.001	1.168	0.092	0.988, 1.349	< 0.001
1907–1911	1.182	0.079	1.027, 1.338	< 0.001	1.096	0.067	0.964, 1.229	< 0.001
1912–1916	0.968	0.053	0.862, 1.073	< 0.001	0.943	0.049	0.846, 1.040	< 0.001
1917–1921	0.888	0.036	0.815, 0.960	< 0.001	0.866	0.036	0.795, 0.938	< 0.001
1922–1926	0.760	0.030	0.699, 0.820	< 0.001	0.770	0.030	0.710, 0.830	< 0.001
1927–1931	0.610	0.028	0.554, 0.666	< 0.001	0.669	0.027	0.614, 0.723	< 0.001
1932–1936	0.483	0.026	0.431, 0.535	< 0.001	0.556	0.026	0.504, 0.607	< 0.001
1937–1941	0.397	0.025	0.347, 0.447	< 0.001	0.468	0.025	0.418, 0.518	< 0.001
1942–1946	0.258	0.025	0.208, 0.308	< 0.001	0.328	0.025	0.277, 0.378	< 0.001
1947–1951	0.121	0.025	0.071, 0.172	< 0.001	0.199	0.026	0.147, 0.250	< 0.001
1952–1956	−0.037	0.026	−0.088, 0.014	0.158	0.060	0.027	0.007, 0.113	0.026
1957–1961	−0.165	0.027	−0.218, −0.112	< 0.001	−0.078	0.028	−0.134, −0.023	0.005
1962–1966	−0.335	0.028	−0.392, −0.279	< 0.001	−0.256	0.030	−0.315, −0.196	< 0.001
1967–1971	−0.504	0.031	−0.565, −0.443	< 0.001	−0.435	0.032	−0.498, −0.371	< 0.001
1972–1976	−0.626	0.033	−0.692, −0.559	< 0.001	−0.607	0.035	−0.677, −0.537	< 0.001
1977–1981	−0.775	0.036	−0.847, −0.703	< 0.001	−0.769	0.038	−0.845, −0.694	< 0.001
1982–1986	−0.872	0.039	−0.950, −0.794	< 0.001	−0.889	0.042	−0.972, −0.807	< 0.001
1987–1991	−1.029	0.048	−1.124, −0.934	< 0.001	−1.061	0.050	−1.160, −0.961	< 0.001
1992–1996	−1.172	0.070	−1.310, −1.035	< 0.001	−1.301	0.073	−1.445, −1.156	< 0.001
1997–2001	−1.338	0.107	−1.549, −1.127	< 0.001	−1.394	0.112	−1.615, −1.172	< 0.001
2002–2006	−1.590	0.202	−1.988, −1.193	< 0.001	−1.543	0.201	−1.938, −1.148	< 0.001
AIC			8.41		AIC		8.36	
BIC			−268.35		BIC		−261.59	
Deviance			9.138		Deviance		15.903	

various age groups, along with a lack of widespread organized screening programs [16]. In Saudi Arabia, despite the rising incidence over several decades, the absence of a nationwide population-based screening program likely contributes to late-stage diagnosis and elevated mortality rates [17]. Furthermore, a recent review from the Eastern Mediterranean region identified knowledge gaps, structural barriers, and low uptake of screening tests (e.g., fecal occult blood tests and colonoscopy) as major obstacles to early detection [18]. Taken together, these findings indicate that the increasing colorectal cancer mortality in Iran underscores the urgent need to implement organized screening

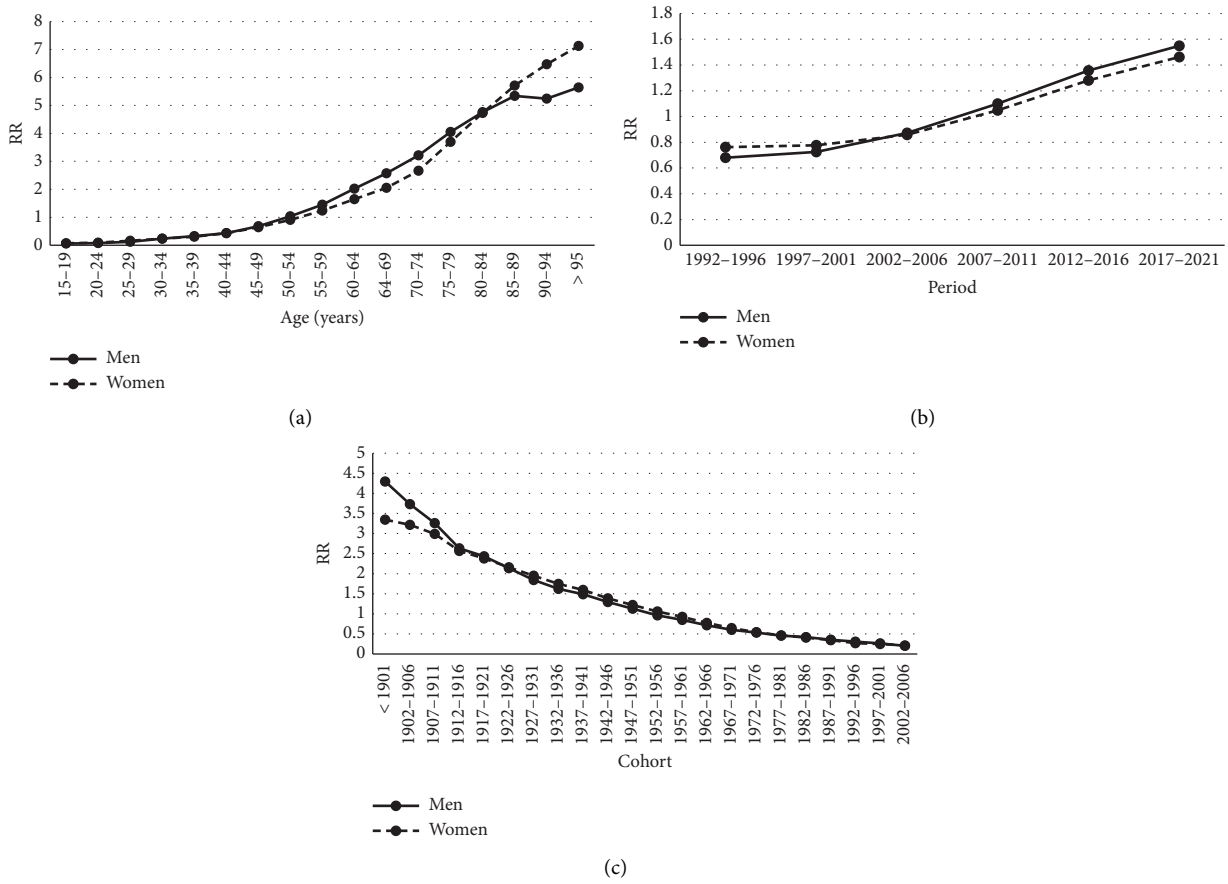


Figure 3: Colorectal cancer mortality relative risks due to (a) age, (b) period, and (c) cohort effects among Iranian men and women.

programs, expand access to early detection services, and strengthen public health education initiatives.

Consistent with our findings, Yu et al. reported an increasing age effect on colorectal cancer mortality [19]. This rise is largely driven by biological factors. Older adults are more vulnerable to malnutrition, which can worsen clinical outcomes and elevate mortality risk [20, 21]. Age-related decline in physiological function also contributes to higher mortality in older age groups [22]. In our study, the RR of death for both men and women aged 50 years and above exceeded one, indicating a higher-than-average risk. Therefore, middle-aged and older adults remain a critical target population for colorectal cancer prevention and control efforts in Iran.

Our results showed an increasing period effect in both men and women, indicating that colorectal cancer mortality has risen over time. A similar pattern has been reported in studies from China [22]. This upward trend may reflect the growing influence of "Westernized" lifestyle factors, including higher consumption of animal fat and red meat, lower vegetable intake, rising obesity, physical inactivity, smoking, and alcohol use [23, 24]. Childhood exposure to antibiotics may also contribute by disrupting the gut microbiome and increasing the risk of inflammatory bowel disease, a known risk factor for colorectal cancer [25].

Similar to our findings, Liu et al. reported a diminishing cohort effect, with individuals born in more recent years experiencing lower mortality rates than earlier generations [26]. Although Figure 2 appears to show a reverse pattern, this is likely due to confounding between age and period effects. The cohort curves in Figure 2 reflect crude trends that do not separate these effects, which can obscure the true generational pattern. In contrast, the APC model provides adjusted estimates that more accurately capture underlying cohort differences. Several factors may explain the declining cohort effect. Younger generations have generally benefited from better childhood nutrition, reducing long-term vulnerability to malnutrition-related health risks [21, 27]. They also tend to have higher educational attainment and greater health awareness, which may lead to improved knowledge of colorectal cancer prevention and screening [26, 28]. Nonetheless, our cohort findings differ from some studies, which may reflect variations in race, nationality, or tumor subsite. For example, a Swedish study showed contrasting cohort effects for right-sided versus left-sided colorectal cancers, with recent cohorts having a higher risk of right-sided cancer but a lower risk of left-sided cancer [29].

One of the study's notable strengths is that it provides the first countrywide estimate of colorectal cancers deaths in Iran over 32 years. Also, we used advanced trend models in this study to determine the role of the three factors, namely, age, period, and cohort. However, this study has several limitations. The GHDx dataset does not provide information on tumor subsites (e.g., right-sided colon, left-sided colon,

or rectal cancers), which may reflect distinct epidemiological patterns and could not be examined in our analysis. Furthermore, reliance on GBD estimates means that important lifestyle risk factors (e.g., diet, physical activity, smoking, and obesity) and genetic influences were not directly available for inclusion. These factors may contribute to the heterogeneity in colorectal cancer mortality and should be examined in future studies. Finally, as all ecological analyses, our findings cannot be generalized to the individual level because doing so may introduce an ecological bias.

5. Conclusion

This study provides a long-term overview of colorectal cancer mortality in Iran, showing a clear increase over the past 3 decades, with strong age and period effects and lower risks in more recent birth cohorts. These findings underscore the need to strengthen national screening strategies, particularly by expanding access to fecal occult blood testing and targeted colonoscopy for adults aged 50 years and older. Increasing public awareness of lifestyle-related risk factors and improving early detection pathways in primary care could further contribute to reducing preventable mortality. The establishment of more accurate cancer registries that capture tumor subsites and include lifestyle and genetic risk information would also support more effective planning and policy decisions.

Nomenclature

ASMR	Age-standardized mortality rate
APC	Age–period–cohort
GHDx	Global health data exchange
GBD	Global burden of disease
APC	Annual percentage change
AAPC	Average annual percentage change
RR	Relative risk
IE	Intrinsic estimator
AIC	Akaike's information criterion
BIC	Bayesian information criterion

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Statement

This study was approved by the Ethics Committee of Shiraz University of Medical Sciences with IR.SUMS.SCHEANUT.REC.1402.106.

Conflicts of Interest

The authors declare no conflicts of interest.

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