Non Comunicable Diseases

Comparing the trend of colorectal cancer before and after the implementation of the Population-Based National Cancer Registry in Iran

MOJTABA SEPANDI[1], YOUSEF ALIMOHAMADI[2]
[1] Gastroenterology and Liver Disease Research Center, Clinical Sciences Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran; [2] Health Research Center, Life style Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran

Keywords

Cancer registration • Colorectal cancer • Trend Analysis • Iran • ITS

Summary

Introduction. *Colorectal cancer is the third most common malignancy and the second leading cause of cancer deaths worldwide. This disease is the fourth most common malignancy in Iran. Since knowing the trend of this cancer is necessary for planning; this study aimed to compare the trend of colorectal cancer before and after implementing the Population-Based National Cancer Registry.*
Methods. *In this time series analysis using secondary data, the autoregressive integrated moving average (ARIMA) was used to predict the future trend. An Interrupted Time Series (ITS) regression model was also used to compare the incidence and mortality of colorectal cancer before and after the setting up of the Iranian National Population-Based Cancer Registry (INPCR).*
Results: *Among Iranian men, an increasing trend in the incidence (from 16.8 in 2019 to 19.5 per 100,000 in 2027) and deaths of colorectal cancer for the coming years was predicted (from 10.2 in 2019 to 11.2 per 100,000 in 2027). A similar pattern was also observed for the incidence of this cancer among females (from 11 in 2019 to 12.3 per 100,000 in 2027), but a reverse pattern was predicted for the trend of deaths among women (from 2.06 in 2019 to 1.93 per 100,000 in 2027). During the years after the implementation of the INPCR, the trend of cases (β: 0.33, $p < 0.001$) as well as deaths due to colorectal cancer was significantly increasing (β: 0.08, $p < 0.001$) among the Iranian population.*
Conclusions. *Probably, part of the increase in the incidence and mortality of colorectal cancer could be due to the improvement of the registration and reporting system of new cancer cases.*

Introduction

Colorectal cancer is a lethal disease and the second leading cause of cancer deaths worldwide [1]. Colorectal cancer morbidity and mortality rates differ around the world. Globally, colorectal cancer is the second most commonly diagnosed cancer in females and the third in males. Rates of both incidence and mortality are substantially higher in males compared to females [2].
Recognized risk factors for colorectal cancer include a positive family history, consumption of processed meats [3], smoking [4], excess body fat [5], a diet containing low fiber and insufficient consumption of dairy products as well as a low level of regular physical activity [6]. Colorectal cancer is the fourth most common malignancy in Iran [7]. The Iranian lifestyle has slowly changed to a Western lifestyle during the last three decades [8]. In recent years, the Iranian population has been facing demographic changes and economic and social developments, which can have significant effects on cancer patterns and trends [9].
The increasing trend of colorectal cancer could be partly due to demographic and lifestyle changes in the Iranian population, lower consumption of vegetables and fruits higher intake of red meat, and the community transition to a sedentary lifestyle [10]. The prominence of cancer registry systems in developing countries is not doubted. Accurate epidemiologic data on cancer is essential, both for research and for the planning and evaluation of programs in cancer prevention and control [11]. Efforts to register cancer in Iran began in the 1950s. In the late 2000s, regional population-based cancer registries were established in some provinces of Iran [12], and several reports were published [13-15]. Because this population-based cancer registration system had some limitations including disagreement in method and data collection as well as lack of appropriate structures and adequate financial support, in the early 2010s the Iranian Ministry of Health planned to launch the Iranian National Population-Based Cancer Registry (INPCR). The main aim of INPCR was to aggregate population-based cancer data at the national level [12]. Up to the year 2014, almost 98% of the Iranian population has been covered by INPCR [12]. Cancer registration is an important part of cancer control programs, and registration data can be used widely in etiologic research, evaluation of the effects of preventive measures, and program development in healthcare services [16]. The use of the cancer registration system in developed countries has led to a reduction in cancer deaths [17]. Cancer registration has shown the effects of early diagnosis and prevention campaigns at a population level [18]. Since knowing the trend of this cancer in the country is necessary for planning, the current study aimed to compare the trend

of colorectal cancer before and after implementing the Population-Based National Cancer Registry in Iran.

Materials and methods

Study design and data source

In this time series analysis using secondary data, we obtained the figures of new cases and deaths due to colorectal cancer from the Gapminder website, which is available at https://www.gapminder.org/data/. These data included all registered new cases and deaths due to colorectal cancer in Iran, per 100,000 populations for both Males and Females which have been diagnosed and registered from 1990 to 2019. Data from this website has been used in previous studies [19, 20].

Data analysis

To compare the average incidence and mortality before and after 2008 the paired t-test was used.

ARIMA model

To predict the future trend, the Autoregressive Integrated Moving Average (ARIMA (p, d, q)) was used. The ARIMA model as a time series analysis prediction method is a combination of an autoregressive and a moving average model [21] which is based on the fitting value of the past data sequence to extrapolate into the future (2020-2027). ARIMA model has been widely used in disease trend prediction [22]. This model is denoted ARIMA (p, d, q) where p is the number of time lags (the order of the model), q is the order of the moving average model, and d is the degree of differencing [22]. The process of the ARIMA model generating involves three steps. First, the Augmented Dickey-Fuller (ADF) test was used to assess the stationarity. Second, p and q were determined from autocorrelation function (ACF) and partial autocorrelation function (PACF) plots. The ACF plot indicates that the time series data follows the AR or autoregressive model. The AR time series model is obtained if the ACF plot decays towards zero or follows a sine wave pattern [23]. PACF gives the partial correlation of a stationary time series with its own lagged values, regressed the values of the time series at all shorter lags [24]. Third, to select the appropriate prediction model, p and q were replaced into the model from smallest to largest values. To select the best model, Akaike's information criterion (AIC) was used [25].

After selecting the best model according to minimum AIC and assessing the fitness of the selected models using different tests the ARIMA (p, d, q) model was used to predict the future trend based on current data. By considering annual time intervals, 30 years from 1990 to 2019 were accounted for in the time series model and the prediction was made up to 2027.

Interrupted time series regression

An Interrupted time series (ITS) was also used to compare the incidence and mortality of colorectal cancer before and after the setting up of the INPCR. In the ITS model, the dependent variable is measured before and after the intervention [26]. In the late 2000s, regional population-based cancer registries were established in some provinces of Iran [12], therefore, 2008 was chosen as the cut-off point for comparing the incidence and mortality of colorectal cancer. Data analyses were conducted using the ITSM (Interactive Time Series Modeling) for prediction, Stata 2017 software for Interrupted Time Series, and Excel 2010 for data management and graphs. The significance level was set at 0.05.

Results

Trend Analysis

According to our results, the average and standard deviation of registered new colorectal cancer cases from 1990 to 2019 among Iranian men and women were 11.9±2.4 and 8.7±1.1 cases per 100,000 populations, respectively. The highest incidence rate of colorectal cancer in men was 16.8 per 100,000 people in 2019, and the lowest rate was 9.29 in 1990. Among women, the highest recorded incidence was 11 in 2019, and the lowest incidence was 7.3, in 1990. Also, the average and standard deviation of registered new deaths due to colorectal cancer from 1990 to 2019 among men and women were 8.4 ± 1.01 and 2.4 ± 0.39 deaths per 100,000 populations, respectively (Tab. I).

Figure 1 shows the annual changes in incidence and mortality by gender. There were more fluctuations among men compared to women, both in incidence and mortality (Fig. 1). The average incidence before and after 2008 among men was 10.24± 0.87 and 14.35 ± 1.65, respectively (p = 0.0001). The average incidence before and after 2008 among women was 7.89 ± 0.49 and 9.91 ± 0.74, respectively (p = 0.0001) (Tab. II).

Prediction

An increasing trend in the incidence as well as deaths due to colorectal cancer for the coming years has been predicted (Fig. 2). Among Iranian men, an increasing trend in the incidence (from 16.8 in 2019 to 19.5 per 100,000 in 2027, ARIMA model with p = 1, q = 1, and AIC = 102 was used [ARIMA (1, 1, 1)] as well as deaths of colorectal cancer for the coming years was predicted (from 10.2 in 2019 to 11.2 per 100,000 in 2027, ARIMA model with p = 1, q = 1, and AIC = 180 was used [ARIMA (1, 2, 1)] (Fig. 2).

A similar pattern also was observed for the incidence of this cancer among females (from 11 in 2019 to 12.3 per 100,000 in 2027, ARIMA model with p = 2, q = 1, and AIC = 144 was used [ARIMA (2, 1, 1)] (Fig. 2), but a reverse pattern was predicted for the trend of deaths among the women (from 2.06 in 2019 to 1.93 per 100,000 in 2027, ARIMA model with p = 1, q = 1, and AIC = 158 was used (ARIMA (1, 2, 1)) (Fig. 2).

Interrupted Time series

The incidence and mortality trends were compared

Tab. I. The incidence and deaths of cancers among the Iranian population, 1990-2019 (proportion per 100,000 population).

Year	Registered cases in Men	Change	Registered Cases in Women	Change	Registered Deaths in Men	Change	Registered Deaths in Women	Change
1990	9.29	-	7.3	-	7.65	-	3.22	-
1991	9.36	0.07	7.33	0.03	7.62	-0.03	3.16	-0.06
1992	9.37	0.01	7.34	0.01	7.57	-0.05	3.12	-0.04
1993	9.6	0.23	7.47	0.13	7.59	0.02	3.05	-0.07
1994	9.54	-0.06	7.45	-0.02	7.5	-0.09	3	-0.05
1995	9.66	0.12	7.51	0.06	7.48	-0.02	2.93	-0.07
1996	9.95	0.29	7.71	0.2	7.51	0.03	2.84	-0.09
1997	9.89	-0.06	7.76	0.05	7.45	-0.06	2.76	-0.08
1998	9.83	-0.06	7.73	-0.03	7.38	-0.07	2.69	-0.07
1999	9.58	-0.25	7.58	-0.15	7.23	-0.15	2.62	-0.07
2000	10	0.42	7.83	0.25	7.33	0.1	2.55	-0.07
2001	10.6	0.6	8.15	0.32	7.5	0.17	2.5	-0.05
2002	10.7	0.1	8.18	0.03	7.57	0.07	2.43	-0.07
2003	10.8	0.1	8.19	0.01	7.68	0.11	2.36	-0.07
2004	11	0.2	8.3	0.11	7.79	0.11	2.31	-0.05
2005	11.5	0.5	8.59	0.29	8.02	0.23	2.26	-0.05
2006	11.9	0.4	8.78	0.19	8.22	0.2	2.22	-0.04
2007	11.9	0	8.82	0.04	8.33	0.11	2.17	-0.05
2008	12.1	0.2	8.91	0.09	8.48	0.15	2.14	-0.03
2009	12.4	0.3	9.02	0.11	8.69	0.21	2.12	-0.02
2010	12.7	0.3	9.16	0.14	8.87	0.18	2.1	-0.02
2011	13.1	0.4	9.36	0.2	8.99	0.12	2.09	-0.01
2012	13.4	0.3	9.5	0.14	9.11	0.12	2.08	-0.01
2013	13.8	0.4	9.7	0.2	9.33	0.22	2.09	0.01
2014	14.5	0.7	9.97	0.27	9.6	0.27	2.11	0.02
2015	15.3	0.8	10.3	0.33	9.93	0.33	2.13	0.02
2016	15.8	0.5	10.6	0.3	10.1	0.17	2.13	0
2017	16	0.2	10.7	0.1	10.1	0	2.11	-0.02
2018	16.4	0.4	10.8	0.1	10.1	0	2.08	-0.03
2019	16.8	0.4	11	0.2	10.2	0.1	2.06	-0.02
P trend	0.001	0.001	0.001	0.008	0.001	0.001	0.001	0.0001

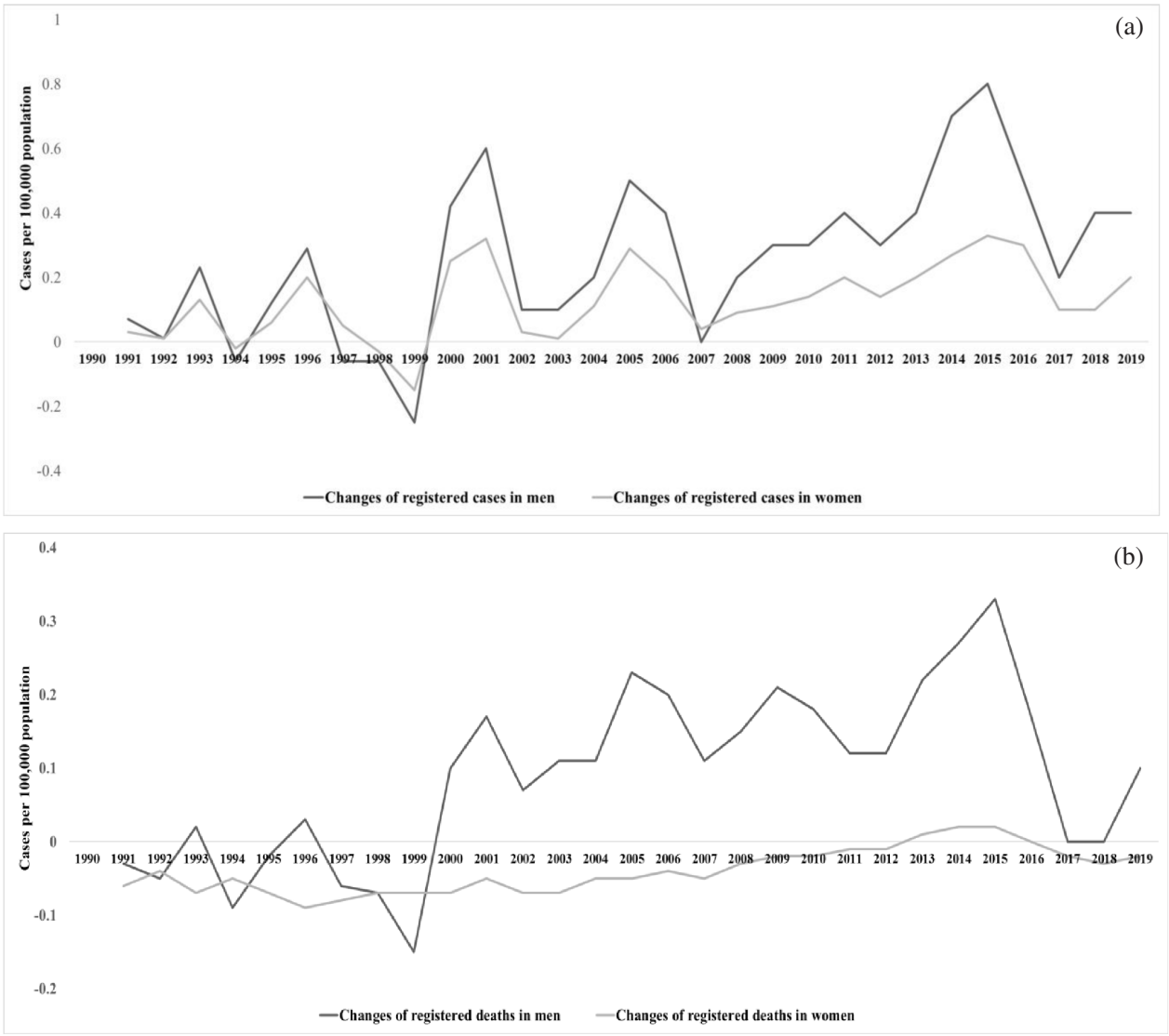
Change: The difference in each year's cases from the previous year.

before and after 2008 through an ITS analysis, the post-intervention (after the implementation of the INPCR) slope changes are significant for the incidence (β: 0.33, $p < 0.001$) and deaths due to colorectal cancer (β: 0.08, $p < 0.001$) (Data not shown). In other words, after the implementation of the INPCR, the number of registered cases as well as deaths had a statistically significant increasing trend among the Iranian population. Although, before and after 2008, the slope of the regression line related to the incidence of the disease is positive, but the incidence has increased more steeply after this year (Fig. 3a). Regarding deaths, the slope of the regression line was negative before 2008, while after the implementation of the INPCR, the registration of deaths due to colorectal cancer increased (Fig. 3b).

Discussion

This study investigated the incidence of colorectal cancer and its mortality in Iran for 29 years, to assess the impact of the national cancer registry on the trend of this cancer in Iran. The results showed that the incidence and mortality rate in Iran increased between 1990 and 2019. Consistent with the results of the present study, Yazdizadeh et al., concluded that the incidence of colorectal cancer in

Fig. 1. The trend of changes in incidence (a) and deaths (b) of colorectal cancer according to gender, 1990-2019 (proportion per 100,000 population).



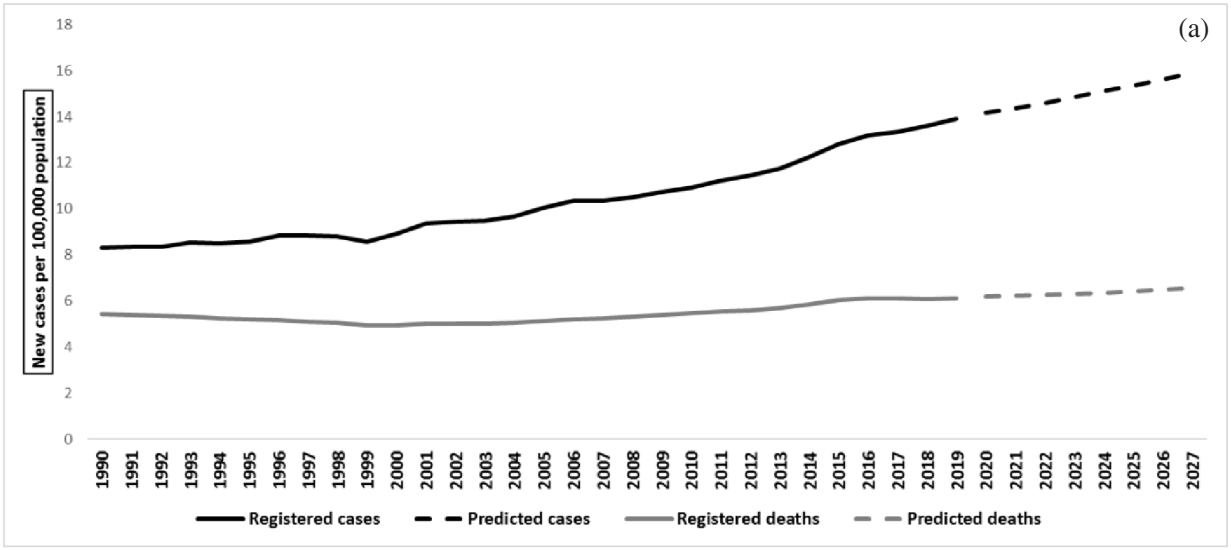
Tehran has increased by 82% over the past 30 years [27]. The results of Mousavi et al.'s study also confirm the increasing trend of colon cancer in Iran [28]. An increasing trend in the incidence of colorectal cancer has also been reported in some European [29, 30] and African [31] countries. An increasing mortality trend has also been reported in several countries in Latin America, the Caribbean, and Asia [32, 33] and this may reflect limited access to early diagnosis and treatment [34]. A study in Iran showed that the five-year survival rate of colorectal cancer is 41 percent and the median survival time is estimated to be 3.5 years [35].

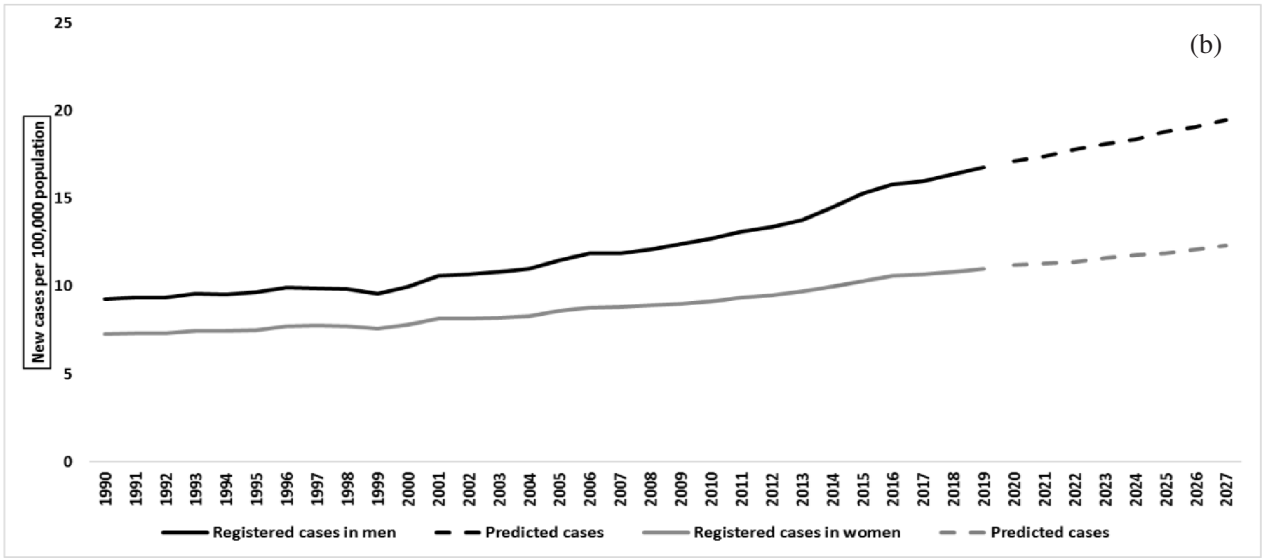
Tab. II. Comparing the average incidence and deaths of colorectal cancer (proportion per 100,000 population), before and after 2008.

Variable	Year	Average	SD	p*
Cases in Men	Before 2008	10.24	0.87	0.0001
	After 2008	14.35	1.65	
Cases in Women	Before 2008	7.89	0.49	0.0001
	After 2008	9.91	0.74	
Deaths in Men	Before 2008	7.63	0.29	0.0001
	After 2008	9.45	0.62	
Deaths in Women	Before 2008	2.67	0.34	0.0001
	After 2008	2.10	0.02	

* Based on paired t-test.

Fig. 2. The prediction of the total incidence and deaths (a), incidence by gender (b), and deaths of colorectal cancer by gender (c), 1990-2027 (proportion per 100,000 population).





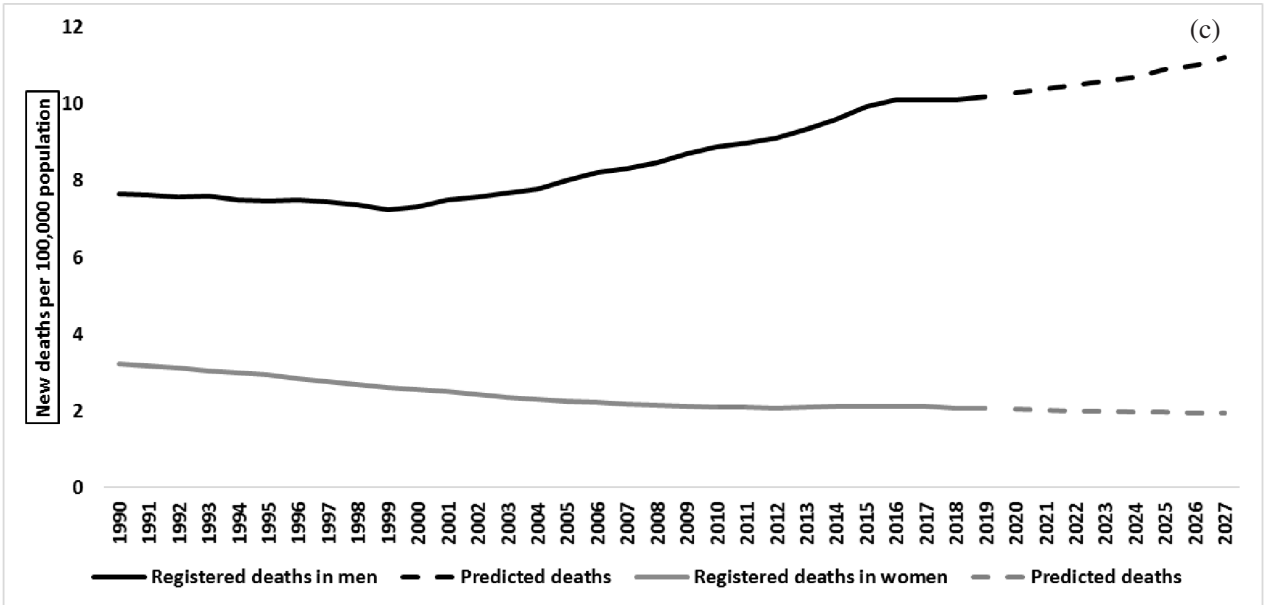
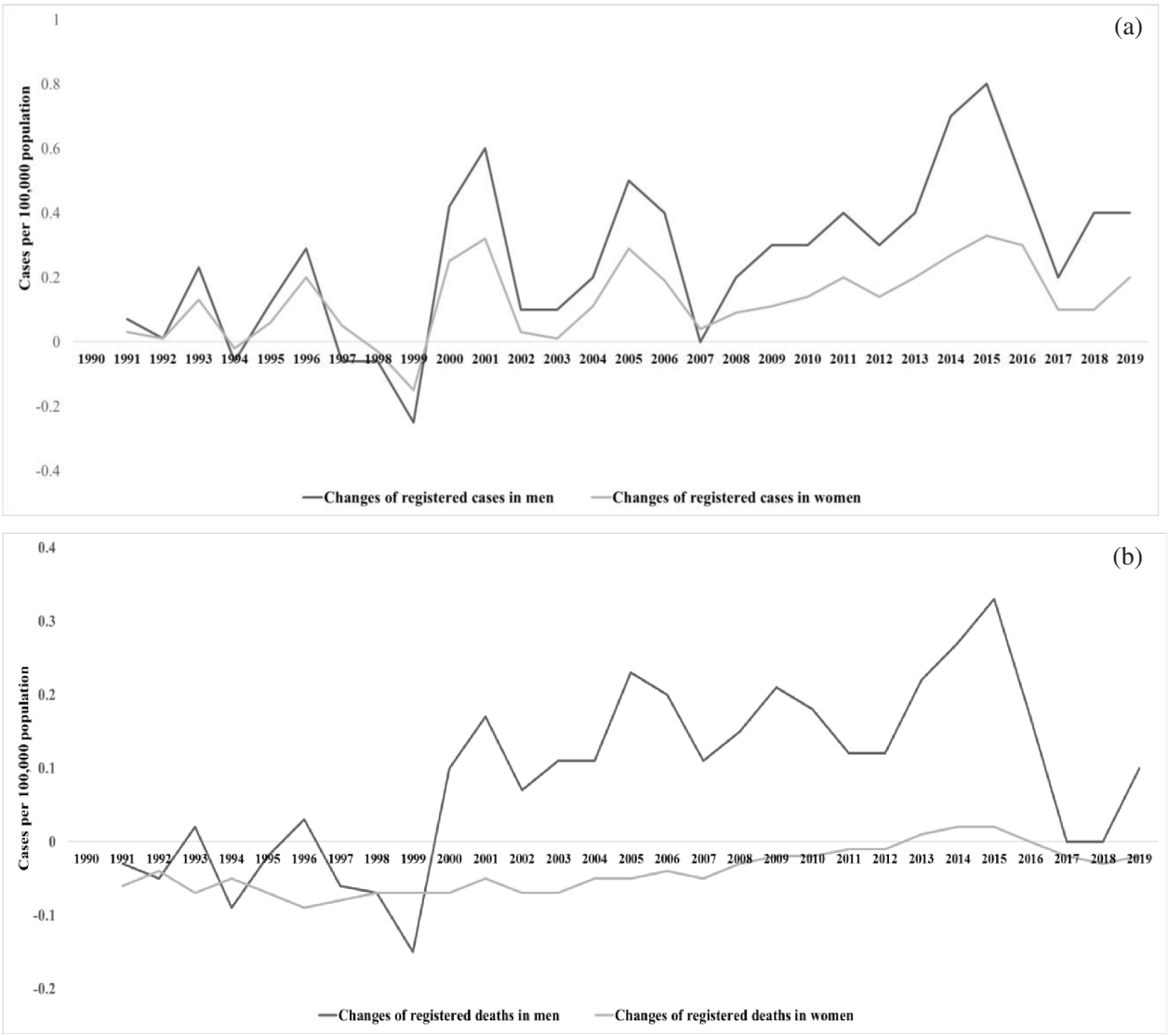


Fig. 3. Interrupted time series analysis of the total number of colorectal cancer cases (a) and deaths (b) from 1990 to 2019 (proportion per 100,000 population), before and after 2008.



A systematic review reported that the average 5-year overall survival rate in the Iranian population is estimated to be 52.5% [36]. A more favorable trend for females regarding mortality was also observed in the present study, which may be attributable, in part, to differential sex exposure to major environmental risk factors. Other studies worldwide confirmed that overall survival is better for women than for men [35]. When the trends of incidence and mortality before and after 2008 were compared, a statistically significant difference was observed before and after this date in terms of incidence and mortality. Since the late 2000s, a population-based registration program in the country as a complement to pathology-based registration has been established and the coverage of the cancer registration system in Iran has been improved [12]. A similar trend of incidence during this period has been observed in the skin [37] and stomach [38, 39] cancers. The current study showed that, during the years after the implementation of the INPCR, the number of registered cases as well as deaths had a significant increasing trend among the Iranian population. Although, before and after 2008, the slope of the regression line related to the incidence of the disease is positive, but the incidence has increased more steeply after this year. Regarding deaths, the slope of the regression line was negative before 2008, while during the years after the implementation of the INPCR, the trend of deaths due to colorectal cancer increased. This implies that probably some colorectal cancer deaths have been missed during the years before the implementation of the INPCR. A study in Canada using ITS analysis to determine the impact of the colorectal cancer screening guideline on the incidence rates of colon and rectal cancer among Canadians showed that the post-guideline slope changes are significant for both cancers [40]. Another study in Taiwan evaluated the influence of a nationwide screening program through the ITS analysis. They concluded that the implementation of this screening program effectively

reduced colorectal cancer mortality [41]. Based on the above explanations, it can be concluded that at least part of the observed increase in the incidence of colorectal cancer in Iran could be due to the improvement of the approach to collecting information related to the cancer registration system. Another explanation for the increase in the incidence of colorectal cancer in Iran could be the increase in the prevalence of risk factors [42]. Diet plays an important role in the development of colon cancer [43, 44]. Iran, as a developing country in the Persian Gulf region, has been faced with the increasing prevalence of cancer risk factors, an aging population, and population growth in recent decades [12]. One of the reasons for the increase in the trend of cancers especially colorectal cancer in Iran is the change in eating habits. In the past decades, fast foods have gradually replaced traditional Iranian foods, which are mainly high in fiber. Studies show that fat consumption in Iran has increased and this has led to an increase in obesity [8, 45]. Obesity and lack of regular physical activity are positively correlated with the risk of developing colorectal cancer [46, 47]. This is while estimates show that only one-third of the Iranian adult population engages in regular physical activity and the prevalence of smoking in Iran is approximately 14% [48].

Our results showed that the incidence and mortality of colorectal cancer are increasing in the whole Iranian population. Colorectal cancer survival is strongly related to the stage of disease diagnosis [49]. For colorectal cancer, accurate and standardized surgery can increase patient survival and significantly reduce the risk of recurrence [50]. In addition, estimates show that in developing countries, a small percentage of patients with colorectal cancers receive radiotherapy [51].

Despite the valuable results, the present study had limitations. First, lack of access to individual data such as family history, age, dietary pattern, and physical activity. Secondly, the observed difference in the incidence and mortality rate of colorectal cancer before and after the implementation of the cancer registration system could be partially due to confounding effects, which could not be adjusted in the present study.

Conclusions

Implementation of population-based cancer registration programs, improved the cancer registration system and the probably part of the increase in the incidence and mortality of colorectal cancer could be attributable to the improvement of the registration and reporting system of new cancer cases. This study provides evidence for the need for further analysis of the cancer registry system. Considering the preventability of colorectal cancer and the increase in the incidence and mortality of this disease, educational interventions are necessary, especially regarding screening programs and early diagnosis methods. Finally, the impact of the cancer registration system should be considered in the interpretation of the results of all cancer research in Iran.

Ethical consideration

This study was reviewed and approved by the ethics committee of Baqiyatallah University of Medical Science (IR.BMSU.REC.1402.033). Patient consent is not applicable.

Data availability statement

The data presented in this study are available on request from the corresponding author.

Informed consent statement

Not applicable.

Conflicts of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Fundings

This study does not have a funding source.

Authors' contributions

Conceptualization, Methodology, Project administration, Supervision, writing – original draft, Writing – review & editing: all authors. All authors read and approved the final manuscript.

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Correspondence: Yousef Alimohamadi, Health Research Center, Life style Institute, Baqiyatallah University of Medical Sciences, Tehran, Iran. E-mail: y.alimohamadi67@gmail.com

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