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Bayesian age-period-cohort projection of cancers in Iran: a modeling study

Hadis Barati[1], Mohamad Amin Pourhoseingholi[2], Gholamreza Roshandel[3] and Seyed Saeed Hashemi Nazari[1*]

Abstract

Introduction Cancer is a significant public health issue in Iran, and its incidence has been on the rise in recent years. The objective of this study is to predict the incidence of total cancer in Iran using a Bayesian age-period-cohort (APC) model.

Methods Utilizing age-period-cohort modeling, this study assessed the multifaceted effects of age, period, and cohort on cancer incidence during the period spanning 2005 to 2017. Key metrics, including the net drift (representing the overall annual percentage change), local drift (indicating annual percentage changes within specific age groups), and longitudinal age curves (depicting expected age-specific rates over time), were computed. Moreover, the evaluation encompassed an analysis of period and cohort relative risks. To project the future age-standardized incidence rates of cancers from 2018 to 2027, Bayesian age-period-cohort analysis integrated nested Laplace approximations.

Result The age-standardized incidence rate and the absolute number of cancer cases in Iran showed an upward trend. The net drift was 1.79% (95% confidence interval, CI: 0.87% to 2.72%) for males and 3.31% (95% CI: 2.49% to 4.14%) for females. Local drifts remained consistently above zero for all age groups from 2005 to 2017, except for the under-5 age group in both males and females, and the 45–49 and 50–54 age groups in females. After accounting for period deviations, the risk of cancer incidence exhibited an exponential increase with age for both sexes. Based on the Bayesian age-period-cohort analysis, it is estimated that there will be around 210,701 new cancer cases in 2027. Moreover, the Age-Standardized Rate (ASR) for cancer is anticipated to reach 240.32 per 100,000 by 2027. The forecasts indicate a rise in cancer incidence rates across all age groups for both males and females.

Conclusion This study underscores the urgency of implementing targeted preventive strategies aligned with demographic shifts and lifestyle factors. Emphasizing the role of robust cancer registries, it advocates for continuous monitoring to inform evidence-based interventions.

Keywords Cancers, Incidence, Prediction, Modeling study, Provinces of Iran, ASR

*Correspondence:
Seyed Saeed Hashemi Nazari
saeedh_1999@yahoo.com
Full list of author information is available at the end of the article

Introduction

Cancer is a significant contributor to mortality on a global scale, posing a major obstacle to efforts aimed at increasing life expectancy [1]. In 2020, the number of newly diagnosed cancer cases (excluding nonmelanoma skin cancer) reached approximately 19.3 million globally, while cancer-related deaths (excluding nonmelanoma skin cancer) amounted to nearly 10.0 million [2].

Similarly, Iran is confronting a considerable health challenge posed by cancer, experiencing higher incidence and mortality rates. According to the latest data from the International Agency for Research on Cancer (IARC) for the year 2020, there were an estimated 131,191 new cancer cases in Iran, leading to 79,136 cancer-related deaths. Unfortunately, these figures are projected to increase in the future [3].

In Iran, the primary factors that increase the risk of cancer comprise the consumption of opium and tobacco, drinking hot tea, inadequate consumption of fruits and vegetables, significant tooth loss, low levels of physical activity, obesity, and dietary patterns [4–6].

Despite the rising prevalence of cancer in Iran over the years [7–12], prior research primarily concentrated on individual factors, such as age-specific incidence rate, which solely examines the effect of age on cancer incidence, overlooking the impact of the interplay between different time periods, birth cohorts, and age on the burden of cancer. Simultaneously, in numerous time-series investigations, researchers solely focus on the diachronic shifts (the period effect) and neglect the intricacies of social transformations over time. Regarding the time dimension, social change encompasses three intertwined "confounding" impacts of age, period, and birth cohort, and these three elements can generate mutually constraining effects. Hence, it is essential to concurrently examine these three impacts within an analytical framework to gain a more precise understanding of the alterations within a specific time dimension and their respective interpretation mechanisms. Age–period–cohort analysis has been a widely utilized approach for evaluating the influences of age, period, and cohort effects on the outcome. The age effect illustrates the disparities in biological or social processes associated with age. Period effects indicate the impacts of the intricate amalgamation of historical events and environmental factors that influence all age groups. The cohort effect underscores the historical distinctions among individuals born in different times [13, 14].

To address this knowledge gap, our study aimed to investigate the association between age, calendar period, and birth cohort with the rising incidence of cancer in Iran, utilizing an age-period-cohort analysis. Moreover, we used the Bayesian age–period–cohort (BAPC) model[15] to predict the incidence cancer in Iran from 2018 to 2027.

Method

Study data

In 1984, the Iranian Parliament passed the "cancer reporting" legislation, leading to the launch of a nationwide cancer registration initiative by the cancer office under the Iranian Ministry of Health. This led to the formation of the national pathology-based registry (INPa), which was active from 1984 to 2013 [16, 17].

Recognizing limitations such as underestimation and inadequate population representation, the INPCR[18], a population-based cancer registration system, was introduced in 2014 to address these issues. Its objectives were to ensure comprehensive, precise, and representative cancer data[19].The INPCR expanded its data resources beyond the INPa by incorporating clinical and paraclinical data from hospitals and mortality data from the deaths registry.

Both INPCR and INPa adhere to international guidelines from the International Association of Cancer Registries (IACR) and the International Agency for Research on Cancer (IARC). Additionally, both registries use the third edition of the International Classification of Diseases for Oncology (ICD-O-3) to code tumor characteristics, ensuring consistency in cancer site classification and facilitating comparability across datasets [20].

To forecast cancer incidence in Iran for 2027, we used corrected data from 2005 to 2013 along with population-based INPCR data from 2014 to 2017, which met strict quality standards, enabling reliable predictions. A Bayesian model was employed to adjust incidence estimates from 2005 to 2013[21].

For correcting the undercount of cancer data through the Bayesian method, we used INPa (pathology-based) data from Iran for 2005 to 2013, which predates the establishment of the INPCR program. The Bayesian method requires a prior, which was provided by the population-based cancer registry in Golestan Province, active since 2005. This registry offered the necessary pathology-to-population ratio to correct the undercounting in cancer registries across Iran. Further details regarding this methodology are available in a separate study[21].

Statistical analysis

In order to calculate several parameters, we employed the age-period-cohort framework. These parameters include: (A) Net drift, which shows the overall log-linear trend across time and birth cohort, and expresses the annual percentage change in the expected age-adjusted rate.(B) Local drifts, which indicate the log-linear trends for each age group across time and birth cohort, and demonstrate

the annual percentage change in the expected age-specific rate over time.(C) Longitudinal age curve, which presents the expected age-specific rates adjusted for period effects in the reference cohort. (D) Period (or cohort) rate ratios (RR), which exhibit the ratio of age-specific rates in each period (or cohort) relative to the reference one.

We've organized the cancer incidence and population data into 5-year periods from 2005 to 2017 and successive 5-year age intervals from less than 1 year to 85 years and older. to conduct age-period-cohort analyses. The birth cohort was determined by subtracting the median age of the interval from the period. Using the age-period-cohort Web Tool provided by the National Cancer Institute[22], we calculated the estimated parameters. For measuring relative rates, we used the reference period interval (2010–2014) and reference birth cohort interval (1970–1974). The significance of estimable parameters and functions was tested using the Wald chi-square test, and all statistical tests were two-sided.

We utilized Bayesian age-period-cohort analysis with integrated nested Laplace approximations to forecast the age-specific incidence cases of cancer for the years 2018 to 2027. The soundness of this approach has been previously established[15]. We provided additional details in Text S2. Finally, we standardized the cancer incidence rates using the World-2000 population[23]. We conducted the Bayesian age-period-cohort analysis using R package BAPC.

The study utilized the average annual percentage change (AAPC) to assess the temporal trends in cancer age-standardized incidence rates (ASRs) for two time periods: 2005–2017 and 2018–2027. These periods represent past and future trends, respectively. To determine the AAPC, a regression line was applied to the natural logarithm of the rates, denoted as $y=\alpha+\beta x+\varepsilon$, where $y=\ln$ (ASR) and $x=$calendar year. The AAPC was then computed as $100\times(\exp(\beta)—1)$. To address over-dispersion, the AAPC for 2018–2027 was adjusted by incorporating the inverse of the standardized error (1/se) of the estimated incidence rate as weights in the regression models.

All analyses of the present research were carried out using R software, version 4.3.1. The study was approved by the Medical Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.PHNS.REC.1399.132).

Result

The number of newly diagnosed Cancer cases increased from 52,425 in 2005 to 126,707 in 2017, and the Cancer ASR increased from 110.43 per 100, 000 to 178.03 per 100,000 during the same period (AAPC = 4.18, 95% confidence interval [CI] 3.18, 6.20). The case numbers increased in both sexes. The ASR increased significantly among males (AAPC = 3.97, 95% CI, 3.08, 5.46) and females (AAPC = 4.56, 95% CI 3.83, 6.01).

The incidence of cancer across age subgroups for both sexes, women and men, is shown in Fig. 1 S1. Additionally, age-specific cancer incidence is increasing across all age groups.

Age-period-cohort analysis

Net drift shows the overall annual percentage change of cancer and the annual percentage changes of cancer in each age group. We found marked sex differences ($p=0.0002$) in net drift with 1.29% (95% confidence interval, CI: 0.61% to 1.97%) for males and 2.74% (95% CI: 2.49% to 3.06%) for females, reflecting increased of cancer incidence for females than males from 2005 to 2017.

In most age groups, local drift values are observed to be above zero, with the exception of males and females under 5 years of age, and females in the 45–49 and 50–54-year age groups (Fig. 1). To assess sex-specific differences in local drift patterns, we conducted a Wald test, which yielded a result approaching significance ($p=0.06$). Although this trend indicates a potential divergence in local drift between males and females, it did not meet the conventional threshold for statistical significance ($p<0.05$).

Figure 2 illustrates the longitudinal age curves of cancer incidence for both sexes. After controlling for period and cohort effects, we found that the distribution of cancer incidence with age exhibited exponential distribution. For both sexes, the cancer incidence showed the rapidly expanding trends from 45 to 49 age group to + 85 age group.

The period (cohort) relative risks (RR) are the ratio of age-specific rates in each period (cohort) relative to the reference period (cohort). We found increased period relative risks during the whole study period after adjusting for age and birth cohort in females. The relative risks were higher in the third period than in the first period (RR = 1.09 in 2017 versus RR = 0.83 in 2005). (Fig. 3).

Cohort relative risks were also found in similar patterns for both sexes. The log RR was highest in the 2010 birth cohort (Fig. 4).

In addition, using the specific results of Wald tests, we found cohort and period effects, and the net drifts and local drifts and cohort deviations were all statistically significant ($p<0.01$) (Table S1).

Cancer incidence projection

We next conducted a Bayesian age-period-cohort analysis to project future Cancer incidence trends in Iran. Our results showed that Between 2018 and 2027, the Cancer

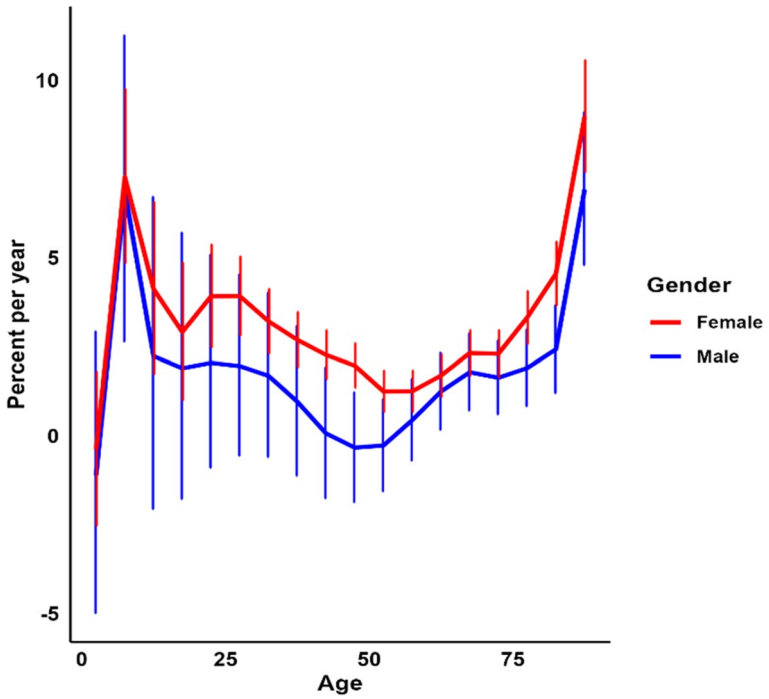

Fig. 1 Local drifts values and the corresponding 95% confidence interval for males and females for cancer disease incidence in Iran from 2005 to 2017

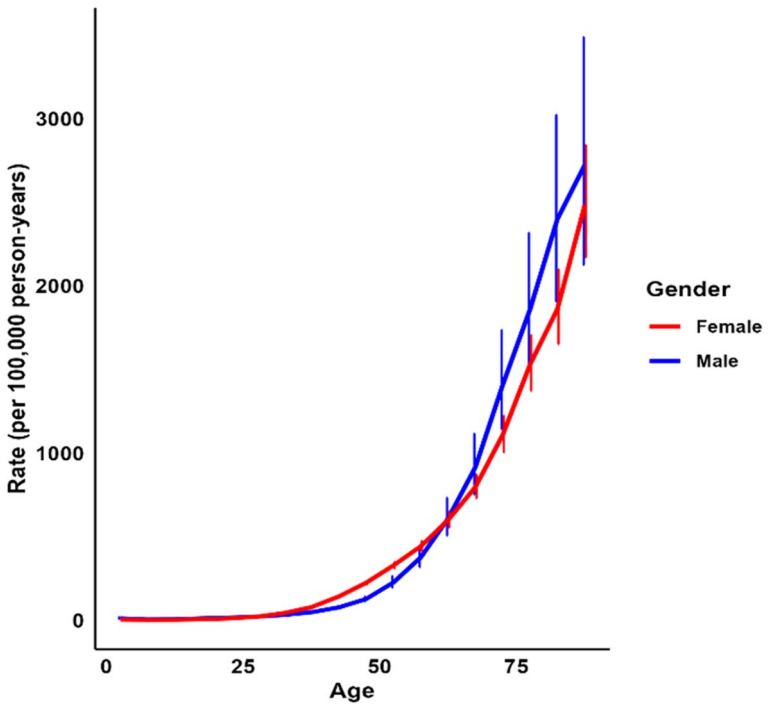

Fig. 2 Fitted longitudinal age curves of cancer disease incidence (per 100,000 person-years) and the corresponding 95% confidence interval for males and females

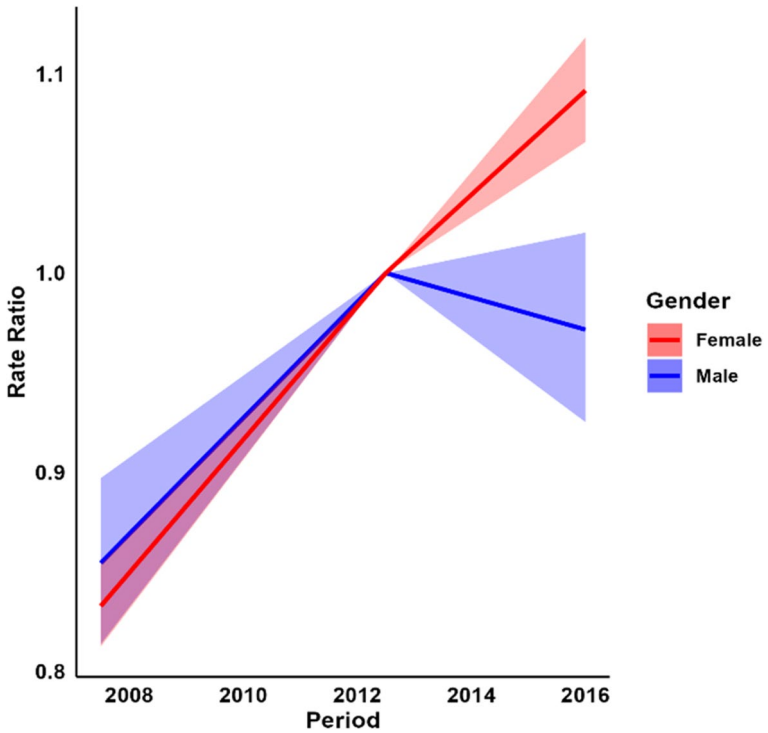

Fig. 3 Relative risk of each period compared with the reference period (2010–2014) adjusted for age and nonlinear cohort effects and the corresponding 95% confidence interval for males and females

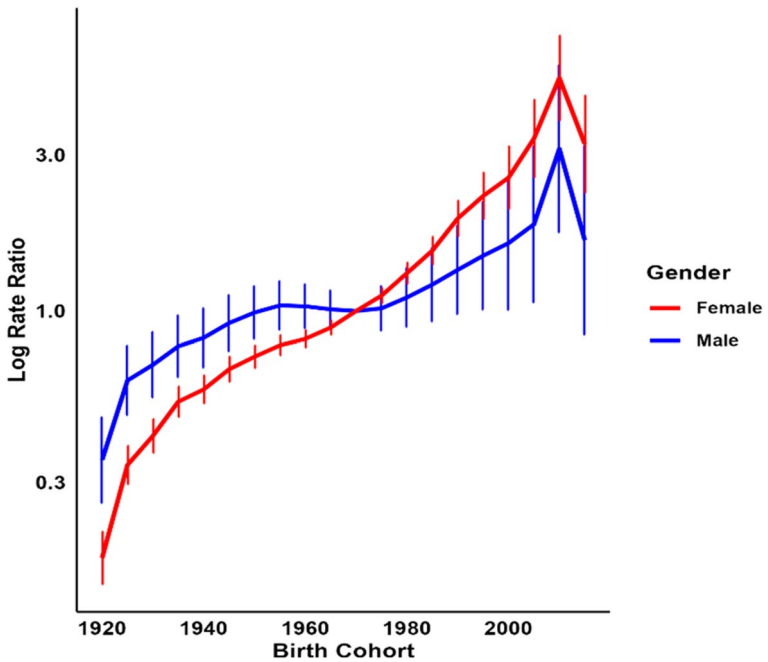

Fig. 4 Log Relative risk of each cohort compared with the reference cohort (cohort 1970–1974) adjusted for age and nonlinear period effects and the corresponding 95% confidence interval

incidence case number will further increase to 210,701 by 2027. The Cancer ASR will increase to 240.32 per 100,000 during the same period (AAPC = 3.34, 95% CI 3.30, 3.35) (Fig. 5).

The forecasts indicate a rise in cancer incidence across all age groups for both males and females (Fig. 2 and 3 S2). The age-standardized incidence rate prediction suggests an increase in cancer for females to 267.52 (AAPC = 1.72, 95% CI 1.64, 1.75) and for males to 235.89 (AAPC = -1.57.34, 95% CI -1.59, -1.57) by 2027 (Fig. 5).

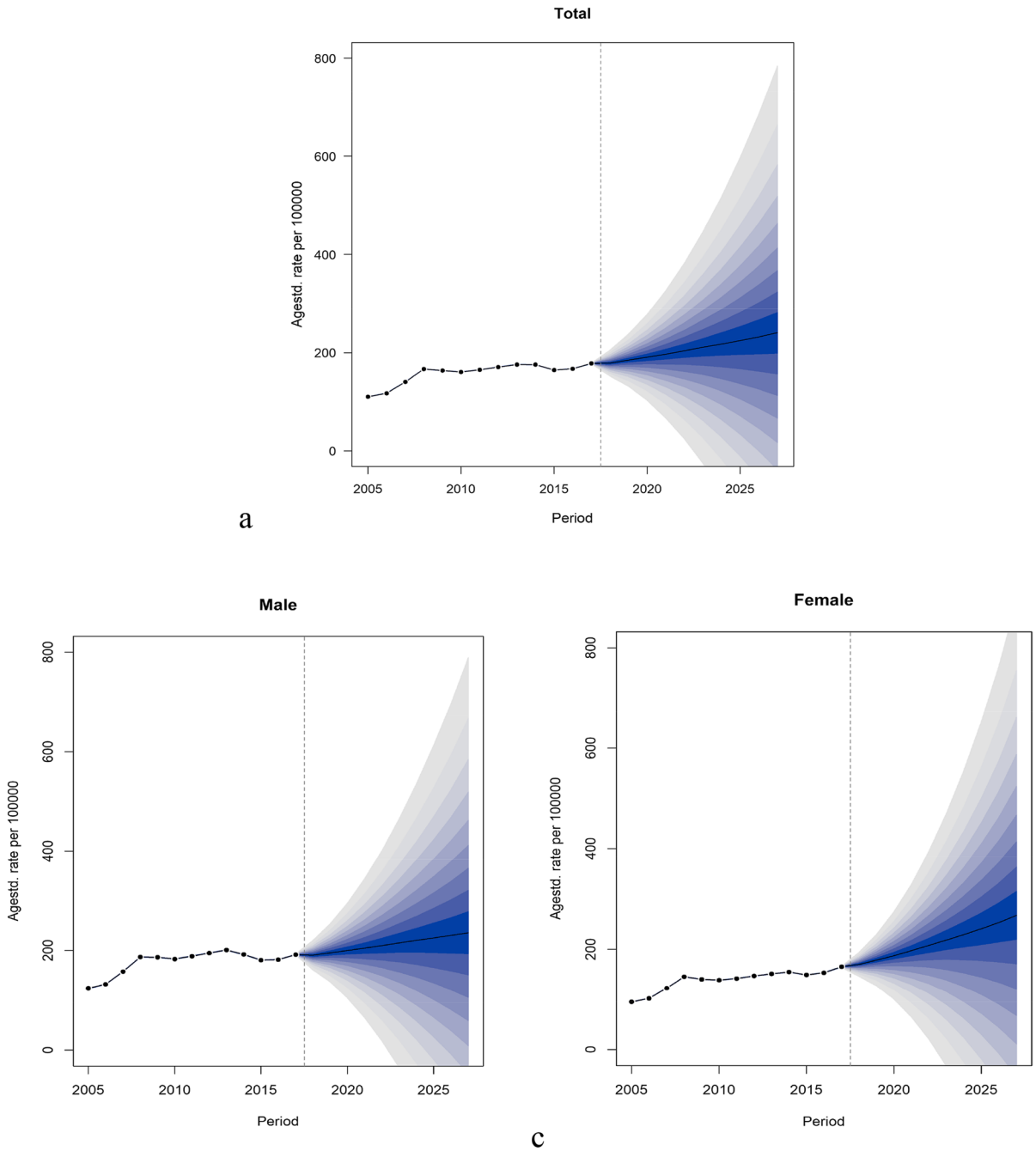

Fig. 5 The temporal trends of age-standardized incidence rates (ASRs, per 100,000) of cancer between 2005 and 2027 in both sexes (**a**), males (**b**), and females (**c**). The dots represent the observational values from cancer ASRs, and the blue shadow denotes the 95% highest density interval of prediction values. The predictive mean value is shown as a black solid line. The vertical dashed line indicates where the prediction starts

Discussion

Results highlight a significant increase in newly diagnosed cancer cases and age-standardized rates (ASR) from 2005 to 2017. The number of cancer cases surged from 52,425 to 126,707, while the ASR rose from 110.43 per 100,000 to 178.03 per 100,000. This substantial rise in cancer incidence reflects a growing public health challenge that requires immediate attention.

One noteworthy observation is the increase in cancer cases in both sexes. The ASR also saw a considerable increase in males and females alike, with females experiencing a higher net drift, indicating a more pronounced rise in cancer incidence for women than men. These findings emphasize the importance of gender-specific considerations in cancer prevention and control strategies.

The analysis of period and cohort relative risks also revealed intriguing patterns. Increased risks over the study period, particularly in females, suggest the influence of changing environment, lifestyle, or other factors during this time frame, especially changes in registration practices This calls for further research to identify the specific drivers behind the rising cancer incidence in Iran.

In comparison, Roshandel and colleagues provided a breakdown of cancer cases between 2014 and 2016. The data indicate that, on average, 104,863 new cancer cases were registered during this period, with men accounting for 52% and women for 48% of these cases. The ASR for all cancers in men and women were 148.5 and 129.3, respectively[24].

Combining the results from both studies, it is evident that cancer is a significant public health concern in Iran, with an alarming increase in incidence over time. The findings underscore the urgency of developing comprehensive cancer control and prevention programs that target both genders and address regional disparities.

This study focused on a Bayesian age-period-cohort analysis to project cancer incidence trends in Iran between 2018 and 2027. The study found that cancer incidence case numbers are expected to increase significantly, reaching 210,701 cases by 2027. The Age-Standardized Rate (ASR) of cancer is also projected to rise to 240.32 per 100,000 individuals during the same period.

This study's findings indicate an upward trend in the incidence of cancer in both men and women, as well as the total population, with a notable increase in the age-standardized rate (ASR) across all groups. This aligns with a study by Roshandel et al., which projected a 42.6% increase in cancer cases by 2025 based on data from 2008 to 2016, predicting a total of 160,400 cases with an ASR of 116.1 per 100,000 [24]. Differences in our findings likely stem from our longer study period and our approach to correcting undercounts through model-based adjustments, while Roshandel's study applied fixed numbers to reduce bias from smaller sample sizes. Consequently, our study's estimates may present a more refined forecast for cancer incidence.

Our findings underscore the necessity of comprehensive public health policies and early detection initiatives, particularly given the projected increase in cancer burden. Effective prevention, awareness, and treatment strategies are critical, especially gender- and age-specific interventions that could mitigate the growing cancer impact in coming years.

A comparison with the national 2018 cancer registry report for Iran reveals consistency in the number of cases and ASR, suggesting the reliability of our corrections. In 2018, the national report indicated 141,641 new cases with an ASR of 173.48 per 100,000 for both sexes, while our estimates projected 146,510 cases with an ASR of 178.75 per 100,000. The close alignment supports the effectiveness of the adjustments applied in this study and validates the APC Bayesian model's projections[25].

International comparisons further affirm our findings. A study in the Kurdistan region of Iraq (2013–2019) found a more than twofold increase in cancer incidence in Erbil and Dohuk, from 73 to 174 per 100,000 in women and from 36 to 85 per 100,000 in men. Their model projects a similar future trend, reinforcing our conclusion of a growing cancer incidence [26]. We included this comparison given cultural, religious, and geographical similarities between Iraq and Iran, particularly in border regions where these parallels are more pronounced [27, 28].

Additionally, an analysis of breast cancer incidence from 1990–2015 in four Asian countries (China, India, Pakistan, and Thailand) demonstrated an increasing trend, especially among individuals aged 50–84. This aligns with our findings and suggests common regional patterns, as Iran shares geographical and epidemiological similarities with these countries [29].

Other international studies show similar trends. In the U.S., a study by Weir et al. showed a significant increase in expected cancer cases for men and women by 2020, in agreement with our findings[30]. Meanwhile, research by Al-Sayegh et al. in Oman found a 23% increase in ASR from 1996 to 2019, with a particularly pronounced rise in women (48%) versus men (7%) [31]. Unlike our study, however, the Omani study observed a relatively stable incidence among men.

Studies examining cancer type distributions, such as Amori et al., highlight differing common cancers by sex, which suggests biological and possibly sex-specific risk factors[9]. Our study also aligns with findings from Yang et al., which emphasize that increased cancer incidence is more pronounced in older age groups[32].

These projections, though based on the best available data and modeling techniques, may vary due to factors such as lifestyle changes, healthcare advancements, and policy interventions. Continuous surveillance and research will be critical for refining these predictions and informing targeted cancer control strategies in Iran [33, 34]. Globally, increasing cancer incidence is driven by demographic shifts, lifestyle factors (e.g., poor diet, physical inactivity, and higher tobacco and alcohol use), and environmental and genetic influences. Thus, a multifaceted approach addressing these drivers is vital for managing cancer incidence.

Our study's strengths include a longer time frame and the use of Bayesian corrections, distinguishing it from previous studies that often relied on fixed numbers for bias correction. From this perspective, our study is among the few that utilized model-based corrected data [21] to enhance the accuracy of cancer incidence predictions. However, limitations exist. Cancer incidence trends may reflect historical diagnostic and reporting patterns, indicating potential registry quality biases that warrant cautious interpretation. Additionally, Our APC model analyzed data in five-year intervals; however, the final interval (2015–2017) is incomplete due to the unavailability of data for 2018–2019. This limitation necessitates an assumption that the trends observed in 2015–2017 would remain stable if extended to a full five-year period.

Finally, although analyzing multiple cancer types across Iran enhances this study's scope, the diversity of risk factors, diagnostics, and treatments among cancer types presents a limitation. Future research may benefit from type-specific analyses to further clarify these patterns.

Conclusion

In conclusion, the research underscores the pressing concern of the escalating burden of cancer incidence in Iran, which is heavily impacted by demographic changes related to age groups and lifestyle choices. To effectively address this challenge, urgent improvements in health systems are required to cater to the healthcare needs of the population. Emphasizing large-scale screening and comprehensive risk factor control strategies is crucial in the fight against cancer and strengthening prevention efforts. The study predicts a rise in cancer cases across all age groups, necessitating a long-term, best-practice approach that prioritizes primary prevention measures targeting smoking and obesity. Additionally, continuous monitoring of cancer trends through reliable population-based cancer registries and national registration sources is essential for timely interventions and progress evaluation.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12885-024-13289-0.

Supplementary Material 1.

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Authors' contributions
HB and SSHN contributed to designing the work; HB and GR: Contributed to the acquisition and revising of the article; SSHN, HB, and MAP: Contributed to the Analysis and revising of the article; SSHN, GR and MAP contributed to the interpretation of data and revising the article; HB, SSHN, and MAP: Contributed to Drafting the work and revising. All authors contributed to the Final approval of the version to be published and the Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data availability
The dataset used and/or analyzed during the current study is available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with ethical standards. The Medical Ethics Committee approved the study procedure of Shahid Beheshti University of Medical Sciences (IR.SBMU.PHNS.REC.1399.132).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Epidemiology of School of Public Health and Safety, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [2]Gastroenterology and Liver Diseases Research Center, Research Institute for Gastroenterology and Liver Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran. [3]Golestan Research Center of Gastroenterology and Hepatology, Golestan University of Medical Sciences, Gorgan, Iran.

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