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Projections of esophageal cancer incidence trend in Jiangsu Province, China: a Bayesian modeling study

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ABSTRACT

Objective: Esophageal cancer has made a great contribution to the cancer burden in Jiangsu Province, East China. This study was aimed at reporting esophageal cancer incidence trend in 2009–2019 and its prediction to 2030.

Methods: The burden of esophageal cancer in Jiangsu in 2019 was estimated using 54 cancer registries' data selected from Jiangsu Cancer Registry. Incident cases of 16 cancer registries were applied for the temporal trend from 2009 to 2019. The burden of esophageal cancer by 2030 was projected using the Bayesian age-period-cohort (BAPC) model.

Results: About 24,886 new cases of esophageal cancer (17,233 males and 7,653 females) occurred in Jiangsu in 2019. Rural regions of Jiangsu had the highest incidence rate. The age-standardized incidence rate (ASIR, per 100,000 population) of esophageal cancer in Jiangsu decreased from 27.72 per 100,000 in 2009 to 14.18 per 100,000 in 2019. The BAPC model showed that the ASIR would decline from 13.01 per 100,000 in 2020 to 4.88 per 100,000 in 2030.

Conclusions: According to the data, esophageal cancer incidence rates were predicted to decline until 2030, yet the disease burden is still significant in Jiangsu. The existing approaches to prevention and control are effective and need to be maintained.

1. Introduction

Esophageal cancer ranks eighth among the most diagnosed cancers worldwide, with an estimated 510,716 new cases in 2022.[1] Histologically, esophageal cancer is primarily classified into two main subtypes: esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC). Generally, 85 % of esophageal cancer cases are ESCC, especially in China.[2] There were 224,012 estimated new esophageal cancer cases in China, accounted for 43.86 % among 185 countries in 2022. Exposure to heavy drinking and smoking are the main risk factors for ESCC, which may result in chronic stimulation and inflammation of the esophageal mucosa.[3] Some other potential factors such as nutritional deficiencies, nitrosamines, betel quid chewing, and pickled vegetables may be partly accountable for the observed incidence, even though the extents of these contributions are unclear.[4,5]

According to data from Jiangsu Provincial Cancer Registry in 2018, the age-standardized esophageal cancer incidence rate by world Segi's standard population was 14.83 per 100,000, which was higher than the national average (13.80 per 100,000).[6,7] To facilitate more efficient allocation of limited health care resources by policymakers and to provide a basis for researchers to assess the effectiveness of interventions or screening for esophageal cancer, it is essential to evaluate the incidence of esophageal cancer from current and future perspectives in Jiangsu Province.

In epidemiology, the age-period-cohort (APC) model was developed in the past decades and widely used to measure the underlying covariates which cause the incidence of a disease, and project the future disease burden. In particular, the Bayesian APC (BAPC) model was proved to be a powerful tool to analyze incidence rates and predict future morbidity.[8] The BAPC model is a Possion regression model where incidence is analyzed according to age, period, and cohort effects.[9] The age impact relates to biological, physiological, and social processes of aging. The period effect corresponds to external factors impacting all age groups at a specific calendar time ranging from economic, social, and environmental factors. The cohort effect represents influence indexing all exposures experienced by a generation from birth.[10]

Our study aimed to estimate the numbers of new esophageal cancer cases in Jiangsu Province in 2019 based on the latest population-based registry data, analyze the temporal trends of esophageal cancer incidence from 2009 to 2019, and predict future incidence rates from

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2020 to 2030, which could provide some further understanding about tendency of esophageal cancer incidence and scientific clues to develop better control and prevention strategies.

2. Materials and methods

2.1. Data source and quality control

Jiangsu Provincial Cancer Registry is one of the largest cancer registries in China, which is responsible for the collection, assessment, and release of cancer data reported by the local population-based cancer registries in Jiangsu Province. All new cancer cases were coded in accordance with the International Classification of Diseases for Oncology, 3rd edition (ICD-O-3) and the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10). In the present study, esophageal cancer incidence data was extracted and analyzed according to ICD-10 coded C15.0-C15.9.

The quality of all cancer registry data was checked and evaluated based on the criteria of Cancer Incidence in Five Continents.[11,12] The indicators of quality measures include the proportion of morphologic verification (MV%), the mortality to incidence (M/I) ratio, the percentage of death certificate-only cases (DCO%), and the steadiness of incidence trends through the years. After quality evaluation, the most recent data from 54 local population-based cancer registries were used to estimate the numbers of new esophageal cancer in 2019, with a population coverage of 56.3 million residents, accounting for 71.75 % of the total population in Jiangsu Province. Qualified and continued incident data from 16 local cancer registries were used to analyze the temporal trends from 2009 to 2019 and project the incidence rates from 2020 to 2030. The indicators of quality measures of 54 cancer registries data and 16 cancer registries were provided in Supplementary Tables 1 and 2, respectively.

2.2. Statistical analysis

A total of 54 cancer registries with qualified cancer statistic data were used to describe the esophageal cancer incidence in 2019. Crude incidence rates were calculated for different areas (urban or rural) and age groups (0 and 1–4, 5–9, 10–14…80–84, and 85+ years). The numbers of new cases were estimated from the age-specific cancer incidence rates from 54 cancer registries, multiplied by the corresponding populations. Each of the cancer registries provided population statistics in the respective regions to the Jiangsu Provincial Cancer Registry. The ASIR was standardized according to the Segi's world standard population.[13]

The temporal trends in the incidence of the esophageal cancer between 2009 and 2019 were examined by fitting Joinpoint Regression Program (Version 5.0.2, https://surveillance.cancer.gov/joinpoint/) to ASIR using the data from 16 cancer registries. To lessen the likelihood of reporting erroneous changes in trends over the time, all models were limited to a maximum of two joinpoints (3-line segments). Trends were expressed as an annual percent change and the Z test was used to assess whether the change was statistically different from zero. In addition, we also reported the average annual percent change (AAPC) in the ASIR of esophageal cancer between 2009 and 2019. The BAPC method was used to project the incidence rate of esophageal cancer for each age group from 2020 to 2030 using R software (version 4.3.0, https://www.r-project.org/). The classic APC model can be formulated as:

$$\gamma_{ij} \sim B(n_{ij}, p_{ij})$$

$$n_{ij} = log\left(\frac{P_{ij}}{1-P_{ij}}\right) = \mu + \theta_i + \Phi_j + \Psi_k$$

It's common knowledge that the traditional APC model is a log-linear Poisson model. It can be formulated: during period j ($j = 1, 2, 3\ldots\ldots, J$), the counts of incidences γ_{ij} in age group i ($I = 1, 2, 3\ldots\ldots, I$), have a binomial distribution with parameters p_{ij} and n_{ij}. Whereas p_{ij} represents the unknown incidence probability, n_{ij} represents the known population size of age group i at period j.[14] In our data-set $I = 18$ and $J = 11$. The logit of the incidence probability is composed of an intercept μ, age termθ_i, period termΦ_j, and cohort termΨ_k. Suppose age is given in five-year intervals whereas period is given on an annual basis, as in our dataset, the cohort index is $k = k\ (i, j) = 5.\ (I - i) + j$. Gaussian random walk (RW) priors of different orders are used by the Bayesian hierarchical approach for the APC parameters of θ, Φ and Ψ. It combines prior knowledge with scanning data to originate a posterior distribution. To prevent parameter values from significantly differing from those in nearby time bands, trends corresponding to age, period, and birth cohort were smoothed using the RW model. The RW1 prior assumes a constant trend across the time scale, while the RW2 prior assumes a linear time trend. In our study, projections for future time points of esophageal cancer incidence rates were achieved by using RW1 prior on the assumption of a constant trend over the time scale. This model was implemented with the software package BAPC Modeling and Prediction package (BAMP v.2.1.3; Institute of Biomedical Engineering, Imperial College, London, UK) using Markov Chain Monte Carlo (MCMC) methods. MCMC stimulations were operated for 1010,000 iterations with the initial 10,000 iterations used as burn-in to minimize the influence of initial values.[15] The inferred median rates and 95 % CI (using 2.5 and 97.5 percentiles of the 1000,000 iterated results) were attained by 1000,000 iterations of model simulations. As a gauge of the model's goodness of fit, the posterior and predictive deviance information criteria (DIC value) were used.[16]

3. Results

3.1. Esophageal cancer incidence in Jiangsu, 2019

We estimated about 24,886 new esophageal cancer cases (17,233 males and 7653 females) in Jiangsu Province in 2019, accounting for 8.85 % and ranking the 4th of all new malignant tumors. The crude and age-standardized incidence rates were 31.70 and 14.17 per 100,000, respectively. Both for males and females, the incidence rates were greater in rural areas than those in urban areas (Table 1).

3.2. Trends in esophageal cancer incidence, 2009–2019

Between 2009 and 2019, AAPC in the ASIR of esophageal cancer was −6.28 % (95 % CI: −6.80 % to −5.75 %). When gender-specific patterns were examined, the incidence rate of esophageal cancer declined regardless of gender. The AAPC was lower in females (−7.75 %, 95 % CI: −8.65 % to −6.85 %) than in males (−5.60 %, 95 % CI: −6.03 % to −5.18 %) during the whole period. When area-specific patterns were examined, the incidence rate declined at an AAPC of −7.45 % (95 % CI: −9.06 % to −5.81 %) in urban areas and −5.39 % (95 % CI: −6.21 % to −4.55 %) in rural areas (Table 2). Analysis of age-specific incidence rates showed a decreasing trend in the age range of 40 to 79 years, and the greatest decreases were seen in younger age groups (40–44 years), with 13.75 % in males, 20.49 % in females, 14.86 % in urban areas, and 15.49 % in rural areas. The incidence remained stable among people over 80 years regardless of urban or rural areas and different genders (Table 3).

3.3. Bayesian APC model

The BAPC models were configured to the overall age-specific incidence rates during 2009–2019. Table 4 shows the variation in deviance during model sequence construction. Compared with age-period (AP) and age-cohort (AC) models, the full three-factor APC model performed better. The DIC of the APC model was 334.81, showing a more favorable statistical fit than the other sub-models (1485.14 for AP, 360.35 for AC). Therefore, the projection of the esophageal cancer incidence rates was based on the APC model.

Table 1
Estimated esophageal cancer incidence by region and gender in Jiangsu in 2019.

Areas	Gender	Cases[a]	Proportion (%)	Rate ($1/10^5$)	ASIR ($1/10^5$)	Rank[b]
All areas	Both genders	24,886	8.85	31.70	14.17	4
	Male	17,233	11.01	43.47	20.88	3
	Female	7653	6.14	19.69	7.72	6
Urban areas	Both genders	10,136	7.35	27.47	12.46	4
	Male	7305	9.59	39.61	19.05	4
	Female	2831	4.59	15.33	6.10	7
Rural areas	Both genders	14,750	10.28	35.45	15.68	3
	Male	9928	12.34	46.83	22.51	3
	Female	4822	7.65	23.62	9.13	6

[a] the estimated esophageal cancer cases in Jiangsu Province according to the crude rate of esophageal cancer incidence from selected registries.
[b] rank of esophageal cancer cases among all estimated cancer cases combined in Jiangsu Province in 2019.
Abbreviation: ASIR, age-standardized incidence rate using world Segi's standard population.

Table 2
Trends in age-standardized incidence rates of esophageal cancer by gender and region from 2009 to 2019.

Areas	Gender	Trend 1		Trend 2		AAPC, % (95% CI)
		Years	APC, % (95% CI)	Years	APC, % (95% CI)	2009-2019
All areas	Both genders	2009-2019	-6.28* (-6.80 to -5.75)	-	-	-6.28* (-6.80 to -5.75)
	Male	2009-2019	-5.60* (-6.03 to -5.18)	-	-	-5.60* (-6.03 to -5.18)
	Female	2009-2019	-7.75* (-8.65 to -6.85)	-	-	-7.75* (-8.65 to -6.85)
Urban areas	Both genders	2009-2011	-12.01* (-20.42 to -2.71)	2011-2019	-6.28* (-7.30 to -5.24)	-7.45* (-9.06 to -5.81)
Rural areas	Both genders	2009-2019	-5.39* (-6.21 to -4.55)	-	-	-5.39* (-6.21 to -4.55)

* The APC or AAPC is significantly different from zero ($P < 0.05$).
Abbreviations: AAPC, average annual percent change; APC, annual percentage change; CI, confidence interval.

Table 3
Trends for age-specific esophageal cancer incidence rates by gender and area in Jiangsu from 2009 to 2019.

Age group, years	AAPC, %				
	All	Male	Female	Urban	Rural
40–44	-14.96[a]	-13.75[a]	-20.49*	-14.86[a]	-15.49[a]
45–49	-13.51[a]	-12.99[a]	-16.15[a]	-13.76[a]	-13.22[a a]
50–54	-11.77[a]	-10.80[a]	-15.34[a]	-12.39[a]	-11.41[a]
55–59	-11.78[a]	-10.30[a]	-16.17[a]	-11.69[a]	-11.41[a]
60–64	-6.68[a]	-5.47[a]	-10.84[a]	-6.60[a]	-6.90[a]
65–69	-6.38[a]	-4.64[a]	-8.32[a]	-6.55[a]	-5.84[a]
70–74	-5.27[a]	-4.55[a]	-7.12[a]	-6.95[a]	-3.42[a]
75–79	-3.40[a]	-3.61[a]	-3.33[a]	-4.10[a]	-2.68[a]
80–84	-0.75	-1.76	-0.60	-2.35	0.00
85+	-0.93	-0.91	-0.44	-1.15	0.40

[a] average annual percent change during 2009 to 2019 significantly different from zero ($P < 0.05$).
Abbreviation: AAPC, average annual percentage change.

Table 4
Comparison of age-period-cohort sub-models for esophageal cancer incidence.

Terms in model	Resid. DF	Residual	Residual Deviance	Deviance	*P* value
Age	104	4653.043		3780.5936	
Age-drift	103	2378.737	1	1504.2876	< 0.001
Age-cohort	98	1244.803	5	360.3542	< 0.002
Age-period-cohort	93	1229.259	5	334.8103	< 0.003
Age-period	98	2369.589	5	1485.1403	< 0.004
Age-drift	103	2378.737	5	1504.2876	< 0.005

Abbreviation: Resid. DF, residual degrees of freedom.

Fig. 1 displays the rough incidence rates of esophageal cancer, aggregated into each 1-year period and 5-year age groups. The group 40 years or younger was eliminated because there were not enough cases. Age, period, and cohort effects were within a comparable range, making it possible to compare the effects' slopes directly. Age effects had an slope up to the age of 80 years and then went down slowly for ages after that (Fig. 1A). While the incidence rate displayed a descending trend with the period among age groups during 40–79 years, other age groups showed no clear pattern (Fig. 1B and Table 3). For the cohort effects plot, an obvious declining pattern was seen in the age groups during 40–79 years and a steady pattern in other age groups from the cohort curves (Fig. 1C).

3.4. Predicted incidence of esophageal cancer

Projected data from 2020 to 2030 suggests that overall ASIR will decrease by an AAPC of −9.33 % (95 % CI: −9.44 % to −9.22 %), which corresponds to average annual reductions in males of −8.35 % (95 % CI:

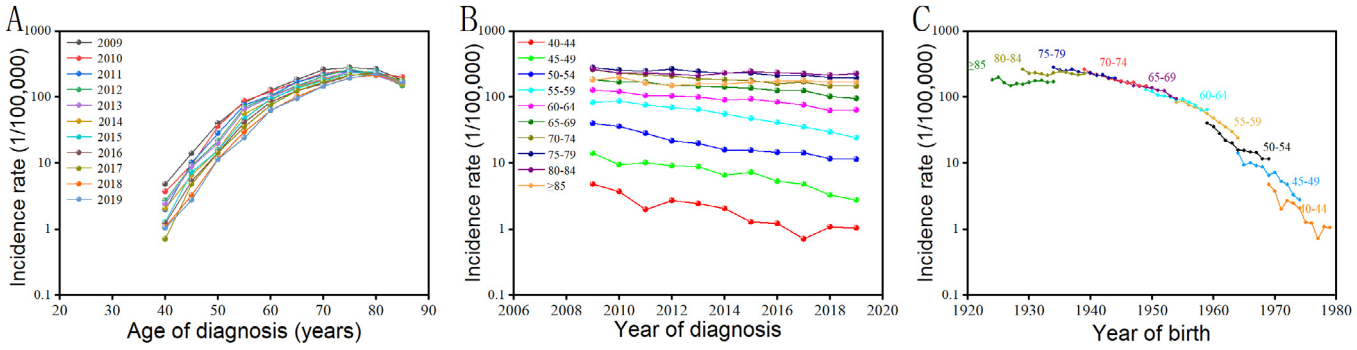

Fig. 1. (A-C) Incidence of esophageal cancer per 100,000 by age (A), period (B), and birth cohort (C) effect.

Table 5
Trends for age-specific esophageal cancer incidence rates by gender and area in Jiangsu from 2020 to 2030.

Areas	Gender	Trend 1		Trend 2		AAPC, % (95% CI)
		Years	APC, % (95% CI)	Years	APC, % (95% CI)	2020–2030
All areas	Both genders	2020-2025	-8.59* (-8.79 to -8.40)	2025-2030	-10.06* (-10.25 to -9.87)	-9.33* (-9.44 to -9.22)
	Male	2020-2025	-7.66* (-7.85 to -7.47)	2025-2030	-9.04* (-9.23 to -8.85)	-8.35* (-8.46 to -8.24)
	Female	2020-2025	-10.65* (-10.87 to -10.42)	2025-2030	-12.25* (-12.48 to -12.03)	-11.45* (-11.58 to -11.33)
Urban areas	Both genders	2020-2025	-9.68* (-9.97 to -9.39)	2025-2030	-11.14* (-11.42 to -10.85)	-10.41* (-10.58 to -10.25)
Rural areas	Both genders	2020-2025	-7.48* (-7.69 to -7.27)	2025-2030	-8.88* (-9.09 to -8.67)	-8.18* (-8.30 to -8.06)

* The APC or AAPC is significantly different from zero ($P < 0.05$).
Abbreviations: AAPC, average annual percent change; APC, annual percentage change; CI, confidence interval.

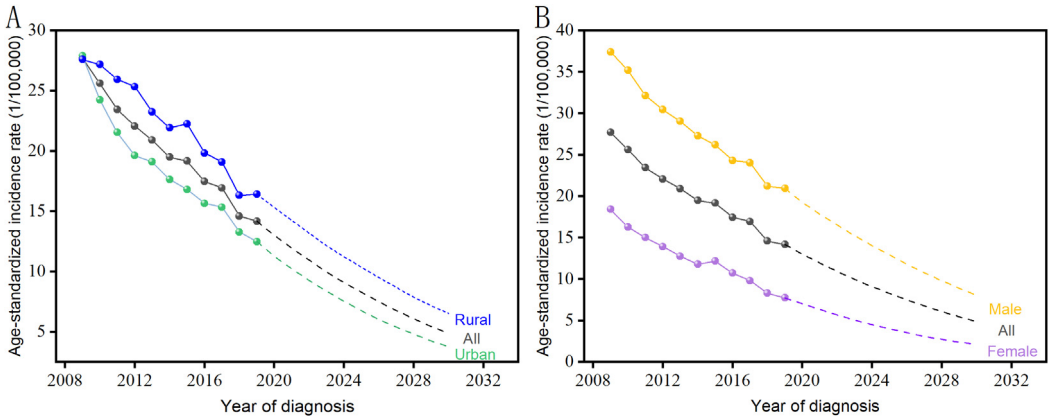

Fig. 2. (A, B) Observed and predicted esophageal cancer age-standardized incidence rate by area (A) and gender (B) of Jiangsu Province from 2009 to 2030.

−8.46 % to −8.24 %) and in females of −11.45 % (95 % CI: −11.58 % to −11.33 %) (Table 5). Similar patterns of decreasing AAPC in incidence rates were found in different areas, with a total decrease in rural areas of −8.18 % (95 % CI: −8.30 % to −8.06 %) and −10.41 % (95 % CI: −10.58 % to −10.25 %) in urban areas. Fig. 2 shows the observed and predicted ASIR of esophageal cancer by gender and area from 2009 to 2030. In addition, we plotted esophageal cancer incidence rates with birth cohorts by age group in different genders and areas from 1924 to 1979 in Fig. 3. Trends of incidence rates for all age groups from 2009 to 2030 were plotted in Fig. 4.

4. Discussion

This is an updated comprehensive analysis of the disease burden of esophageal cancer in Jiangsu Province, East China by using the most recent representative data collected from 54 qualified cancer registries covering about 56 million population and forecasts to 2030. It was estimated that about 24,886 esophageal cancer cases occurred in Jiangsu in 2019. The overall ASIR in Jiangsu in 2019 was 14.17 per 100,000, which was still higher than national average (13.80 per 100,000).[7] The incidence rates for the genders differed by two to three times, with males accounting for around 70 % of cases. This disparity was also found in many parts of the world, which supports our results.[17]However, the reason for the significant gender difference in the risk of esophageal cancer is not clear and needs to be further explored. Compared with the urban area, the ASIR in rural areas was much higher. Some earlier investigations came to the same result.[18,19] One of the reasons might be that urban residents are more knowledgeable of cancer prevention than rural ones, as seen by urban regions' lower smoking prevalence.[20]

In our study, we analyzed the trend in the ASIR of esophageal cancer over an 11-year period from 2009 to 2019 based on 16 cancer registries which had continuous data. The results showed that the ASIR of esophageal cancer in Jiangsu showed a downward trend regardless of urban or rural areas and different genders in the past 11 years. This result was consistent with the national incidence pattern between 2011 and 2015 and with the data found in most East Asian countries.[17,19] Smoking is one of the main risk factors for ESCC.[3] In certain high-income nations, declines in ESCC incidence have been verified and are largely attributable to the drop in smoking prevalence.[21] The decrease in the incidence rates of esophageal cancer in Jiangsu Province over the past

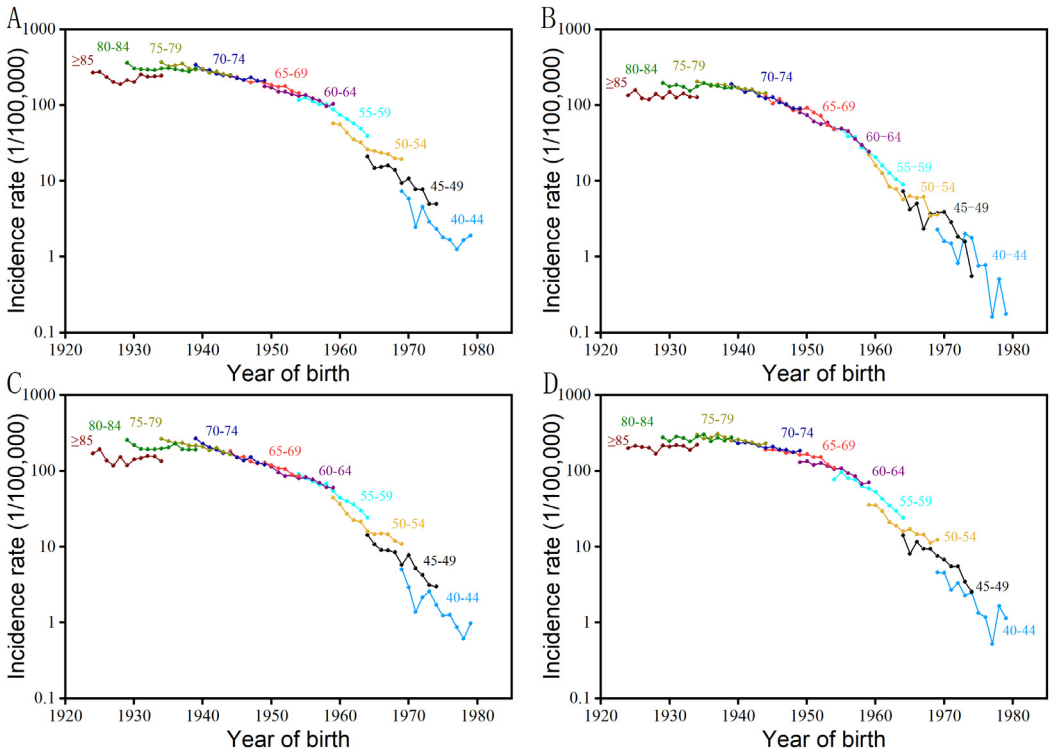

Fig. 3. (A-D) Esophageal cancer incidence with different birth cohorts by age groups in Jiangsu Province, for males (A); for females (B); for urban residents (C); and for rural residents (D).

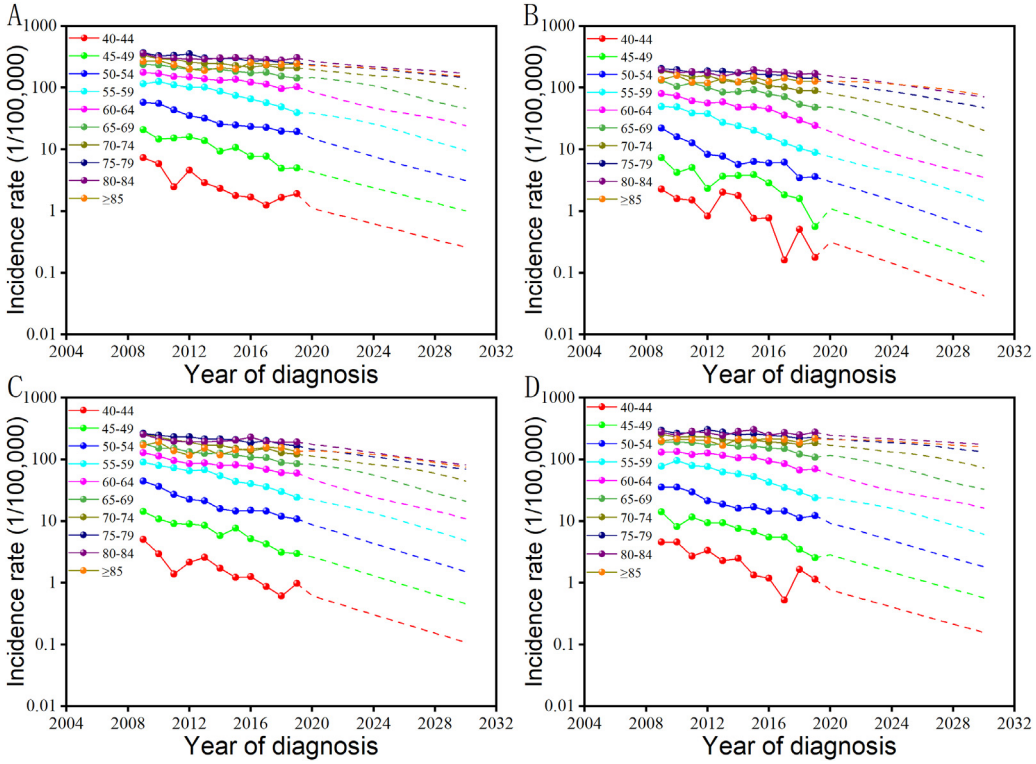

Fig. 4. (A-D) Trends for age-specific incidence rates during 2009–2019 and predicted from 2020 to 2030 in Jiangsu Province, for males (A); for females (B); for urban residents (C); and for rural residents (D).

11 years may also be related to the decline in the prevalence of smoking. A study using data from 31 provinces in China based on 5 national representative surveys from 2007 to 2018 showed that the prevalence of current smoking among adults in East China has decreased from 29.4 % to 23.4 % between 2007 and 2018, with annual rate of change of 1.9 % ($P<0.05$).[20]

In a Bayesian APC analysis, age is often the most important variable as it implies consistent extrinsic factors, such as exposure accumulation. Our studies also found a convincing relationship between age and the incidence of esophageal cancer. The age-specific incidence dramatically increased after 40 years and reached the peak in the age group of 80–84 years. In addition, various age groups showed varying declining tendencies from 2009 to 2019. The greatest decrease was seen in younger age groups (40–44 years), while the incidence remained stable among people over 80 years of age. This may imply that the younger the population, the more they can profit from precautions, and as a result, these precautions may lead to an acceleration in the falling burden of esophageal cancer in the future. Our results also demonstrated that cohort has a strong association with esophageal cancer incidence, possibly due to cohort-related causes such as changes in eating habits and improved hygiene.[22] Like some other countries, China has seen tremendous economic development and sociodemographic and cultural transformation, which have also prompted various lifestyle changes during the past few decades.

Several researches have used BAPC models to examine esophageal cancer rates and generated short-term estimates.[23-25] Melina predicted the future trend of the ESCC burden by APC models using data from 42 registries in 12 countries. It was found that the incidence of ESCC would continue decreasing in most parts of the world, while the incidence rates of EAC were anticipated to increase sharply across high-income countries up to 2030.[21] Based on the supposition that historical trends in age, period, and cohort will persist into the future, we also used Bayesian APC models to predict the incidence rates in Jiangsu Province and found that the ASIR of esophageal cancer will drop continuously by 2030, especially in women and urban areas. According to our findings, although the incidence of esophageal cancer in Jiangsu will continue to decline over the next 11 years, the cancer still has to be treated seriously due to its high malignancy and poor survival.[26]

According to our knowledge, this is the first attempt to comprehensively explain historical and projected esophageal incidence patterns using provincial data in China, and thereby providing some useful information for other regions to control the disease. Although our projections for the future were based on long-term data from highly reliable population-based cancer registries and an extrapolation of rates using Bayesian APC models that have undergone empirical evaluation, there are a few limitations that should be mentioned. First, underreporting and misdiagnosis could happen in cancer registration, especially in less developed regions; therefore some of these estimates of esophageal cancer may be underestimated. In addition, underreported incidences might arise if a patient's address in the clinic or pathology center of the referred cities was wrongly documented. Second, trend-based projections contain a high degree of uncertainty since they are by definition dependent on the risky assumption that incidence trends seen in the past would persist in the future.[27] Ideally, prediction models should include credible data on risk variables. In support of the method employed, BAPC models have proven to provide reliable estimates.[28-30] Third, the projections were based on 16 registries with continuous data covering about 22 % of the provincial population each year. This coverage percentage was higher than that reported by Chen et al. in their estimates of the 2025 cancer statistics in China.[31] But there may be an unknown degree of uncertainty in current estimates that cannot be ignored. Fourth, due to the lack of predicted population in Jiangsu Province until 2030, the number of esophageal cancer cases cannot be calculated. Finally, this study did not analyze the incidence of esophageal cancer by histological type, because most of the histological types in this province are ESCC.

5. Conclusions

In summary, the ASIR of esophageal cancer is expected to continue to decrease in Jiangsu in the coming years. The existing approaches to prevention and control are effective and need to be maintained. People over 80 years do not show a substantial change in incidence, and more preventative actions are required to lower risk factor exposure in younger age groups, and therefore lower the likelihood of developing esophageal cancer as they get older.

Declaration of competing interest

We declare that we have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author contributions

R.H. and J.Z. were responsible for the study concept and design. W.M., Y.F., and B.J. acquired data. W.M. and Y.F. analyzed and interpreted data. W.M. drafted the manuscript, and all authors revised it for important intellectual content. The authors take full responsibility for data analysis and result interpretation of this article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jncc.2024.11.004.

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