

Article The Burden of Esophageal Cancer in China From 2013 to 2030 A Dynamic Cohort Modeling Study

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Abstract

Background: This study aimed to predict the disease burden of esophageal cancer (EC) over the period 2013-2030 in China.

Methods : A dynamic cohort Markov model was developed to simulate the EC prevalence, disability-adjusted life years (DALY), and the medical direct expenditure based on gender. JoinPoint Regression Program was used to calculate the average annual percentage change (AAPC) of EC prevalence and DALY rates, while the regression model was applied to analyze the changing trend of economic burden over time.

Results: The predicted DALY rates per 100 000 people increased in both-sex (219.17 - 252.39) and males (302.89 – 384.31), while it decreased in females (131.21- 115.91). The years of life lost (YLL) accounted for the majority of DALYs. The AAPC were 0.8%(95% CI, 0.8%-0.9%), 1.4%(95% CI, 1.3%- 1.5%), and -0.7% (95% CI, -0.8%- -0.7%) in both-sex, males and females, respectively. The medical direct expenditure in both-sex, males, and females was predicted to increase by 165.35%, 194.04%, and 94.20%, respectively.

Conclusions: EC still caused a severe burden on society. YLL was responsible for the majority of the DALYs, which highly suggesting the implementation of accurate prevention like screening and early diagnosis and treatment programs.

1. Introduction

In 2012, the noncommunicable diseases (NCDs) were responsible for 68% of the world's deaths, and cancer was the second leading cause of death after cardiovascular disease worldwide[1]. Esophageal cancer (EC) was still one of the malignant tumors over the world. Over half of the worldwide EC occurs in China [2]. EC was estimated as the fifth most common cancer and the fourth leading cause of cancer-related death in China [3]. In 2012, there were an estimated 286.7 thousand new cases and 210.9 thousand deaths. The incidence and mortality were $21.17/10^5$ and $15.18/10^5$, and it was about 2.3 times higher in males than in females^[4, 5]. From 2001 to 2011, EC incidence showed a decreasing trend with an average annual percent change (AAPC) of -0.9%[4]. Similarly, the EC mortality had the same changing trend, with the AAPC of -1.1%[5].

Though EC incidence and mortality were predicted by national cancer center to decrease over time, EC still placed a considerable burden on society, families, and individuals. Over 90% of EC patients with a clear cancer stage diagnosed as invasive cancer[6]. Among the invasive cancer stage, about 20% of them had already developed distant metastasis[6]. The overall 5-year survival rate was about 18.4%[5]. Moreover, it was difficult to treat invasive stage cancer, especially for patients with distant metastasis, which could not only result in a decline in the quality of life but also a heavy economic burden. The overall average hospital expenditure per patient was US\$ 11028.5 from 2002 to 2011 using the purchasing power parities 2017, with an average annual increase of 6.3% [6, 7].

There is growing concern and awareness about the increasing burden of EC not only from the health perspective but also from the economic conditions. Though the burden of EC morbidity and mortality had been fully documented, the prevalence, premature death, disability, and economic burden due to EC have not been fully characterized in China. Consequently, this study aimed to address the current information gaps in the understanding of burden of EC through the estimation of the prevalence, disability-adjusted life years (DALY) and medical direct expenditure based on both-sex. Specifically, the study findings could inform the policy decision-markers with key insights to reduce the growing burdens of EC.

2. Methods

The study examined the EC burden from 2013 to 2030 by prevalence, DALYs and medical direct expenditure through simulating a dynamic cohort Markov model using the TreeAge Pro 2019. DALYs were calculated by the years of life lost (YLL) due to premature death in the population and the years lived with disability (YLD) for people with EC that using methodology recommended by the World Health Organization (WHO)[8]. The study calculated the YLD based on the EC prevalence rather than EC incidence. Total annual medical direct expenditure presented the economic burden. Moreover, the study predicted the changing trend of EC burden overtime. Additionally, the changing trends in prevalence rates and DALYs for both sex were analyzed using the AAPC and 95% confidence index (95%CI)[9].

2.1 Model structure

The dynamic cohort Markov model with five states was conducted, including new people, health, EC, EC-specific death, and other death. The model structure was displayed in Fig. 1. And the new people presented the newborn. The arrows presented the transition direction of the cohort population on a yearly basis, and EC specific death did not assume as an absorbing state. Moreover, “no remission” of people in the EC state towards the health state. The proportion of people transferred between different states was estimated by the transition probabilities. The study used the following formula to do the transition from rate to probability: $p = 1 - \exp(-r)$, where p was the probability, and r was the rate[10].

The number of people transferred from the state of new people to health state and other death using the following calculations: $T_{\text{-newtohealth}} = R_b \times \text{Count_alive} \times (1 - M_{\text{-Inf}})$ $T_{\text{-newtodeath}} = 1 - T_{\text{-newtohealth}}$. Where $T_{\text{-newtohealth}}$ presented the number of people transferred from the state of new people to health state, and $T_{\text{-newtodeath}}$ presented the number of people transferred from the state of new people to the state of other death, R_b was the birthrate, Count_alive was the number of people still alive among each simulation cycle, including number of people in the health state and EC state. $M_{\text{-Inf}}$ was infant mortality. The transition probability from health to EC states assumed as the EC annual incidence probability. The death probability of health was computed as the difference between the population death probability and EC disease-specific death probability. The majority of death in the state of EC attributed to disease-specifically, a small part of them was dead caused by other reasons.

2.2 Data inputting and estimation of key model parameters

Population data from baseline year (2012) to 2018 was collected from the National Bureau of Statistics of China except that the infant mortality was drawn from the China Health and family planning statistical yearbook 2017[11, 12]. The population trend for subsequent years was drawn from the United Nations population division, including birthrate, population mortality, infant mortality, and sex-ratios[13]. The birthrate for males and females was calculated by the birthrate for both-sex multiplied by the sex-ratio. Population mortality and infant mortality for males and females were computed by the mortality data of both-sex combined with the sex-ratio and the risk ratios of the mortality in males compared to females, where the risk ratios were obtained from the Tabulation on the 2010 population census of the people's republic of China. And the risk ratio of population mortality was 1.31, while it was 0.95 for infant mortality[14]. EC Prevalence in 2012, the average age at onset and duration of EC were estimated using the DisMod model that developed for the calculation of the Global Burden of Disease Study (GBD)[15]. The average age at death was computed by average age onset plus duration of EC. The EC incidence and mortality in 2012, the fatality, and the AAPC of incidence and mortality were obtained from published data of the National Office for Cancer Prevention and Control[5, 16]. The key parameters that used for calculation of DALYs set as following: the discount rate was 0.03, the age-weighting was 0.1658, age-weighting parameter was 0.04. The calculation of standard life expectancy at death due to EC was the difference between the standard life expectancy at birth and the average ages at death due to EC. Standard life expectancy at birth was drawn from the National Bureau of Statistics of China and the United Nations population division[11, 13]. Disability weight was estimated using values addressed in the Disability weights for the Global Burden of Disease (GBD) 2013 study and clinic stage data for China. According to the GBD report, the disability weight of EC diagnosis/ therapy and control (stage I-II), cancer with pre-terminal metastasis (stage III), and terminal phase(IV) were 0.288, 0.451, and 0.540, respectively[17]. EC clinic stage was collected from a 10- year multicenter retrospective survey, and the constitution of stage I-II, stage III, and stage IV was 45.5%, 33.8%, and 20.7%, respectively[6]. Consequently, the weighted average disability weight was 0.395. The calculation of annual medical direct expenditure per patient was using the data in 2012 drew from a 10-year multicenter retrospective survey, and for the subsequent year, assumed it increased at a constant value of 6.27% [6]. It was changed into US dollars using the purchasing power parities 2017[7]. Tables 1 and 2 summarized the detail inputting parameters. Besides, the changing trend of medical direct expenditure was analyzed using the regression model with an exponential transition for medical costs. Meanwhile, long-term changing trends of prevalence rates and DALYs were simulated by the JoinPoint Regression Program software 4.7.0.0[18].

Table 1
Birthrate and population mortality by years

Year	Birthrate			Population mortality		
	Both sex	Male	Female	Both sex	Male	Female
2013	0.012080	0.012860	0.011183	0.007160	0.008094	0.006179
2014	0.012370	0.013169	0.011451	0.007160	0.008094	0.006179
2015	0.012070	0.012759	0.011291	0.007110	0.008038	0.006136
2016	0.012950	0.013689	0.012114	0.007090	0.008015	0.006119
2017	0.012430	0.013140	0.011628	0.007110	0.008039	0.006137
2018	0.010940	0.011565	0.010234	0.007130	0.008060	0.006153
2019	0.011930	0.012611	0.011160	0.007121	0.008050	0.006145
2020–2024	0.010645	0.011170	0.010063	0.007823	0.008842	0.006750
2025–2029	0.009808	0.010211	0.009368	0.008686	0.009820	0.007496
2030	0.009460	0.009769	0.009130	0.009692	0.010960	0.008367
Note: Birthrate and population mortality from 2013 to 2018 were obtained from the national Bureau of Statistics of China, then it were collected from the United Nations population division						

Table 2
Other Model inputting

Parameters Male Female	Reference		
Initial cohorts probability (2012)			
New people	0	0	-
Health	692666146	660599867	[11]
Esophageal cancer	531157	242830	*
Disease-specific death	149000	61900	[5]
Other death	5462368	4021658	
Birthrate	Table 1		
Infant mortality			
2013	0.009273	0.009761	[12]
2014	0.008687	0.009145	[12]
2015–2019	0.007905	0.008321	[12]
2020–2024	0.008193	0.008624	[13]
2025–2029	0.007061	0.007433	[13]
2030	0.006162	0.006487	[13]
Annual incidence of EC in 2012	0.000293	0.000127	[16]
AAPC for incidence of EC	0.000	0.025	[16]
Fatality of EC	0.290	0.268	[5]
Mortality for EC	0.00021	0.00009	[5]
AAPC for mortality of EC	0.000	0.027	[5]
Mortality for other reasons	Table 1		
Standard Life expectancy at death due to esophageal cancer			
2012–2014	13.86	16.80	[11]
2015–2019	14.68	17.80	[11]
2020–2024	15.20	18.28	[13]
2025–2029	15.76	18.79	[13]

Note: * predicted by the DisMod model.

Parameters	Male	Female	Reference
2030	16.34	19.28	[13]
Average age at onset	64.8	66.0	*
Durations	3.3	3.3	*
Disability weight	0.395	0.395	[6, 17]
Cost of EC in 2012 (\$)	13980.6	13980.6	[6]
Note: * predicted by the DisMod model.			

2.3 Validation

The study conducted the internal validation of this model by comparing the EC incidence for both-sex that was simulated by the model with the estimates that were predicted by the National Office for Cancer Prevention and Control from which the input EC incidence for males and females were drawn. We computed the Goodness-of-fit analyses by plotting the model predictions versus the national estimates, fitting a linear curve without intercept. The squared linear correlation coefficient (R^2) simulated by the linear regression was used to examine the Goodness-of-fit of the model.

3. Results

3.1 Validation

The results simulated by the model closely matched the estimates predicted by the National Office for Cancer Prevention and Control: the regression line slope was 1.01, and the R^2 was 0.99, which demonstrated the good consistency between the two estimates. The results for the internal validation were presented in Appendix 1.

3.2 EC disease prevalence

The changing trend of EC prevalence and prevalence rates over time was addressed in Fig. 2 and Fig. 3. Overall, the EC prevalence in both-sex and males showed an increasing trend, while it showed a decreasing trend in females. In both-sex, the EC prevalence rate was expected to peak at $67.88/10^5$ in 2019 and then decreased to $64.54/10^5$. The AAPC was 0.3% (95% CI: 0.3–0.3). In males, it was predicted to increase constantly, from $81.97/10^5$ in 2013 to $96.39/10^5$ in 2030. And the AAPC was 0.9% (95%CI:0.9%-1.0%). In females, it decreased from $38.92/10^5$ to $31.5764.54/10^5$. However it was predicted to peak at $41.26/10^5$ in 2016. And the AAPC was -1.2% (95%CI: -1.3% - -1.2%). Compared to 2013, the prevalence increased by 23.20% and 11.17% in males and both-sex, while it decreased by 13.72% in females. For both-sex, it peaked at 962.02 thousand in 2021 and then decreased to 933.44 thousand in 2030. For males, it increased from 575.54 thousand to 709.08 thousand from 2013 to 2030, while for females, it peaked at 280.45 thousand in 2017 and then decreased to 224.36 thousand.

3.3 DALYs and its annual average percent change

Detail calculations of DALYs were reported in Table 3, and the AAPC was displayed in Fig. 4. The DALYs increased by 32.93% in males, while it decreased by 6.05% in females. It was 2.3–3.3 times higher in males than in females. The DALYs in males showed a constant increasing from 2126.62 thousand to 2826.99 thousand from 2013 to 2030. However, it peaked at 1007.26 thousand in 2018 then decreased to 823.74 thousand in 2030 in females. Noticeable, the YLL accounted for about 92% of DALYs, while YLD only accounted for 2%.

Overall, the DALY rates per 100000 people increased in both-sex and males, while it decreased in females. However, in the first three years, they all presented an obvious increase. In both-sex, it peaked at 261.78 in 2021 then decreased to 252.42 in 2030. The AAPC was 0.8%(95% CI, 0.8%- 0.9%). In males, it showed a constant increasing, from 302.89 to 384.30. The AAPC was 1.4%(95% CI, 1.3%- 1.5%). In females, it was predicted to peak at 147.42 in 2017 and then decreased to 115.92. The AAPC was - 0.7%(95% CI, -0.8%- -0.7%).

Table 3
The projected DALYs of the esophageal cancer

Year	Male (thousand)			Female (thousand)		
	YLLs	YLDs	DALYs	YLLs	YLDs	DALYs
2013	1948.66	177.96	2126.62	798.72	78.05	876.77
2014	2111.47	187.88	2299.36	855.35	81.29	936.64
2015	2231.27	195.14	2426.41	891.83	83.15	974.97
2016	2317.46	200.56	2518.02	912.18	84.01	996.19
2017	2381.80	204.66	2586.47	921.71	84.17	1005.88
2018	2430.50	207.89	2638.38	923.43	83.84	1007.26
2019	2468.82	210.47	2679.29	919.76	83.14	1002.90
2020	2502.32	212.50	2714.82	912.29	82.17	994.46
2021	2526.46	214.04	2740.51	901.61	80.97	982.59
2022	2544.84	215.27	2760.11	888.48	79.64	968.12
2023	2559.42	216.27	2775.70	873.83	78.21	952.05
2024	2571.36	217.12	2788.48	858.19	76.73	934.93
2025	2582.86	217.86	2800.72	842.23	75.22	917.45
2026	2591.65	218.31	2809.96	825.64	73.64	899.28
2027	2597.01	218.65	2815.66	808.30	72.05	880.35
2028	2601.00	218.90	2819.90	790.86	70.47	861.32
2029	2604.02	219.10	2823.12	773.44	68.89	842.34
2030	2607.73	219.25	2826.99	756.41	67.34	823.74

3.4 Projected medical direct expenditure

The trend of medical direct expenditure was displayed in Fig. 5. Overall, the annual medical direct expenditure increased constantly, and it was 2.5–3.8 times higher in males than in females. From 2013 to 2030, in both-sex, it increased by 165.35%, from 4.24 billion to 11.26 billion. In males, it increased by 194.04%, from 3.02 billion to 8.89 billion, while it increased by 94.20% in females, from 1.22 billion to 2.37 billion. Also, the model examined the proportions of the medical direct expenditure on EC in the total health expenses and the personal cash health expenses from 2013 to 2018. As shown in Appendix 2, Compared to 2013, the proportion of the medical direct expenditure in the total health expenses

decreased by 23.4% (0.47% vs. 0.36%) in 2017, while it decreased by 10.8% (1.39% vs. 1.24%) in the personal cash health expenses.

4. Discussion

This was the first modeling simulation of the EC burden in China. The model predicted that the EC prevalence increased from 835.6 thousand to 933.2 thousand, and the EC prevalence rates increased from $60.98/10^5$ to $64.53/10^5$ from 2013 to 2030. The DALYs rate per 100 000 people increased from 302.89 to 384.31 in males, and from 219.17 to 252.39 in both-sex, while it decreased from 131.21 to 115.91 in females. Our study demonstrated that the burden of EC was higher in males. The main reason may be that males were more exposed to risk factors such as tobacco and alcohol consumption[19].

Sun XB's study estimated that the DALYs rate per 100 000 people was 1150 in males and 490 in females in China[20]. This estimation was considerably higher than in our study. And this difference could be explained by the difference in EC incidence and mortality that used in the calculation of DALYs. Sun XB's study was conducted bases on the Feicheng County, which was one of the areas that had the highest EC incidence and mortality, with the incidence and mortality of $160.78/10^5$ and $122.26/10^5$ in males and $81.36/10^5$ and $94.40/10^5$ in females [20]. However, the estimates of the EC incidence and mortality in our study were drawn from the national level, which was substantially lower than in Feicheng County. Another reason for this discrepancy may be was the estimates of YLD. Prevalence YLD was estimated in our study, while incidence YLD was calculated in Sun XB's study. In Contrast, the results of the study suggested that our estimated DALY rates were substantially higher than in many other countries including developing and developed countries[19, 21]. For example, the DALY rates per 100 000 people were predicted to about 120 in males and 68 in females in 2015 in Iran, while in the United Kingdom and Japan, it was 88 and 69 in both-sex respectively 2008[21].

Over the past decades, fewer data were available on the medical expenditure estimation of EC, even though a few countries had reported the estimation of the costs of EC[22, 23]. Past studies more discussed the economic burden due to EC on the average expenditure per patient, average expenditure per clinic visit, and average daily expenditure. Besides, the median medical direct expenditure varied by geographical distribution[24]. However, the inputting of medical expenditure in our study was derived from a 10-year multicenter retrospective survey on the medical expenditure on EC from 2002 to 2011 that might fully present the medical expenditure from the national level[6]. According to our study, the total economic burden of EC will increase constantly over the next few decades. And it will be higher in males than in females for all the predicted years. Although the EC incidence decreased in females, the economic burden increased over time, which may be driven by the increasing population and the growth of medical prices. The proportion of the medical direct expenditure on EC in the total health expenses and the personal cash health expenditure addressed a decreasing trend, which indicated that the growth rate of total health expenditure and personal health expenditure was higher than that of medical direct expenses on EC.

“Health China 2030” has set a goal for chronic disease management: premature mortality from major chronic diseases was reduced by 30% percent. The EC incidence and mortality displayed a decreasing trend over time. However, the results of our study showed that the disease burden based on the DALYs and medical direct expenditure attributed by EC presented an increasing trend. It was still much room for the improvement of the accurate prevention and control of the EC. The most effective strategy could be the screening and early diagnosis and treatment, which also had been highlighted by the “Health China 2030”. Moreover, early diagnosis and treatment are essential to reduce premature death and improve the patients’ quality of life: the 5-year survival rate for early EC could reach 95%[25]. Besides, the costs and effectiveness should be considered due to the scarcity of medical resources and other competing diseases. However, health economists should pay more attention to the EC screening ages and gender difference from the perspective of cost-effectiveness for recommending accurate screening. Furthermore, strengthening health education and health promotion in schools for achieving the goal of health for everyone.

Some limitations must be considered. First, the external validation of the model had not been fully examined since there were no comparable published data. However, the results of our study demonstrated a good internal validation. In addition, our model approved the good face validity, not only because that the model structure could correctly represent the dynamic cohort of EC, but also because the model was developed based on the structure on DisMod II which was conducted from the perspective of the global burden of disease studies. Second, our study could underestimate the total economic burden of EC, since it ignores the medical indirect costs and the indirect costs. Hopefully, in the future, the indirect costs could be calculated for providing better estimates.

5. Conclusion

EC still caused a serious disease burden in China. And it was higher in males than in females. YLL was accounted for the majority of DALYs. Comprehensive strategies should be performed for the improvement of EC prevention and control. Screening and early diagnosis and treatment are highly recommended for that. However, the cost and effectiveness of the screening should be considered. Besides, the process management of clinical screening and treatment should be strengthened to reduce the occurrence of complications such as bleeding, perforation and abdominal pain, and to ensure the safety of participants. Moreover, health promotion and health education should be suggested to improve the opportunity EC screening, and to manger the behavioral risk exposure and promote healthy lifestyles.

Abbreviations

EC
esophageal cancer
DALY
disability-adjusted life year
YLL

years of life lost

YLD

years lived with disability

AAPC

average annual percentage change

Declarations

Ethics approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

Consent for publication

The informed consent was not performed, because the study does not contain human participants.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests

Author Contributions

Yuanyuan Li; methodology, Yuanyuan Li and Xueshan Sun; software, Yuanyuan Li; formal analysis, Yuanyuan Li; writing—review and editing, Yuanyuan Li; writing—original draft preparation, Junfang Xu; methodology, Yuxuan Gu and Xiaoqian Hu; visualization, Xuemei Zhen and Xueshan Sun; investigation, Hengjin Dong; project administration, Hengjin Dong; supervision.

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Figures

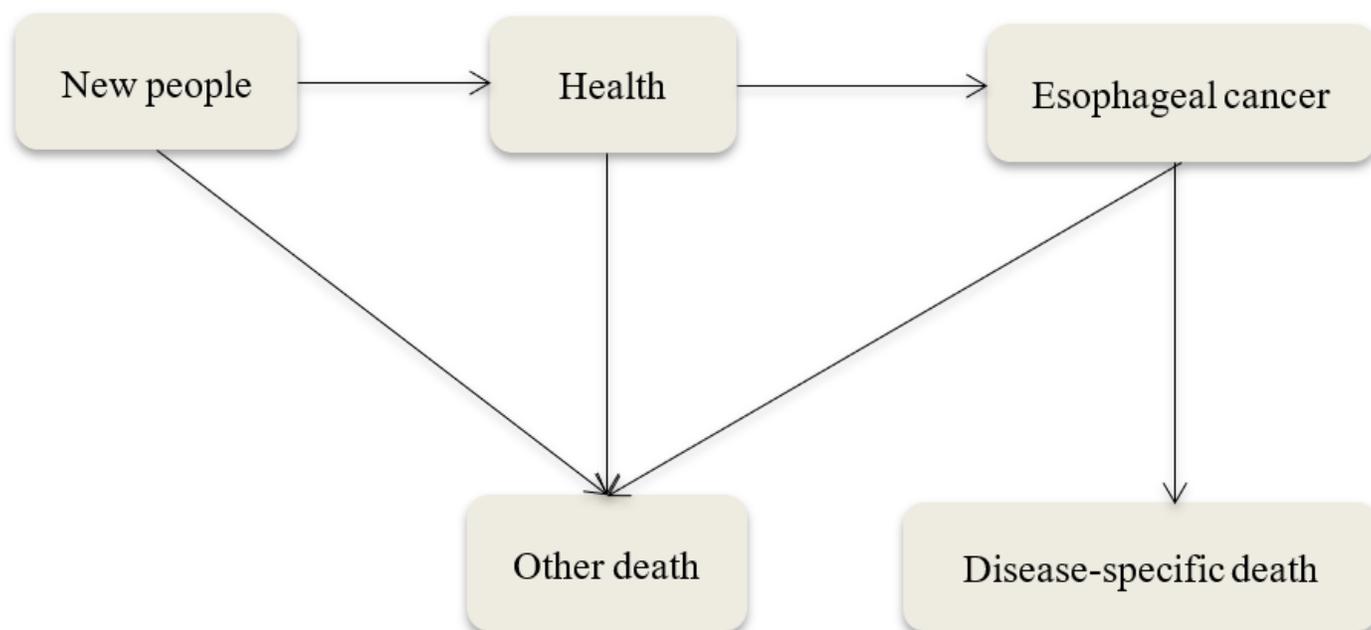


Figure 1

Dynamic Cohort Esophageal cancer Markov Model with five states

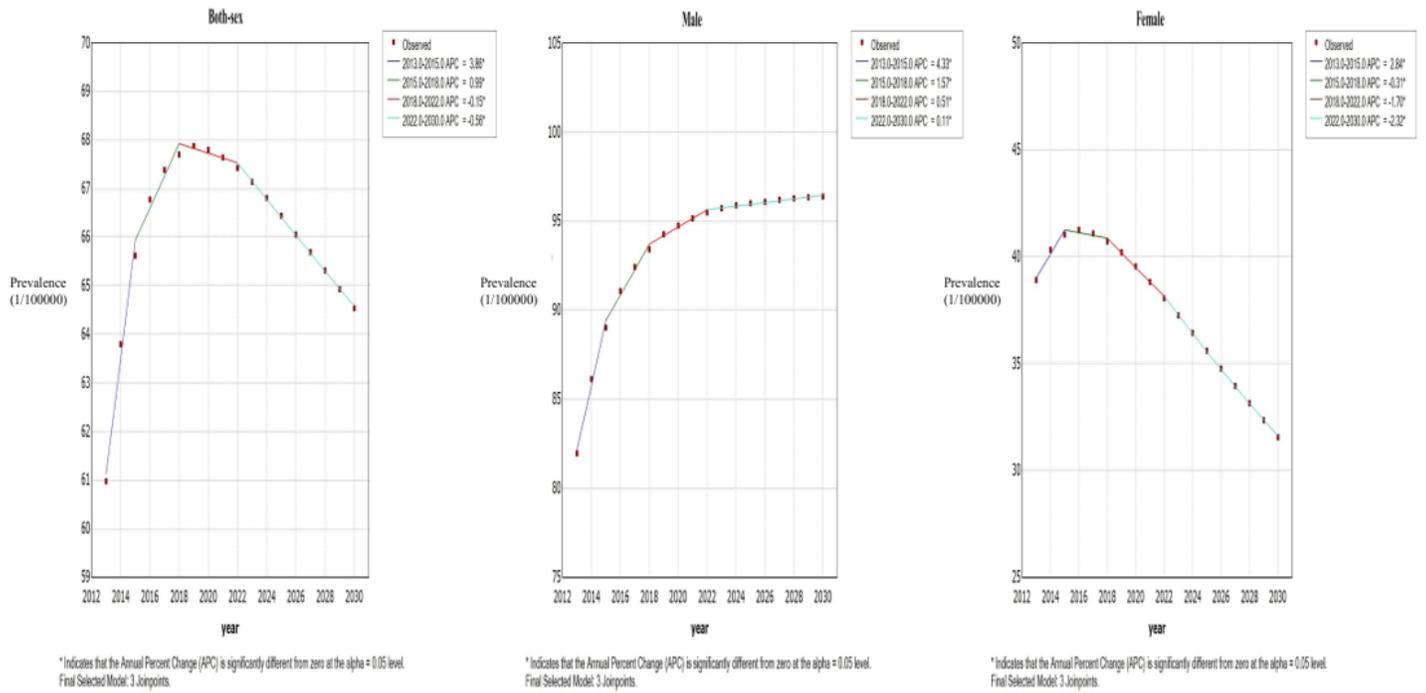


Figure 2

The predicted changing trend of the prevalence of EC from 2013 to 2030

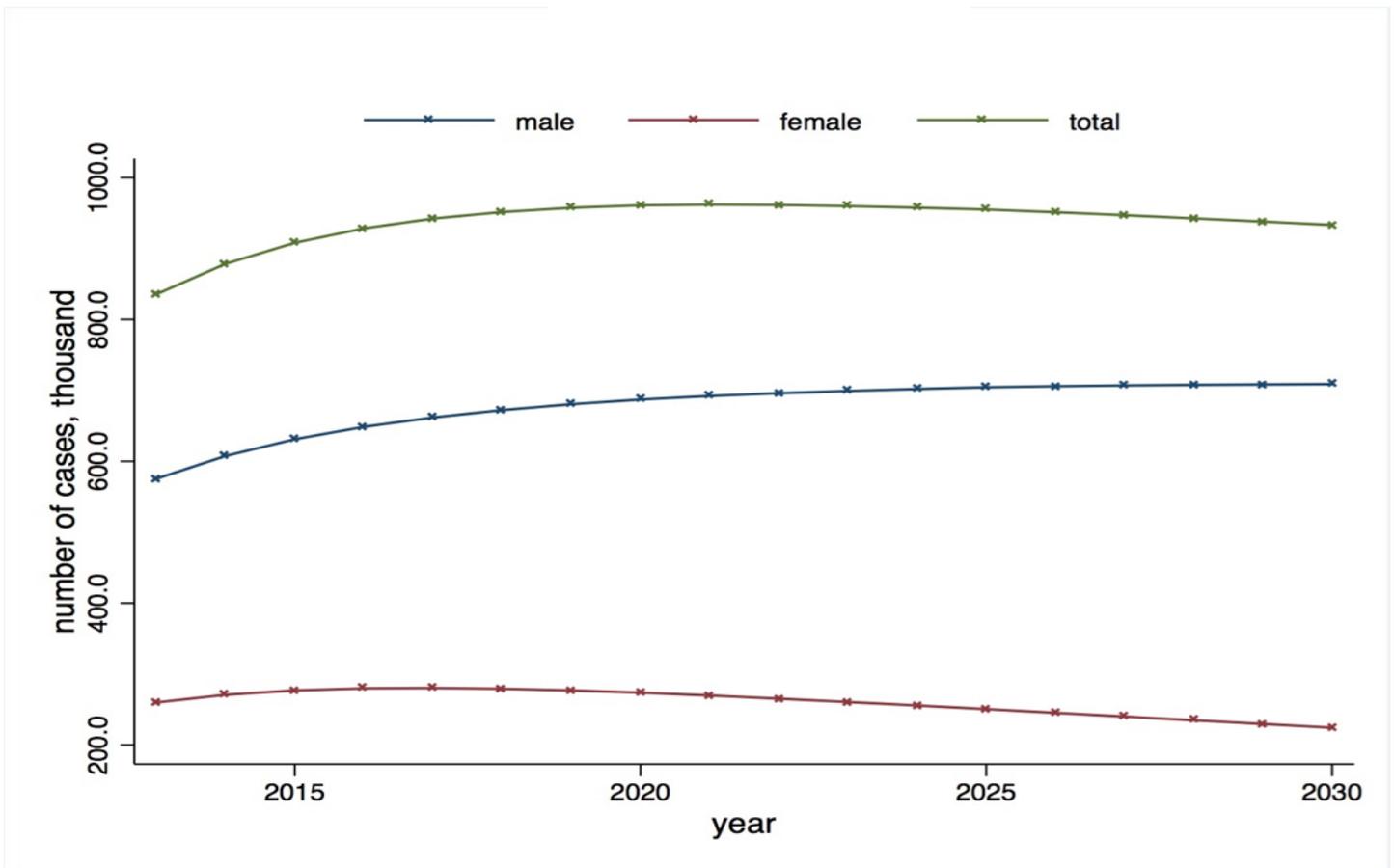


Figure 3

The predicted changing trend of the EC prevalence rates from 2013 to 2030

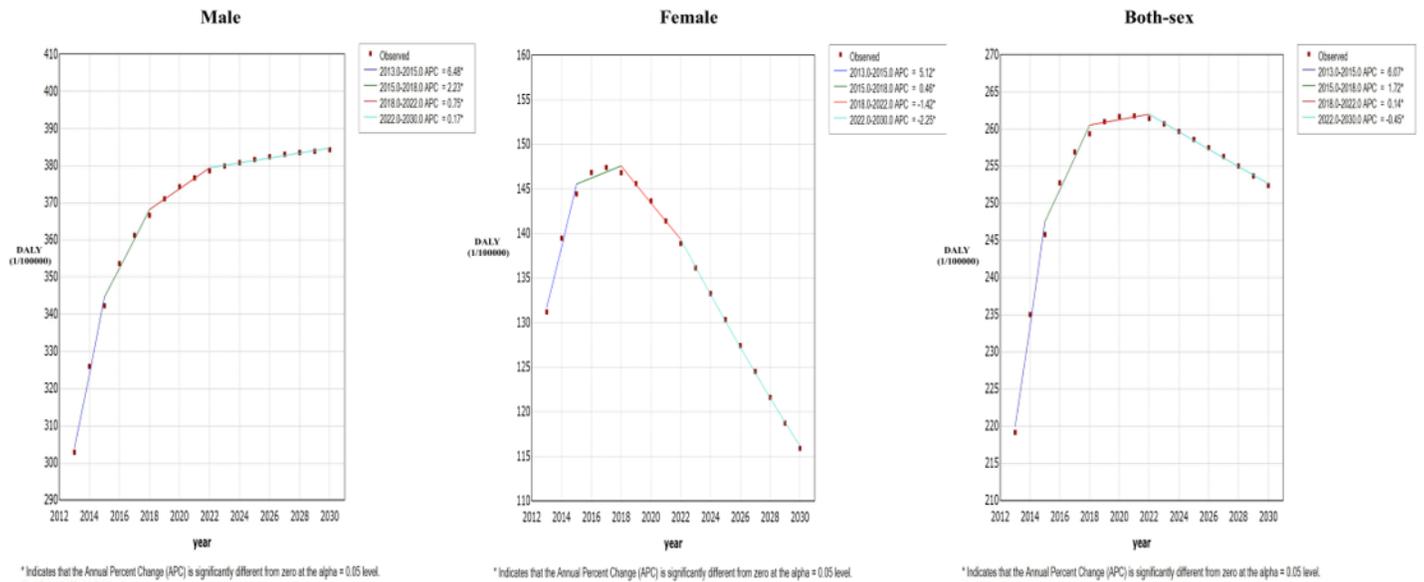


Figure 4

The predicted changing trend of the DALYs due to EC from 2013 to 2030

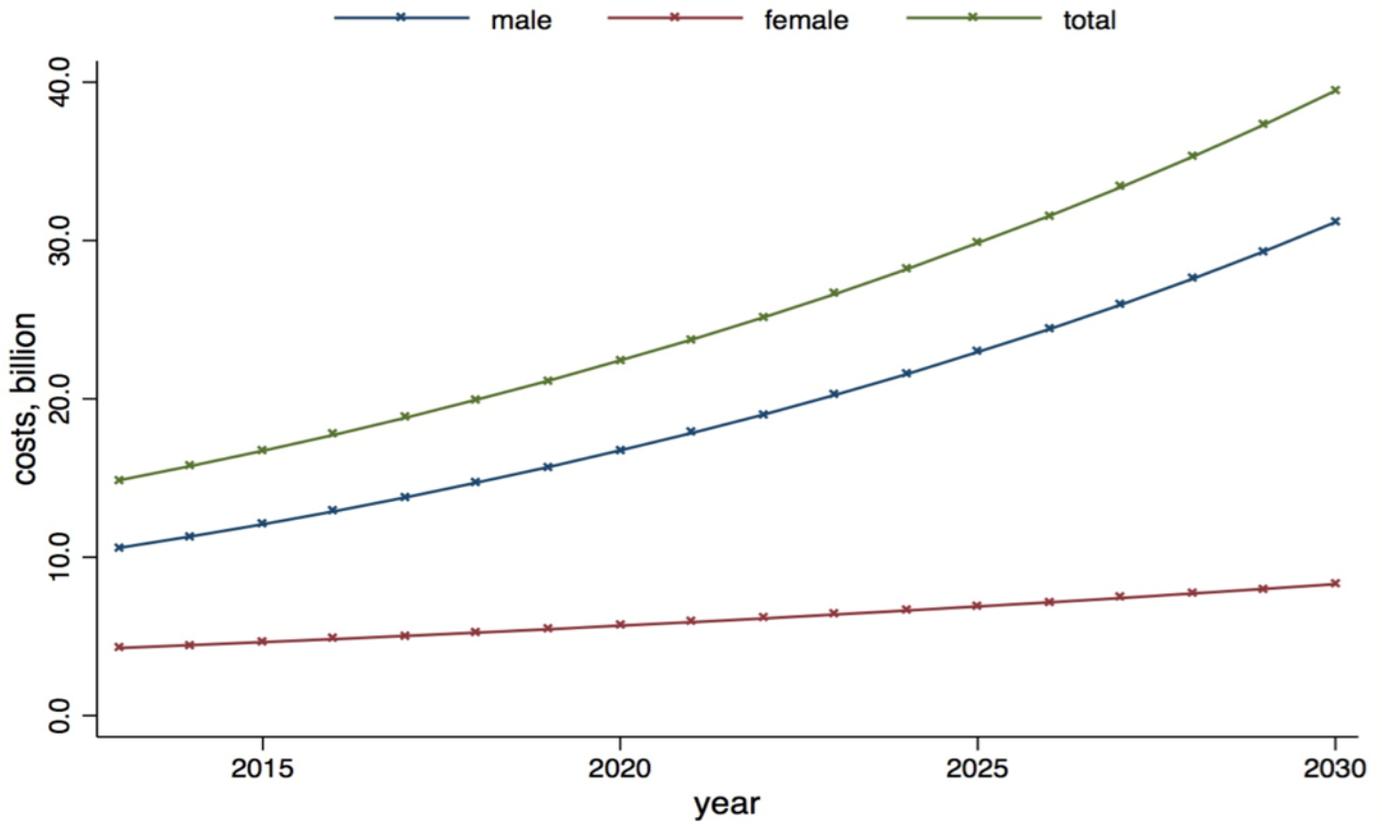


Figure 5

The predicted medical direct expenditure of esophageal cancer from 2013 to 2030

Supplementary Files

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- [Supplement.docx](#)