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Future of cancer incidence in Shanghai, China: Predicting the burden upon the ageing population

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ABSTRACT

Aim: The age-specific cancer patterns have changed significantly over the last few decades in urban Shanghai. Predicting the cancer incidence in an ageing population can help to anticipate future resource needs, evaluate primary prevention strategies, and inform further research studies.

Materials and Methods: Annual cancer cases and population data from 1988 to 2013 were collected from Shanghai Cancer Registry. A Bayesian age-period-cohort model was applied to project the future cancer incidence with demographical changes from 2014 to 2025.

Results: From 1988 through 2013, the urban population aged < 65 years decreased by 19.5%, while the population aged ≥ 65 years increased by 58.4%. In the same period, cancer cases increased by 66.0% (from 8315 to 13,806) and 88.6% (from 7448 to 14,048) in these two populations, respectively. From 2014–2025, the population size is expected to decrease by an additional 29.6% in people aged < 65 years, while it will increase by an additional 68.3% in people aged ≥ 65 years. Correspondingly, the model predicts an 87.5% and 143.4% increase in cancer cases for these two populations, respectively. The most pronounced increase was found in thyroid cancer in both sexes, followed by prostate, kidney, and colon cancer in men. In women, lung, kidney, and cervical cancer in women was expected to increase.

Conclusions: The number of cancer cases in urban Shanghai, especially in older people, is expected to significantly increase in the next decade. Particular strategies targeting the elderly are required to combat the cancers.

1. Introduction

Cancer incidence and mortality have been increasing in China, making cancer the leading cause of death since 2010 and a major public health concern [1]. Much of the increasing burden of cancer is attributable to population growth and socio-demographic changes [2]. As the economic center of China, Shanghai has gained remarkable achievements in both economy and healthcare infrastructure in the last few decades. For example, the life expectancy in Shanghai has increased from 73.3 years in 1982 to 82.5 years in 2013 [3].

One of the resultant socio-demographic changes in Shanghai is the dramatic increase in the number of older adults (age ≥ 65). Specifically, there has been a three-fold increase in the population size of older people in urban Shanghai over the last four decades, from 0.34 million in 1973 to 1.15 million in 2013 [3]. The proportion of older people in urban Shanghai was recorded as high as 18.6% in 2013. Since cancer occurs more commonly in older adults [4,5], the ageing population of Shanghai is expected to markedly increase in a concomitant number of cancer diagnoses. Moreover, the shifting trend to Western diets, change in occupational pattern, increased high risk behaviors (e.g. excessive calorie intake and physical inactivity), and changes in established cancer risk factors (e.g. smoking, hepatitis virus infection,

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and ambient air pollution) could result in an alteration of the cancer profile in Shanghai [6,7].

The incidence rate can serve as a crude proxy for shifting patterns of disease within a population, as well as clues to the changing risk factors [8]. This information is critical for the understanding and planning of the disease burden, and permits an evolution of the Shanghai Health System to respond to future challenges. Previous studies have described the cancer incidence trends in Shanghai but these were of retrospective design and consequently lack insight into the future burden of cancer [9–12]. To address this need, we used data on those diagnosed with 27 selected cancers in urban Shanghai between 1988 and 2013 to project both the future number of cancer patients and cancer incidence to 2025.

2. Methods

2.1. Study data

2.1.1. Cancer cases

Cancer case data from 1988 to 2013 were obtained from the Shanghai Cancer Registry, which was officially established in 1963 and is one of the largest population-based Cancer Registries in China. Meanwhile, Shanghai Cancer Registry is also one of the earliest associate global members of the International Association of Cancer Registries (IACR). Incident cases of cancer were identified by ICD-10 codes. A total of 27 cancer sites were extracted, by gender, age (5-year interval from 0 to 4 to ≥ 85 years), and year of diagnosis, from the Shanghai Cancer Registry. The registration area for this study covered the ten original urban districts in Shanghai, including Huang Pu, Nan Shi (incorporated into Huang Pu in 1993), Lu Wan (incorporated into Huang Pu in 2011), Xu Hui, Chang Ning, Jing An, Pu Tuo, Zha Bei (incorporated into Jing An in 2015), Hong Kou, and Yang Pu.

2.1.2. Population data

The population was stratified by gender and age (5-year interval from 0 to 4 to ≥ 85 years), and by urban areas at the end of each year during the study period. Data were provided by the Shanghai Municipal Bureau of Public Security. The mid-year population estimate by gender was based on the populations at the ends of two consecutive calendar years and used as the average annualized population, a surrogate for person-years at risk. The population data used for the projection of cancer incidence were estimated via the Cohort Component Method [13]. The age-specific birth and death rates were obtained from the Sixth National Population Census conducted in 2010. We postulated that the death rates were constant from 2010 to 2025, while birth rates were likely to experience a minor increase because of the "two-child" policy. Consequently, the birth rate in 2010 was multiplied by 1.1 to better match the actual circumstance.

2.2. Statistical analysis

2.2.1. Historic cancer incidence: 1988 through 2013

We used the cancer incidence rate (crude incidence rate and age-standardized incidence rate [ASR]) and estimated annual percentage change (EAPC) to quantify the cancer burdens and trends [14]. The ASR was derived from the incidence standardized by world population (WHO 2000). A regression line was fitted to the natural logarithm of the rates i.e., $y = \alpha + \beta x + \varepsilon$, where $y = \ln(\text{rate})$, and x = calendar year, and the EAPC was calculated as $100\times(exp(\beta)\text{-}1)$. We calculated the EAPC for period 2014–2025 with the inverse of standardized error (1/se) of estimated incidence rate as the weights in the regression models.

2.2.2. Future cancer incidence: 2014 through 2025

We aimed to project age-specific cancer incidence for 12 years in the future (2014–2025) based on the demographics changes, by conducting a Bayesian age-period-cohort (APC) analysis with integrated nested Laplace approximation (INLA). This has been well documented and validated elsewhere [15,16]. Briefly, since the expectation that effects adjacent in time might be similar, the second-order random walk (RW2) model with inverse-gamma prior distribution was used for age, period and cohort effects. RW2 assumes independent mean-zero normal distribution on the second differences of all time effects. This is a natural target for smoothing, since the second differences in APC models are identifiable. Consider the age effects, say, and then the RW2 prior is given by:

$$f(\alpha|\ \kappa_\alpha) \propto \kappa_\alpha^{\frac{I-2}{2}} \exp\left(\frac{\kappa_\alpha}{2}\sum_{i=3}^{I}(\alpha_i - 2\alpha_{i-1} + \alpha_{i-2})^2\right)$$

$$= \kappa_\alpha^{\frac{I-2}{2}} \exp\left(-\frac{1}{2}\alpha^T Q\alpha\right)$$

$$Q = \kappa_\alpha \begin{bmatrix} 1 & 2 & 1 & & & & \\ -2 & 5 & -4 & 1 & & & \\ 1 & -4 & 6 & -4 & 1 & & \\ & \ddots & \ddots & \ddots & \ddots & \ddots & \\ & & 1 & -4 & 6 & -4 & 1 \\ & & & 1 & -4 & 5 & -2 \\ & & & & 1 & -2 & 1 \end{bmatrix},$$

where i denotes the age index running from 1 to $I = 5$ in this study, because we projected the cancer incidence of people aged 0–84 and the age was divided into 5 groups (0–19, 20–34, 35–49, 50–64, and ≥65 years). Moreover, κ_α^{-1} denotes the variance parameter. Note that Q is rank deficient. To complete the RW2 model specification, we use the usual conjugate hyperprior for the precision, κ_α ˜ *Gamma(α, λ)*. This leads to the full conditional $\kappa_\alpha|\alpha$ ˜ *Gamma(α + 0.5 rank(Q), λ + 0.5α´Qα)*, which may be directly simulated. In this study, we used the parameter default values $\alpha = 1$ and $\lambda = 0.00005$.

We also projected the cancer burden on the assumption that the population size would not significantly change from 2014–2025, in order to ascertain the effect of an ageing population. Moreover, since the sharply increase in thyroid and prostate cancers in recent years, we excluded the cancer cases in 2008–2013 to overcome the effects of "surveillance bias", wherein "the more we look, the more we find", on thyroid and prostate cancer incidences [17]. And then we used the data from 1988 to 2007 to predict the future burden of these two cancers. All age groups were included in this analysis because age-specific projections based on full data sets are more accurate for the younger age groups [18].

All statistics were performed using R program (Version 3.4.4, R core team). The Bayesian age-period-cohort model was conducted with BAPC [16] and INLA packages [19] in R.

3. Results

3.1. All cancer sites

Fig. 1 displays the shifting age distribution in the urban Shanghai population between 2010 and 2025. Specifically, from 1988 through 2013, the urban population aged < 65 years decreased by 19.5% (from 6.36 million to 5.12 million); whereas the population aged ≥ 65 years increased by 58.4% (from 0.68 million to 1.08 million). In the same period, the cancer cases increased by 66.0% (from 8315 to 13,806) and 88.6% (from 7448 to 14,048) in the populations aged < 65 and ≥65, respectively. From 2014–2025, the population size is expected decreased by an additional 29.6% in people aged < 65 years, while it is expected to increase by an additional 68.3% in people aged ≥ 65 years. Correspondingly, an 87.5% and 143.4% increase in cancer cases are anticipated for those two populations, respectively.

With respect to gender, cancer cases increased from 9197 in 1988 to 14,423 in 2013 with a crude incidence of 4.22 for EAPC in men. For women, there was a 104.9% increase in cancer cases with a crude incidence of 6.13 for EAPC during the period (from 6566 to 13,431;

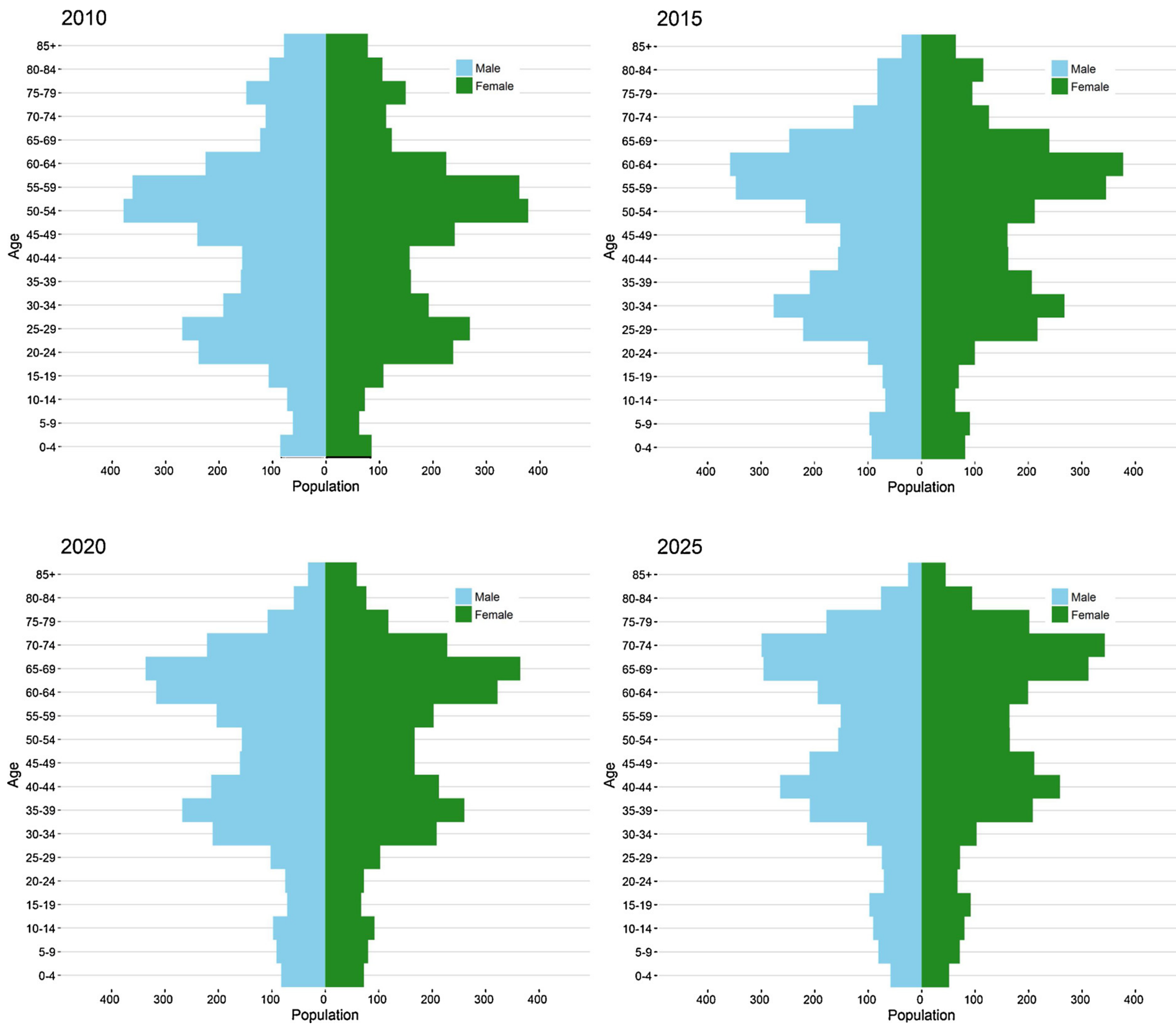

Fig. 1. The gender-specific age distribution in urban Shanghai population in 2010, 2015, 2020, and 2025. (The age distribution in 2010 was derived from the Sixth National Population Census conducted in 2010. The X-axis is on a scale of thousands).

Table 1). From 2014–2025, an additional 120.5% and 109.8% increase in cancer cases are anticipated for men (from 14,423 to 31,808) and women (from 13,431 to 28,172), respectively (Table 1; Supplement Fig. 1). Furthermore, the crude incidence of cancer increased on average by 8.59% (95% CI, 6.31%–10.63%) and 8.09% (95% CI, 6.12%–11.47%) for men and women per year from 2014 through 2025, respectively.

3.2. Site specific data

As shown in Fig. 2, most of the cancers were increased in terms of crude incidence in both genders from 1988 through 2025. The most pronounced increase was observed for thyroid cancer in both genders, followed by prostate, kidney, and colon cancer in men, and lung, kidney, and cervical cancer in women (Table 1). In men, the thyroid cancer incidence increased on average by 14.73% per year from 1988 to 2013, and by 23.55% per year between 2014 and 2025. In women, the thyroid cancer incidence increased on average by 18.98% and 19.33% per year during the 1988–2013 and 2014–2025 periods, respectively. In terms of absolute cancer case number, the highest percentage change was observed for prostate cancer in men and thyroid cancer in women, with the number of newly diagnosed prostate cancer cases increased from 86 in 1988 to 1269 in 2013, which then further increased to 9610 in 2025. The number of thyroid cancer cases increased from 99 in 1988 to 1714 in 2013 and further increased to 7132 in 2025, respectively. However, the increasing trends of thyroid cancer in both genders and prostate cancer in men were slowing when took the “surveillance bias” into account (Supplement Figs. 2–4).

For oesophageal, stomach, and liver cancer in men, both the crude incidence and newly diagnosed cancer cases reduced from 1988 to 2013 and were expected to further decrease from 2014 to 2025 (Table 1; Fig. 2). While in women, the significant reduction in incidence was only observed for liver cancer throughout the study period. The incidence of oesophageal and stomach cancer decreased from 1988 to 2013, whereas they increased from 2014 to 2025. Conversely, for ovarian and other uterine adnexa cancers, the crude incidence increased between 1988 and 2013 and then decreased between 2014 and 2025 (Table 1; Fig. 2).

Based on the absolute case number for cancer incidence, the leading cancer sites in 1988 were lung, stomach, liver, and oesophageal cancer in men, and stomach, breast, lung, and liver cancer in women (Fig. 3). In 2013, the leading four cancer sites were lung, stomach, colon, and prostate cancer in men, and breast, lung, thyroid, and colon cancer in women. In 2025, the leading cancer sites were expected to be prostate, thyroid, lung, and colon cancer in men, and thyroid, lung, breast, and colon cancer in women. The ranking for most cancers was stable over the study period. The prostate cancer in men, and kidney and thyroid cancer in both genders experienced the most pronounced increase in

Table 1
The trends and projections of cancers in Shanghai based on the change in demographics.1988–2025.

Cancer site	ICD10 code	Male							Female						
		Cases			EAPC of CIR		EAPC of ASR		Cases			EAPC of CIR		EAPC of ASR	
		1988	2013	2025	1988–2013	2014–2025	1988–2013	2014–2025	1988	2013	2025	1988–2013	2014–2025	1988–2013	2014–2025
	All sites combined[†]	9197	14423	31808	4.22**	8.59**	1.74**	3.57**	6566	13431	28172	6.13**	8.09**	2.10**	3.75**
Oral cavity and pharynx	C00-14	318	391	460	0.63*	0.89*	−0.70*	0.24	159	163	172	0.14	0.23*	−1.27**	−1.44**
Oesophagus	C15	543	385	333	−1.49**	−0.47*	−3.88**	−1.42**	254	150	198	−3.45**	0.54*	−5.57**	−1.29**
Stomach	C16	2091	1659	1234	−3.01**	−3.23**	−3.18**	−4.23**	1137	910	979	−1.48**	0.74*	−2.50**	−2.58**
Colon	C18	471	1429	2972	2.13**	4.54**	1.95**	3.28**	488	1306	2809	3.75**	6.01**	1.85**	3.04**
Rectum and anus	C19-21	376	993	1223	2.45**	0.63	1.52**	0.19	358	697	1146	2.44**	3.49**	0.73**	2.31**
Liver	C22	1265	1168	738	−1.19**	−3.22**	−1.95**	−4.31**	539	537	454	−0.07	−0.78**	−2.25**	−2.19**
Gallbladder	C23-24	108	222	485	1.44*	4.25**	0.88*	2.27**	164	335	453	1.74**	1.98**	0.64	0.74*
Pancreas	C25	258	670	1256	1.52**	3.19**	1.30**	2.39**	193	539	1065	2.76**	3.49**	1.70**	2.20**
Larynx	C32	137	160	183	0.79	0.23	−1.52**	−1.09**	29	9	5	-#	-#	-#	-#
Lung	C33-34	2417	3210	4300	0.74*	1.15**	−1.57**	0.19	887	1969	6120	2.38**	6.52**	0.61*	3.97**
Breast	C50	–	–	–	–	–	–	–	1059	2494	3539	4.27**	3.49**	2.39**	3.11**
Cervix uteri	C53	–	–	–	–	–	–	–	166	339	700	5.08**	6.33**	4.26**	4.72**
Corpus uteri	C54	–	–	–	–	–	–	–	137	359	421	4.22**	2.04**	2.37**	1.63**
Ovary and other uterine adnexa	C56,C57.0-4	–	–	–	–	–	–	–	234	370	247	1.94**	−0.49*	0.88*	−1.83**
Prostate	C61	86	1269	9610	14.89**	13.78**	9.36**	10.32**	–	–	–	–	–	–	–
Kidney etc.	C64-66,C68	108	647	1288	6.75**	7.42**	6.30**	3.49**	70	358	996	7.55**	4.74**	5.65**	4.00**
Bladder	C67	279	575	1075	1.48**	3.19**	0.63*	1.28**	88	183	272	1.29**	1.49**	0.96**	1.11**
Brain and CNS	C70-72	197	323	432	0.59*	2.17**	0.35	1.01**	164	417	593	2.10**	0.99**	1.75**	0.39
Thyroid	C73	43	584	5269	14.73**	23.55**	10.76**	13.33**	99	1714	7132	18.98**	19.33**	10.65**	12.92**
Non-Hodgkin lymphoma	C82-85,C96	141	307	393	0.64**	0.35*	−9.30**	−2.97**	118	257	378	1.05**	2.12**	−2.29**	−2.77**
Multiple myeloma	C88 + C90	22	100	130	6.38**	0.47*	4.00**	−1.22**	18	68	107	4.11**	4.74**	3.67**	3.69**
Leukaemia	C91-95	180	223	297	0.92*	0.51*	0.53*	0.14	136	175	250	0.93*	0.99**	0.75*	0.61**

Note: Cancer with few cases (< 50 per year) were excluded.
EAPC: estimated annual percentage change in cancer incidence. CIR: crude incidence rate; ASR: age-standardized incidence rate.
[†] the combination of cancer sites listed above.
** $p < 0.001$.
* $p < 0.05$.
# cannot calculate due to scarcity of cases.

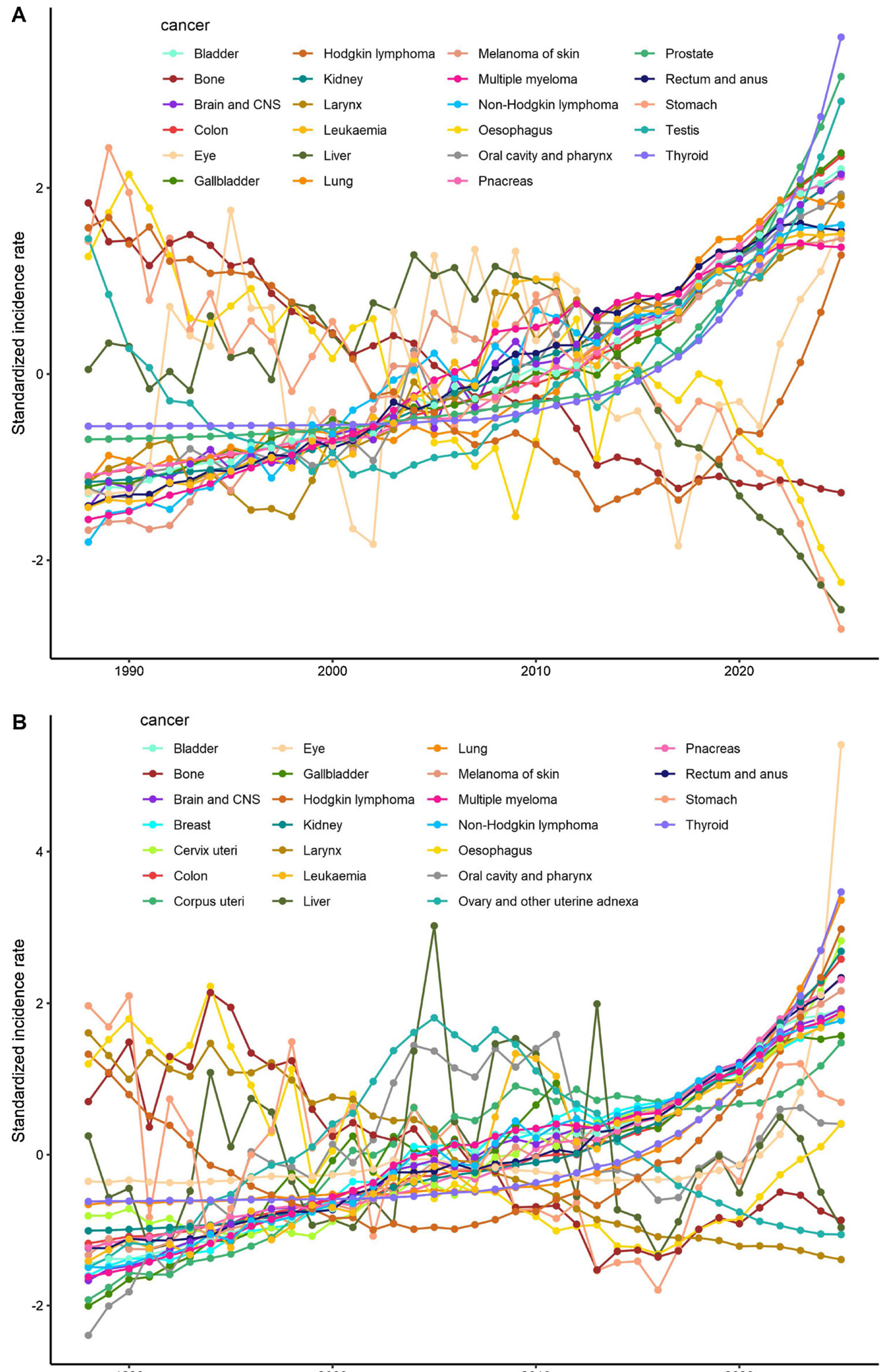

Fig. 2. The temporal trends of cancer incidences from 1988 to 2025. (A: men; B: women. All incidences have been standardized by their means and standard errors.).

the ranking. In contrast, gastrointestinal cancers, such as liver and stomach cancer, in both genders decreased dramatically in the ranking.

3.3. Effects of the ageing population and cancer risk factors

We also projected the future cancer cases based on the assumption that the urban Shanghai population will not change from 2014 to 2025. In this scenario, incident cancer cases were expected to increase by 95.4% to 26,971 in people < 65 years old, and by 98.6% to 27,893 in people aged ≥ 65 years, respectively (Fig. 4). The EAPC of crude incidence in these two populations was 9.21 (95% CI, 6.49–10.43) and 8.19 (95% CI, 6.87–9.43), respectively. Briefly, a total of 45,519 cancer cases in older people will be prevented if the urban Shanghai population remains constant over the next 12 years, whereas an additional 10,829 people aged < 65 will develop cancer.

The change in ASRs approximates to the change in risk factors. As

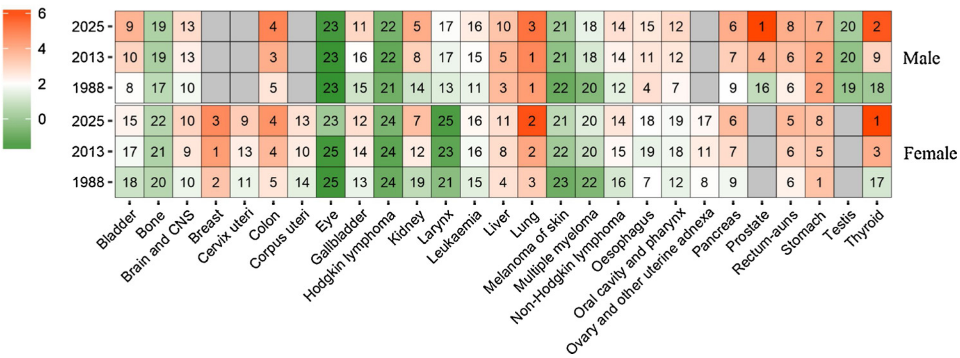

Fig. 3. The ranks of cancers in terms of their incidence in urban Shanghai in 1988, 2013, and 2025. (All incidences are in log scale. Brick red represents the higher incidence, while forest green represents the lower incidence. Gray means no data available.) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article).

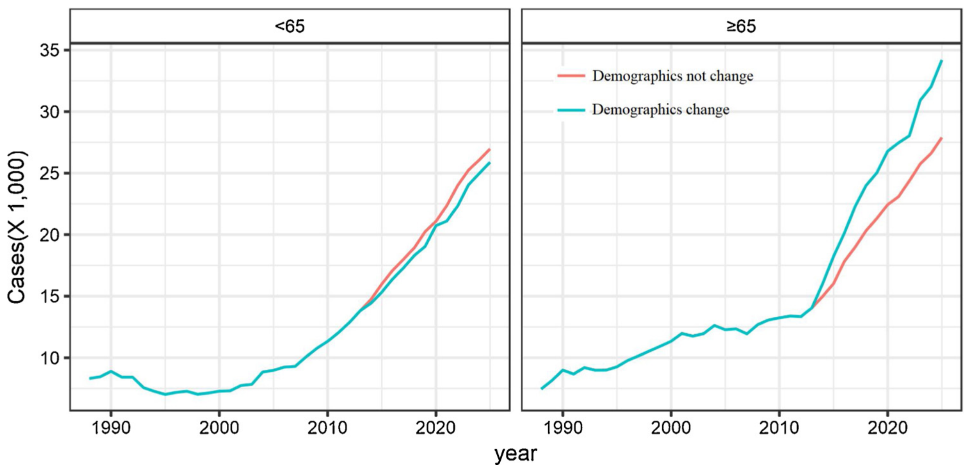

Fig. 4. The anticipated cancer cases with or without demographic changes from 2014 to 2025.

shown in Table 1, we also calculated the EAPC of ASRs for each cancer site and all sites combined. For all cancer sites, the EAPCs were lower when compared with the EAPCs of crude incidences in both genders, while the cancer trends have not changed remarkably in most cancers from 1988 to 2025. Thyroid cancer was still found to be the most rapidly increasing cancer in both genders, followed by prostate cancer in men, and cervical cancer in women. However, although ASRs reduced for laryngeal, multiple myeloma, and non-Hodgkin lymphoma cancer in men, and oral cavity and pharynx, oesophageal, stomach, and non-Hodgkin lymphoma cancer in women, the crude incidences increased throughout the study period.

4. Discussion

The burden of cancer on the urban Shanghai population has significantly increased over the last few decades, and is expected to rise sharply over the next decade, with the greatest increase borne by older people. By 2025, approximately 60% of all cancer cases will be diagnosed in people aged ≥ 65 years. Alarmingly, certain cancer sites that have been diagnosed less frequently in the past, such as thyroid and prostate cancer, will be among those with the greatest increase in incidence. This represents a remarkable shift in the cancer pattern in urban Shanghai.

The increase in cancer cases has been generally attributed to the change in cancer-related risk factors, population size, and population age structure [20]. In urban Shanghai, the population size decreased by 12.0% from 1988 to 2013 and we anticipated an additional 12.5% decrease by 2025. However, while the overall resident numbers in Shanghai has strikingly increased by 87.5% from 1988 through 2013, the number of professional physicians has decreased from 4.2 per 1000–2.4 per 1000 during this period [3]. This decrease might suggest that further shrinkage of health resource in Shanghai is likely, thereby imposing severe challenges on diagnosis and treatment of diseases that include cancer. On the other hand, the Shanghai population is still ageing, especially in the urban districts. The expanding aged population could be viewed as a sign of improved medical facilities and healthcare in Shanghai over the past decades. More importantly, this could herald a heavy disease burden in the geriatric population in the near future. For example, certain cancers are expected to increase in terms of absolute case numbers although their incidences may reduce. To address the anticipated surge in cancer incidence specifically in older adults, significant investments in research and targeted measures are needed. On the one hand, there should be a greater emphasis on primary prevention and early detection, such as eradication of *Helicobacter pylori*, wider implementation of HBV and HPV vaccination, and effective screening for cervical and colorectal cancer, are warranted [21–23]. On the other hand, growing evidence from diverse types of cancers such as breast, prostate, and glioblastoma suggest that age at diagnosis is a critical factor for both cancer biology and response to treatment [24–26]. As a result, randomized clinical trials and non-randomized clinical studies are urgently needed to identify clinically beneficial and cost-effective treatments tailored to older patients [27].

Apart from the effect of the ageing population, the changes in cancer-related risk factors should also be considered in the prediction of future cancer burden. The Shanghai government has made great efforts to counter cancer in the last few decades. The most remarkable achievement has been seen in the persistent decrease of liver cancer in both genders [28], which was mainly ascribed to the disseminated and long-term HBV vaccination programme in children [29]. In 2017, Shanghai initiated its HPV vaccination programme; the accumulative protective effect at the population level can be expected to emerge in the next few decades [30]. Moreover, a smoking ban has been completely in place for public places in Shanghai since 2017, albeit this is much later compared to other countries [31,32]. However, experiences from Western countries have already shown that decreasing incidence of lung cancer and oropharyngeal cancer can be expected from the contemporarily low smoking rate because of the cohort effect of smoking cessation [33]. However, risk factors for cancer development are complicated and multilevel, and therefore hard to measure and disentangle. In the current study, we found that the ASRs of most cancers will still increase, albeit the ageing effect has been adjusted for. These data might indicate that much more attention should be placed on other underlying risk factors, such as obesity, diabetes, and air pollution. Previous epidemiological studies have suggested that immediate health promotion interventions are required to counter the high prevalence of obesity and diabetes in Shanghai [34,35], which are expected to subsequently result in a higher number of cancer cases [36–38].

In this study, we found an alarming surge in thyroid cancer case in both genders. This unexpected expansion has been observed in the United States too [39]. Although the reasons for this increase are not completely understood, they may partly relate to the improved scrutiny and access to care in recent years [17]. However, the effects of screening activities are difficult to account for in cancer projections. For other cancer sites among those with the greatest relative increase, such as prostate and colorectal cancer, the shift in diet and lifestyle in the urban Shanghai population might be one of the reasons for these striking changes, because Asian immigrants in America have also experienced a sharp increase in these types of cancer [27].

Shanghai is a metropolis with developed medical facilities, a completed health system, and improved medical levels but it is also characterized by a large, ageing population. With the progression of urbanization in China, more and more cities will expand with more than ten millions residents over the next few decades. The ageing population and increasing cancer burden will be a major challenge encountered by most cities. Predicting future incident cancer cases helps health managers and policy makers anticipate the resources needed to screen, diagnose, and treat patients with newly diagnosed with cancer while providing ongoing care to care survivors.

Some limitations regarding this study should be noted here. First, only the urban population was included in the analyses, while major parts of population in Shanghai are living in suburb districts. Second, immigration to urban Shanghai in the future has not been considered in predicting the size of the population. Third, the alterations in risk factors for certain cancers and the effect of increased screening coverage cannot be taken into account in the Bayesian APC model.

5. Conclusions

In summary, the number of cancer cases in urban Shanghai, particularly in older people, is expected to vastly increase over the coming years. Consequently, resources needed for cancer prevention, screening, early detection, and treatment will need to concomitantly increase. Broadly speaking, renewed government interest in national healthcare reform should include a substantial focus on the elderly.

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Contributors

Study design: TZ, XC, ZL
Data collection: ZL, HY, QF, NC
Data analyses: ZL, YJ
Results interpretations: All authors.
Manuscript writing: ZL, TZ, XC, YJ, HY, CS
Manuscript proofing: TZ, XC, WY

Declaration of interest

We declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.canep.2019.03.004.

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