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Breast cancer mortality in Chinese women: does migrant status play a role?

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ABSTRACT

Purpose: It is unclear whether migration would affect the mortality risk of breast cancer. In this study, we compared breast cancer mortality among three Chinese populations: Guangzhou (GZ)-born women, Hong Kong (HK)–born women, and HK residents who were born outside HK (HK immigrant), with the aim to explore the impact of migrant status on breast cancer mortality.
Methods: We applied an age–period–cohort model to annual age-specific mortality rates of breast cancer among GZ-born, HK-born, and HK-immigrant women from 2003 to 2016, respectively. We also projected mortality rates from 2017 to 2030.
Results: Annual age-standardized mortality rate of breast cancer in women aged 35 years or older was 9.18, 9.17, and 9.83 per 100,000 population, for GZ-born, HK-born, and HK-immigrant women, respectively. A decreasing trend was found in the post-1950s cohorts of GZ-born women and in the post-1960s cohorts of two HK populations. Annual mortality rates of breast cancer in these populations were projected to decrease among the 35–64 years age group and increase among the 65 years and older age group in 2017–2030.
Conclusions: We found higher age-specific mortality rates of breast cancer in HK-immigrant women compared with HK- and GZ-born women, suggesting that immigration status might have an impact on breast cancer mortality.

Background

Breast cancer is one of the most common cancers in women. Globally, it was estimated that 2.09 million women were newly diagnosed with breast cancer, and 0.63 million died from breast cancer in 2018 [1]. Previous studies have identified several risk factors of breast cancer incidence and mortality, including genetic factors such as family history, BRCA1/2 carrier, and estrogen [2]; reproductive and hormonal factors such as menstrual life, nulliparity, first live birth age, and breastfeeding [3–5]; and lifestyle

Ethics approval and consent to participate: Not applicable.

Consent for publication: Not applicable.

Availability of data and material: The data that support the findings of this study are available from the Census and Statistics Department (CSD) of Hong Kong and the Guangzhou Municipal Center for Disease Control and Prevention (GZCDC) but restrictions apply to the availability of these data, which were used under license for the present study and, thus are not publicly available. However, data are available from the corresponding authors on request and with permissions from the CSD of Hong Kong and GZCDC.

Competing interests: None.

Authors' contributions: S.Z. and L.Y. conceived and designed the work. L.Y., G.L., and H.D. acquired the data. S.Z. carried out the analysis in this work. S.Z., L.Y., and D.H. interpreted data and drafted the article. All authors revised the article and approved the final version.

The authors have no conflicts of interest to disclose.

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factors such as obesity [6–8], physical activity, dietary habits [9], and smoking [10]. Besides these risk factors, migrant status has also been proposed to associate with breast cancer. For example, one early study in Sweden showed that the attack rate of breast cancer tended to be different between immigrants and native Caucasian populations [11]. A study in Canada found that Asian immigrants less likely received mammography screening than did nonimmigrants [12]. Moreover, similar breast cancer survival rates for Asian immigrants and native Caucasian women were reported by a U.S. study [13], but another study reported that the survival rates of Asian immigrants were worse than those of native Asian women [14]. However, no studies have been conducted to compare breast cancer mortality between immigrant and nonimmigrant women within the same ethnicity and culture, to our best knowledge.

Breast cancer is the fourth leading cause of death among cancers in Chinese women, and the age-standardized mortality rate increased from 5.7 to 8.8 deaths per 100,000 women throughout the past 10 years in China [1,10,15]. The incidence rate and prognosis of breast cancer showed socio-economic and spatial heterogeneities in mainland China. Economically developed urban areas in China had higher incidence rates of breast cancer and better prognoses than underdeveloped urban and rural areas [10]. It has been reported that the 5-year survival rate of breast cancer patients in Shanghai, one of the most industrialized cities in China, was 78% in 1992–1995 [16], much higher than the survival rate in a rural area near Shanghai (58% in 1992–2000) [17]. Both rates were significantly lower than the rate of 89% reported for U.S. women in 1999–2005 [18].

In this study, we compared the mortality rates of breast cancer between Chinese women in Hong Kong (HK) and Guangzhou (GZ). Both cities share similar ethnicity (>90% of female residents are Chinese) [19], culture, and dietary habits. Multiple migration waves from mainland China to HK occurred in the last century, including a major migration inflow during the Chinese Civil War (from 1945 to 1950) and several small-scale inflows in the 1950s, 1970s, and 1990s [20–23]. Overall, 87.8% of these immigrants were Chinese originally from the Guangdong province, where GZ is the capital city [24]. Previous studies found that child immigrants in Hong Kong had a higher risk of cardiovascular diseases [25] and wheezing disorders [26]. However, to date, there are no studies that have compared the breast cancer mortality of immigrants and HK origin residents although such comparison could provide important evidence to understand the role of immigration in cancer mortalities.

This study was aimed to assess the age, period, and cohort effects on breast cancer mortality during the study period of 2003–2016 and to project mortality rates up to 2030 in three Chinese populations: GZ-born women, HK-born women, and HK women who were born outside HK (HK immigrant). We chose these three populations based on the following reasons: (1) they are ethnically homogeneous and share the same culture and dietary habits, (2) GZ-born and HK-immigrant women had similar early life experiences, and (3) HK-immigrant and HK-born women likely share similar screening and health care seeking behavior. Specifically, we hypothesize that if migrant status plays an important role in breast cancer mortality, HK-immigrant women could show different patterns of age, period, and cohort effects from the homeland population (represented by GZ) and HK-born population.

Methods

Data source

The HK and GZ population data by age, gender, ethnicity, and birthplace were obtained from the Census and Statistics Department of Hong Kong and the Guangzhou Municipal Center for Disease Control and Prevention, respectively. The Hong Kong data were divided into HK born and HK immigrants who were born outside HK (including mainland China, Macau, and Taiwan). The death registry data of Hong Kong in 2003–2016 were obtained from the Census and Statistics Department. GZ is the capital city of the nearest province (Guangdong province) in mainland China to HK. Compared with the majority of the other parts in mainland China, GZ has similar environmental conditions and living habits as in HK. The death registry data of GZ in 2003–2016 were obtained from Guangzhou Municipal Center for Disease Control and Prevention. Breast cancer mortality data were retrieved from the death registry data using the International Classification of Diseases version 10 codes C50, C50.0–C50.9 after 2000 for both GZ and HK. Given the low incidence of breast cancer in men and young women, only the mortality data from women aged 35 years or older were included in this study. Annual mortality rate was calculated for single-year age groups, and age-standardized mortality rates were calculated based on the World Health Organization world standard population in 2000 [27]. We also did a stratified analysis for the age groups of 35–64 years and 65 years and older. The cutoff age at 65 years was selected because nearly 50% of the breast cancer incidences aged above 65 years [28].

Statistical analysis

We applied an age–period–cohort (APC) model with a Poisson distribution to annual mortality rates of breast cancer by single-year age groups from 35 to 85 years and older for GZ-born, HK-born, and HK-immigrant women, respectively. The APC model has long been applied to incidence or mortality data of cancers and chronic diseases, and more technical details can be found in a review by Holford [29]. The best-fit APC model was selected by minimizing the deviance and the Akaike Information Criteria [30]. We bootstrapped the sample data from the whole datasets 100 times and fitted an APC model to each sample to check the sensitivity and fitting performance of the final APC model. Probability maps were also plotted in Supplementary Figure 1 to show the percentiles of all the fitting values that observed data fell at for each data point [31,32]. Overall, all the models achieved the satisfactory goodness of fit.

It is well known that the APC model has an identifiability problem because of the linear correlations between age, period, and cohort variables; therefore, only the second-order differences could be estimated from this model [33,34]. Statistical significance of age, period, and cohort effects was tested by log-likelihood ratio tests between the full models and nested submodels of age–period, age–cohort, and period–cohort effects. Furthermore, t tests were applied to test the statistical significance of the age effect difference between the three populations. We did not test for the period effects and the effects of pre-1930 cohorts because the data of early cohorts could be imprecise because of insufficient data sample. Further details of this limitation can be found in the Discussion section.

By fixing the period effect at its average level, we used the age–cohort submodel to project the trend of mortality rates in those aged 35 years or older from 2017 to 2030 [35,36]. We used the second-order autoregressive time series to extrapolate the cohort effects, in which each point estimate was derived from the data of two preceding cohorts. The 95% credible intervals were estimated by using a chain-ladder model with a Poisson distribution [31,32,37].

The P value less than .05 indicated statistical significance. All the analyses were conducted by the package "apc" of R version 3.4.3 (R Core Team, R Foundation for Statistical Computing, Vienna, Austria, 2013, http://www.R-project.org/) [38].

Results

During the study period, annual age-standardized mortality rate of breast cancer was 9.83, 9.17, and 9.18 per 100,000 women, for HK-immigrant, HK-born, and GZ-born women aged 35 years or older, respectively (Table 1). An increasing trend of mortality rates over age was observed for all these populations, with occasional exceptions. Women in HK had significantly higher mortality rates than GZ-born women among most of the age groups, and the largest difference was found in those aged 70 years and older (Table 2). HK-immigrant women had a higher mortality risk than HK-born women in younger and older age groups, whereas no significant difference was found in the age groups of 35–39 and 55–69 years, and a significant lower rate in the 45–54 years age group.

Detailed information about the model goodness-of-fit and prediction performance is shown in Supplementary Tables 1–3. The APC model generally fitted well to annual single-year mortality rates of breast cancer among the three Chinese female populations (Figs. 1 and 2). In women aged 35–64 years, a slow rising trend of breast cancer mortality was observed before 2014 among all the populations, but a clear declining trend was found post-2014. The projection to the year 2030 shows that breast cancer mortality rate decreases in this younger age group, and the most dramatic change occurs in HK-born women. The trends of mortality in older women aged 65 years and older were less consistent. The mortality rates of GZ-born women consistently increased after 2003, but a turnover point was found in 2009, and the rates increased since 2012. The mortality rates of HK-born and HK-immigrant women remained relatively stable in older women, whereas GZ-born older women had a lower mortality rate, which is projected to surpass the former around 2025. In both age groups combined, annual mortality rates of age 35 years or older are projected to remain stable in 2017–2030, with an average annual rate of 32, 22, and 27 deaths per 100,000 women among the HK-immigrant, HK-born, and GZ-born populations.

The effect estimates of age, period, and cohort for GZ-born, HK-immigrant, and HK-born women are shown in Figure 2. The trend of the age effects is consistent between HK-born and GZ-born women, with a fast-rising trend for those aged 35–50 years, a plateau for 50–75 years, and a rising trend again in 75 years and above. The period effects are largely consistent between the three populations. The cohort effects show an inverse “U” shape in all three populations with a peak clearly observed in the 1930s, whereas multiple peaks were found in HK-immigrant and HK-born women. A decreasing trend was found among the post-1960s cohorts of GZ-born women and in the post-1950s cohorts of two HK populations. For the 1941–1950 cohort, breast cancer mortality risk was relatively lower for GZ-born than HK-immigrant and HK-born women, whereas the 1956–1965 GZ-born cohort has a relatively higher risk than HK-immigrant and HK-born women (Table 3).

Discussion

In this study, we projected the trend of age-specific mortality rates up to year 2030 in the age groups of 35–64, 65 years and older, and both combined, separately for these populations. In the combined group, the projection shows a steady trend, which is consistent with another study in HK [39,40]. The mortality rate of breast cancer is projected to continuously increase in older women but simultaneously decrease in the 35–64 age group. Projected increase in the elderly could be associated with more frequent diagnosis of cancer at advanced stages resulting in poorer survival [40,41]. A similar situation was reported in the United States and the United Kingdom, which could also be applied to the HK context

Table 1
Age-specific mortality rates of breast cancer and age-standardized mortality rates (per 100,000 female population) in HK from 2003 to 2016 and in GZ from 2003 to 2016

Age group (y)	HK immigrant				HK born				GZ born			
	2003–2007	2008–2012	2013–2016	Whole period	2003–2007	2008–2012	2013–2016	Whole period	2003–2007	2008–2012	2013–2016	Whole period
35–39	5.83	7.18	3.51	5.67	5.36	4.5	5.12	5.95	5.55	5.19	5.49	5.4
40–44	10.93	13.14	10.62	12.11	11.7	10.11	11.09	11.61	11.33	9.7	8.6	9.91
45–49	17.44	17.04	17.68	17.06	18.02	17.19	18.61	18.83	21.17	16.09	18.32	18.39
50–54	25.08	29.35	22.61	24.38	28.31	25.92	28.82	27.32	27.16	24.19	28.94	26.68
55–59	27.37	34.97	33.72	30.61	26.66	28.93	32.82	30.46	28.16	27.63	34.5	30.29
60–64	33.86	36.62	37.37	34.26	38.31	34.36	36.79	35.06	24.81	27.94	31.56	28.76
65–69	25.95	31.46	37.26	29.07	35.8	25.21	29.41	29.56	28.92	25.42	33.14	29.43
70–74	31.18	29.48	32.68	30.91	31.69	26.43	35.83	28.47	34.54	37.38	31.32	34.59
75–79	38.9	35.26	39.33	39.26	22.65	24.92	29.45	28.8	34.86	38.03	33.75	35.69
80–84	59.01	56.68	43.42	56.1	38.88	39.48	41.87	43.06	40.05	43.95	53.24	46.86
85+	86.53	86.83	70.24	82.8	44.88	38.61	40.77	43.67	51.52	62.87	52.47	55.83
Age standardized	9.6	10.28	9.61	9.83	9.34	8.45	9.73	9.17	9.18	8.66	9.56	9.18

Age-standardization was based on the World Health Organization world standard population in 2000 [27].

Table 2
Comparison of age-specific mortality rates of breast cancer (per 100,000 female population) between the HK-born, HK-immigrant and GZ-born women

Age group (y)	HK immigrant vs. HK born			HK immigrant vs. GZ born			HK born vs. GZ born		
	Difference	95% CI	*P* value*	Difference	95% CI	*P* value*	Difference	95% CI	*P* value*
35–39	0.09	0.06, 0.13	<.0001	0.03	0, 0.07	.0672	−0.06	−0.08, −0.03	<.0001
40–44	0.1	0.05, 0.15	.0001	0.2	0.15, 0.25	<.0001	0.1	0.05, 0.14	<.0001
45–49	−0.05	−0.12, 0.02	.1454	−0.15	−0.23, −0.07	.0002	−0.1	−0.17, −0.03	.0033
50–54	−0.22	−0.31, −0.13	<.0001	−0.07	−0.16, 0.02	.1417	0.15	0.09, 0.22	<.0001
55–59	0.34	0.26, 0.42	<.0001	0.25	0.18, 0.33	<.0001	−0.09	−0.15, −0.02	.0066
60–64	0.08	−0.01, 0.18	.0967	1.09	1, 1.18	<.0001	1.01	0.9, 1.12	<.0001
65–69	0.13	0.03, 0.23	.0144	0.17	0.06, 0.28	.0025	0.04	−0.08, 0.16	.5358
70–74	0	−0.13, 0.13	.9756	−0.47	−0.58, −0.36	<.0001	−0.47	−0.62, −0.32	<.0001
75–79	1.7	1.57, 1.84	<.0001	0.32	0.19, 0.44	<.0001	−1.39	−1.51, −1.26	<.0001
80–84	1.84	1.6, 2.09	<.0001	0.98	0.82, 1.15	<.0001	−0.86	−1.11, −0.61	<.0001
85+	5.88	5.74, 6.02	<.0001	3.77	3.62, 3.92	<.0001	−2.11	−2.28, −1.95	<.0001

CI = confidence interval.
* *P* value of *t* test.

[36]. Increased awareness against breast cancer, early diagnosis, and improved cancer therapies in both HK and GZ women could possibly explain the projected trends [10,42–44], but further investigations on the underlying reasons are needed.

Interestingly, we observe a higher mortality rate among HK-immigrant women than the other two, particularly in older women (Fig. 1). Consistently, in the cohort effects, we identified a faster increasing trend in the 1920–1930 cohorts and multiple peaks in the 1940–1950 cohorts in HK-immigrant women (Fig. 2). These cohorts correspond to the first immigration wave during the Chinese Civil War (1945–1950s), and the second during the Culture Revolution (late 1960s–1970s) [45]. Hence, we speculate that many of the 1940–1950 cohorts of HK immigrants had probably suffered from the Chinese Civil War and the Great Chinese Famine between 1959 and 1961 during their puberty and adolescence before they fled to HK [20–23]. Those who moved from mainland China to HK after the famine could have worse early life experience and less healthy physical conditions than the HK-born population, which could affect the survival odds from breast cancer in their later life. Our findings echo the previous findings that women who experienced severe famine during their childhood and early adulthood had a higher risk of breast cancer than those without famine exposure [46]. Another possible explanation is the implementation of the one-child policy in the late 1970s [47,48], which has been found to be associated with increased breast cancer risk in mainland China [10]. It is of note that mortality rates might also be affected by many other factors such as socioeconomic status, lifestyle (obesity and smoking), mammography screening, early diagnosis of breast cancer, and accessibility to effective treatments. In the past decades, the mainland China has experienced a fast economic growth, and an epidemiologic transition has been found in cardiovascular diseases since more people adopted westernized lifestyle [49]. This could also explain the rapid increase of breast cancer mortality among GZ-born women in this study. Therefore, further studies are warranted to explain the high mortality rate in the HK immigrants.

The cohort effects became consistent across the three populations in the post-1960 cohorts, but inconsistent for the pre-1960 cohorts. This could be because of fast economic development of mainland China after 1980s, with an annual increase rate of 8.5% in mainland China [50,51]. The consistency of the post-1960 cohorts could also be (partly) because of an increased age at first childbirth among the GZ-born women [52]. We also projected that the older GZ-born women had a faster increase in mortality rates in the next 14 years (Fig. 1). The HK-born women had a higher mortality rate than the GZ-born women among those aged over 70 years, but the two mortality rates appear similar among younger age groups (Table 2). This might be the result of rapid development in living conditions among the younger generation of GZ-born women during the economic boom after the 1980s [50,51].

Breast cancer mortality is determined by both survival profile and incidence rate. In our data, age-standardized mortality rates

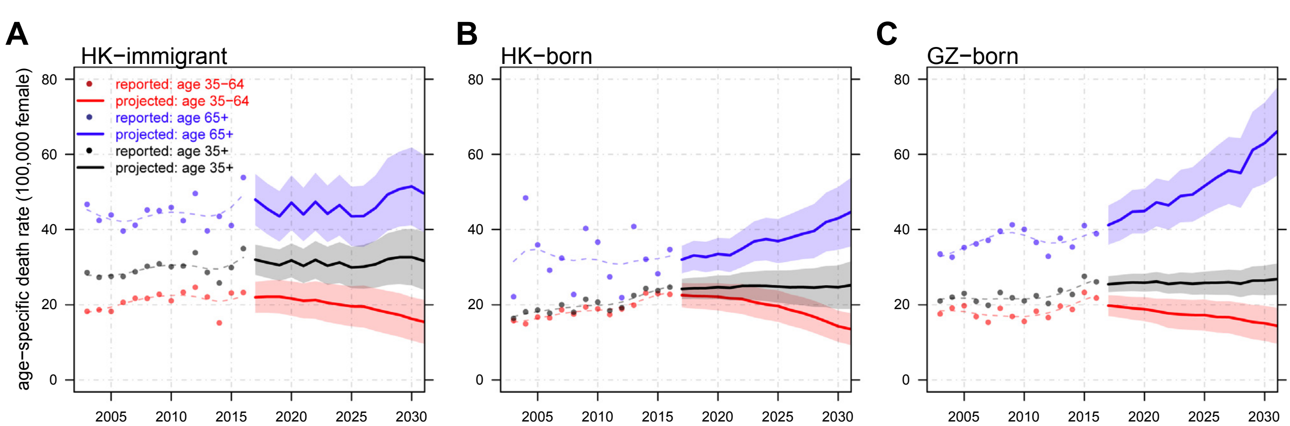

Fig. 1. Observed and projected age-specific mortality rates of breast cancer in 2003–2030, among (A) HK-immigrant, (B) HK-born, and (C) GZ-born women, by the 35–64 years (red), 65 years and older age groups (blue), and both combined (black). In each panel, observed data are plotted as dots, *LOESS* smoothed data as broken line, projected rates as solid line, and the shaded areas are 95% credible intervals of projected rates. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

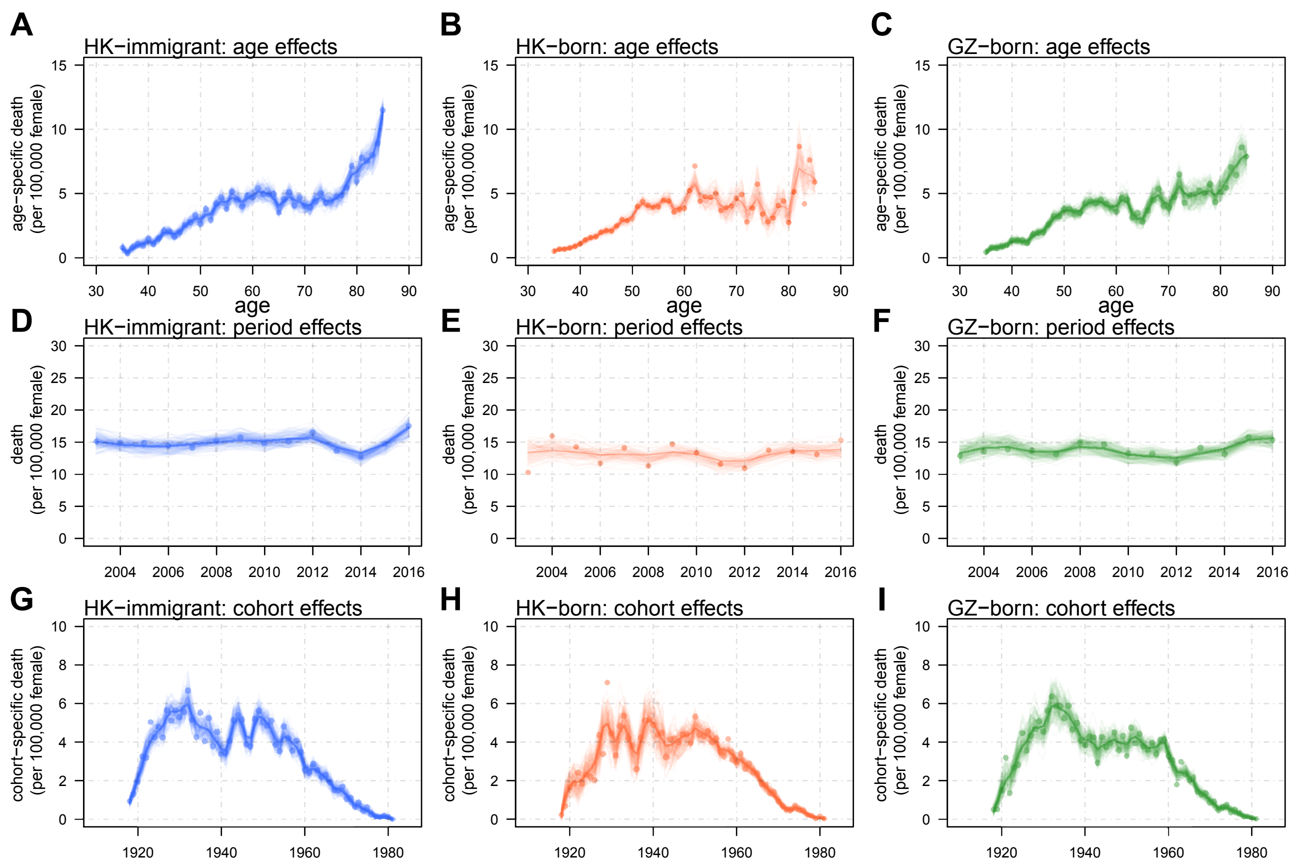

Fig. 2. Estimates of the age, period, and cohort effects on breast cancer mortality of HK-immigrant (panels A, D, and G), HK-born (panels B, E, and H), and GZ-born (panels C, F, and I). In each panel, dots are observed age-specific mortality rates, thick lines are mortality rates predicted from the APC model, and thin lines are the estimated from the APC models fitted to the 100 subdatasets randomly sampled by bootstrapping.

were found similar between the three populations. Age-standardized incidence rate in 2008 was 45.8 and 46.6 per 100,000 women in HK and GZ, respectively [53,54]. There is no strong evidence to suggest distinctive survival profiles between HK-born and GZ-born women. One study of the U.S. Asians from 1988 to 2005 demonstrated that immigrant status could partially explain the disparities in breast cancer survival rates between immigrants and local-born people, although they had different ethnicities [14]. Unfortunately, we do not have the incidence rate in HK immigrants. Future work is warranted when individual data become available for migrant status, cancer incidence, and mortality.

The strengths of our study lie in several aspects. First, we compared the immigrants with the other two ethnically homogeneous Chinese populations, and these three populations share similar culture and dietary habits. However, most previous studies often compared the data of minority immigrants with those of local populations with different ethnicities [11–14]. Second, our data were from two large and representative Chinese cities and divided into three groups according to birthplace and immigration status. We were able to compare the age, period, and cohort effects of immigrants with those in local-born populations and also with a representative population from the place of origin.

Table 3
Comparison of cohort-specific mortality rates of breast cancer (per 100,000 female population) between the HK-born, HK-immigrant, and GZ-born women

Cohort	HK immigrant vs. HK born			HK immigrant vs. GZ born			HK born vs. GZ born		
	Difference	95% CI	*P* value*	Difference	95% CI	*P* value*	Difference	95% CI	*P* value*
1931–1935	1.69	1.58, 1.8	<.0001	1.06	0.94, 1.18	<.0001	−0.63	−0.75, −0.52	<.0001
1936–1940	1.14	1.01, 1.28	<.0001	0.77	0.67, 0.86	<.0001	−0.38	−0.52, −0.24	<.0001
1941–1945	1.15	1.02, 1.28	<.0001	−0.2	−0.34, −0.12	.0001	−1.38	−1.5, −1.26	<.0001
1946–1950	−0.21	−0.35, −0.07	.0026	−0.5	−0.64, −0.42	<.0001	−0.32	−0.46, −0.18	<.0001
1951–1955	0.61	0.49, 0.73	<.0001	0.68	0.57, 0.78	<.0001	0.07	−0.04, 0.18	.2344
1956–1960	0.36	0.26, 0.46	<.0001	0.76	0.66, 0.86	<.0001	0.4	0.31, 0.49	<.0001
1961–1965	0.11	0.03, 0.18	.0078	0.34	0.25, 0.42	<.0001	0.23	0.17, 0.3	<.0001
1966–1970	0.19	0.11, 0.27	<.0001	−0.2	−0.25, −0.09	<.0001	−0.36	−0.42, −0.29	<.0001
1971–1975	−0.27	−0.32, −0.21	<.0001	0.02	−0.04, 0.08	.5636	0.28	0.22, 0.35	<.0001
1976–1980	0.12	0.05, 0.19	.001	−0.2	−0.32, −0.16	<.0001	−0.36	−0.43, −0.29	<.0001

CI = confidence interval.
* *P* value of *t* test.

Our study has some limitations. First, ecology fallacy cannot be avoided in this ecological study. Second, we do not have the records of the exact immigration time for individual subjects, so the assumption that the immigrants had similar early life exposure to the origin populations might not hold in some HK immigrants who came to HK in their early childhood. Third, there are many other factors that could have driven the temporal change of breast cancer mortality but remained unadjusted in our model, such as screening programs, promotion of the public awareness of breast cancer, and health services. Last but not least, due to the lack of incidence rate and individual data as well as the descriptive nature of the APC model, further individual-based research is needed to elucidate the mechanisms behind the discrepant patterns across these Chinese populations.

Conclusions

We found that HK-immigrant women had slightly higher age-specific mortality rates among three populations of Chinese women that share similar culture. The findings suggest that migrant status might somehow have affected the breast cancer mortality of Chinese women.

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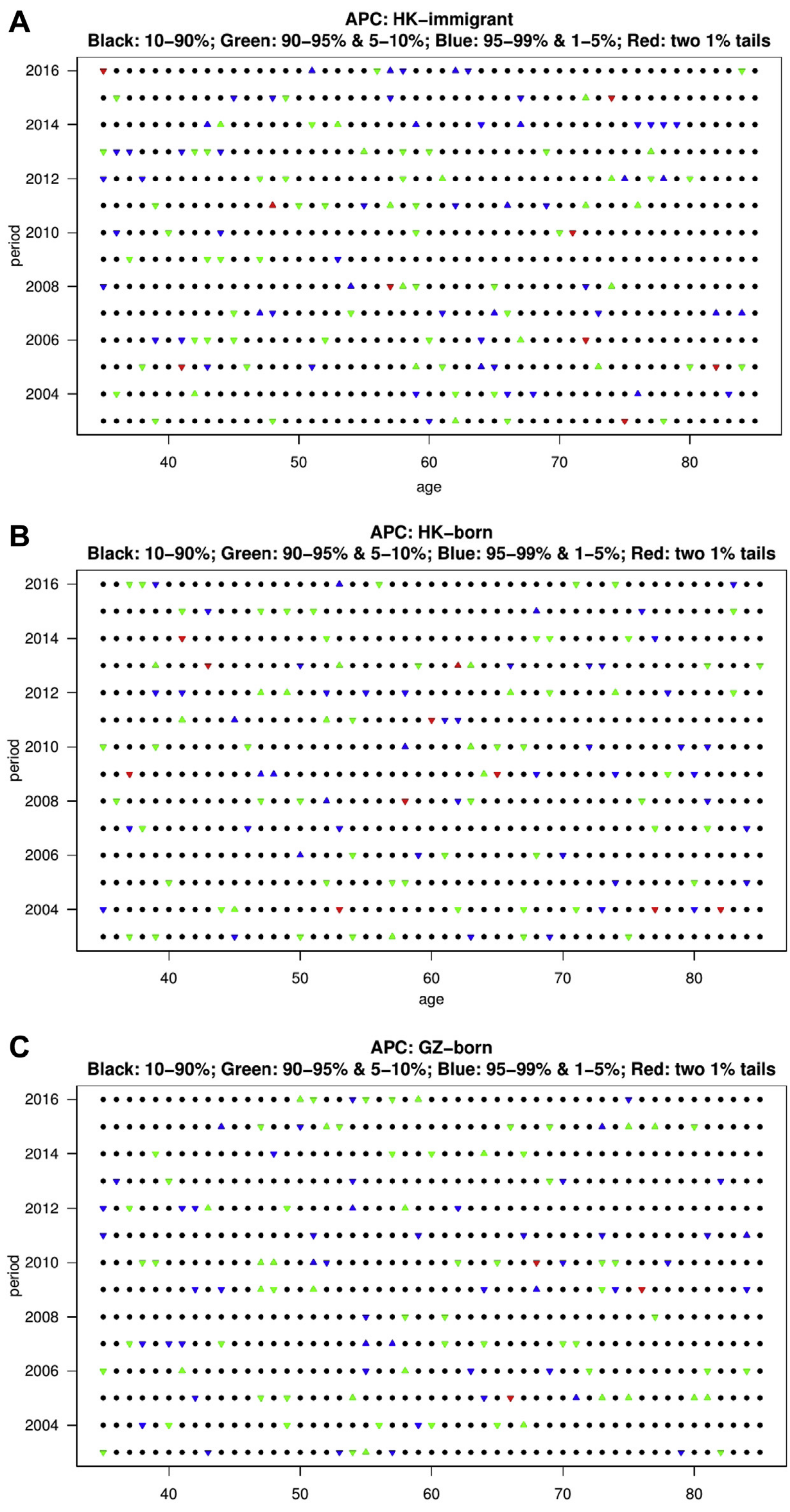
Appendix



Supplementary Figure 1. The fitting performance of the age-period-cohort models by age and period, among (A) the HK-immigrant, (B) HK-born and (C) GZ-born women. The black dots represent the fitting values are within the 80% quantile of the Poisson distribution according to the observation; green triangles are for 5–10% (upward) and 90–95% (downward); blue triangles are for 1–5% (upward) and 95–99% (downward); and red triangles are for the two 1% tails. The closer the APC model fit is to the median (i.e., 50% percentile) of one prior Poisson distribution the better the fitting performance. Thus, a higher proportion of black dots indicates a higher goodness of fit. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Supplementary Table 1
The fitting performance of the age-period-cohort models among Hong Kong immigrant women (HK-immigrant)

Model[a]	AIC	Increase of deviance	Decrease in d.f.	*P*-value of LR tests
Full APC model	3214.6	NA	NA	NA
Submodels				
AP	3200.5	109.9	62	<.001
AC	3210.5	19.8	12	.07
PC	4169.6	1053.0	49	<.001
Ad	3197.8	131.2	74	<.001
Pd	4580.4	1587.8	111	<.001
Cd	4170.0	1077.4	61	<.001
A	3217.8	153.2	75	<.001
P	5519.5	2528.9	112	<.001
C	4465.4	1374.8	62	<.001
t	4577.7	1609.1	123	<.001
tA	4597.7	1631.1	124	<.001
tP	5516.8	2550.1	124	<.001
tC	4741.0	1774.4	124	<.001
Constant only	5536.8	2572.2	125	<.001

A = age model; AC = age-cohort model; Ad = age drift model; AP = age-period model; AIC = Akaike information criterion; C = cohort model; Cd = cohort drift model; d.f. = degree of freedom; LR = likelihood ratio; P = period model; PC = period-cohort model; Pd = period drift model; t = trend model; tA = trend age model; tC = trend cohort model; tP = trend period model.
[a] The codes for the submodels are as follows.

Supplementary Table 2
The fitting performance of the age-period-cohort models among women born in Hong Kong (HK-born)

Model[a]	AIC	Increase of deviance	Decrease in d.f.	*P*-value of LR tests
Full APC model	2889.6	NA	NA	NA
Submodels				
AP	3032.2	266.6	62	<.001
AC	2879.1	13.4	12	.337
PC	3033.6	242.0	49	<.001
Ad	3019.9	278.3	74	<.001
Pd	4211.5	1543.9	111	<.001
Cd	3021.9	254.3	61	<.001
A	3152.1	412.5	75	<.001
P	4442.8	1777.2	112	<.001
C	3164.2	398.6	62	<.001
t	4199.2	1555.6	123	<.001
tA	4331.5	1689.9	124	<.001
tP	4430.5	1788.9	124	<.001
tC	4247.6	1606.0	124	<.001
Constant only	4562.7	1923.1	125	<.001

AIC = Akaike information criterion; d.f. = degree of freedom; LR = likelihood ratio.
[a] The submodel codes are the same as in Supplementary Table 1.

Supplementary Table 3
The fitting performance of the age-period-cohort models among women born in Guangzhou (GZ-born)

Model[a]	AIC	Increase of deviance	Decrease in d.f.	*P*-value of LR tests
Full APC model	3133.5	NA	NA	NA
Submodels				
AP	3162.1	152.6	62	<.001
AC	3136.7	27.2	12	.007
PC	3348.0	312.5	49	<.001
Ad	3158.7	173.3	74	<.001
Pd	3785.2	873.7	111	<.001
Cd	3345.2	333.8	61	<.001
A	3307.5	324.0	75	<.001
P	3793.4	883.9	112	<.001
C	3563.3	553.8	62	<.001
t	3781.8	894.4	123	<.001
tA	3930.5	1045.1	124	<.001
tP	3790.1	904.6	124	<.001
tC	3940.8	1055.3	124	<.001
Constant only	3938.8	1055.3	125	<.001

AIC = Akaike information criterion; d.f. = degree of freedom; LR = likelihood ratio.
[a] The submodel codes are the same as in Supplementary Table 1.