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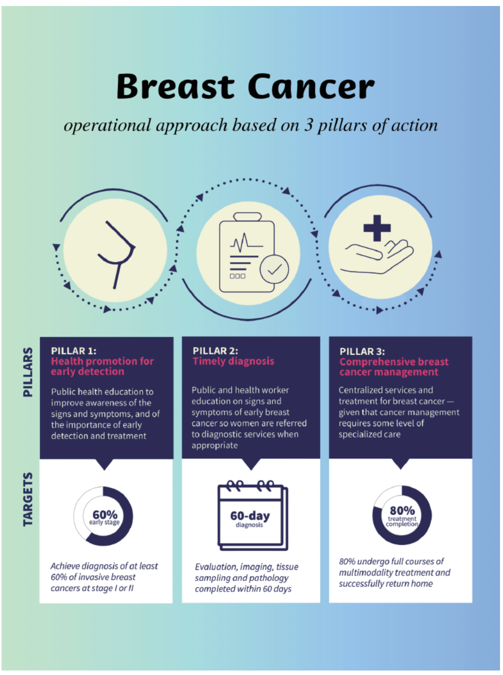

BREAST CANCER PREVENTION AND CONTROL ISSUE

Preplanned Studies

Vital Surveillances

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Cover Image: adapted from the World Health Organization, https://www.who.int/multi-media/details/global-breast-cancer-initiative-operational-approach-based-on-3-pillars-of-action.

This week's issue was organized by Guest Editor Linhong Wang.

Preplanned Studies

Breast Cancer Screening Coverage — China, 2018–2019

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Summary

What is already known about this topic?

In 2015, only 18.9% of adult women underwent breast cancer screening in China.

What is added by this report?

Breast cancer screening coverage for women aged 20 years and above in China reached 22.3% during 2018–2019. Women with lower socioeconomic status had lower screening coverage. There were significant variations across the provincial-level administrative divisions.

What are the implications for public health practice?

The promotion of breast cancer screening requires the maintenance of national and local policies, as well as financial support for screening services. In addition, there is a need for the strengthening of health education and the improvement of accessibility to health services.

Breast cancer became the most commonly diagnosed form of cancer worldwide in 2020, with approximately 2.3 million women affected, surpassing the number of new cases of lung cancer for the first time. It is still the primary cause of cancer mortality in women and is also the fifth most common cause of cancer deaths globally (*1*). China had 24% of newly diagnosed cases and 30% of cancer-related deaths worldwide in 2020 (*2*). The age-standardized incidence of breast cancer increased from 17.07 per 100,000 in 1990 to 35.61 per 100,000 in 2019 over the past three decades (*3*). Early detection, along with available, low-cost, and effective treatment, can result in improved cancer staging upon presentation and reduced mortality. To combat this rising incidence of breast cancer since the 1990s, China implemented a free screening program nationally in 2009 for rural women aged 35–64 years. During the course of the study, 18.9% of all women aged 20 and above and 25.7% of women aged 35 to 64 participated in breast cancer screening (*4*), slightly higher than rates in the early 2010s (*5*). This study aimed to provide an update on the current status of breast cancer screening levels in China, estimating the screening rates across subgroups using the latest nationally and provincially representative surveillance data. The findings showed that 22.3% of women aged 20 years and above and 30.9% of women aged 35–64 years have ever participated in breast cancer screening in China. Lower screening uptake was noted among women from lower socioeconomic status (SES); with considerable variations observed across provincial-level administrative divisions (PLADs).

This study utilized data from the sixth field survey named China Adults Chronic Disease and Nutrition Surveillance, which is part of the China Chronic Disease and Risk Factor Surveillance (CCDRFS), to estimate the latest uptake of breast cancer screening in China (*6*). The field survey was conducted from August 2018 to June 2019 in 298 districts/counties across all 31 PLADs directly under the central government in Chinese mainland. A multistage and cluster randomized sampling approach was used to select adults aged 18 years or older who had lived at their residence for more than 6 months in the past year, were not pregnant, and did not have serious health conditions or illnesses that would prevent participation, including intellectual disability or language disorders. Trained local health staff conducted interviews with all participants to collect information on major chronic diseases and related risk factors. Female participants were also asked about their breast cancer screening history and the date of their most recent screening, if applicable. The Ethical Committee of the National Center for Chronic and Noncommunicable Disease Control and Prevention and Chinese Center for Disease Control and Prevention approved the CCDRFS survey, and all participants provided written informed consent. A total of 184,876 participants completed the survey, yielding a response rate of 97.4%. After data cleaning, 184,509 participants (including 109,317 females) were included in the basic database. For the final analysis, 15,354 female participants were excluded due to their age being less than 20 years old, having incomplete sociodemographic data, or lacking responses to the breast cancer screening question. All estimates were weighted based on China's 2010 census, which was released by the National Bureau of Statistics. The chi-square test was used to analyze differences in unordered categorical variables, and logistic regression was employed to investigate trends with ordered categorical variables. A multiple logistic regression analysis based on complex sampling design was conducted, and standard errors (SEs) were estimated using Taylor linearization with a finite population correction. Statistical significance was determined using a two-sided *P*-value of less than 0.05. All statistical analyses were performed using SAS software (version 9.4, SAS Institute Inc., Cary, USA).

This study included a total of 93,963 female participants who were 20 years of age or older. As of 2018–2019, 54.8% of Chinese women lived in rural areas, 37.3% had received primary school education or less, and 46.4% had undergone health examinations within the past three years (Table 1).

In 2018–2019, among women aged 20 years and above, 22.3% [95% confidence interval (*CI*): 21.1%–23.5%] of women reported undergoing at least one lifetime screening for breast cancer. The rate was higher in women aged 35 to 64 years with a prevalence of 30.9% (95% *CI*: 29.2%–32.5%) (Table 2). When considering the past three years, 20.5% of women had undergone screening. The highest ever screening rate was among women aged 40–49 years, with a prevalence of 36.0% (95% *CI*: 33.9%–38.2%), while women aged 70 years and above had the lowest screening rates (4.3%, 95% *CI*: 3.7%–4.9%). The study also found that reporting breast screening was less likely among women with the lowest education level (16.6%, 95% *CI*: 15.3%–18.0%) or income (17.2%, 95% *CI*: 15.4%–19.1%), unemployed women (14.8%, 95% *CI*: 12.6%–17.0%), and women who had not undergone a health examination during the past 3 years (14.3%, 95% *CI*: 13.2%–15.4%). Urban women (24.5%, 95% *CI*: 22.4%–26.6) were more likely to undergo screening than rural women (20.6%, 95% *CI*: 18.8%–22.4%). Additionally, women living in eastern China had higher screening rates (27.0%, 95% *CI*: 25.1%–29.0%) than those in central (20.6%, 95% *CI*: 18.3%–22.8%) and western China (16.7%, 95% *CI*: 14.9%–18.6%).

A multivariate logistic regression analysis was conducted on women between the ages of 35 and 64. Results showed that the odds of receiving breast cancer screening were higher among rural women compared to urban women [odds ratio (*OR*)=1.25, 95% *CI*: 1.03–1.50]. However, the likelihood of breast cancer screening in eastern China was still higher compared to

TABLE 1. Sociodemographic characteristics of female participants aged 20 years and above, 2018–2019.

Characteristic	No. of participants (*N*=93,963)	Weighted proportion (%)*
Age (years)		
20–29	5,047	24.2
30–39	10,178	21.0
40–49	17,921	22.3
50–59	25,555	15.4
60–69	24,377	9.5
70 and above	10,885	7.7
Residence		
Urban	44,176	45.2
Rural	49,787	54.8
Location		
East	35,196	42.2
Middle	27,851	32.4
West	30,916	25.5
Education		
Primary or less	51,956	37.3
Secondary	24,755	29.9
High	10,640	14.7
College or above	6,612	18.0
Household income per capita (CNY)		
Q_1 (<7,200)	17,022	15.3
Q_2 (7,200–14,999)	19,310	19.0
Q_3 (15,000–24,999)	16,170	18.0
Q_4 (25,000 and above)	20,672	25.7
Don't know/refused	20,789	21.9
Employment status		
Employed	57,093	66.3
Housework	21,016	19.5
Retired	11,013	6.0
Unemployed	4,841	8.2
Health examination in the past 3 years		
No	56,992	53.6
Yes	36,971	46.4
Self-assessed health status		
Poor or fair	47,820	54.1
Good	46,143	45.9

Abbreviation: CNY=Chinese Yuan.

* Proportions are weighted to represent the national total population with poststratification for age, and urban/rural residence.

TABLE 2. Breast cancer screening rates among Chinese adult women by sociodemographic factors — China, 2018–2019.

Sociodemographic variable	Screening rates among 20 years and above					Screening rates among 35–64 years	
	Ever screened (%) (95% *CI*)				Screened in 3 years (%) (95% *CI*)	Ever screened (%) (95% *CI*)	*OR* (95% *CI*)
	Total	Urban	Rural	*P* value*			
Total	22.3 (21.1, 23.5)	24.5 (22.4, 26.6)	20.6 (18.8, 22.4)	<0.0001	20.5 (19.3, 21.7)	30.9 (29.2, 32.5)	
Age (years)							
20–29	10.8 (9.1, 12.6)	11.5 (8.7, 14.2)	10.3 (8.2, 12.4)	0.5242	10.6 (8.9, 12.3)	–	–
30–39	27.3 (25.5, 29.2)	29.8 (27.2, 32.4)	25.3 (22.3, 28.2)	0.0413	25.7 (23.7, 27.6)	–	–
40–49	36.0 (33.9, 38.2)	39.2 (35.6, 42.8)	33.7 (30.5, 36.9)	0.0510	33.4 (31.3, 35.4)	–	–
50–59	27.3 (25.4, 29.1)	31.1 (28.1, 34.2)	24.5 (21.7, 27.3)	0.0075	24.3 (22.6, 26.0)	–	–
60–69	14.7 (13.5, 16.0)	19.2 (17.1, 21.3)	11.5 (9.5, 13.5)	<0.0001	12.4 (11.2, 13.6)	–	–
70 and above	4.3 (3.7, 4.9)	6.6 (5.4, 7.8)	2.7 (2.0, 3.4)	<0.0001	3.4 (2.8, 3.9)	–	–
P value for difference	<0.0001	<0.0001	<0.0001		<0.0001		
Residence							
Urban	–	–	–		22.7 (20.7, 24.7)	34.4 (31.7, 37.2)	1.00 (Reference)
Rural	–	–	–		18.8 (17.1, 20.6)	28.2 (25.7, 30.8)	1.11 (0.86, 1.43)§
P value for difference					<0.0001	<0.0001	
Geographic location							
East	27.0 (25.1, 29.0)	29.2 (26.2, 32.2)	24.7 (21.2, 28.1)	0.1018	25.1 (23.2, 27.1)	37.1 (34.5, 39.6)	1.58 (1.33, 1.88)
Middle	20.6 (18.3, 22.8)	22.1 (17.7, 26.5)	19.6 (17.2, 22.1)	0.3440	18.5 (16.3, 20.6)	28.8 (25.7, 31.9)	1.22 (0.99, 1.50)
West	16.7 (14.9, 18.6)	17.5 (14.6, 20.5)	16.2 (13.6, 18.8)	0.5390	15.5 (13.8, 17.3)	23.5 (20.9, 26.2)	1.00 (Reference)
P value for difference	<0.0001	<0.0001	0.0003		<0.0001	<0.0001	
Education							
Primary or less	16.6 (15.3, 18.0)	16.3 (13.8, 18.9)	16.7 (15.0, 18.4)	0.8299	15.0 (13.7, 16.3)	22.2 (20.3, 24.0)	1.00 (Reference)
Secondary	25.1 (23.3, 26.9)	25.9 (23.3, 28.4)	24.7 (22.0, 27.3)	0.5658	22.9 (21.2, 24.6)	33.8 (31.7, 35.8)	1.41 (1.23, 1.62)§
High	27.5 (25.1, 29.9)	29.0 (25.9, 32.1)	25.3 (21.3, 29.3)	0.1867	25.5 (23.2, 27.8)	39.0 (35.8, 42.2)	1.40 (1.15, 1.70)§
College or above	25.2 (22.8, 27.7)	26.6 (23.9, 29.2)	20.3 (15.0, 25.6)	0.0573	24.1 (21.7, 26.5)	48.7 (45.2, 52.2)	1.84 (1.49, 2.28)§
P value for trend	<0.0001	<0.0001	<0.0001		<0.0001	<0.0001	

TABLE 2. (Continued)

Sociodemographic variable	Screening rates among 20 years and above					Screening rates among 35–64 years	
	Ever screened (%) (95% *CI*)				Screened in 3 years (%) (95% *CI*)	Ever screened (%) (95% *CI*)	*OR* (95% *CI*)
	Total	Urban	Rural	*P* value*			
Household income per capita (CNY)							
Q_1 (<6,000)	17.2 (15.4, 19.1)	16.2 (12.6, 19.8)	17.5 (15.4, 19.6)	0.5789	15.4 (13.7, 17.2)	23.7 (21.1, 26.2)	1.00 (Reference)
Q_2 (6,000–12,499)	19.1 (17.7, 20.6)	19.7 (17.5, 21.9)	18.9 (16.9, 20.8)	0.6290	17.8 (16.3, 19.2)	26.9 (25.0, 28.8)	1.08 (0.93, 1.24)
Q_3 (12,500–23,999)	24.4 (22.4, 26.4)	24.4 (22.0, 26.9)	24.4 (21.3, 27.6)	0.9978	22.5 (20.6, 24.4)	33.4 (31.2, 35.7)	1.21 (1.04, 1.40)
Q_4 (24,000 and above)	29.7 (27.6, 31.7)	30.0 (27.4, 32.6)	28.9 (24.5, 33.3)	0.7105	27.4 (25.3, 29.4)	40.8 (38.5, 43.1)	1.36 (1.16, 1.58)
Don't know or refused	18.3 (16.5, 20.1)	20.1 (17.3, 23.0)	16.8 (14.4, 19.3)	0.1148	17.0 (15.2, 18.7)	25.6 (22.9, 28.3)	0.93 (0.79, 1.11)
P value for trend†	<0.0001	<0.0001	<0.0001		<0.0001	<0.0001	
Employment status							
Employed	23.7 (22.4, 25.1)	26.7 (24.4, 28.9)	21.6 (19.6, 23.6)	0.0035	22.1 (20.8, 23.4)	31.6 (29.8, 33.3)	1.00 (Reference)
Housework	19.4 (17.5, 21.4)	20.2 (16.7, 23.6)	19.1 (16.6, 21.6)	0.6575	17.8 (15.9, 19.7)	28.1 (25.8, 30.4)	1.01 (0.92, 1.11)
Retired	26.1 (23.5, 28.6)	26.1 (23.4, 28.8)	25.6 (12.8, 38.3)	0.9390	21.4 (18.9, 23.9)	33.1 (29.7, 36.6)	0.95 (0.81, 1.11)
Unemployed	14.8 (12.6, 17.0)	15.3 (12.5, 18.1)	14.2 (10.6,17.7)	0.6478	13.9 (11.7, 16.1)	28.7 (24.7, 32.7)	0.90 (0.72, 1.22)
P value for difference	<0.0001	<0.0001	0.0068		<0.0001	0.0085	
Health examination in past 3 years							
No	14.3 (13.2, 15.4)	13.1 (11.4, 14.9)	14.9 (13.5, 16.4)	0.1577	12.5 (11.5, 13.6)	19.4 (17.9, 20.9)	1.00 (Reference)
Yes	31.8 (30.2, 33.4)	33.4 (31.2, 35.7)	29.8 (27.3, 32.4)	0.0628	30.0 (28.4, 31.6)	45.6 (43.7, 47.6)	3.17 (2.95, 3.41)
P value for difference	<0.0001	<0.0001	<0.0001		<0.0001	<0.0001	
Self-assessed health status							
Poor or fair	23.0 (21.6, 24.4)	25.9 (23.7, 28.1)	20.8 (18.8, 22.8)	0.0026	21.0 (19.7, 22.4)	31.1 (29.3, 32.9)	1.15 (1.05, 1.27)
Good	21.6 (20.2, 22.9)	23.1 (20.7, 25.4)	20.3 (18.2, 22.3)	0.1232	20.0 (18.6, 21.3)	30.6 (28.6, 32.6)	1.00 (Reference)
P value for difference	0.0464	0.0053	0.5666		0.1275	0.6084	

Note: The screening rates presented in this study are weighted proportions that have been adjusted for age through poststratification to ensure representation of the entire national population.
Abbreviation: *CI*=confidence interval; CNY=Chinese Yuan.
* *P* value denotes the difference between urban screening coverage and rural screening coverage in women aged 20 years and above.
† Participants who responded with "don't know/refused" were excluded from the calculation.
§ The model accounted for the interaction between residence and education.

western China (*OR*=1.58, 95% *CI*: 1.33–1.88). Additionally, the odds of screening were three times higher among women who had received a health examination within the past three years compared to those who had not (*OR*=3.17, 95% *CI*: 2.95–3.41) (Table 2).

In Beijing, over 40% of women aged 20 years and above and more than 60% of women aged 35–64 years underwent screening, and in economically developed eastern coastal PLADs such as Jiangsu Province, Zhejiang Province, Tianjin, and Shanghai, more than 30% of women aged 20 years and above and 40% of women aged 35–64 years underwent screening. In contrast, the Xizang (Tibet) Autonomous Region, Guizhou Province, and Hebei Province demonstrated the lowest rates of screening, all below 10%. Refer to Figure 1 for more details.

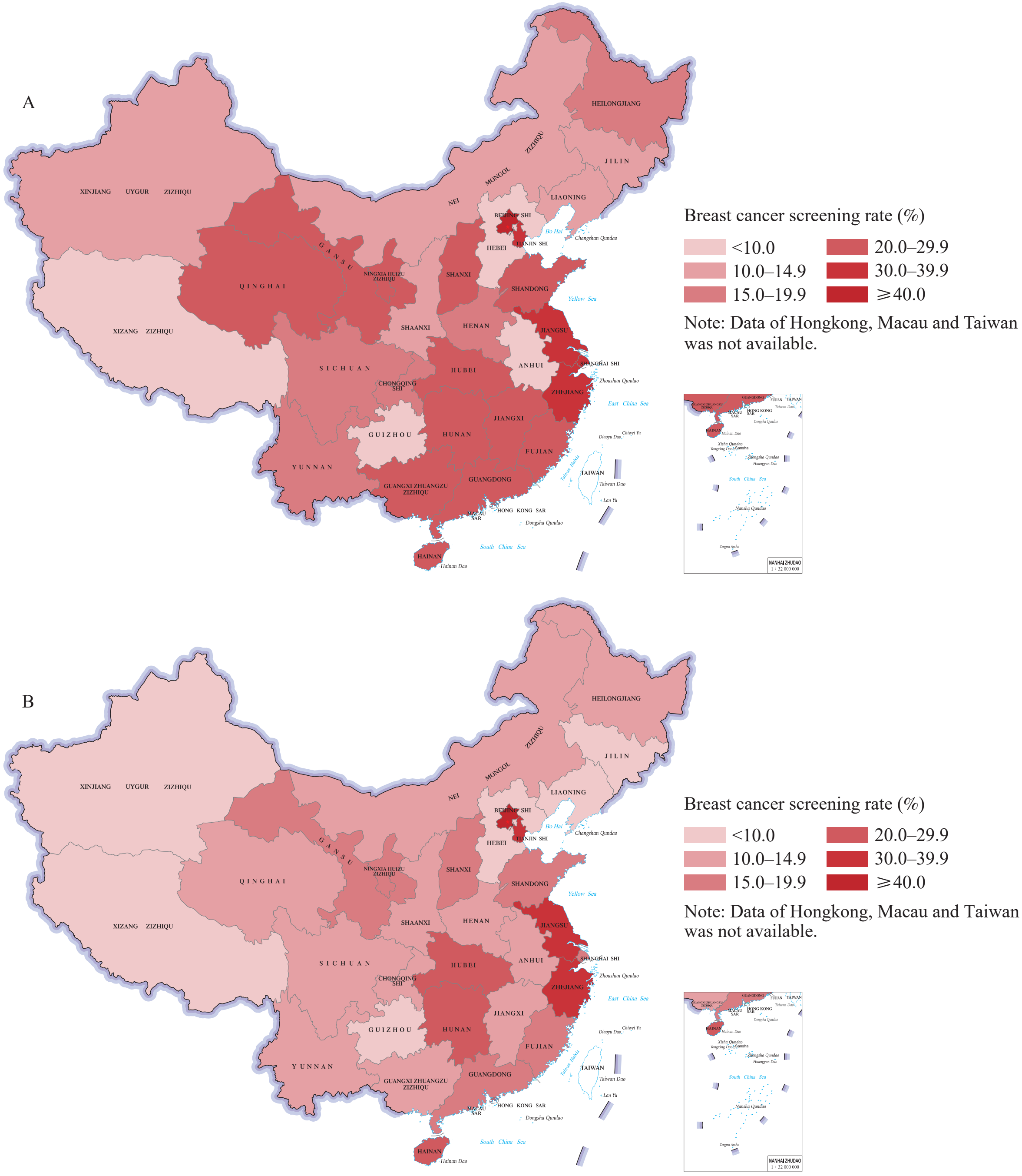

FIGURE 1. Provincial variations in breast cancer screening coverage in adult women in China, 2018–2019. (A) Screening rate among 20 years and above; (B) Screening rates among 35–64 years.

DISCUSSION

According to the findings of the China CDC, the use of breast cancer screening among adult women in China continues to be inadequate. Although there has been a slight increase in breast cancer screening rates for women aged 20 years and above, as well as for those aged 35–64 years, when compared to the statistics of 2015, the breast cancer screening coverage is still way below the standard in developed countries (*7*). As of 2018, more than 1,700 counties had conducted breast cancer screening programs (*8*). Since 2022, the scope of free screening services has been broadened to include both urban and rural women. However, this study reveals that despite the expansion of breast cancer screening programs, the proportion of women availing of screening services is still considerably low.

Numerous factors have the potential to restrict the uptake of cancer screening in women, including but not limited to low socioeconomic status, cultural barriers, and cancer fatalism (*9*). Upon conducting this study, we discovered that women who underwent health examinations were significantly more likely to obtain cancer screening even when other potential restricting factors were accounted for. This outcome underscores the significance of both accessible health services and effective health education.

There are two limitations to be taken into account. Initially, the self-reported screening history may have been subject to recall bias. To minimize this, the interviewers were instructed to carefully define and explain the types of breast cancer screening and assist participants in recalling the timing of their last test. Second, the CCDRFS did not collect information on the reasons for non-participation in screening.

Based on nationally and provincially representative survey data from 2018–2019, this study provides the most current estimate of breast cancer screening coverage in China. Women aged 20 years and older had a breast cancer screening coverage of 22.3%, while women aged 35–64 years had a coverage of 30.9%. Women with lower socioeconomic status had lower screening coverage, and there were still significant disparities across PLADs. To increase the utilization of breast cancer screening, it is crucial to continue national and local policies and provide financial support for breast cancer screening services. Additionally, health education and accessibility of health services should be strengthened, particularly in targeted age groups, those with low SES, and underdeveloped PLADs, to encourage more women to participate in screening.

Conflicts of interest: No conflicts of interest.

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Preplanned Studies

Breast Cancer Awareness and Association with Frequency of Screening Among Women — China, 2020

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Summary

What is already known about this topic?

Breast cancer awareness plays a crucial role in promoting screening attendance, enabling early detection, and improving survival rates associated with breast cancer. Nevertheless, a persistent issue is the low public awareness of breast cancer warning signs and risk factors.

What is added by this report?

Breast cancer awareness rate was 10.2%, with particularly low rates among never-screened and inadequately screened women. Factors associated with low awareness levels included low income, agricultural occupation, limited educational attainment, smoking, and the absence of professional recommendations.

What are the implications for public health practice?

Consideration should be given to effective health education and delivery strategies aimed at women who have never been screened or have received inadequate screening.

Breast cancer is the most prevalent cancer among women worldwide (*1*). Early detection of breast cancer can enhance survival rates, while delayed diagnoses are often linked to low breast cancer awareness, such as recognizing early warning signs (*2*). Furthermore, insufficient awareness acts as a barrier to both attending screening appointments and adhering to follow-up procedures. Breast cancer awareness among Chinese women has been documented as low (*3*); however, the data have not been updated in recent years. Notably, only 25% of women in China have undergone breast cancer screening (*4*), and limited information is available on breast cancer awareness among never-screened or inadequately screened women.

This population-based cohort study on female breast cancer encompassed 63,219 participants, with an average of 5.3 person-years of follow-up. The findings revealed a breast cancer awareness rate of 10.2%, with particularly low rates among never-screened and inadequately screened women. Factors associated with low awareness levels included low income, agricultural occupation, limited educational attainment, smoking, and the absence of professional recommendations. These results highlight the urgent need for effective health education and targeted delivery strategies to mitigate breast cancer risks.

The study population was derived from the breast cancer cohort study in Chinese women, a population-based cohort focused on precise prevention of breast cancer (*5*). During 2008–2009, 81,191 women aged 25–70 years participated in breast cancer screening and completed an in-person interview. From March 2018 to October 2020, the original participants were followed, and other eligible women residing in the same areas, aged 25–70 years, and not pregnant, were recruited. Ultimately, a total of 63,219 women who completed the interview, clinical examination, and sample collection were included in the standardized cohort. All study participants provided informed consent.

In this study, trained research personnel administered a 30-minute self-developed questionnaire to collect information on participants' demographic characteristics, reproductive history, lifestyle and behaviors, family history, and knowledge of breast cancer. The frequency of breast cancer screening (i.e., clinical examination, ultrasound, and mammography) was assessed based on the most recent date recorded in the baseline data and participants' self-reported screening history. Consequently, women were categorized into three groups: never screened, screened more than three years ago, and screened within the past two years.

The primary outcome assessed in this study was breast cancer awareness at follow-up, measured through a 12-item questionnaire and in-person interviews. The questionnaire comprised three sections: 1) identification of lump and non-lump symptoms, 2) recognition of modifiable and non-modifiable risk factors, and 3) engagement in breast self-examination (BSE). We utilized a modified definition for breast cancer awareness based on the Breast Cancer Awareness Measure (BCAM) and its applicability within the context of China (*6*). A woman was deemed to be aware of breast cancer if she met the following criteria: identification of at least three symptoms among the list of five provided, acknowledgment of a minimum of one non-modifiable risk factor from the list of three provided, and reported BSE in the past year. Additionally, we established definitions for knowledge of symptoms and risk factors (Table 1).

We estimated the overall breast cancer awareness rate by screening frequency. The bootstrap method, employing 500 resampling iterations, was utilized to calculate 95% confidence intervals (*CI*). The χ^2 test with Rao-Scott correction was implemented to evaluate differences. A mixed-effect regression model, featuring a random intercept for the county, was fitted to investigate associations between screening frequency, demographic and socioeconomic factors, behaviors, family history, professional recommendations, and interaction terms, in relation to breast cancer awareness, while controlling for age and its quadratic and cubic terms. Subsequently, the ggeffects package enabled the calculation of age-specific awareness fitted values by maintaining other covariates at constant values. All analyses were conducted using SAS (version 9.4; SAS Institute, Cary, USA) and R software (version 4.2.2; R Foundation for Statistical Computing, Vienna, Austria).

In the standardized cohort of 63,219 participants, the mean age was 47.5 years (standard deviation=11.0).

TABLE 1. Breast cancer awareness by frequency of screening among women — China, 2020.

Item	Overall		Frequency of screening [% (95% *CI*)][§§]			
	N	Rate [% (95% *CI*)]	Never (*n*=22,331)	Screened over 3 years (*n*=23,573)	Screened within 2 year (*n*=16,839)	*P*
1 Breast cancer symptoms						
1.1 Lump in breast	62,517	50.0 (49.6–50.4)	46.5 (39.9–53.1)	42.5 (37.4–47.5)	65.4 (59.6–71.1)	<0.001
1.2 Lump under armpit	62,517	42.7 (42.3–43.1)	40.1 (32.4–47.9)	34.9 (30.4–39.5)	57.1 (51.4–62.9)	<0.001
1.3 Puling in of nipple	62,517	37.5 (37.1–37.8)	34.6 (27.7–41.5)	30.5 (26.3–34.7)	51.1 (44.0–57.3)	<0.001
1.4 Discharge from nipple	62,518	37.9 (37.5–38.3)	34.6 (27.6–41.5)	30.9 (26.8–35.0)	52.1 (45.9–58.4)	<0.001
1.5 Pain in breast	62,518	44.2 (43.8–44.6)	39.4 (31.6–47.3)	37.7 (32.8–42.7)	59.7 (53.2–66.1)	<0.001
2 Risk factors related to breast cancer						
2.1 Menarche before age 12 years	62,519	20.8 (20.4–21.1)	19.7 (14.5–24.9)	16.8 (13.6–20.0)	27.7 (22.2–33.2)	<0.001
2.2 Reproductive history	62,519	22.5 (22.2–22.9)	20.9 (15.6–26.3)	18.1 (15.1–21.2)	30.9 (26.0–35.8)	<0.001
2.3 Menopause after age 55 years	62,519	21.7 (21.3–22.0)	20.5 (15.2–25.8)	17.7 (14.7–20.7)	28.8 (23.6–34.0)	<0.001
2.4 Drinking alcohol	62,517	28.6 (28.2–29.0)	25.6 (19.3–31.9)	24.0 (21.0–26.9)	39.1 (33.8–44.5)	<0.001
2.5 Taking hormones	62,519	29.7 (29.3–30.0)	26.1 (19.7–32.5)	24.8 (21.7–27.9)	41.2 (35.2–47.2)	<0.001
2.6 Family history of breast cancer	62,517	34.7 (34.3–35.1)	31.5 (24.6–38.3)	29.4 (25.7–33.0)	46.6 (39.3–53.9)	<0.001
3 Breast self-examination	62,743	20.2 (19.9–20.5)	8.1 (5.5–10.6)	13.9 (10.3–17.4)	45.2 (36.4–54.0)	<0.001
4 Knowledge of breast cancer symptom*	62,517	41.0 (40.6–41.4)	37.2 (29.9–44.6)	33.8 (29.5–38.1)	56.1 (50.2–62.1)	<0.001
4.1 Knowledge of non-lump symptoms[†]	62,517	38.2 (37.8–38.5)	34.7 (27.8–41.7)	31.3 (27.2–35.4)	52.4 (46.2–58.6)	<0.001
5 Knowledge of breast cancer risk factors[§]	62,517	27.7 (27.3–28.1)	24.8 (18.7–30.9)	22.9 (19.9–25.9)	38.5 (33.1–43.8)	<0.001
5.1 Knowledge of changeable factors[¶]	62,517	33.4 (33.0–33.8)	29.6 (22.2–37.0)	28.3 (25.0–31.6)	45.7 (39.4–52.0)	<0.001
5.2 Knowledge of unchangeable factors**	62,517	37.1 (36.7–37.5)	33.8 (26.5–41.1)	31.5 (27.9–35.1)	49.2 (42.1–56.4)	<0.001
6 Breast cancer awareness[††]	62,654	10.2 (9.9–10.5)	3.9 (1.9–6.0)	6.1 (4.2–8.1)	24.4 (18.2–30.6)	<0.001

Abbreviation: *CI*=confidence interval.

* identify >3 symptoms.

† identify at least 1 non-lump symptom (1.3, 1.4, and 1.5).

§ identify >2 risk factors.

¶ identify at least 1 changeable risk factor (2.2, 2.4, and 2.5).

** identify at least 1 unchangeable risk factor (2.1, 2.3, and 2.6).

†† meet 4, 5.2, and 6, simultaneously.

§§ 476 cases are missing.

Among these individuals, 53.1% had attained a primary school education or lower, 68.3% reported a monthly household income per capita of 3,000 CNY or less, 15.0% had a family history of cancer, 1.1% were smokers, and 4.8% were drinkers (data not shown).

The overall breast cancer awareness rate was found to be 10.2% (95% *CI*: 9.9%–10.5%), with a notably lower rate observed among women who had never been screened or had not been screened in over 3 years (Table 1). Knowledge regarding breast cancer symptoms varied, with 37.5% to 50.0% of the surveyed women being aware of the different symptoms. In comparison, awareness of risk factors was lower than that of symptoms, with figures ranging from 20.8% to 34.7%.

More specifically, 38.2% (95% *CI*: 37.8%–38.5%) of the participants were able to correctly identify non-lump symptoms, 27.7% (95% *CI*: 27.3%–28.1%) demonstrated knowledge of risk factors, and 20.2% (95% *CI*: 19.9%–20.5%) reported having conducted a BSE within the past year. For each of these items, the awareness rate among women who had been screened within the past two years was significantly higher compared to those who had never been screened or had not been screened in over three years.

Breast cancer awareness was notably higher in women who had been screened within the past two years (*OR*=6.26, 95% *CI*: 4.36–9.01) and those screened over three years ago (*OR*=1.99, 95% *CI*: 1.36–2.91), compared to unscreened women (Table 2). A significant interaction was observed between screening frequency, household income, education, and awareness. Middle and high household income levels, as well as junior school education or higher, were associated with increased awareness. However, these associations were diminished in women screened within two years and those screened over three years, rendering them insignificant. Additionally, breast cancer awareness was linked to nonagricultural occupations, alcohol consumption, family history of cancer, and professional recommendations for screening. Comparable patterns were found for knowledge of symptoms, risk factors, and BSE. Nevertheless, elevated odds in women screened over three years were not observed for knowledge of symptoms and risk factors. In contrast, a high frequency of screening amplified the disparities in knowledge attributed to education.

Figure 1 displays the age-specific breast cancer awareness among women, broken down by the frequency of screening. It was found that overall breast cancer awareness, understanding of symptoms and risk factors, as well as BSE, were notably higher in women who had been screened within the past two years compared to those in other groups. Additionally, breast cancer awareness in women under the age of 50 was observed to be higher than in their older counterparts.

DISCUSSION

Our study demonstrates that 10.4% of women possess awareness of breast cancer, with the lowest level of awareness observed among those who have never undergone screening. Lower awareness is associated with socioeconomic factors such as low socioeconomic status, agricultural occupations, smoking, and lack of professional recommendations for screening. To the best of our knowledge, this is the largest cohort study to date that examines breast cancer awareness in Chinese women and specifically analyzes awareness according to screening frequency. These findings emphasize the necessity for health education initiatives targeting breast cancer, particularly for women who have never been screened or have undergone inadequate screening.

Consistent with prior research conducted in China (18.6%) (*3*), the present study identifies a substantial gap in breast cancer awareness among Chinese women, primarily due to their limited knowledge of risk factors and BSE practices. Regardless of screening frequency, fewer than 40% of women were found to be aware of both modifiable and non-modifiable risk factors for breast cancer. In this investigation, we employed a modified definition of BCAM that does not include older age as a non-modifiable factor, which consequently led to more challenging questions and decreased levels of awareness. This decision was made based on the observation that peak breast cancer incidence in Chinese women occurs around menopause, rather than increasing with age (*7*). Gaining knowledge of non-modifiable risk factors not only enables women to assess their own risk but also encourages adherence to routine screening and timely diagnosis (*8*). While BSE is not widely endorsed as a method for reducing mortality (*9*), conducting regular BSEs can positively impact women's awareness and facilitate early detection (*10*).

Increased awareness of breast cancer contributes to higher rates of screening attendance and subsequent diagnoses (*2*). Our study findings reveal a notably low level of awareness among unscreened women,

TABLE 2. Associations between screening frequency, potential factors, and breast cancer awareness among women — China, 2020.

Independent variable	Model 1: breast cancer awareness*		Model 2: knowledge of breast cancer symptom†		Model 3: knowledge of breast cancer risk factor§		Model 4: breast self-examination¶	
	OR (95% *CI*)	*P*	*OR* (95% *CI*)	*P*	*OR* (95% *CI*)	*P*	*OR* (95% *CI*)	*P*
Frequency of screening (*vs*. never)								
Screened over 3 years	1.99 (1.36–2.91)	<0.001	0.98 (0.88–1.09)	0.69	0.99 (0.86–1.13)	0.83	2.03 (1.67–2.46)	<0.001
Screened within 2 years	6.26 (4.36–9.01)	<0.001	1.42 (1.24–1.62)	<0.001	1.44 (1.23–1.68)	<0.001	4.59 (3.76–5.60)	<0.001
Occupation (*vs*. agricultural occupation)								
Non-agricultural occupation	1.78 (1.63–1.94)	<0.001	1.31 (1.24–1.39)	<0.001	1.58 (1.49–1.67)	<0.001	1.57 (1.46–1.68)	<0.001
Housework/unemployed	1.24 (1.14–1.36)	<0.001	0.93 (0.89–0.98)	0.003	1.10 (1.04–1.16)	<0.001	1.20 (1.12–1.27)	<0.001
Household income per capita per month (*vs*. <1,000)								
1,000–2,999	2.00 (1.43–2.79)	<0.001	1.64 (1.50–1.80)	<0.001	1.56 (1.40–1.74)	<0.001	1.28 (1.07–1.53)	0.007
3,000 and more	3.07 (2.19–4.30)	<0.001	2.22 (2.01–2.45)	<0.001	2.45 (2.18–2.75)	<0.001	1.41 (1.17–1.69)	<0.001
Education (junior school and higher *vs*. primary school and lower)	2.20 (1.83–2.64)	<0.001	1.80 (1.69–1.92)	<0.001	1.59 (1.48–1.71)	<0.001	1.28 (1.14–1.43)	<0.001
Pregnancy (*vs*. never)								
1 pregnancy	1.17 (0.89–1.53)	0.26	1.26 (1.08–1.46)	0.003	1.13 (0.96–1.33)	0.13	1.19 (0.97–1.47)	0.10
2 pregnancies and more	1.02 (0.78–1.33)	0.89	1.31 (1.13–1.52)	<0.001	1.05 (0.90–1.23)	0.51	1.11 (0.91–1.36)	0.31
Smoking (smoker *vs*. non-smoker)	0.75 (0.48–1.18)	0.21	0.70 (0.57–0.86)	<0.001	0.71 (0.56–0.91)	0.006	0.90 (0.68–1.18)	0.44
Alcohol (drinker *vs*. non-drinker)	1.26 (1.12–1.42)	<0.001	1.04 (0.95–1.13)	0.40	1.00 (0.92–1.10)	0.91	1.25 (1.13–1.38)	<0.001
Family history of cancer (Yes *vs*. No)	1.25 (1.16–1.34)	<0.001	1.30 (1.24–1.36)	<0.001	1.16 (1.10–1.22)	<0.001	1.24 (1.17–1.32)	<0.001
Professional recommendation (Yes *vs*. No)	>3.34 (3.13–3.57)	<0.001	1.29 (1.23–1.36)	<0.001	1.30 (1.24–1.37)	<0.001	5.62 (5.32–5.93)	<0.001
Interaction between household income and screening frequency (*vs*. low × never)								
Middle × screened over 3 years	1.02 (0.69–1.51)	0.94	1.03 (0.91–0.16)	0.65	1.21 (1.05–1.40)	0.009	0.93 (0.75–1.15)	0.51
Middle × screened within 2 years	0.77 (0.53–1.12)	0.17	1.07 (0.94–1.24)	0.31	1.02 (0.87–1.20)	0.77	0.92 (0.74–1.14)	0.43
High × screened over 3 years	0.86 (0.58–1.28)	0.47	0.93 (0.81–1.05)	0.24	0.94 (0.80–1.09)	0.39	0.86 (0.69–1.07)	0.17
High × screened within 2 years	0.67 (0.46–0.97)	0.04	1.05 (0.91–1.22)	0.49	0.81 (0.69–0.96)	0.01	0.92 (0.74–1.14)	0.43
Interaction between education and screening frequency (*vs*. primary school × never)								
Junior school × screened over 3 years	0.94 (0.75–1.17)	0.58	1.21 (1.11–1.32)	<0.001	1.15 (1.04–1.27)	0.004	1.02 (0.89–1.17)	0.77
Junior school × screened within 2 years	0.74 (0.61–0.91)	0.003	1.10 (1.00–1.20)	0.04	1.11 (1.00–1.22)	0.04	0.99 (0.87–1.14)	0.92

Note: All four models are adjusted for age, quadratic term, and cubic term of age.
Abbreviation: *OR*=odds ratio; *CI*=confidence interval.
* In Model 1, the dependent variable is breast cancer awareness (*6*).
† In Model 2, the dependent variable is knowledge of all five breast cancer symptoms (*4*).
§ In Model 3, the dependent variable is knowledge of all six breast cancer risk factors (*5*).
¶ In Model 4, the dependent variable is breast self-examination (*3*).

emphasizing the urgent need to prioritize this population in future health education programs. Additionally, our results demonstrate a positive correlation between breast cancer screening and awareness, as well as socioeconomic disparities. However, this effect may diminish over time. When the screening interval exceeds 3 years, participants' awareness drops to levels comparable to those of unscreened individuals. This highlights the importance of regular health education initiatives to maintain and promote breast cancer prevention awareness at the population level.

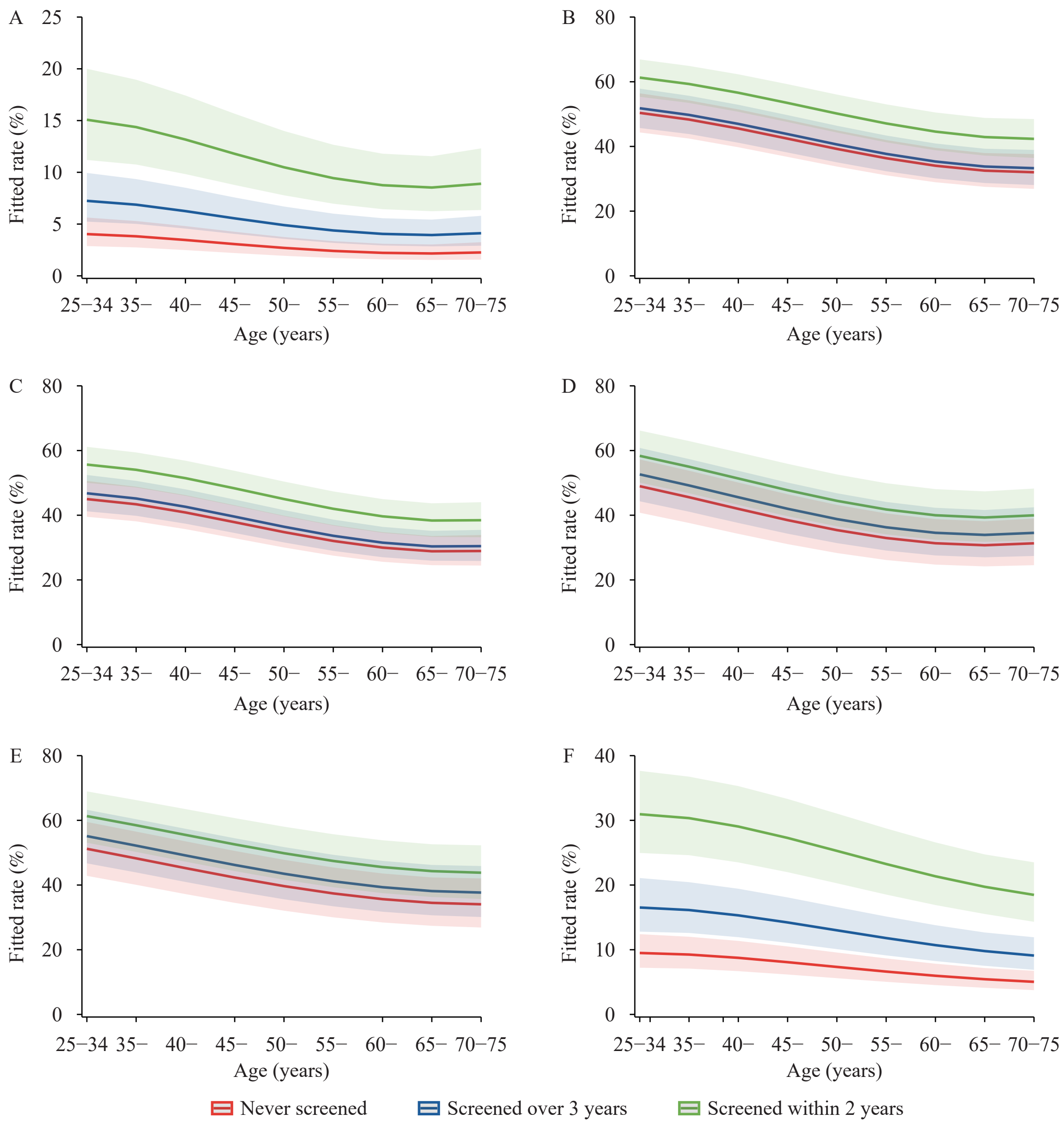

FIGURE 1. Fitted age-specific breast cancer awareness by frequency of screening among women — China, 2020. (A) Breast Cancer Awareness; (B) Knowledge of breast cancer symptoms; (C) Knowledge of breast cancer non-lump symptoms; (D) Knowledge of modifiable breast cancer risk factors; (E) Knowledge of non-modifiable breast cancer risk factors; (F) Breast self-examination.

Conversely, frequent screening has been found to slightly exacerbate the disparity in awareness among groups with different education levels. This phenomenon can be partially attributed to the lack of targeted health education strategies for women with lower education levels. In line with previous research (*8*), our study reveals that women exhibiting lower awareness are more likely to be older, smokers, possess lower education and income, and lack professional recommendations. Our findings offer insights into potential areas for targeted health education, including the utilization of informational booklets, verbal interactions, and future investigation of effective intervention strategies.

A primary limitation of this study is the lack of consideration for the impact of baseline breast cancer awareness among newly recruited participants. However, this is unlikely to alter the conclusion as all participants reside in the same geographic regions and share similar demographic attributes and cultural backgrounds.

In conclusion, awareness of breast cancer remains limited in China, particularly among women who have not received screening or have been inadequately screened. Emphasis should be placed on implementing effective health education and targeted delivery strategies within this population.

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Preplanned Studies

Depressive Symptoms and Sleep Duration as Risk Factors for Breast Cancer — China, 2020

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Summary

What is already known about this topic?

Psychological and lifestyle factors are known to potentially play a significant role in the development of breast cancer. However, current evidence-based studies present controversial findings on the associations between depression, sleep duration, and breast cancer risk.

What is added by this report?

This study investigated the potential risk factors of depressive symptoms and short sleep duration for breast cancer within the Breast Cancer Cohort Study in Chinese Women. The findings revealed that women experiencing depressive symptoms and short sleep duration exhibited a heightened risk of developing breast cancer, particularly among the older population.

What are the implications for public health practice?

Public policy ought to prioritize early health education interventions targeting psychological factors in order to facilitate the prevention of breast cancer.

Breast cancer is the most common cancer and a leading cause of morbidity and mortality among women worldwide (*1*). In China, approximately 420,000 new breast cancer cases occur annually, accounting for 16.72% of all new cancer cases. Psychological and lifestyle factors, such as depression and poor sleep, may be more prevalent among breast cancer patients. Depression significantly impacts individuals' daily lives, affecting approximately 300 million people worldwide (*2*). In China, the prevalence rates of depression are 5.4% for women and 2.7% for men (*3*). Sleep is essential for emotional and physical health, and poor sleep habits may increase the risk of cancer and mental disorders (*4*). Persistent insomnia can exacerbate depressive symptoms; indeed, sleep disorders and depression often co-occur and interact. The roles of depression and sleep duration in breast cancer development have been investigated in numerous studies, but the results have been inconsistent.

This study aimed to examine the associations of depressive symptoms and sleep duration with breast cancer among Chinese women using data from the breast cancer cohort study in Chinese women (BCCS-CW). Our findings indicated that women with depressive symptoms experienced an increased risk of breast cancer, particularly in middle-aged and elderly age groups. These results suggest that breast cancer prevention measures and interventions should consider addressing psychological factors.

The BCCS-CW is a large prospective study conducted by the Chinese Center for Disease Control and Prevention across three provincial disease control centers and nine hospitals. The study collected standardized population-based data from Chinese Han women diagnosed with breast cancer. The study design has been previously reported in detail (*5*). The Ethics Committees of the Chinese Center for Disease Control and Prevention provided approval for the BCCS-CW study, and all participants gave written informed consent prior to participating in face-to-face interviews.

Between 2018 and 2020, the BCCS-CW enrolled 112,118 women who had previously been recruited for a population-based cohort study in 2008. A total of 63,495 women had standardized information collected for analysis in this study. However, only 63,018 participants were included in the final analysis. A total of 477 participants were excluded due to missing data for essential variables, depression scores, or sleep duration, or because of the presence of extreme values.

During the BCCS-CW, multiple data collection methods were employed, including questionnaires, physical measurements, surgical examinations, breast ultrasound and mammography, as well as laboratory tests. A self-developed questionnaire, validated by experts, was utilized to gather basic information via standardized face-to-face interviews carried out by trained and qualified interviewers. The collected data encompassed demographic characteristics such as age and education level.

Depression was assessed in this study using the Center for Epidemiological Studies-Depression (CES-D) Scale, which is included in the BCCS-CW questionnaire and was originally developed for assessing depressive symptomatology in the general population. The CES-D Scale consists of 20 items that evaluate the feelings and behaviors of participants during the previous week. Each item is scored on a scale from 0 (not at all) to 3 (a lot), with higher CES-D scores indicative of more severe depressive symptoms. The total CES-D score ranges from 0 to 60, and scores over 19 are considered reflective of depression.

In this study, participants self-reported their sleep duration in response to the question: "In the past month, how much sleep did you get per night (in hours and minutes)?" Sleep durations ranging from 1 to 23 hours were considered valid and recorded in hours and minutes. Sleep duration was then categorized as follows: <7 hours, ≥7 hours and <9 hours (reference range), or ≥9 hours. Sleep satisfaction was assessed using a 5-point Likert scale, with questionnaire items scored as 1 for very satisfied, 2 for satisfied, 3 for neutral, 4 for dissatisfied, and 5 for very dissatisfied.

Statistical analyses were conducted using SPSS (version 25.0; IBM Corp., Armonk, NY, USA) and R (version 4.2.0; R Development Core Team, Vienna, Austria) software. Continuous data were reported as means±standard deviations, while categorical data were presented as numbers (percentages). For continuous variables, *t*-tests and analyses of variance were employed, whereas the chi-squared test was applied to categorical variables. Logistic regression analysis was utilized to calculate odds ratios (*OR*s) and 95% confidence intervals (*CI*s).

To identify factors associated with depression and sleep duration, univariate and multivariate logistic regression models were constructed employing the "enter" method, with breast cancer as the dependent variable. Significant factors in the univariate models were incorporated as independent variables in the multivariate model, which was adjusted for age, education, marital status, annual family income, and history of benign breast disease. A stratified analysis was also conducted according to menopausal status.

Trend tests were performed by categorizing sleep duration into three groups: less than 7 hours, between 7 and 9 hours, and 9 or more hours. Two-tailed *P*-values of less than 0.05 were deemed statistically significant. The GGally R package was employed to create a matrix scatterplot depicting age groups, CES-D scores, and sleep duration.

A total of 63,018 Chinese women were included in the analysis, comprising 700 breast cancer cases. Baseline characteristics of the participants are displayed in Table 1. The average age at enrollment was 50.78±11.01 years. Among the participants, 53.05% had an education level of primary school or less, 68.29% had a monthly per capita household income of less than 3,000 CNY, 43.63% were postmenopausal, and more than 70% reported their families' economic and social status as average. There was a significant difference in age distribution between the breast cancer and control groups (t=7.35, P<0.001), and the mean CES-D score was higher in the breast cancer group (t=2.24, P=0.019). Additionally, the breast cancer group had a shorter sleep duration (t=−2.41, P=0.016) and a lower rate of sleep satisfaction compared to the control group (14.31% *vs*. 7.32%).

Figure 1 illustrates the distribution of depressive symptoms across various age groups. The average CES-D score and the likelihood of depression were observed to increase with age, particularly among older women. The prevalence of depression in each age group was as follows: 20–30 years, 3.2%; 31–40 years, 3.3%; 41–50 years, 2.8%; 51–60 years, 4.1%; 61–70 years, 5.8%; and >70 years, 6.9%.

Figure 2 displays the relationships among age group, CES-D score, and sleep duration, with linear correlations identified among these variables in both the breast cancer and control groups. For the entire cohort, a positive correlation was found between the CES-D score and age (r=0.130, P<0.001), whereas a negative correlation was observed between the CES-D score and sleep duration (r=−0.077, P<0.001). Additionally, a negative correlation was noted between sleep duration and age (r=−0.068, P<0.001).

The univariate logistic regression analysis revealed that the CES-D score, sleep duration, and sleep satisfaction were significantly associated with breast cancer risk (Table 2). After controlling for age, education level, average monthly income, and social status, participants with short sleep duration possessed an *OR* for incident breast cancer of 1.265 (95% *CI*: 1.045, 1.531), while those reporting low sleep satisfaction had an *OR* of 1.174 (95% *CI*: 1.071, 1.285).

Stratified analysis by menstrual status demonstrated that low sleep satisfaction (*OR*=1.162; 95% *CI*: 1.029,

TABLE 1. The demographic characteristics of the participants of the BCCS-CW, 2020.

Variable	Overall *N* (%)	Breast cancer *N* (%)	Control *N* (%)	t/χ^2	*P* value
Age, mean (SD)	50.78±11.01	53.34±9.22	50.75±11.02	7.35	<0.001
Sleep duration, mean (SD)	7.29±1.90	7.09±2.16	7.29±1.90	–2.41	0.016
CES-D score, median (IQR)	3.00 (7.00)	4.00 (6.00)	3.00 (7.00)	2.24	0.019
Education				8.60	0.014
Primary school and below	33,402 (53.05)	393 (56.30)	33,009 (53.01)		
Junior/senior high school/technical school	27,175 (43.16)	292 (41.83)	26,883 (43.18)		
Junior college and above	2,384 (3.79)	13 (1.87)	2,371 (3.81)		
Marital status				1.38	0.240
Unmarried	6,040 (9.58)	58 (9.29)	5,982 (9.60)		
Married	56,978 (90.42)	642 (91.71)	56,336 (90.40)		
Average monthly income, CNY				21.83	<0.001
<1,000	12,842 (20.40)	168 (24.07)	12,674 (20.36)		
1,000–2,999	30,147 (47.89)	355 (50.86)	29,792 (47.85)		
3,000–4,999	13,994 (22.23)	106 (15.19)	13,888 (22.31)		
≥5,000	5,978 (9.49)	69 (9.88)	5,909 (9.49)		
Menopause				89.64	<0.001
Yes	27,495 (43.63)	368 (52.57)	27,127 (43.53)		
No	32,453 (51.50)	258 (36.86)	32,195 (51.67)		
Benign breast disease history				2271.40	<0.001
Yes	933 (1.49)	162 (23.18)	771 (1.24)		
No	61,847 (98.51)	537 (76.82)	61,310 (98.76)		
Sleep satisfaction				33.55	<0.001
Very satisfied	13,542 (21.58)	96 (13.73)	13,446 (21.67)		
Satisfied	27,395 (43.65)	313 (44.78)	27,082 (43.64)		
Neutral	15,934 (25.39)	190 (27.18)	15,744 (25.37)		
Dissatisfied	5,502 (8.77)	94 (13.45)	5,408 (6.71)		
Very dissatisfied	382 (0.61)	6 (0.86)	376 (0.61)		
Economic status				22.72	<0.001
Very good	2,815 (4.47)	25 (3.58)	2,790 (4.48)		
Good	8,025 (12.75)	75 (10.74)	7,950 (12.77)		
Common	48,313 (76.73)	516 (73.93)	47,797 (76.77)		
Poor	3,333 (5.29)	67 (9.60)	3,266 (6.25)		
Very poor	475 (0.75)	15 (2.15)	460 (0.74)		
Social status				5.02	0.025
Very good	4,265 (6.77)	42 (6.02)	4,223 (6.78)		
Good	9,356 (14.86)	92 (13.18)	9,264 (14.88)		
Common	47,464 (75.39)	530 (75.93)	46,934 (75.38)		
Poor	1,659 (2.63)	30 (4.30)	1,629 (2.62)		
Very poor	217 (0.34)	4 (0.57)	213 (0.34)		

Abbreviation: IQR=interquartile range; BCCS-CW=the Breast Cancer Cohort Study in Chinese Women; SD=standard deviation; CNY=Chinese Yuan.

1.311) served as a risk factor for breast cancer in menopausal women (Table 3). In premenopausal women, both depression (*OR*=1.507; 95% *CI*: 1.010, 2.249) and low sleep satisfaction (*OR*=1.192; 95% *CI*: 1.024, 1.388) contributed to an elevated risk of breast cancer.

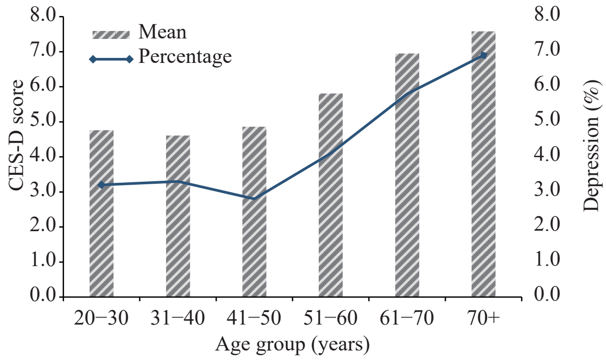

FIGURE 1. The distribution of depressive symptoms among Chinese women of different age groups in the BCCS-CW, 2020.
Abbreviation: CES-D score=center for epidemiological studies-depression scale; BCCS-CW=the Breast Cancer Cohort Study in Chinese Women.

DISCUSSION

In this study, we examined population-based data from a large, ongoing prospective study involving Chinese Han women diagnosed with breast cancer. Our objective was to investigate whether depression and brief sleep duration serve as risk factors contributing to the onset of breast cancer. The findings suggest that depressive symptoms, limited sleep duration, and reduced sleep satisfaction could all be considered risk factors for the development of breast cancer. Consequently, it is crucial that preventive measures and interventions focus on addressing these psychological factors, given their potential impact on the progression of cancer.

Depression, a prevalent mental disorder, is characterized by its primary symptoms of low mood and anhedonia, which can significantly impede an individual's ability to lead a normal life. In this study, 4.4% of the female participants were found to be suffering from depression, with the CES-D scores displaying an increase with age. Notably, the highest prevalence of depression (6.9%) was observed among participants who were 70 years or older, aligning with findings from earlier studies (*2*).

Prior to accounting for potential confounders, our findings revealed an association between breast cancer incidence and depression, consistent with earlier prospective studies (*6*). Although multivariable logistic regression results did not corroborate this association across the entire cohort, it remained evident among the premenopausal population. Nevertheless, the overall epidemiological evidence supporting an association between depression and breast cancer remains inconclusive (*7*–*8*). Discrepancies among study findings may be attributed to variations in lifestyle and cultural factors across countries, as well as the inclusion of age groups with differing breast cancer incidence rates. To validate these findings, additional large-scale prospective cohort studies are warranted.

Insufficient sleep has been found to negatively impact individuals' health and increase the risk of cancer. Furthermore, poor sleep quality may contribute to compromised immune function and heightened risk of metabolic disorders, potentially leading to obesity and implications for melatonin release. However, the precise mechanisms underpinning these relationships remain elusive. In our study, we observed a link between low sleep satisfaction and increased risk of breast cancer among Chinese women. Specifically, we found that short sleep duration (OR=1.265, P=0.016) constituted a risk factor for breast cancer, while long sleep duration (OR=1.164, P=0.206) did not. Nevertheless, our subgroup analyses did not yield significant associations between sleep duration and breast cancer risk.

Notably, prior research investigating the connection between sleep and breast cancer has produced inconsistent findings (*9*). Several prospective studies and meta-analyses (*10*) have not substantiated the association between sleep duration and breast cancer risk. Potential explanations for these discrepancies include variations in criteria for categorizing sleep duration across studies as well as potential biases arising from participants' self-reported data.

The present study has several limitations that warrant acknowledgment. Firstly, the data were derived from the BCCS-CW study, in which depressive symptoms and sleep characteristics were assessed only once. Consequently, the analysis was restricted to examining the associations between depression, sleep duration, and sleep satisfaction with

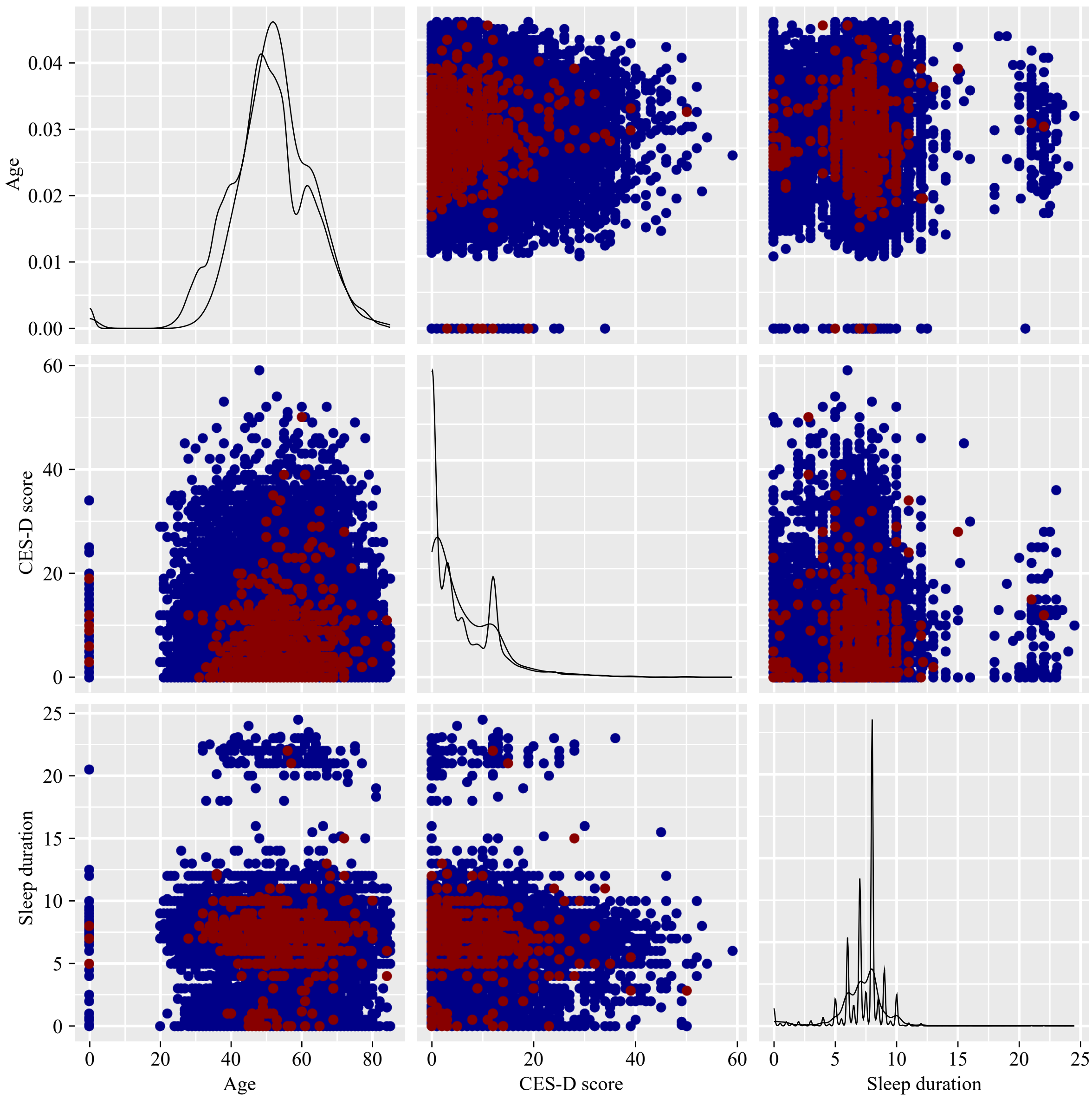

FIGURE 2. The correlation between age group, CES-D score, and sleep duration in the BCCS-CW, 2020.
Note: In the presented figure, red dots correspond to the breast cancer group, while blue dots represent the control group. The histograms positioned diagonally illustrate the distribution of age, CES-D scores, and sleep duration. Meanwhile, the scatterplots positioned above and below the diagonal display the relationships between these variables.
Abbreviation: CES-D score=center for epidemiological studies-depression scale. BCCS-CW=the Breast Cancer Cohort Study in Chinese Women.

breast cancer within the Chinese female population. Furthermore, it is only possible to hypothesize if these variables have a causal connection to breast cancer incidence. Lastly, potential information bias might exist due to the reliance on self-reported subjective feelings of participants for certain variables.

The results of this research suggest that public policy should prioritize early psychological interventions and health education as preventative measures for breast cancer, particularly in premenopausal women. Additionally, it is essential to conduct large-scale, prospective cohort studies with follow-up assessments to determine the causal relationships and identify the most effective time for intervention.

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TABLE 2. Univariate and multivariate logistical regression analyses of correlates of breast cancer.

Variable	Univariate analyses		Multivariate analyses	
	OR (95% *CI*)	*P* value	*OR* (95% *CI*)	*P* value
Age	1.021 (1.015, 1.028)	<0.001	1.021 (1.013, 1.030)	<0.001
CES-D score	1.102 (1.002, 1.023)	0.020	1.005 (0.994, 1.017)	0.359
Sleep satisfaction	1.263 (1.167, 1.367)	<0.001	1.174 (1.071, 1.285)	0.001
Average monthly income (CNY)	0.874 (0.800, 0.954)	0.003	0.966 (0.875, 1.067)	0.498
Social status	1.154 (1.108, 1.308)	0.025	0.988 (0.863, 1.132)	0.865
Education				
Primary school and below	Reference	1	Reference	1
Junior/senior high school/technical school	0.912 (0.783, 1.062)	0.238	1.156 (0.966, 1.384)	0.113
Junior college and above	0.461 (0.265, 0.801)	0.006	0.805 (0.450, 1.438)	0.463
Sleep duration				
7–9 h	Reference	1	Reference	1
<7 h	1.529 (1.281, 1.825)	<0.001	1.265 (1.045, 1.531)	0.016
≥9 h	1.148 (0.909, 1.449)	0.248	1.164 (0.920, 1.472)	0.206

Abbreviation: CES-D score=Center for epidemiological studies depression scale; *OR*=ddds ratio; *CI*=confidence interval; CNY=Chinese Yuan.

TABLE 3. Multivariate logistical regression analyses in the subgroups divided by menstrual status.

Variable	Menopausal		Premenopausal	
	OR (95% *CI*)	*P* value	*OR* (95% *CI*)	*P* value
Age	1.033 (1.018, 1.048)	<0.001	0.988 (0.974, 1.002)	0.092
Depression	0.145 (0.020, 1.036)	0.054	1.507 (1.010, 2.249)	0.045
Sleep satisfaction	1.192 (1.024, 1.388)	0.024	1.162 (1.029, 1.311)	0.015
Average monthly income (CNY)	1.088 (0.925, 1.281)	0.310	0.834 (0.724, 0.961)	0.012
Social status	1.033 (0.832, 1.283)	0.767	1.014 (0.832, 1.236)	0.891
Education				
Primary school and below	Reference	1.000	reference	1.000
Junior/senior high school/technical school	1.132 (0.848, 1.510)	0.399	1.192 (0.935, 1.520)	0.157
Junior college and above	0.757 (0.368, 1.556)	0.488	1.795 (0.556, 5.791)	0.328
Sleep duration				
7–9 h	Reference	1.000	reference	1.000
<7 h	1.322 (0.956, 1.828)	0.091	1.237 (0.956, 1.600)	0.106
≥9 h	1.135 (0.763, 1.688)	0.531	1.230 (0.896, 1.689)	0.201

Abbreviation: *OR*=Odds ratio; *CI*=Confidence interval; CNY=Chinese yuan.

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Vital Surveillances

Trends in Incidence Rates, Mortality Rates, and Age-Period-Cohort Effects of Female Breast Cancer — China, 2003–2017

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ABSTRACT

Introduction: This study reported the trends in female breast cancer incidence and mortality rates in China, and analyzed the corresponding age-period-cohort effects.

Methods: Data from 22 population-based cancer registries in China between 2003 and 2017 were analyzed. Age-standardized incidence rates (ASIR) and mortality rates (ASMR) were calculated using Segi's world standard population. Joinpoint regression was employed to evaluate trends, and age-period-cohort effects were examined using the intrinsic estimator method.

Results: The ASIR for female breast cancer exhibited a more rapid increase in rural areas compared to urban areas across all age groups. The most substantial increase was observed in the 20–34 age group in rural areas [annual percent change (APC)=9.0%, 95% confidence interval (*CI*): 7.0%–11.0%, *P*<0.001]. The ASMR for females under 50 years old remained stable from 2003 to 2017 in both urban and rural areas. However, the ASMR for females over 50 in rural areas and those over 65 in urban areas demonstrated a significant increase, with the most pronounced increase observed among females over 65 in rural areas (APC=4.9%, 95% *CI*: 2.8%–7.0%, *P*<0.001). Age-period-cohort analysis revealed increasing period effects and decreasing cohort effects for female breast cancer incidence and mortality rates in both urban and rural settings. Notably, the cohort effect for incidence displayed a slight upward trend for females born between 1983 and 1992 in rural areas.

Conclusions: Our study revealed a rapid increase in breast cancer incidence among younger generations and an accelerated mortality rate in older populations residing in rural areas. To effectively address the growing burden of female breast cancer in China, it is essential to develop and implement targeted intervention strategies.

Breast cancer in females represents one of the most rapidly increasing malignancies in China (*1*–*3*). Projections estimate that over 400,000 new diagnoses and over 100,000 fatalities will transpire by 2030 within the nation (*4*). Consequently, it is crucial to establish targeted intervention strategies for this cancer to avert it from developing into a significant public health issue.

Despite recent advances, there remains a gap in understanding the trends in incidence and mortality rates of female breast cancer in China. The present study aimed to examine these trends from 2003 to 2017, focusing on age groups and geographic distribution. Joinpoint regression modeling and age-period-cohort analyses were employed in this investigation. Additionally, this research can be used to evaluate the effectiveness of current cancer screening initiatives and inform future policy-making in China.

METHODS

Cancer Registry Data

The present study analyzed datasets of female breast cancer (C50, ICD-10) from 22 population-based cancer registries in China (11 urban and 11 rural) between 2003 and 2017. The pooled data included 183,521 female breast cancer cases and 41,831 cancer-related deaths from a population of 329,750,392 person-years. Of these, 167,998 cases and 37,341 deaths were from urban areas with 274,073,539 person-years, and 15,523 cases and 4,490 deaths were from rural areas with 55,676,853 person-years.

Given the rarity of female breast cancer among individuals below 20 years of age, data from this population were excluded from subsequent analyses. Incidence and mortality rates were computed using 5-year age intervals (20–24, 25–29, ..., 80–84, ≥85) and stratified by 5-year periods (2003–2007, 2008–2012, 2013–2017) and geographical classification (urban and rural).

Statistical Analysis

The age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) were calculated utilizing Segi's world standard population. Joinpoint regression analysis was conducted for trend examination, and the annual percent changes (APC) and average annual percent change (AAPC) were reported. The age-period-cohort effects were analyzed using the intrinsic estimator method, and risk ratios were provided. Statistical analyses were carried out with Stata (version 13.0, Stata Corporation, College Station, Texas, USA) and Joinpoint software (version 4.6.0.0, Applications Branch, National Cancer Institute, Bethesda, USA).

RESULTS

Trends in Incidence Rate

In all regions, the ASIR for female breast cancer in individuals over 20 years old increased from 46.34 per 100,000 in 2003 to 68.78 per 100,000 in 2017, with an AAPC of 2.5% [95% confidence interval (*CI*): 2.0%–2.9%]. The ASIR was higher in urban areas compared to rural areas.

The ASIR for female breast cancer demonstrated a significant increase across most age groups between 2003 and 2017. However, an exception was observed in the urban 50–64 age group, where the ASIR increased rapidly from 2003 to 2008 (APC=4.5%, 95% *CI*: 3.4%–5.7%, *P*<0.001). Following this period, the upward trend slowed between 2008 and 2017 (APC=1.5%, 95% *CI*: 1.0%–1.9%, *P*<0.001). Notably, in comparison to urban areas, the ASIR experienced a faster increase in rural areas across all age groups. The most prominent rise was observed in the 20–34 age group in rural areas, with an APC of 9.0% (95% *CI*: 7.0%–11.0%, *P*<0.001) throughout the entire period (Figure 1A, 1B, 1C). Corresponding trend analysis results for incidence rates can be found in Supplementary Table S1 (available at https://weekly.chinacdc.cn/).

Trends in Mortality Rate

Across all regions, the ASMR for females with breast cancer aged 20 and above experienced an increase from 11.12 per 100,000 in 2003 to 11.67 per 100,000 in 2017, exhibiting an AAPC of 0.9% (95% *CI*: 0.4%–1.3%).

For females over 20 years old, the ASMR increased more rapidly in rural areas (APC=2.4%, 95% *CI*:

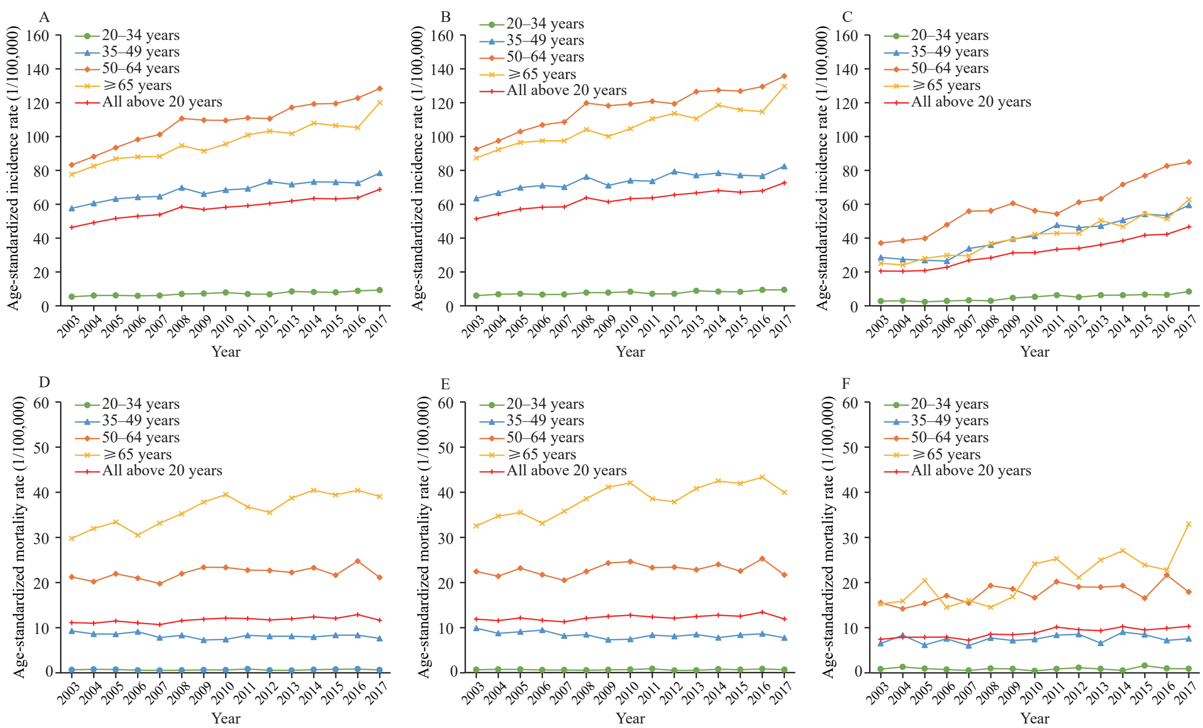

FIGURE 1. Trends in incidence and mortality rates of female breast cancer by age group and area, 2003–2017. (A) Incidence rates across all areas. (B) Incidence rates in urban settings. (C) Incidence rates in rural settings. (D) Mortality rates across all areas. (E) Mortality rates in urban settings. (F) Mortality rates in rural settings.

1.7%–3.2%, *P*<0.001) compared to urban areas (APC=0.6%, 95% *CI*: 0.2%–1.1%, *P*=0.013). When examining the data by age group, the ASMR for the 20–34 age group exhibited stability in both urban and rural areas from 2003 to 2017. The ASMR for the 35–49 age group in urban areas declined between 2003 and 2009 (APC=–3.6%, 95% *CI*: -6.4% to –0.7%, *P*=0.020) and then stabilized. In contrast, the ASMR for the 50–64 age group in rural areas and the over-65 age group in both areas showed significant increases, with the most substantial increase observed in the over-65 age group in rural areas (APC=4.9%, 95% *CI*: 2.8%–7.0%, *P*<0.001) (Figure 1D, 1E, 1F). The corresponding mortality rate trend analyses are provided in Supplementary Table S2 (available at https://weekly.chinacdc.cn/).

Trends in Age Distribution of Female Breast Cancer Incidence

In urban areas, the age distribution trends of female breast cancer incidence rates were consistent across three study periods. The ASIR exhibited a rapid increase starting from the 20–24 age group. During 2003–2012, a plateau in the incidence rate was observed between the 45–49 and 70–74 age groups, followed by a rapid decline. In the period of 2013–2017, the incidence rate continued to increase, albeit at a slower pace, beginning at the 45–49 age group and peaking within the 60–64 age group. The rate then exhibited a gradual decrease until the 70–74 age group and subsequently declined rapidly (Figure 2B).

In rural regions, the ASIR reached its peak within the 55–59 age group during the periods of 2003–2007 and 2008–2012. However, between 2013 and 2017, the rate experienced a plateau spanning from the 45–49 age group to the 60–64 age group (Figure 2C).

The incidence rates showed an increase for cohorts from 1933 to 1988 (ages 25–74) in urban areas, and for cohorts from 1923 to 1993 (ages 20–84) in rural areas (Figure 3A, 3B).

Trends in Age Distribution of Female Breast Cancer Mortality

In both urban and rural settings, there is a positive association between age and ASMRs, with rates increasing as age increases (Figure 2E, 2F).

The mortality rates exhibits an increase across all cohorts in both urban and rural settings (Figure 3C, 3D).

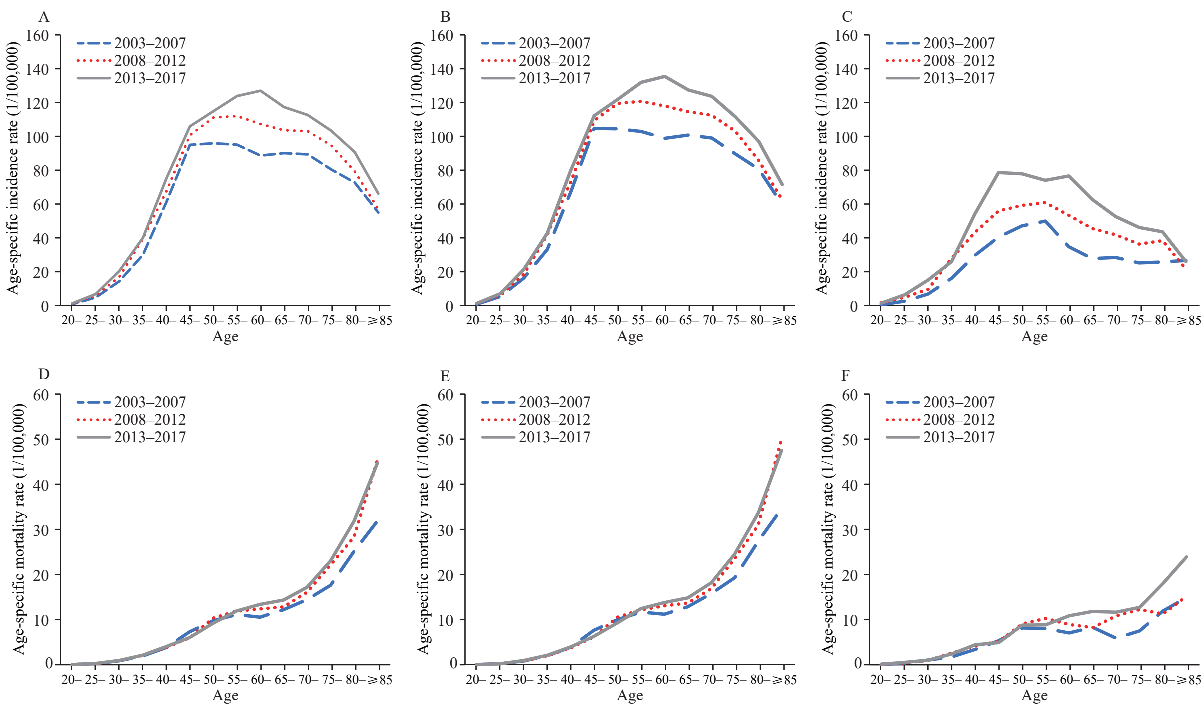

FIGURE 2. The age-specific incidence and mortality rates of female breast cancer, by time period and area. (A) Incident rates in all areas. (B) Incident rates in urban areas. (C) Incident rates in rural areas. (D) Mortality rates in all areas. (E) Mortality rates in urban areas. (F) Mortality rates in rural areas.
Note: Each line represents the connection of age-specific rates for a 5-year period.

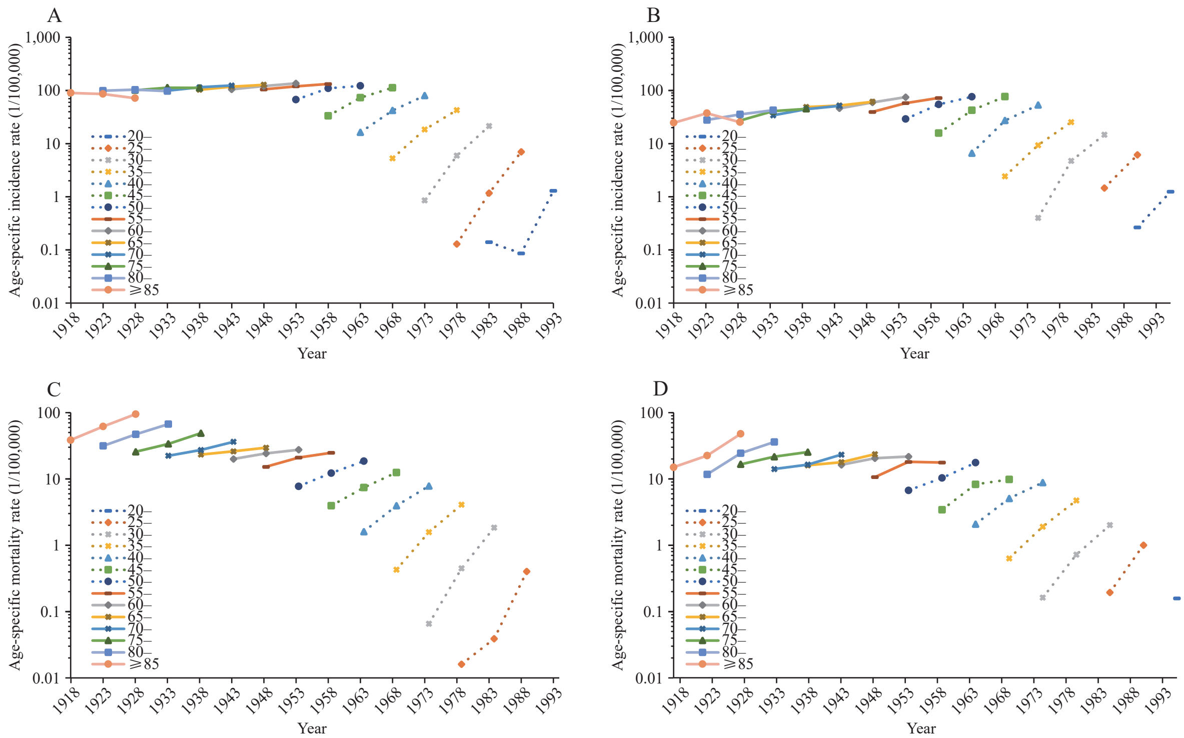

FIGURE 3. The birth cohort-specific incidence and mortality rates of female breast cancer, by area. (A) Incident rates in urban areas. (B) Incident rates in rural areas. (C) Mortality rates in urban areas. (D) Mortality rates in rural areas. Results were not shown in age group 20–24 if the age-specific rate is 0.
Note: Each line represents the connection of cohort-specific rates for a 5-year age group.

Results of Age-Period-Cohort Models

The age, period, and cohort effects exhibited similarity across urban and rural areas. In both regions, the age effect on female breast cancer incidence rates increased significantly from the 20–24 age group, reaching a peak in the 45–49 age group. Subsequently, the age effect decreased gradually within the following age groups. As for mortality rates, the age effect escalated significantly within the 20–24 age group, peaking in the 50–54 age group. A slight decrease occurred thereafter, followed by a resurgence in the 65–69 age group for urban areas and the 70–74 age group for rural areas (Figure 4).

The incidence and mortality rates demonstrated a period effect, with increases observed from 2003 to 2017.

In urban regions, there was a consistent decline in the cohort effect on both incidence and mortality rates. Conversely, in rural areas, the cohort effect on incidence rates exhibited a rapid decrease, followed by a minor resurgence observed among those born between 1983 and 1992. As for mortality rates in rural areas, the cohort effect initially declined, but experienced a slight increase for the cohort born between 1928 and 1937, and subsequently showed a continuous decrease thereafter (Figure 4).

DISCUSSION

Age effect: The present study revealed that the incidence rate of female breast cancer was the highest among the age group of 45–70 years, consistent with global observations (*5*). In this investigation, the peak age effect for female breast cancer incidence occurred in the 45–49-year-old group. Luan et al (*6*) assessed the age-period-cohort effects on female breast cancer incidence in Hong Kong, Shanghai, and White and Black populations in Los Angeles. Although the age effect also peaked in the 45–49-year-old group in Shanghai, distinct patterns were observed in the other three populations. These diverse age effect patterns across various populations might be attributable to the potential differences in the prevalence of tumor-related genes (*7*).

Ding et al. (*8*) discovered a rapid increase in breast cancer mortality rates from the 20–24 age group to the 45–49 age group, followed by a slower rate of increase. Wang et al. (*9*) noted that the age effects of breast cancer mortality plateaued in the 55–59 age group and then gradually declined in Japan and Korea, while the

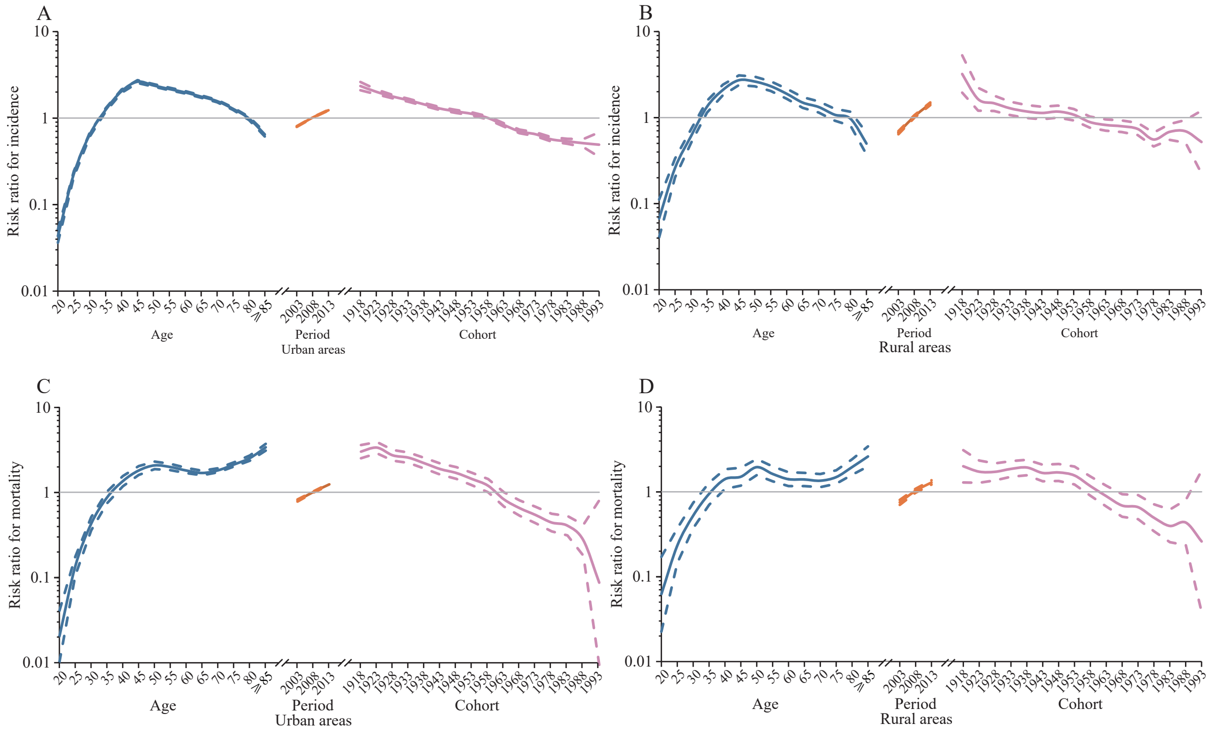

FIGURE 4. The result of age-period-cohort analysis of incidence and mortality rates of female breast cancer, by area. (A) Incident rates in urban areas. (B) Incident rates in rural areas. (C) Mortality rates in urban areas. (D) Mortality rates in rural areas. ote: Blue solid and dash lines represent the age effect and 95% confidence interval. Orange solid and dash lines represent the period effect and 95% confidence interval. Pink solid and dash lines represent the cohort effect and 95% confidence interval.

age effect consistently increased with age in Singapore. In the present study, a small peak in the female breast cancer mortality rates was observed within the 50–54 age group. Further investigation is necessary to determine the reasons for the elevated risk in this particular age group.

Period effect: Our study identified increasing period effects in female breast cancer incidence and mortality rates from 2003 to 2017, aligning with findings from previous research (*8–10*). This observation suggests that socioeconomic transformations and modernized lifestyle changes may constitute the primary factors contributing to the rise in breast cancer incidence and mortality in China.

Screening strategies are crucial influencing factors for incidence and mortality trends in breast cancer. Krishnamoorthy et al (*11*) conducted an analysis of worldwide breast cancer incidence rate trends across various regions. Their findings indicated that the Americas had the highest breast cancer incidence, but it was the one region in which the incidence rate had been declining. Likewise, the period effect in the Americas displayed a decreasing trend. These findings suggest that the breast cancer screening programs in the Americas have reached a saturation point, and their health benefits have become evident. However, due to the limited coverage of screening programs in China, the period effect has not yet been reversed. Drawing on the experiences of the Americas, it can be predicted that the period effect and the ASIR for breast cancer will continue to rise for an extended period in China.

Cohort effect: Our research identified a decreasing cohort effect in incidence and mortality rates for female breast cancer, consistent with findings from previous studies (*6,8–10*). This decline in cohort effect suggests that older birth cohorts face a higher risk of developing female breast cancer than younger cohorts. The possible reasons for this reduction may include healthier living habits and enhanced health awareness among younger generations, along with improvements in public health policies and clinical diagnosis and treatment options in recent years.

It is important to note, however, a slight upsurge in cohort effect was observed among younger populations in rural areas of China. This reversal may result from an increased exposure to emerging risk factors, such as sedentary lifestyles (*12*), changes in reproductive behaviors (e.g., delayed first childbirth, nulliparity, and oral contraceptive pill use), and diminished breastfeeding practices (*13*). These factors come in addition to well-established risks such as physical inactivity, excessive body weight, and diabetes (*14*).

The early diagnosis rate for female breast cancer in China was significantly higher than that observed for other types of cancer (*15*). Our data further revealed that between 2003 and 2017, the mortality rate for female breast cancer increased at a slower pace than the incidence rate. This evidence suggests that current screening programs have yielded substantial benefits through early detection and treatment. However, it is critical to recognize that effective primary prevention strategies for addressing new risk factors remain limited. Without them, reducing breast cancer incidence in the short term may be unattainable. As such, there is a pressing need to develop comprehensive public health intervention strategies, particularly for younger generations and vulnerable populations.

In the current study, we utilized continuous surveillance data from 22 cancer registries spanning 2003 to 2017, offering a more accurate depiction of trends in rates as compared to alternative multi-sectional datasets. Additionally, the use of ICD-10 coding for cancer registry data enhances the precision of our analysis. Nonetheless, some limitations exist within this dataset, primarily due to its restricted population coverage, particularly in rural areas. This results in increased fluctuation within trends and broader 95% *CI* for risk ratio point estimation. Furthermore, the observation period in this study is relatively shorter than those found in research conducted in other countries.

In conclusion, the present study examined the period from 2003 to 2017 and found increasing incidence rates of breast cancer across all age groups and geographic locations. However, rising mortality rates were observed predominantly among women over 50 years old, particularly in rural areas. These trends can be primarily attributed to period effects, while cohort effects generally decreased. Notably, a slight upward trend was detected for younger generations in rural regions. Consequently, it is crucial to adjust and refocus current intervention strategies for female breast cancer in China to adequately address the growing burden of this disease.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Trends for age-standardized incidence rates of female breast cancer for any time segments identified in joinpoint analysis by age group and area, 2003–2017.

Age, years	Area	Trend 1			Trend 2			2003–2017		2013–2017	
		Years	APC (95% *CI*)	*P*	Years	APC (95% *CI*)	*P*	AAPC	*P*	AAPC	*P*
20–34	All	2003–2017	3.5 (2.7, 4.3)	<0.001*	–	–	–	3.5 (2.7, 4.3)	<0.001*	3.5 (2.7, 4.3)	<0.001*
	Urban	2003–2017	2.6 (1.7, 3.6)	<0.001*	–	–	–	2.6 (1.7, 3.6)	<0.001*	2.6 (1.7, 3.6)	<0.001*
	Rural	2003–2017	9.0 (7.0, 11.0)	<0.001*	–	–	–	9.0 (7.0, 11.0)	<0.001*	9.0 (7.0, 11.0)	<0.001*
35–49	All	2003–2017	1.8 (1.4, 2.2)	<0.001*	–	–	–	1.8 (1.4, 2.2)	<0.001*	1.8 (1.4, 2.2)	<0.001*
	Urban	2003–2017	1.4 (1.0, 1.8)	<0.001*	–	–	–	1.4 (1.0, 1.8)	<0.001*	1.4 (1.0, 1.8)	<0.001*
	Rural	2003–2017	6.2 (5.2, 7.2)	<0.001*	–	–	–	6.2 (5.2, 7.2)	<0.001*	6.2 (5.2, 7.2)	<0.001*
50–64	All	2003–2008	5.0 (3.9, 6.2)	<0.001*	2008–2017	1.7 (1.3, 2.2)	<0.001*	2.9 (2.4, 3.3)	<0.001*	1.7 (1.3, 2.2)	<0.001*
	Urban	2003–2008	4.5 (3.4, 5.7)	<0.001*	2008–2017	1.5 (1.0, 1.9)	<0.001*	2.5 (2.1, 3.0)	<0.001*	1.5 (1.0, 1.9)	<0.001*
	Rural	2003–2017	5.8 (4.7, 6.8)	<0.001*	–	–	–	5.8 (4.7, 6.8)	<0.001*	5.8 (4.7, 6.8)	<0.001*
≥65	All	2003–2017	2.5 (2.1, 2.9)	<0.001*	–	–	–	2.5 (2.1, 2.9)	<0.001*	2.5 (2.1, 2.9)	<0.001*
	Urban	2003–2017	2.3 (1.9, 2.7)	<0.001*	–	–	–	2.3 (1.9, 2.7)	<0.001*	2.3 (1.9, 2.7)	<0.001*
	Rural	2003–2017	6.7 (5.8, 7.6)	<0.001*	–	–	–	6.7 (5.8, 7.6)	<0.001*	6.7 (5.8, 7.6)	<0.001*
All≥20	All	2003–2008	3.8 (2.6, 5.0)	<0.001*	2008–2017	1.8 (1.3, 2.2)	<0.001*	2.5 (2.0, 2.9)	<0.001*	1.8 (1.3, 2.2)	<0.001*
	Urban	2003–2008	3.4 (2.1, 4.7)	<0.001*	2008–2017	1.5 (0.9, 2.0)	0.013*	2.1 (1.6, 2.7)	<0.001*	1.5 (0.9, 2.0)	<0.001*
	Rural	2003–2017	6.2 (5.6, 6.9)	<0.001*	–	–	–	6.2 (5.6, 6.9)	<0.001*	6.2 (5.6, 6.9)	<0.001*

Abbreviation: APC=annual percent change; AAPC=average annual percent change; *CI*=confidence interval.
* *P*<0.05.

SUPPLEMENTARY TABLE S2. Trends for age-standardized mortality rates of female breast cancer for any time segments identified in joinpoint analysis by age group and area, 2003–2017.

Age, years	Area	Trend 1			Trend 2			2003–2017		2013–2017	
		Years	APC (95% *CI*)	*P*	Years	APC (95% *CI*)	*P*	AAPC	*P*	AAPC	*P*
20–34	All	2003–2017	0.6 (−1.4, 2.6)	0.552	–	–	–	0.6 (−1.4, 2.6)	0.552	0.6 (−1.4, 2.6)	0.552
	Urban	2003–2017	0.4 (−1.9, 2.8)	0.722	–	–	–	0.4 (−1.9, 2.8)	0.722	0.4 (−1.9, 2.8)	0.722
	Rural	2003–2017	0.7 (−3.7, 5.4)	0.730	–	–	–	0.7 (−3.7, 5.4)	0.730	0.7 (−3.7, 5.4)	0.730
35–49	All	2003–2017	-0.7 (−1.5, 0.1)	0.073	–	–	–	-0.7 (−1.5, 0.1)	0.073	-0.7 (−1.5, 0.1)	0.073
	Urban	2003–2009	-3.6 (−6.4, -0.7)	0.020*	2009–2017	0.8 (−1.1, 2.7)	0.400	-1.1 (−2.6, 0.3)	0.100	0.8 (−1.1, 2.7)	0.400
	Rural	2003–2017	1.1 (−0.4, 2.7)	0.144	–	–	–	1.1 (−0.4, 2.7)	0.144	1.1 (−0.4, 2.7)	0.144
50–64	All	2003–2017	0.7 (0.0, 1.4)	0.052	–	–	–	0.7 (0.0, 1.4)	0.052	0.7 (0.0, 1.4)	0.052
	Urban	2003–2017	0.5 (−0.2, 1.2)	0.150	–	–	–	0.5 (−0.2, 1.2)	0.150	0.5 (−0.2, 1.2)	0.150
	Rural	2003–2017	1.8 (0.6, 3.0)	0.006*	–	–	–	1.8 (0.6, 3.0)	0.006*	1.8 (0.6, 3.0)	0.006*
≥65	All	2003–2017	2.1 (1.4, 2.7)	<0.001*	–	–	–	2.1 (1.4, 2.7)	<0.001*	2.1 (1.4, 2.7)	<0.001*
	Urban	2003–2017	1.8 (1.1, 2.5)	<0.001*	–	–	–	1.8 (1.1, 2.5)	<0.001*	1.8 (1.1, 2.5)	<0.001*
	Rural	2003–2017	4.9 (2.8, 7.0)	<0.001*	–	–	–	4.9 (2.8, 7.0)	<0.001*	4.9 (2.8, 7.0)	<0.001*
All≥20	All	2003–2017	0.9 (0.4, 1.3)	<0.001*	–	–	–	0.9 (0.4, 1.3)	<0.001*	0.9 (0.4, 1.3)	<0.001*
	Urban	2003–2017	0.6 (0.2, 1.1)	0.013*	–	–	–	0.6 (0.2, 1.1)	0.013*	0.6 (0.2, 1.1)	0.013*
	Rural	2003–2017	2.4 (1.7, 3.2)	<0.001*	–	–	–	2.4 (1.7, 3.2)	<0.001*	2.4 (1.7, 3.2)	<0.001*

Abbreviation: APC=annual percent change. AAPC=average annual percent change; *CI*=confidence interval.
* *P*<0.05.

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