Contents lists available at ScienceDirect

### Journal of the National Cancer Center

journal homepage: www.elsevier.com/locate/jncc



### Full Length Article

# The burden and long-term trends of breast cancer by different menopausal status in China



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#### ARTICLE INFO

Keywords: Breast cancer Menopausal status Long-term trends China

#### ABSTRACT

*Background:* The burden of breast cancer in women of different menopausal status has not been assessed in China previously. We aim to evaluate and project the burden of breast cancer in different menopausal status in China.

*Methods:* The incidence and mortality of breast cancer were estimated using the data of 554 cancer registries in 2017 and the trends of incidence and mortality of 112 cancer registries from 2010 to 2017. Data from 22 continued cancer registries from 2000 to 2017 were applied for long-term trend projection to 2030 using the Bayesian ageperiod-cohort model. Menopausal status was stratified by age, with premenopause defined as chronological age <45 years, perimenopause defined as 45–54 years, and postmenopause defined as  $\geq$ 55 years.

*Results*: Approximately 352,300 incident cases and 74,200 deaths of breast cancer occurred in China in 2020, contributing to 2.6 million disability-adjusted life years (DALYs). Perimenopausal women had the highest incidence, prevalence, and DALYs rates, with the rates being 100.3 per 100,000, 819.2 per 100,000 and 723.1 per 100,000 persons. While postmenopausal women had the highest mortality rates (25.5 per 100,000 persons). From 2000 to 2017, the largest increase in incidence and mortality for breast cancer was observed in postmenopausal women with an average annual percentage change (AAPC) of 5.6% and 2.94%. The number of breast cancer cases and deaths will increase to 452,000 and 98,800 in 2030, resulting in 3.2 million DALYs.

*Conclusions:* The burden of breast cancer is rapidly increasing in China and varies among different menopausal status. Specific prevention and control strategies for women in different menopausal status will be more helpful in reducing the rapidly growing trends of breast cancer.

#### 1. Introduction

Breast cancer is one of the most common cancers and the leading cause of cancer death among women worldwide. According to GLOBO-CAN 2020, there were an estimated 2.3 million new breast cancer cases and 685,000 deaths worldwide in 2020.<sup>1</sup> The burden of breast cancer in China was relatively low during the past decades. However, since the 1990s, the disease burden of breast cancer has been sharply increased, especially in urban areas.<sup>2</sup> Breast cancer has become the heaviest burden of cancer among Chinese women, with approximately 412.3 disability-adjusted life years (DALYs) per 100,000 persons in 2019.<sup>3</sup>

Women in different menopausal status may have diverse risk factors, histological types, and molecular characteristics of breast cancer.<sup>4-6</sup> For example, high body fat increases the risk of breast cancer in postmenopausal women, while the relationship between excess body weight and breast cancer remains controversial in premenopausal women.<sup>4,5</sup> The incidence of premenopausal and postmenopausal breast cancer may reflect the two different rate patterns, which may relate to estrogen receptor (ER) expressions.<sup>6-8</sup> Anderson et.al found that incidence rates of ER-positive breast cancer in postmenopausal women continued to increase, but for those early ER-negative breast cancer, the incidence rate reached a plateau or declined.<sup>9</sup> Different menopausal status in women may affect the effectiveness of mammography screening. Early screening of breast cancer is more difficult in premenopausal women due to high breast density, which may lead to later stages at diagnosis.<sup>10</sup> Notably, the prognosis of breast cancer was also different between younger and older patients. The subtypes of breast cancer, were more serious in premenopausal women, while postmenopausal women were usually diagnosed with luminal breast cancer, with relatively better outcomes.<sup>6</sup>

https://doi.org/10.1016/j.jncc.2024.04.007

Received 12 December 2023; Received in revised form 12 April 2024; Accepted 30 April 2024

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In addition, changes of age structures also affect the distribution of different menopausal status of breast cancer.<sup>11</sup> Thus, distinguishing the burden of breast cancer and analyzing the temporal trends under different menopausal status should be beneficial for optimizing breast cancer prevention and control strategies.

This study aims to quantify the disease burden of breast cancer for Chinese women in different menopausal status in 2020, including incidence, mortality, prevalence, and DALYs, evaluate the long-term trends of breast cancer incidence and mortality from 2000 to 2017, and forecast the breast cancer burden to 2030.

#### 2. Materials and methods

#### 2.1. Data source

The data of breast cancer were obtained from the National Central Cancer Registry of China (NCCR), China Cancer Registry Annual Report 2020, and previous studies.<sup>12,13</sup> Details on the NCCR database were described in a previous study.<sup>12</sup> In this study, we extracted data coded as C50 in ICD-10 from the database to analyze the breast cancer burden.

In order to estimate the years lived with disability (YLDs), breast cancer was divided into four types of sequelae: diagnosis and primary therapy phase, controlled phase, metastatic phase, and terminal phase. The duration of each sequelae was divided according to the Global Burden of Disease (GBD) Study 2017, and the disability weights were obtained from our previous study.<sup>14,15</sup> The standard reference life table for calculating the years of life lost (YLLs) caused by premature death was derived from the GBD 2019.16 The standard reference life table was constructed based on the lowest observed age-specific mortality rates by gender and location across all estimation years from all locations with populations over 5 million. National population data by 5-year age group and region were obtained from the National Bureau of Statistics of China (http://data.stats.gov.cn/) and World Population Prospects 2019 (https://population.un.org/). Individual registry population data, which was provided by local registries, were obtained from Public Security Bureaus or calculations based on census data.

#### 2.2. Definition of menopausal status

We defined menopause status based on chronological age of diagnosis or death.<sup>17</sup> The three-menopause status (premenopause, perimenopause, and postmenopause) were defined as chronological age <45 years, 45–54 years, and  $\geq$ 55 years, respectively.

#### 2.3. Statistical analysis

The incidence and mortality of breast cancer were estimated using the data of 554 cancer registries in 2017 and the trends of incidence and mortality of 112 cancer registries from 2010 to 2017. The trends from 2010 to 2017 were obtained by fitting a logarithmic Poisson regression model. The age-specific incidence and mortality combined with population data were used to estimate the number of cases and deaths of breast cancer in 2020. According to previous studies (Supplementary online P1), the 10-year prevalence of breast cancer at age k was estimated based on the incidence rates and survival rates in a specific year.<sup>18</sup> We calculated the number of YLLs by multiplying each death with the expected life expectancy for that age group obtained from a standard life table. To estimate the YLDs, the prevalence for each phase is multiplied by its corresponding disability weights. The total YLDs were calculated as the sum of values for each general stage of breast cancer. DALYs were estimated as the sum of YLLs and YLDs.

The long-term trends over 18 years from 2000 to 2017 was analyzed using continuous qualified data from 22 cancer registries. The average annual percent change (AAPC) and APC were estimated using Joinpoint regression (vision 4.9.0). A maximum of 2 Joinpoint restricted models to reduce the likelihood of erroneous changes in trend. Z test was used to evaluate whether these changes were statistically different from zero. The Bayesian age-period-cohort model was used to project the breast cancer burden to 2030. Decomposition analysis was used to analyze changes in the proportion of burden attributed to demographic factors and age-specific rates.<sup>19,20</sup> We used exact Poisson tests to estimate the 95% confidence intervals (CIs).<sup>21,22</sup>

#### 3. Results

### 3.1. Breast cancer incidence, prevalence, mortality, and DALYs in China, 2020

In 2020, there were an estimated 352,300 (95% CI, 346,900-357,700) new breast cancer cases, and 74,200 (95% CI, 71,200–76,800) deaths occurred in China, with the 10-year prevalence being 2.79 million (95% CI, 2.75–2.84 million), resulting in 2.63 million (95% CI, 2.55–2.72 million) DALYs, of which 84.8% were attributed to YLLs and 15.2% attributed to YLDs (Table 1, Fig. 1, Supplementary Table 1). The age-standardized incidence, prevalence, mortality, and DALYs rates of breast cancer were 31.92, 255.12, 6.27, and 235.71 per 100,000 persons, respectively. The age-standardized incidence, prevalence, mortality, and DALYs rates of breast cancer in urban areas were higher than those in rural areas (Table 1).

#### 3.2. The burden of breast cancer by menopausal status

#### 3.2.1. Incidence

An estimated approximately 63,100 (95% CI, 61,800–64,600) premenopausal, 127,100 (95% CI, 125,700–128,400) perimenopausal, and 162,100 (95% CI, 159,500–164,700) postmenopausal women were diagnosed with breast cancer in 2020. Perimenopausal women had the highest breast cancer incidence among the three-menopause status, with the crude and age-standardized incidence rates being 100.32 (95% CI, 99.24–101.41) and 99.23 (95% CI, 98.15–100.31) per 100,000 persons, respectively. For different regions, the age-standardized incidence was similar in urban and rural areas among premenopausal women, but higher in urban areas than in rural areas among perimenopausal and postmenopausal women (Table 1).

#### 3.2.2. Prevalence

The 10-year prevalence for premenopausal, perimenopausal, and postmenopausal breast cancer was 518,200 (95% CI, 507,100–529,800), 1,037,600 (95% CI, 1,026,500–1,048,800), and 1,238,600 (95% CI, 1,219,600–1,257,900), respectively. Similar to the incidence rates, premenopausal women had the lowest crude breast cancer prevalence rate (137.49 per 100,000 persons), whereas perimenopausal women had the highest crude breast cancer incidence rate (819.17 per 100,000 persons). The age-standardized prevalence was higher in urban areas than in rural areas among women in the three status (Table 1).

#### 3.2.3. Mortality

An estimated approximately 7400 (95% CI, 6900–7900) premenopausal, 19,700 (95% CI, 19,200–20,300) perimenopausal, and 47,100 (95% CI, 45,600–48,700) postmenopausal women died from breast cancer in 2020. Both the crude and age-standardized mortality rates were lowest in premenopausal women (1.96 vs. 1.17 per 100,000 persons) and highest (25.84 vs. 24.82 per 100,000 persons) in postmenopausal women. For different regions, the age-standardized mortality rate was similar in urban and rural areas among premenopausal women, but higher in urban areas than in rural areas among postmenopausal women (Table 1).

#### 3.2.4. DALYs

Breast cancer caused 442,200 (95% CI, 415,600–470,600) DALYs in premenopausal women, 915,900 (95% CI, 892,500–939,700) DALYs in perimenopausal women, and 1275,300 (95% CI, 1,238,600–1 313,100)

# Table 1 The incidence, mortality, prevalence and DALYs of breast cancer by menopausal status and region in China, 2020.

Status	Total (95% CI)			Urban (95% CI)			Rural (95% CI)		
	Number (thousand)	Crude rate (per 100,000)	ASR (per 100,000)	Number (thousand)	Crude rate (per 100,000)	ASR (per 100,000)	Number (thousand)	Crude rate (per 100,000)	ASR (per 100,000)
All									
Incidence	352.29	51.16	31.92	254.61	57.68	34.12	97.68	39.52	27.33
	(346.92-357.73)	(50.38-51.96)	(31.43-32.46)	(251.31-258.00)	(56.93-58.44)	(33.64–34.59)	(95.62–99.78)	(38.69-40.38)	(26.71-27.93)
Mortality	74.26	10.78	6.27	52.80	11.96	6.55	21.45	8.68	5.62
	(71.77-76.83)	(10.42-11.16)	(6.04-6.50)	(51.29-54.36)	(11.62-12.32)	(6.34-6.77)	(20.48-22.47)	(8.29-9.09)	(5.36-5.91)
Prevalence*	2794.47	405.85	255.12	2052.85	465.05	277.03	741.62	300.10	209.09
	(2753.17-2836.46)	(3998.50-4119.50)	(2510.80-2592.70)	(2026.79-2079.22)	(459.15-471.03)	(273.26-280.89)	(726.38-757.24)	(293.93-306.42)	(204.55-213.80)
DALYs	2633.42	382.46	235.71	1845.32	418.04	243.90	788.10	318.90	217.03
	(2546.73-2723.42)	(369.87-395.53)	(227.21-244.68)	(1793.86-1898.31)	(406.38-430.04)	(236.37-251.73)	(752.88-825.10)	(304.65-333.88)	(206.61-228.04)
Premenopausal									
Incidence	63.14	16.75	10.09	43.63	18.82	10.31	19.50	13.44	9.48
	(61.76-64.55)	(16.39–17.13)	(9.85-10.36)	(42.84-44.45)	(18.48–19.17)	(10.08-10.54)	(18.93-20.1)	(13.04-13.85)	(9.16–9.79)
Mortality	7.39	1.96	1.17	5.00	2.16	1.17	2.39	1.65	1.14
	(6.93–7.88)	(1.84-2.09)	(1.09–1.25)	(4.74-5.27)	(2.05 - 2.27)	(1.11 - 1.24)	(2.19-2.61)	(1.51-1.80)	(1.04-1.25)
Prevalence*	518.24	137.49	82.87	363.94	156.99	85.97	154.31	106.34	74.90
	(507.06-529.79)	(134.52-140.55)	(80.81-85.01)	(357.32-370.74)	(154.13-159.92)	(84.13-87.90)	(149.74-159.05)	(103.19-109.61)	(72.45-77.46)
DALYs	442.18	117.31	70.56	296.71	127.99	70.02	145.47	100.25	69.07
	(415.57-470.63)	(110.25-124.86)	(65.83-75.72)	(282.04-312.19)	(121.66-134.66)	(66.00-74.34)	(133.53-158.44)	(92.02-109.19)	(63.09-75.62)
Perimenopausal									
Incidence	127.07	100.32	99.23	87.57	102.39	101.48	39.51	96.02	94.55
	(125.71-128.45)	(99.24-101.41)	(98.15-100.31)	(86.74-88.39)	(101.43-103.35)	(100.52-102.43)	(38.96-40.06)	(94.69-97.36)	(93.22-95.89)
Mortality	19.74	15.58	15.20	13.21	15.44	15.16	6.53	15.87	15.28
	(19.20-20.28)	(15.16-16.01)	(14.78-15.63)	(12.89-13.53)	(15.08-15.82)	(14.79–15.53)	(6.31-6.76)	(15.34-16.42)	(14.75-15.81)
Prevalence*	1037.60	819.17	810.29	729.02	852.49	844.85	308.58	749.94	738.44
	(1026.49-1048.76)	(810.4-827.98)	(801.56-819.06)	(722.19-735.85)	(844.49-860.47)	(836.88-852.80)	(304.30-312.91)	(739.54–760.45)	(728.08-748.93)
DALYs	915.90	723.09	710.18	617.14	721.65	711.90	298.76	726.06	705.50
	(892.52-939.68)	(704.63-741.86)	(691.83-728.84)	(603.29-631.14)	(705.46–738.03)	(695.78-728.18)	(289.23-308.54)	(702.91-749.83)	(682.51-729.13)
Postmenopausal									
Incidence	162.08	87.63	90.32	123.41	99.46	102.18	38.66	63.51	66.12
	(159.46-164.74)	(86.21-89.07)	(88.90-91.73)	(121.72-125.12)	(98.10-100.84)	(100.84-103.54)	(37.73-39.62)	(61.99-65.08)	(64.61-67.69)
Mortality	47.13	25.48	24.82	34.60	27.88	26.84	12.53	20.59	20.69
	(45.63-48.68)	(24.67-26.32)	(24.03-25.61)	(33.65-35.57)	(27.12-28.66)	(26.11-27.57)	(11.98-13.11)	(19.68-21.53)	(19.80-21.59)
Prevalence*	1238.62	669.70	697.81	959.89	773.61	803.13	278.74	457.89	482.97
	(1219.62-1257.91)	(659.42-680.12)	(687.39–708.38)	(947.27-972.62)	(763.44–783.87)	(792.85-813.52)	(272.35-285.28)	(447.40-468.64)	(472.24-493.93)
DALYs	1275.34	689.55	702.57	931.47	750.70	758.47	343.87	564.89	588.65
	(1238.64–1313.11)	(669.71–709.97)	(682.63-723.05)	(908.53-954.99)	(732.22–769.66)	(740.03-777.41)	(330.12-358.13)	(542.29-588.30)	(565.72-612.38)

\* 10-year prevalence of breast cancer. Abbreviations: ASR, age-standardized rate using world Segi's standard population; DALYs, disability-adjusted life years.



Fig. 1. The incidence, prevalence, mortality, and DALYs of breast cancer in China, 2020. (A) Incidence; (B) Prevalence; (C) Mortality; (D) DALYs. DALYs, disabilityadjusted life years.

DALYs in postmenopausal women, of which over 85% were attributed to YLLs and less than 15% attributed to YLDs for breast cancer patients in all of the three status (Table 1, Supplementary Table 1). The crude DALYs rate was the lowest (117.31 per 100,000 persons) in premenopausal women and the highest (723.09 per 100,000 persons) in perimenopausal women. The age-standardized DALYs rates were higher in urban areas than in rural areas for the three menopausal status (Table 1).

# 3.3. Trends for breast cancer incidence, prevalence, mortality and DALYs from 2000 to 2017

From 2000 to 2017, the age-standardized incidence and prevalence rates of breast cancer showed rapid increase, with the AAPC being 4.98% (95% CI, 4.47%–5.49%) and 5.62% (95% CI, 5.10%–6.14%), respectively. The age-standardized mortality and DALYs rates showed slightly increasing trends, with an AAPC less than 2%. For different regions, the age-standardized incidence, mortality, prevalence, and DALYs rates in rural regions increased higher than those in urban regions (Fig. 2, Table 2).

For different menopausal status, the most rapid increase of the age-standardized incidence, mortality, prevalence, and DALYs rates were observed in postmenopausal women, with the AAPC being 5.58% (95% CI, 4.89%–6.28%), 2.94% (95% CI, 2.44%–3.44%), 5.95% (95% CI, 5.07%–6.84%), and 2.96% (95% CI, 2.47%–3.45%), re-

spectively. Perimenopausal women showed a relatively slow increase in incidence (AAPC: 4.57%, 95% CI: 3.64%–5.50%) and prevalence (AAPC: 4.74%, 95% CI: 4.26%–5.22%) than postmenopausal and premenopausal women. Notably, the mortality (AAPC: 0.21%, 95% CI: -0.54% to 0.96%) and DALYs (AAPC: 0.52%, 95% CI, -0.18% to 1.23%) rates remained stable in perimenopausal women. As for different regions, both the age-standardized incidence and prevalence rates showed highly increasing trends in urban and rural regions among the three menopausal status, especially in rural regions (Table 2, Supplementary Fig. 1). To note, the age-standardized mortality and DALYs rates showed slightly downward trends in perimenopausal women with the AAPC being -0.93% (95% CI, -1.47% to -0.40%) and -0.73% (95% CI, -1.22%to -0.24%). The trends for age-standardized YLLs and YLDs are provided in Supplementary Table 2.

## 3.4. Projection of the burden of breast cancer incidence, mortality, prevalence, and DALYs

The projections for the future burden of breast cancer incidence, mortality, prevalence, and DALYs by different menopausal status through 2030 by region in China are presented in Table 3 and Supplementary Tables 3 and 4. By 2030, the number of estimated breast cancer new cases and deaths will rise to 452,000 (95% CI, 446,000–458,000), 3,557,600 (95% CI, 3,512,300–3,603,700) and 98,800 (95% CI, 96,000–101,700), with an increase of 28.30% in cases, 27.31% in



Fig. 2. The trends of incidence, prevalence, mortality, and DALYs rate for breast cancer in China during 2000–2017 and prediction from 2018 to 2030. (A) Incidence; (B) Prevalence; (B) Mortality; (D) DALYs. DALYs, disability-adjusted life years.

prevalence, and 32.97% in deaths compared to 2020. When dividing the burden of breast cancer into the change of age-specific rate and demographic factors, an increase of 24.30% in breast cancer cases, 23.30% in prevalence, and 29.07% in deaths can be attributed to the changes of age-specific rates, with only approximately 4% of the increased burden owing to demographic factors (population size increase or aging) (Table 3, Fig. 3). The changes for the burden of YLLs and YLDs were similar to those of the incidence and mortality (Supplementary Table 5).

#### 4. Discussion

This study systematically estimated the breast cancer burden of different menopausal status in China in 2020 by using the updated data from the National Cancer Center, analyzed the long-term trends from 2000 to 2017, and predicted the burden to 2030. So far, this is the first study in China to report the burden of breast cancer by different menopausal status. We estimated that there were 352,300 new breast cancer cases and 74,300 breast cancer deaths among Chinese women, resulting in 2.63 million DALYs in 2020. The age-standardized incidence and prevalence rates of breast cancer showed rapid increases from 2000 to 2017, especially for postmenopausal women with an AAPC of 5.58%. The incidence, mortality, prevalence, and DALYs will have a 28.30%, 32.97%, 27.82%, and 22.98% increase up to 2030 compared to 2020, respectively.

The results of our study were slightly different from GLOBOCAN and GBD studies.<sup>1,16</sup> The age-standardized incidence and mortality of breast cancer were 31.92/100,000 and 7.43/100,000 respectively, lower than the estimated value of GLOBOCAN 2020 (39.1/100,000 for incidence and 9.5/100,000 for mortality).<sup>1</sup> The possible reason for this difference may be due to the different data sources. The GLOBOCAN estimated breast cancer incidence and mortality using the average incidence and mortality rates of 23 cancer registries' data from 2000 to 2012, which had a relatively high burden of breast cancer in these regions. The agespecific incidence rate had two peaks at age 50 and 60 years, respectively, which was similar to the previous study,<sup>23</sup> but earlier than Western countries<sup>24,25</sup> and later than Japan and South Korea.<sup>26,27</sup> In 2020, the 10-year prevalence and YLDs of breast cancer were 2.79 million and 263.3 thousand person-years, respectively, lower than the estimated results of the GBD groups.<sup>28</sup> This may be because the estimation of the GBD disease burden also used second-hand data, and the data reached to 2012 only, covering a small population and unable to accurately reflect the cancer burden in China.

Trend analysis showed that from 2000 to 2017, the incidence, prevalence, and YLDs of breast cancer continued to increase. The agestandardized incidence, mortality, prevalence, and DALYs rates of postmenopausal women increased the most rapidly, similar to the results of a previous study.<sup>29</sup> The rapid development of social economy, acceleration of urbanization, and changes of lifestyle and behavior patterns may be the reasons for the rapid increase of postmenopausal breast can-

#### Table 2

The trends of age-standardized rates (ASR) of breast cancer incidence, mortality, prevalence and DALYs rates in women by different menopausal status in China, 2000–2017.

Status	Total, % (95% CI)	Urban, % (95% CI)	Rural, % (95% CI)	
All				
Incidence	4.98*(4.47-5.49)	2.50*(2.00-2.99)	6.81*(6.25-7.38)	
Mortality	1.84*(1.45-2.22)	0.39*(0.04-0.73)	2.45*(1.74-3.17)	
Prevalence#	5.62*(5.10-6.14)	2.48*(1.90-3.07)	8.52*(8.01-9.03)	
DALYs	1.71*(1.34-2.08)	0.27(-0.05-0.59)	2.41*(1.71-3.10)	
Premenopausal				
Incidence	4.98*(4.21-5.76)	2.44*(1.99-2.90)	7.64*(5.94–9.36)	
Mortality	0.89*(0.10-1.69)	-0.75(-1.98-0.49)	2.12*(0.80-3.47)	
Prevalence <sup>#</sup>	5.52*(4.74-6.30)	2.40*(1.90-2.91)	9.79*(8.82-10.78)	
DALYs	1.25*(0.51-2.00)	-0.42(-1.47-0.65)	2.42*(1.14-3.72)	
Perimenopausal				
Incidence	4.57*(3.64–5.50)	1.57*(0.60-2.55)	6.08*(5.31-6.85)	
Mortality	0.21(-0.54-0.96)	$-0.93^{\circ}(-1.47 - 0.40)$	0.80(-0.61-2.23)	
Prevalence#	4.74*(4.26-5.22)	1.44*(0.79-2.11)	7.47*(6.69-8.26)	
DALYs	0.52(-0.18-1.23)	$-0.73^{\circ}(-1.22-0.24)$	1.18(-0.18-2.55)	
Postmenopausal				
Incidence	5.58*(4.89-6.28)	3.25*(2.66-3.85)	5.88*(3.80-8.01)	
Mortality	2.94*(2.44-3.44)	1.31*(0.87–1.76)	3.52*(2.58-4.46)	
Prevalence <sup>#</sup>	5.95*(5.07-6.84)	3.16*(2.49-3.83)	8.80*(7.90-9.72)	
DALYs	2.96*(2.47-3.45)	1.34*(0.92-1.77)	3.51*(2.60-4.42)	

\* Average annual percent change during 2000 to 2017 is significantly different from zero (P < 0.05).

<sup>#</sup> 10-year prevalence of breast cancer.Abbreviations: ASR, age-standardized rate using world Segi's standard population; DALYs, disability-adjusted life years.

cer in China. According to the Health and Nutrition Survey of Chinese Residents, the traditional diet patterns in China have shifted to high-fat and calorie diets like the Western diet patterns. The obesity rates in adult women increased from 7.6% in 2002 to 11.7% in 2010.<sup>30</sup> Continued low

birth rate and breastfeeding rate may be other reasons for the high burden of breast cancer. The growing incidence for premenopausal breast cancer may attributed to reproductive factors. In China, the total fertility rate declined sharply between 1970 (5.9 births per woman) to 2010 (1.7 births per woman).<sup>31,32</sup> The government initiated two strategies, the "two-child policy" in 2015 and the "three-child" policy in 2021, to stimulate childbirth, but the effect was less than expected.<sup>33,34</sup> According to the National Health Service Survey, the 5-month breastfeeding rate decreased from 64.5% in 1993 to 24.1% in 2013.35 Oral contraceptives and hormonal menopausal therapy among perimenopausal women were risk factors for breast cancer.<sup>36-38</sup> In Western countries, the incidence of breast cancer at age 50-59 years decreased during 2000-2012, mainly due to the decline in the use of estrogen-related treatment after the Women's Health Survey published in 2002.<sup>36,37</sup> In China, the proportion of oral contraceptives and hormonal menopausal therapy was relatively low and had a small effect on the burden of breast cancer.<sup>39</sup> In addition, the growing aging population in China may also be a driving factor to the growth of breast cancer.<sup>11,20,40</sup>

The mortality rate of breast cancer remained stable in urban areas, but showed a small increase in rural areas. Notably, the mortality rate of breast cancer among perimenopausal women in urban areas showed a slightly downward trend, with approximately 1% decline per year. The trend of YLLs was similar to the mortality rates. The mortality was influenced by socioeconomic factors, the stage of first diagnosis, and the treatment level of breast cancer.<sup>41-44</sup> In Western countries, the mortality rate of breast cancer declined by approximately 39% between 1985 and 2015, owing to the early screening projects and improvement in clinical treatment therapies in the 1980s.<sup>45,46</sup> In China, there are two ongoing screening projects for breast cancer.<sup>47</sup> One is the "Screening for Breast Cancer and Cervical Cancer Program" for rural women, initiated in 2009, aiming at screening 1.2 million 35–64 years old rural women. To 2019, the project was incorporated into basic public health services and

#### Table 3

Predicted burden of new breast cancer cases, deaths, prevalence and DALYs in China and changes between 2020 and 2030 apportioned into changes because of age-specific rate and demographics by region.

Region		No. (95% CI), 10 <sup>3</sup>	No. (95% CI), 10 <sup>3</sup>		Change between 2020 and 2030, %		
	2020	2025	2030	Total change	Change due to demographics	Change due to age-specific rate	
Total							
Cases	352.29	402.27	451.97	28.29	4.00	24.29	
	(346.92-357.74)	(396.59-408.03)	(446.03-458.01)				
Deaths	74.26	86.89	98.78	33.02	3.96	29.06	
	(71.77-76.83)	(84.21-89.66)	(95.96-101.69)				
Prevalence <sup>#</sup>	2794.47	3175.04	3557.61	27.31	4.01	23.30	
	(2742.22-2836.46)	(3131.63-3219.12)	(3512.33-3603.68)				
DALYs	2633.42	2960.28	3237.40	22.94	4.02	18.92	
	(2546.73-2723.42)	(2869.59-3054.50)	(3144.70–3333.96)				
Urban							
Cases	254.61	298.41	347.95	36.66	12.95	23.71	
	(251.31-257.96)	(294.86-302.01)	(344.12-351.84)				
Deaths	52.80	62.22	73.11	38.47	12.94	25.53	
	(51.29–54.36)	(60.58–63.90)	(71.35–74.92)				
Prevalence <sup>#</sup>	2052.85	2398.07	2781.29	35.48	12.95	22.53	
	(2026.79-2079.22)	(2370.14-2426.34)	(2751.33-2811.69)				
DALYs	1845.32	2085.79	2352.16	27.47	12.96	14.51	
	(1793.86–1898.31)	(2031.74–2141.25)	(2295.87-2410.24)				
Rural							
Cases	97.68	103.86	104.02	6.49	-11.97	18.46	
	(95.62–99.78)	(101.73–106.03)	(101.91–106.18)				
Deaths	21.45	24.67	25.67	19.67	-11.94	31.61	
	(20.48-22.47)	(23.63–25.76)	(24.61-26.77)				
Prevalence <sup>#</sup>	741.62	776.97	776.33	4.68	-11.96	16.64	
	(715.44–757.24)	(761.48–792.78)	(761.00-791.98)				
DALYs	788.10	874.50	885.24	12.33	-11.95	24.28	
	(752.88-825.1)	(837.84–913.24)	(848.83–923.72)				

<sup>#</sup> 10-years prevalence cases.

Abbreviations: DALYs, disability-adjusted life years.



Change due to demographic factors Change due to age-specific rate Total change

Fig. 3. Decomposition of changes in cases, prevalence, deaths, and DALYs due to age-specific rates and demographic factors in China, 2020–2030. DALYs, disabilityadjusted life years.

rolled out nationwide. The coverage of breast cancer screening at the population level for women aged 35–64 years has gradually increased over the last decade, from 23% in 2013 to 31% in 2019.<sup>48</sup> The screening rate in urban regions were higher than that in rural regions (23% vs 20.6%).<sup>49</sup> The other project was launched in urban areas in 2012, aiming to screen urban women aged 45–74 years. However, the long-term effect of the two projects on breast cancer has not been observed. Screening-related harms and overdiagnosis also need further evaluation.

Early detection of breast cancer will also be conducive to improving the survival of breast cancer,<sup>50</sup> whereas the proportion of stage I breast cancer was only 25.8% in China, much lower than that in the United States (49.4%).<sup>51</sup> Breast cancer therapy has progressed substantially over the past years and needs to be decided in a multidisciplinary setting, taking molecular subtype and locoregional tumor load into account.<sup>52</sup> Primary conventional surgery is not the optimal choice for all patients any more. For example, neoadjuvant therapy has become a new option for triple-negative and HER2-positive early breast cancer.<sup>52</sup> For metastatic breast cancer, adding targeted therapy to endocrine therapies could prolong the progression-free survival by 4.6 months for postmenopausal women patients.<sup>53</sup> From the public health perspective, living standards and the state of the healthcare system are also related to the dynamic change of mortality.<sup>44</sup>

As a strength, we combined the most representative and high-quality updated breast cancer data to estimate the burden of breast cancer. The burden of breast cancer on different menopausal status was reported for the first time in China, which would help to more accurately formulate strategies in breast cancer prevention and control. Nonetheless, the study has several limitations. Firstly, the long-term trends of breast cancer from 2000 to 2017 were analyzed based on data only from 22 high-quality cancer registries, which may inadequately reflect the trends in China. Secondly, due to lack of individual level menopause information, the menopausal status was classified using age as a proxy index, which may lead to non-differential misclassification of some cases. This is, however, inevitable because detailed menopause data is not obtained in cancer registry database. Finally, because of the lack of individual risk factors, the prediction of breast cancer burden only took age, period, and cohort effect into account. Further research is needed to assess the impact of a single risk factor or combined risk factors on breast cancer burden.

#### 5. Conclusion

This study systematically estimated the burden of breast cancer and predicted the burden to 2030. The total burden of breast cancer continues to increase in China, especially among perimenopausal and postmenopausal women. Specific prevention and control strategies for different menopausal women will be more helpful in reducing the rapidly growing burden of breast cancer.

#### Declaration of competing interest

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

#### Acknowledgments

We sincerely thank all the local cancer registry staff in China for their contribution to data collection, validation, and routine analyses. We also thank the CAMS Innovation Fund for Medical Sciences (grant number: 2021-I2M-1-011) that supported this study.

#### Author contributions

R.Z., S.L. and W.W. performed the study design. R.Z. and S.L. conducted the data analyses. S.L. drafted the original manuscript. S.L., S.Z., S.W., and W.W. performed the revision and edition. W.W. supervised and led the study.

#### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jncc.2024.04.007.

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