


ORIGINAL ARTICLE

Urban rural disparity in female breast cancer incidence rate in China and the increasing trend in parallel with socioeconomic development and urbanization in a rural setting

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Keywords

Healthy diet; obesity and/or overweight; prevention of female breast cancer; socioeconomic development; urbanization.

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Abstract

Background: Worldwide breast cancer incidence correlates with socioeconomic status and increases in parallel with westernization, however urban–rural disparity and trends have not been adequately investigated in China.

Methods: The age standardized rate (ASR) of female breast cancer by population-based cancer registration was compared between urban Shijiazhuang city and rural Shexian County in relation to socioeconomic status. The increasing trend of breast cancer in Shexian County from 2000–2015 was examined using Joinpoint analysis and the correlation with gross domestic product (GDP) per capita was analyzed.

Results: In 2012, the ASR of female breast cancer in Shijiazhuang was more than three times higher than in Shexian County (45.5/1 00 000 vs. 13.8/1 00 000; $P < 0.01$) when the GDP per capita was 2.6 times higher (US\$6964.80 vs. US\$2700). In parallel with rapid socioeconomic development and urbanization, the biennial ASR of female breast cancer in Shexian county has increased significantly from 2.8/1 00 000 in 2000–2001 to 17.3/1 00 000 in 2014–2015, with an average biennial percent change of +10.2% ($P < 0.01$). The Pearson correlation between ASR and GDP was significantly positive ($r = 0.94$, $P < 0.01$).

Conclusion: The incidence of breast cancer in women in China is increasing along with lifestyle westernization and changing reproductive patterns associated with socioeconomic development and urbanization. Urgent prevention measures, including the development of a healthy diet, giving birth at a younger age, an increase in breastfeeding, limiting menopause estrogen therapy, and control of alcohol consumption, are required.

Introduction

In China, the risk factors for breast cancer are significantly different between urban and rural women, and risk transitions have taken place in parallel with socioeconomic development and urbanization over the past three decades. There has been a steady increase in the prevalence of overweight and obese conditions, reduced physical activity, reduced fertility and breastfeeding, older age at first birth, and earlier age of menarch.¹ However, the changing epidemiology of breast cancer has been inadequately documented. For

example, although China has the world's largest urban–rural disparity in socioeconomic development,² the difference in age standardized incidence rate (ASR) of breast cancer in women reported between 77 Chinese cities and 100 counties for 2011 was merely 31.6 vs. 21.0 per 100 000,³ much smaller than that the difference reported between developed and developing countries according to GLOBOCAN 2012 (73.4 vs. 31.3 per 100 000).⁴ These statistics suggest that urban–rural classification criteria may be flawed. By highlighting a striking urban–rural disparity in female breast cancer

between urban Shijiazhuang city and rural Shexian county in Hebei province and a progressively increasing trend from 2000–2015 in Shexian County in parallel with socioeconomic development and urbanization, this paper aims to draw the attention of health policy-makers to the urgent need for breast cancer prevention in China.

Methods

Shexian

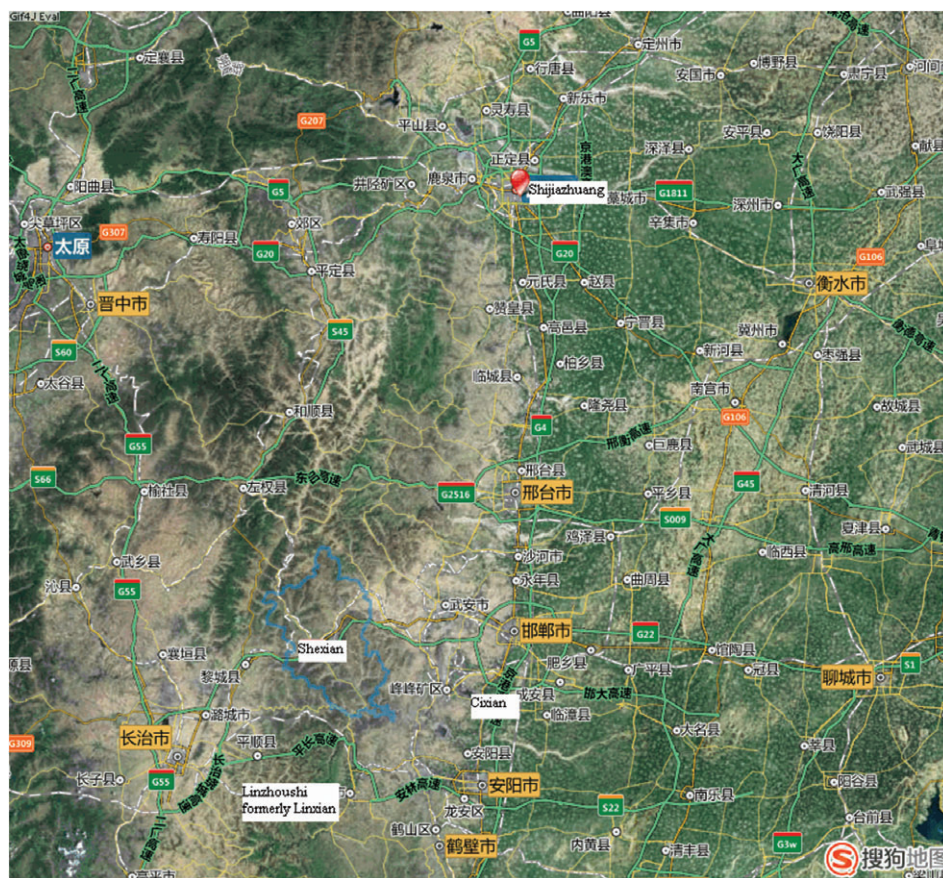
Shexian County is located 200 km southwest of Shijiazhuang city, which is the capital city of Hebei province. Shexian County is an entirely mountainous region that joins the three provinces of Hebei, Henan, and Shanxi (Fig 1). In 2012, its population was 408 998. Shexian County is a northern neighbor of Linxian County of Henan province and a northwestern neighbor of Cixian County of Hebei province. All three counties have been noted for extraordinary high incidence rates of esophago-gastric cancers.⁵ Shexian is a rural agricultural county, consisting of a town and 580 villages. In 2012, 48% of the population lived in the town, and 52% in villages. Town economy relies on employment in the iron/steel, thermal

power, agricultural product, food manufacture, and tourist industries; while the rural population is engaged in growing rice, wheat, persimmon, Chinese prickly ash, and walnuts. The diet in Shexian has traditionally been of agrarian style, with a staple food of rice or steamed buns flavored with vegetables, soybean, pork, or eggs, although since the 1990's a transition has occurred toward a more westernized style of diet. Occupational manual exertion is the primary physical activity for villagers, but in town the majority of people aged ≥ 60 walk or jog in the morning or evening.

Shijiazhuang city

Shijiazhuang is located 200 km northeast of Shexian County (Fig 1). At the beginning of the 20th century, it was not an urban city and consisted of over a dozen villages. The villages were located at the crossing point of the north-south bound Peking–Wuhan railway and the east-west bound Shijiazhuang–Taiyuan railway. Prime urbanization began in 1953 when it was chosen by the Chinese central government as the capital of Hebei Province and one of cities with development priority during the first national five-year program (1953–1957). During

Figure 1 Geographic location of urban Shijiazhuang city (upper right) at the foot of Taihang Mountain and Shexian county located 250 km southwest in the Taihang mountain ranges.



the program, the North China Pharmaceutical Corporation, the largest antibiotic factory in Asia, and five modern textile plants were established in Shijiazhuang city. Upon completion of the five-year program, the total number of municipal employees had increased from 81 067 to 182 188, and the total municipal population from 182 188 to 376 792.

Population-based tumor registration

Population-based cancer registration was established in Shexian County in 1999 and in Shijiazhuang City in 2010, by the National Central Cancer Registry of China (NCCRC) and the International Association of Cancer Registration (IACR). The Chinese Ministry of Health provides a running budget. Cancer diagnoses are reported to local cancer registries from multiple sources, including local hospitals and community health centers, as well as the local Urban Resident Basic Medical Insurance Program and the New Rural Cooperative Medical Scheme, public insurance programs with almost complete coverage of registered urban or rural residents since 2011. Data quality is supervised and assessed annually by NCCRC before publication.

Population data

Population data concerning the gender and age distribution in Shexian County and Shijiazhuang city was obtained from the Population Division of the local Public Security Bureau (Fig 2). The 2012 population in Shexian County was 408 998 (male: female ratio 1.07:1), and in urban Shijiazhuang was 2, 374 827 (male: female ratio 0.95:1).

Statistical methods

Age-specific incidence rates were calculated by dividing the number of new cancer cases by the number of people at age intervals of 0, 1–4, 5–9...80–84, 85+. The rates were then multiplied by the proportion of people in that age interval using Segi's standard world population (a hypothesized 100 000 people),⁶ and then added to obtain the ASR. The Segi world standard population was first introduced by Segi in 1960, drawn from a pooled population of 46 countries and modified by Doll *et al.* in 1966. The Segi–Doll world standard population is used throughout the world to standardize incidence rates for comparison.

The difference in ASR of female breast cancer between Shexian County and Shijiazhuang city was tested using approximate methods described by Esteve *et al.*⁷ Briefly, the approximate method uses the formula: $Z = (t_1 - t_2) / \sqrt{m_1 t_1 + m_2 t_2} / (m_1 m_2)$, where t_1 and t_2 are the

rates to be compared and m_1 and m_2 are person-years of observation, to calculate the value of Z , assumes that Z obeys standard normal distribution. If the Z value is > 1.96 , the hypothesis of equality of the rates between the two populations is rejected at a level of significance of $\alpha = 0.05$.

The trends of biennial ASR of female breast cancer in Shexian between 2000 and 2015 were analyzed using Join-Point Analysis 4.2.0.2 (<http://surveillance.gov/joinpoint>). Pearson's correlation coefficient between biennial ASR of breast cancer incidence and the corresponding gross domestic product (GDP) value in Shexian County from 2000–2015 was analyzed by bivariate correlation using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA).

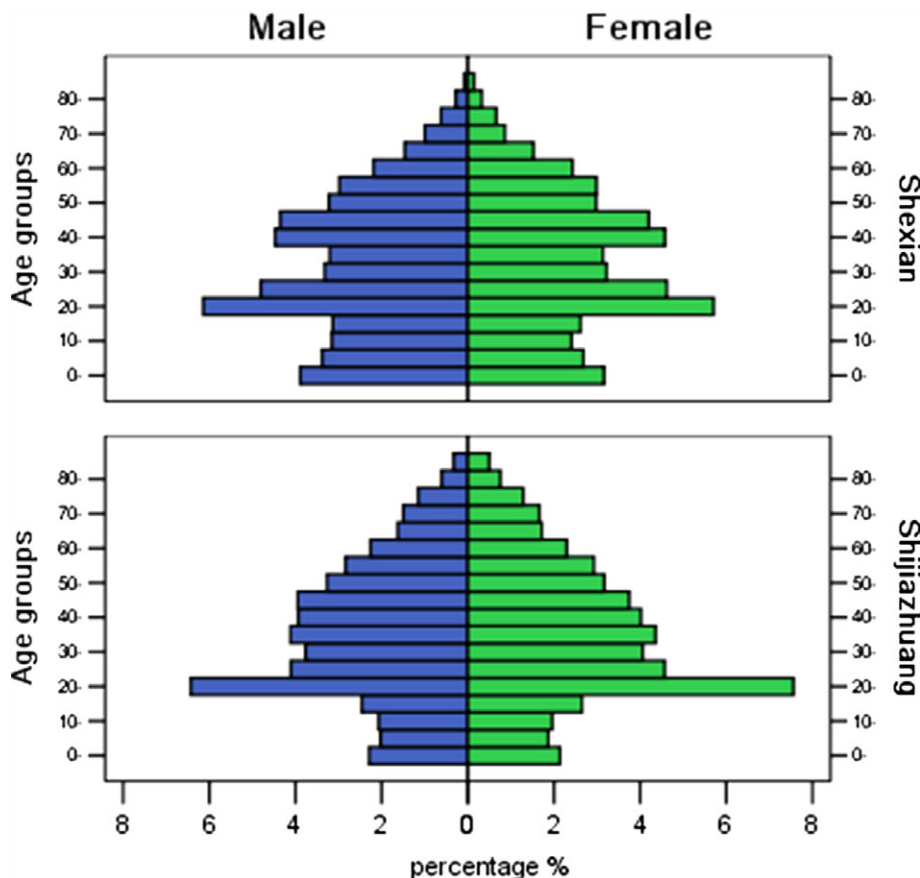
The study was approved by the Institutional Ethics Review Board of the Fourth Hospital of Hebei Medical University.

Results

Comparison of 2012 demographic and lifestyle characteristics

Although both regions started from a rural agrarian background 60 years ago, Shexian is considerably underdeveloped in comparison to Shijiazhuang. As shown in Table 1, in which demographic and socioeconomic data obtained from government websites^{8–12} or published papers^{13,14} are listed, the GDP per capita in 2012 was 2.6 times higher in Shijiazhuang than in Shexian County (US\$6964.80 vs. US\$2700). The annual disposable income per person was US\$1538 for Shijiazhuang but only US\$750 for Shexian residents. Shijiazhuang residents spent more of their disposable income on diet than those in Shexian (40% vs. 20%). The proportion of animal food in the diet was higher in Shijiazhuang ($> 30\%$) than in Shexian ($< 10\%$). Regarding physical activity, Shijiazhuang residents led a more sedentary lifestyle because of the greater availability of white-collar jobs and the fact of living in a relatively more built-up environment. By contrast, Shexian residents are physically more active as a result of working in agricultural roles or walking. As is true in other non-metropolitan areas of China, women in both regions seldom smoke cigarettes or drink alcohol. The prevalence of daily smoking in men is higher in Shexian than in Shijiazhuang (40% vs. 35%), whereas the prevalence of habitual alcohol drinking is the opposite (Shijiazhuang 38% vs. Shexian 25%). Although the prevalence of an overweight condition was similar between the two areas, obesity incidence was higher in urban Shijiazhuang than in rural Shexian women (23.2% vs. 17.1%). In addition, the population in Shijiazhuang is older than in Shexian: the percentage of residents aged < 25 in Shexian was 36.29% compared to 31.46% in

Figure 2 Comparison of the population pyramids between rural Shexian County and urban Shijiazhuang city in 2012.



Shijiazhuang and of residents aged ≥ 65 years was 11.15% and 6.98%, respectively (Fig 2). A four-year difference in life expectancy was observed between Shijiazhuang and Shexian in 2012 (75 vs. 71 years). The birth rate was higher in Shexian than in Shijiazhuang (1.8 vs. 1.1). Shexian women give birth four years younger than Shijiazhuang women (23 vs. 27 years), and breastfeeding is more common among Shexian than Shijiazhuang women (95% vs. 60%) (Table 1).

Comparison of 2012 age standardized incidence rate (ASR) of female breast cancer

Of the 1 217 437 women registered in Shijiazhuang City in 2012, 726 breast cancer cases were diagnosed, for a crude incidence rate of 59.6/1 00 000. Breast cancer accounted for 28.7% of all new cancer cases and was the most commonly diagnosed cancer in women. In contrast, in Shexian in 2012 only 36 breast cancer cases were diagnosed among the 197 416 women, for a crude incidence rate of 18.1/1 00 000. Breast cancer accounted for only 6.6% of all new cancer cases in Shexian women. It was the fifth most

common cancer after stomach, esophageal, cervical, and lung cancers.

The ASR of female breast cancer was 3.3 times higher in Shijiazhuang than in Shexian (45.5 vs. 13.8/1 00 000; $P < 0.01$), and the cumulative incidence rate for 0–74 years was 3.5 times higher (5.2% vs. 1.5%; $P < 0.01$). These differences between Shijiazhuang and Shexian are much larger than the corresponding differences reported between 77 Chinese cities and 100 Chinese counties for 2011 (31.6 vs. 20.1/1 00 000, $P < 0.05$; 3.5% vs. 2.2%, $P < 0.05$, respectively) (Table 2).³

In addition to female breast cancer, the ASR of lung cancer in men in Shijiazhuang was also significantly higher than in Shexian (46.5 vs. 30.0/1 00 000; $P < 0.01$), but not in women (19.0 vs. 20.8/1 00 000). Other significantly higher cancer incidence included colorectal (22.8 vs. 11.9/1 00 000, $P < 0.01$ in men; 14.9 vs. 9.3/1 00 000, $P < 0.01$ in women), kidney (6.9 vs. 2.2/1 00 000, $P < 0.05$ in men; 3.9 vs. 0.5/1 00 000, $P < 0.05$ in women), pancreatic (3.1 vs. 0.1/1 00 000, $P < 0.01$ in men; 2.4 vs. 0.8/1 00 000, $P < 0.10$ in women), thyroid (1.9 vs. 0.1/1 00 000, $P < 0.05$ in men; 3.9 vs. 0.8/1 00 000, $P < 0.05$ in women), prostate (5.3 vs. 0.7/1 00 000, $P < 0.01$), and ovarian cancer (7.0 vs. 2.1/1 00 000, $P < 0.05$) (Table 3).

Table 1 Comparison of demographic and lifestyle characteristics between urban Shijiazhuang and rural Shexian in 2012

Demographic	Urban Shijiazhuang	Rural Shexian
Population (2012)	2374827 ⁸	408,995 ⁹⁻¹²
% of urban population (2012)	100% ⁸	48% ⁹⁻¹²
Altitude (m above sea level)	30–100 m	1000 m
Latitude N	37°27'~38°47'	36°17'~36°55'
GDP per capita 2012 (US\$)	6964.8 ⁸	2700 ⁹⁻¹²
Annual net income per person 2012 (US\$)	3000 ⁸	1200 ⁹⁻¹²
Annual disposable income per person 2012 (US\$)	1538 ⁸	750 ⁹⁻¹²
% of annual disposable income spent on diet 2012	40% ⁸	20% ⁹⁻¹²
% of animal products in diet (as opposed to plant food) 2012	> 30% ⁸	< 10% ⁹⁻¹²
% of people that regularly exercise 2010	60% ⁸	10% ⁹⁻¹²
% of people employed in manual labour 2010	20% ⁸	70% ⁹⁻¹²
% daily smoker men 2010	35% ⁸	40% ⁹⁻¹²
% habitual alcohol drinker men 2010	38% ⁸	25% ⁹⁻¹²
Fertility rate 2012	1.1 ⁸	1.8 ⁹⁻¹²
Age of menarch 2012 (years)	12.0 ⁸	13.0 ⁹⁻¹²
Age at first birth 2012 (years)	27 ⁸	23 ⁹⁻¹²
Age at menopause 2012 (years)	55.8 ⁸	55.5 ⁹⁻¹²
Breastfeeding 2012	60% ⁸	95% ⁹⁻¹²
Household automobile 2015 (%)	40 ⁸	12 ⁹⁻¹²
Household mobile phone 2015 (%)	100 ⁸	90 ⁹⁻¹²
Household refrigerator 2015 (%)	100 ⁸	60 ⁹⁻¹²
% overweight male (BMI ≥ 24 kg/m ²) 18–69 years, 2004	43.7 ^{13,14}	30.2 ¹³
% overweight female (BMI ≥ 24 kg/m ²) 18–69 years, 2004	36.7 ^{13,14}	35.4 ¹³
% obese male (BMI ≥ 28 kg/m ²) 18–69 years, 2004	19.9 ^{13,14}	14.5 ¹³
% obese female (BMI ≥ 28 kg/m ²) 18–69 years, 2004	23.2 ^{13,14}	17.1 ¹³
% aged < 25	31.46 ⁸	36.29 ⁹⁻¹²
% aged ≥ 65	11.15 ⁸	6.98 ⁹⁻¹²
Life expectancy in 2012 (years)	75 ⁸	71 ⁹⁻¹²

BMI, body mass index; GDP, gross domestic product.

Conversely, the ASR of stomach cancer in men in Shexian is 5.7 times higher than in Shijiazhuang (162.0 vs. 28.5/1 00 000; $P < 0.01$) and 9.3 times higher in women (71.5 vs. 7.7/1 00 000; $P < 0.01$); esophageal cancer is 4.6 times higher in men (72.1 vs. 15.7/1 00 000; $P < 0.01$) and 8.8 times higher in women (36.2 vs. 4.1/1 00 000; $P < 0.01$); and liver cancer is 3.2 times higher in women (13.3 vs. 4.2/1 00 000; $P < 0.01$). In addition to upper gastrointestinal cancer, the ASR of cervical cancer is three times higher in Shexian compared to Shijiazhuang women (25.0 vs. 8.4/1 00 000; $P < 0.01$). All of these cancer types are infection-related, associated with disadvantaged socioeconomic development (Table 3).

Socioeconomic development and urbanization and risk factors for non-communicable diseases between 2000–2015 in rural Shexian County

Shexian is traditionally a rural agrarian county, but as is the case in most of eastern and central China, rapid socioeconomic development and urbanization has taken place since 1978, particularly in the last two decades. From 2000

to 2015, a boom in real estate development led to a shift in the economy from agricultural and heavy industry toward service and tourism. Overall, the annual GDP of Shexian County increased from US\$860 to US\$3000.⁹⁻¹² In addition to increasing income and supply of manufactured food, a transition in diet has gradually take place, with the staple starch food or soybean formerly consumed replaced by increasing proportions of high-energy animal products, such as saturated fat, meat, eggs, and milk. In recent decades, most young or middle-aged villagers joined the rural–urban migrant population. From 2000 to 2015, the proportion of town residents increased from 22.4% (85 000/3 80 000) to 54.8% (230 000/4 20 000), representing an increase of 170%, with an annual increase of 10.7%.⁹⁻¹² As a result of the altered diet, reduced physical activity, and migration from a rural to an urban environment, lifestyles are becoming increasingly westernized.

In addition to rural–urban migration, the construction of cement or bitumen roads linking villages to the town had commenced in 2000 and was completed by the end of 2005, thus reaching all 580 villages.⁹⁻¹² Each day, buses run between the town and villages, picking up villagers to and from work and shopping. Thus, the villagers' diet has also changed.

Table 2 Comparison of female breast cancer incidence rates

Age group	Urban Shijiazhuang 2012	Rural Shexian 2012	77 Chinese cities 2011†	100 rural counties 2011†
0~	0.00	0.00	0.00	0.00
1~	0.00	0.00	0.00	0.00
5~	0.00	0.00	0.05	0.00
10~	0.00	0.00	0.00	0.00
15~	0.00	0.00	0.00	0.16
20~	0.00	0.00	1.04	1.27
25~	7.37	5.29	4.54	5.16
30~	22.84	7.59	13.81	11.37
35~	41.52	15.57	33.28	25.39
40~	77.42	21.36	61.29	48.90
45~	136.96	46.52	93.09	68.33
50~	150.13	57.40	100.80	63.64
55~	153.57	49.10	106.99	72.58
60~	159.09	30.17	96.21	61.63
65~	127.56	32.09	91.27	44.65
70~	165.09	28.36	87.65	38.76
75~	88.37	37.00	82.30	32.56
80~	27.88	0.00	72.84	24.96
85+	8.37	0.00	48.85	15.81
Crude rate (1/10 ⁵)	59.63	18.24	46.74	28.43
ASR (China) (1/10 ⁵)	48.54	11.33	33.66	22.59
ASR (1/10 ⁵)	45.52	13.83	31.63	20.96
Cum rate 0–74 years (%)	5.18	1.47	3.45	2.21

†Source Jia *et al.*, 2015.³ ASR, age standardized incidence rate.

Consumption of sausage, soda, and potato chips has become common in children. In the past, walking was the principle means of transportation in this mountainous area, but now with greatly improved road conditions, more and more villagers are in possession of cars and motorbikes.

In parallel with economic growth and urbanization, the prevalence of an overweight condition (body mass index [BMI] ≥ 24 kg/m²) in women aged 18–69 in Shexian tripled from 1991 (11.0%) to 2010 (33.0%), and the prevalence of obesity (BMI ≥ 28 kg/m²) in women aged 18–69 reached 15% in 2010 (Table 1).¹³ Meanwhile, the county has also experienced rapid population aging. The proportion of residents aged ≥ 60 increased from 7.9% in 2000 to 13.9% in 2015.^{9–12} Women in Shexian rarely smoke or drink alcohol. As a result of the one child policy that was in place from 1978 to 2013, the total fertility rate has remained stable at 1.8 in Shexian County from 2000 through 2015.^{9–12} We retrospectively surveyed the average age of menarche using a randomly chosen sample of high school girls, and observed a decrease from age 13.8 years in 2000 to 12.4 years in 2015.

Increasing female breast cancer incidence and positive correlation with GDP growth in rural Shexian County, 2000–2015

In JoinPoint Analysis, the biennial ASR of female breast cancer in Shexian County between 2000 and 2015

increased over 500% from 2.8/1 00 000 to 17.3/1 00 000 (average biennial percent change [ABPC] = +10.2%; $P < 0.01$) (Table 4, Fig 3). In Pearson correlation analysis, a significant positive correlation was observed between increasing biennial ASR of breast cancer and the biennially averaged GDP ($r = 0.94$, $P < 0.01$) (Table 4).

Notably, although breast cancer incidence increased significantly between 2000 and 2015 in Shexian county, parallel with socioeconomic development and urbanization, by 2012, the ASR was still less than a third of the rate in Shijiazhuang City (13.8 vs. 45.5/1 00 000; $P < 0.01$), while the GDP per capita was US\$ 2700 vs. US\$6964, respectively. These results suggest that this trend will continue to increase in Shexian.

Discussion

Worldwide breast cancer incidence increases with industrialization and urbanization

Worldwide, the incidence of breast cancer increases in parallel with socioeconomic development. According to GLOBOCAN 2012, the ASR in developed countries (73.4/1 00 000) was 2.4 times higher than in developing countries (31.3/1 00 000).⁴ In the present study, we found that although Shijiazhuang and Shexian had had a similar

Table 3 Comparison of ASR of major cancer types, 2012

Tumor site	Cases		Rank		Incidence rate (1/10 ⁵)		Percentage (%)		ASR World (1/10 ⁵)		P†
	USZ	RSX	USZ	RSX	USZ	RSX	USZ	RSX	USZ	RSX	
Male											
Lung (C33–34)	786	72	1	3	67.9	33.4	25.2	9.3	46.5	30.0	< 0.01
Stomach (C16)	469	389	2	1	40.5	180.4	15.1	50.2	28.5	162.0	< 0.01
Colorectal (C18–21)	381	29	3	5	32.9	13.7	12.2	3.7	22.8	11.9	< 0.01
Liver (C22)	279	46	4	4	24.1	21.3	9.0	5.9	17.4	18.5	
Esophagus (C15)	266	172	5	2	23.0	79.8	8.5	22.2	15.7	72.1	< 0.01
Kidney (C64–66,68)	114	5	6	8	9.9	2.3	3.7	0.6	6.9	2.2	< 0.05
Prostate (C61)	106	2	7	10	9.2	0.9	3.4	0.3	5.3	0.7	< 0.01
Leukemia (C91–95)	104	9	8	6	9.0	4.2	3.3	1.2	6.5	4.0	< 0.20
Bladder (C67)	101	5	9	8	8.7	2.3	3.2	0.6	5.8	3.0	< 0.20
Lymphoma (C81–85,88,90,96)	100	8	10	7	8.6	3.7	3.2	1.0	6.3	3.1	< 0.10
Pancreas (C25)	50	0	11	11	4.3	0.0	1.6	0.0	3.1	0.1	< 0.01
Larynx (C32)	39	4	12	9	3.4	1.9	1.3	0.5	2.4	1.6	
Gallbladder (C23–24)	38	4	13	9	3.3	1.9	1.2	0.5	2.4	1.6	
Thyroid (C73)	29	0	14	11	2.5	0.0	0.9	0.0	1.9	0.1	< 0.05
Brain (C70–72)	27	9	15	6	2.3	4.2	0.9	1.2	2.0	4.5	< 0.05
Nasopharynx (C11)	21	5	16	8	1.8	2.3	0.7	0.6	1.3	2.1	
Bone (C40–41)	14	9	17	6	1.2	4.2	0.4	1.2	0.9	4.1	< 0.01
All Male Cancer	3114	775			269.1	359.5	100.0	100.0	187.5	325.2	< 0.01
Female											
Breast (C50)	726	36	1	5	59.6	18.2	28.7	6.6	45.5	13.8	< 0.01
Lung (C33–34)	346	46	2	4	28.4	23.1	13.7	8.4	19.0	20.8	
Colorectal (C18–21)	260	22	3	7	21.4	11.1	10.3	4.0	14.9	9.3	< 0.05
Stomach (C16)	137	166	4	1	11.3	83.2	5.4	30.3	7.7	71.5	< 0.01
Cervix (C53)	132	64	5	3	10.8	32.1	5.2	11.7	8.4	25.0	< 0.01
Corpus uteri (C54)	126	18	6	8	10.4	9.0	5.0	3.3	7.9	7.0	
Ovary (C56)	112	6	7	11	9.2	3.0	4.4	1.1	7.0	2.1	< 0.05
Lymphoma (C81–85,88,90,96)	93	6	8	11	7.6	3.0	3.7	1.1	5.5	2.5	< 0.10
Esophagus (C15)	79	86	9	2	6.5	43.1	3.1	15.7	4.1	36.2	< 0.01
Liver (C22)	74	30	10	6	6.1	15.0	2.9	5.5	4.2	13.3	< 0.01
Leukemia (C91–95)	66	8	11	10	5.4	4.0	2.6	1.5	4.6	5.3	
Thyroid (C73)	60	2	12	15	4.9	1.0	2.4	0.4	3.9	0.8	< 0.05
Kidney (C64–66,68)	60	1	12	16	4.9	0.5	2.4	0.2	3.9	0.5	< 0.05
Pancreas (C25)	44	2	13	15	3.6	1.0	1.7	0.4	2.4	0.8	< 0.10
Bladder (C67)	21	4	14	13	1.7	2.0	1.7	0.2	1.4	2.0	
Gallbladder (C23–24)	20	5	15	12	1.6	2.5	0.8	0.9	1.3	2.3	
Brain (C70–72)	12	18	16	8	1.0	9.0	0.5	3.3	1.0	7.3	< 0.01
Bone (C40–41)	11	9	17	9	0.9	4.5	0.4	1.6	0.8	4.0	< 0.01
Nasopharynx (C11)	9	0	18	17	0.7	0.0	0.4	0.0	0.7	0.0	
Larynx (C32)	1	3	19	14	0.1	1.5	0.0	0.5	0.1	1.1	< 0.01
All Female Cancer	2527	547			207.6	274.2	100.0	100.0	150.4	230.7	< 0.01

†Calculated using the approximate method for the comparison of incidence of a disease in two groups as described in Esteve *et al.* 1994.⁷ ASR, age-standardized incidence rate; RSX, rural Shexian; USZ, urban Shijiazhuang.

agrarian economy before 1953, 60 years of unequal development since then has resulted in significant urban–rural disparity in breast cancer incidence: 45.5 vs. 13.8/1 000 000 in 2012. This difference is much larger than that reported between 77 Chinese tumor registration cities and 100 counties in 2011 (31.6 vs. 21.0/1 000 000).³

Although GLOBOCAN 2012 reported that breast cancer ASR incidence in China was among the lowest of all

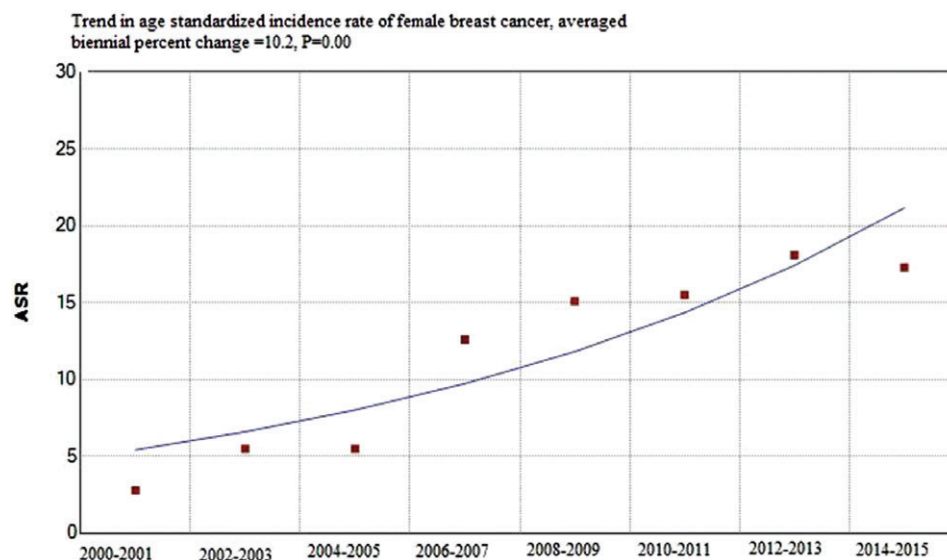
countries,⁴ since that time rapid social economic development and changing reproductive patterns have seen the Chinese rate increase twice as fast as the average global rate.¹ By 2012, the ASR of female breast cancer in Shijiazhuang city (45.5/1 000 000) reached the level of countries with a high human development index (45.2/1 000 000),⁴ about half of the rate of Northern American women (91.6/1 000 000).⁴ Although the rate in Shexian County was still

Table 4 Biennial ASR of female breast cancer 2000–2015 and average biennial GDP in Shexian County

	2000–2001	2002–2003	2004–2005	2006–2007	2008–2009	2010–2011	2012–2013	2014–2015	ABPC _{1–8}	P <
Standardized incidence rates (1/100)										
Breast (C50)	2.8	5.5	5.5	12.6	15.1	15.5	18.1	17.3	10.2	0.00**
GDP US\$	880	1175	1480	1765	2050	2180	2710	2950		

** $P < 0.01$. ABPC, average biennial percent change; ASR, age standardized incidence rate; GDP, gross domestic product.

Figure 3 Trends in biennial age standardized incidence rates (ASR) of female breast cancer in rural Shexian County between 2000 and 2015 by JoinPoint Analysis 4.2.0.2. Average biennial percent change 10.2, $P = 0.00$.



low in 2012 (13.8/1 00 000), it increased over 500% between 2000 and 2015, from 2.8 to 17.3 per 100 000, with an ABPC of +10.2% ($P < 0.01$).

Breast cancer burden expected to increase in China

Because of significant disparity in socioeconomic development, modernization and urbanization in China still has a long way to go. Hong Kong is the most westernized city in China, with the highest breast cancer incidence of all Chinese cities; however, this rate is still lower than Singapore.¹⁵ In Hong Kong, the ASR of female breast cancer rose on average 1.7% per annum between 1976 and 2010. On the basis of these trends, Wong *et al.* predicted that the female breast cancer ASR would increase from 56.7 in 2011–2015 to 62.5/1 00 000 in 2021–2025.¹⁶ Between 2010 and 2015, urbanization in China was taking place at a rate of 3.1% annually. By 2015, 55.6% of the Chinese population had moved into cities, leading to a percentage of city dwellers 29.4% higher than in 1990.¹⁷ Generations of women affected by the family planning program (implemented from the late 1970s until the early 2010s) have not reached the peak age of incidence (around 50 years old), thus the effect of the family planning program has not yet been

fully realized. As a result of these factors, breast cancer incidence is expected to increase in the coming years.

Breast cancer prevention

Marked urban–rural disparity and the rising rate of breast cancer incidence in parallel with socioeconomic development and urbanization suggest breast cancer is preventable.¹⁸ The American Cancer Society Guidelines on nutrition and physical activity for cancer prevention recommend maintaining a healthy body weight, increasing physical activity, and minimizing alcohol intake to reduce the risk of developing breast cancer.¹⁹ Based on the distribution of major breast cancer risk factors in a representative sample of Mainland Chinese women ($n = 17\ 078$) participating in the Chinese National Family Planning and Reproductive Health Survey, Linos *et al.* predicted modest reductions in menopausal hormone and alcohol use, and that weight maintenance could prevent 270 000 of the 2.5 million cases of breast cancer that would occur by 2021 (among the total population of 130.3 million Chinese women aged 35–49 years in 2001).^{1,20}

In conjunction with the prevention measures recommended for adults, dietary patterns in childhood have a significant effect on the risk of breast cancer. In a study of

Asian emigrants to Hawaii and the United States mainland, mothers recalled their children's diets during different age periods. The results indicated that soy offers protection against breast cancer in those who have a high intake during childhood, but that the effect decreases in adolescence and adulthood.²¹ A prospective cohort study from China confirmed this finding.²² In recent decades in China, however, western-style fast food and high-sugar drinks have become more and more popular among children and fried chicken, hot sausages, or processed meat have replaced the traditional Chinese diet of soybeans or puffed rice. Overweight and obese conditions have increased and the age of menarche among girls has significantly decreased as a result of these high calorie and high fat diets. Ma *et al.* reported that the age of menarche among urban Chinese girls decreased from 13.5 years in 1979 to 12.27 years between 2003 and 2005.²³ A study by Iqbal *et al.* found that each year decrease in the age of menarche significantly increased the risk of breast cancer (odds ratio 1.67, 95% confidence interval 1.09–2.56; $P = 0.02$).²⁴ Considering that childhood and adolescent exposure has a significant impact on adult breast cancer risk, limiting the development of an unhealthy food industry aimed at children should be a priority in China.²⁵

The predominance of breast cancer cases in younger women has been observed in Mainland China since the 1980s. In 2008, breast cancer was diagnosed in 78% of women aged < 65 in China, compared to 57% in the United States.²⁶ In China, the increasing ASR of breast cancer is particularly rapid in women aged < 50. The rate peaks at 50 years of age and then subsequently plateaus or declines. This pattern suggests that exposure to breast cancer risk factors differs significantly between women born before and after westernization. However, as the older generation dies out and the birth cohort effect disappears, age distribution will gradually approach that of western countries.²⁶ In the present study, the age distribution in Shexian County was younger than in Shijiazhuang city, and that in 100 Chinese counties was younger than in 77 cities (Fig 4). The predominance of younger breast cancer cases is biologically relevant. The positive rate of hormone receptor in these younger patients is significantly lower than in breast cancer patients aged ≥ 50 .²⁶ Because hormone receptor-negative breast cancer is generally more aggressive than positive, such as basal-like cancer or triple negative breast cancer, younger breast cancer patients have a poorer prognosis on average than postmenopausal women with breast cancer in China.²⁶ A recent meta-analysis including 21 941 breast cancer patients and 864 177 controls concluded that breast feeding was associated with a reduced risk of developing triple-negative breast cancer (odds ratio 0.79, 95% confidence interval 0.66–0.94; $P = 0.01$).²⁷ Therefore, encouraging breastfeeding as a preventive policy may

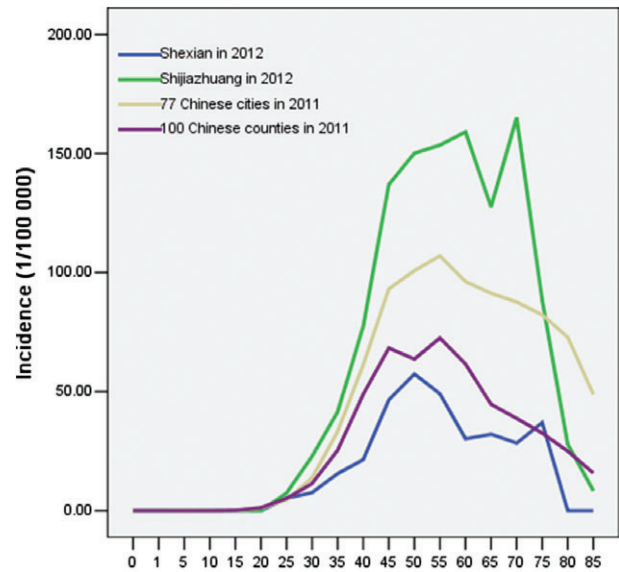


Figure 4 Urban-rural comparison of age-specific incidence curves of female breast cancer in China.

produce a positive effect in China, especially after the one child policy was discontinued in 2013.

Another major concern with breast cancer in China is that although the incidence and mortality rates are low at present, the prognosis is very poor, especially in rural women. The five-year relative survival rate of breast cancer in Chinese women was only 73.0% in 2003–2005²⁸ compared to 91% in American women in 2005–2011.²⁹ Along with differences in treatment practices between the two countries,²⁶ another important cause for the substantial difference in survival is the stage at which the cancer is detected. Less than 1% of breast cancer patients in China were detected with carcinoma in situ at diagnosis in 1999–2008,³⁰ whereas in the United States the proportion was 20% in both non-Hispanic white and African American women in 2013.³¹ This difference is determined to a large extent by different screening techniques. Although population-based breast cancer screening has been practiced for nearly half a century in developed countries and breast cancer has been proven as one of the few cancers for which screening is a successful weapon, the coverage of mammography screening for breast cancer is still very low in China. The overall mammography screening rate in China was only 21.7% in 2010,³² while population-based mammography screening in America women was 68.5% in 2008.³³ Therefore, specific screening schemes tailored for high-risk groups, such as women with low birth rates, reduced breast-feeding, obesity, or a positive family history of cancer should be incorporated into primary health service programs.

Previous studies of urban-rural disparity in cancer in China have defined urban or rural population according to

administration level.³⁴ Prefecture-level cities (e.g. a province-governing city) or municipalities are considered urban, while county or county-level cities are regarded as rural. However, in addition to the urban and suburban population, a typical Chinese prefecture-level city also includes several rural counties. When the latter are misclassified as urban, the real urban–rural difference is diluted. For example, the difference in ASR of female breast cancer in 77 Chinese cities (31.6/1 00 000) and 100 counties (21.0/1 00 000) reported by Jia *et al.*³ was much smaller than that reported between more and less developed countries in GLOBOCAN 2012 (73.4 vs. 31.3 per 100 000).⁴ This may also explain the inconsistent results for urban–rural disparity in cancer so far reported in China.^{34,35} As a result, we limited our comparison to pure urban and rural female populations and found a much larger disparity (45.5/1 00 000 vs. 13.8/1 00 000).

A limitation of this study may lie in the representativeness of Shexian County for rural China. Because Shexian County has been endemic for esophagogastric cancers, it may be socioeconomically more disadvantaged than other counties in China and may have a somewhat lower incidence rate of breast cancer in women. However, situated in northern central China, Shexian County is socioeconomically more developed than most counties in southwestern and northwestern China. In 2010, it had a total product value of 21.4 billion RMB yuan (US\$3.6 billion). Its economy was ranked 19th during 2001–2005 and 13th during 2006–2010 among 136 counties in Hebei province.¹¹

In conclusion, we found a threefold urban–rural disparity in the breast cancer incidence rate between sample rural and urban regions in China. The rate in urban Chinese women has reached the level of countries with a high human development index, according to GLOBOCAN 2012. The rate in both urban and rural settings will continue to increase in parallel with socioeconomic development and urbanization. To reduce the increasing burden, interventions targeted at modifiable risk factors, such as improving the quality of food provided to children, weight control to avoid overweight or obese conditions, giving birth at a younger age, and increases in physical activity, breastfeeding, and breast cancer screening, should be incorporated into public health programs.

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Disclosure

No authors report any conflict of interest.

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