

RESEARCH ARTICLE

Mortality Characteristics and Prediction of Female Breast Cancer in China from 1991 to 2011

Xiao-Jun Shi^{1,2}, William W Au^{1,3}, Ku-Sheng Wu¹, Lin-Xiang Chen¹, Kun Lin^{1*}

Abstract

Aims: To analyze time-dependent changes in female breast cancer (BC) mortality in China, forecast the trend in the ensuing 5 years, and provide recommendations for prevention and management. **Materials and Methods:** Mortality data of breast cancer in China from 1991 to 2011 was used to describe characteristics and distribution, such as the changes of the standardized mortality rate, urban-rural differences and age differences. Trend-surface analysis was used to study the geographical distribution of mortality. In addition, curve estimation, time series modeling, Gray modeling (GM) and joinpoint regression were performed to estimate and predict future trends. **Results:** In China, the mortality rate of breast cancer has increased yearly since 1991. In addition, our data predicted that the trend will continue to increase in the ensuing 5 years. Rates in urban areas are higher than those in rural areas. Over the past decade, all peak ages for death by breast cancer have been delayed, with the first death peak occurring at 55 to 65 years of age in urban and rural areas. Geographical analysis indicated that mortality rates increased from Southwest to Northeast and from West to East. **Conclusions:** The standardized mortality rate of breast cancer in China is rising and the upward trend is predicted to continue for the next 5 years. Since this can cause an enormous health impact in China, much better prevention and management of breast cancer is needed. Consequently, disease control centers in China should place more focus on the northeastern, eastern and southeastern parts of China for breast cancer prevention and management, and the key population should be among women between ages 55 to 65, especially those in urban communities.

Keywords: Epidemiological characteristics - female breast cancer - prediction - standardized mortality - China

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Introduction

Breast cancer is by far the most frequent cancer among women with an estimated 1.38 million new cancer cases diagnosed in 2008 (23% of all cancers) (Ferlay et al., 2010). Breast cancer is also the leading cause of cancer deaths for women in both developing (269,000 deaths, 12.7% of total) and developed regions. The estimated 189,000 deaths in the latter are almost equal to the estimated number of deaths from lung cancer (188,000 deaths) (Bray et al., 2010; Ferlay et al., 2010; Shin et al., 2010). According to the most updated cancer registries in China, breast cancer has become the most common female cancer. Furthermore, the mortality of breast cancer has increased markedly in Chinese women during the past decade.

Many epidemiological studies report that breast cancer mortality rates have been increasing, especially in developing countries. These studies mainly describe incidence and mortality rates, and trends for breast cancer by population (race/ethnicity), location, age and calendar time (Franco et al., 2009; Lazcano et al., 2009; Lopez et al., 2009; Curado et al., 2011). However, there is very

limited information about tendency and prediction on these incidence and mortality of breast cancer in China. Consequently, Chinese scientists have to speculate on trends of dynamic changes about the standardized mortality rate, urban-rural differences and age differences by each province and city (Yang Ling et al., 2005; Chen et al., 2006; Roy et al., 2012; Chun et al., 2012; Powell et al., 2012). Prediction of the trends and identification of geographic patterns of breast cancer mortality, based on population and location, may provide impetus to conduct further investigations and can direct health resources for the development of more useful prevention and management policies.

Among epidemiologic studies, the statistical methods used were mostly purely spatial analyses using the discrete Poisson, Bernoulli, and multinomial models. These investigations show that different spatial patterns in mortality are most likely the result of different underlying processes stemming from demographic, socio-economic, health behavioral, and relevant risk factors (Li et al., 2003; Smigal et al., 2006; Franco et al., 2009; Lazcano et al., 2009; Lopez et al., 2009; Bambhroliya et al., 2012; Burau, et al., 2012; Sexton et al., 2012). Trend surface

¹Department of Preventive Medicine, ³MPH Education Center, Shantou University Medical College, Shantou, ²NanShang Meternity & Child care Hospital of Shenzhen, China *For correspondence: klin@stu.edu.cn

analysis is a means of separating a mapped variable into two components: the trend and the residuals. Trend surface analysis not only shows the overall distribution of the disease, but also reflects disease variation in local areas, as well as the regional distribution and trend of disease (Huanxin et al., 1991). Therefore, our investigation aimed to document the epidemiological characteristics and distribution of breast cancer, and the dynamic changes in standardized mortality rate (SMR), age and urban-rural differences. Trend-surface analysis, as one of the most widely used global surface-fitting procedures, was used to reflect geographical distribution and trends of disease. In addition, we probed available data to estimate the potential trend distribution of the disease, and provide enhanced impetus for prevention and management of breast cancer.

Materials and Methods

Data Source

Data came from the nation-wide cancer mortality survey for the period 1991-2011 of the National Cancer Control Office, Ministry of Public Health. Data collection followed the rules and standards of the International Agency for Research on Cancer (IARC) and the International Association for Cancer Registration.

Evaluation of data quality was based on three aspects, including diagnosis reliability, data integrity and coding quality. The death cases of these surveys were about 1.5-10.5% more than that reported by the public security organizations. To ensure reliability, data were collected by doctors having specified professional knowledge. Due to the recent development of Cooperative Health Services in rural areas, the popularization of medical net, and the availability of medical treatment and service for each individual before death, the causes of death became better documented. In addition, the reliability of the data was routinely checked by professionals using standard criteria. The data were also compared with data from the same areas in which there was a completed report and registration system of causes of death and the result was consistent with mean test and fitting test. Therefore, the quality of these surveys and the data are credible (China health statistics yearbook, 2007a; 2007b; Ping, 2008; Zhu; 2008; China health statistics yearbook, 2009a; 2009b; Ping; 2009; China health statistics yearbook, 2010a; 2010b; China health statistics yearbook, 2011a; 2011b; Ping, 2012).

Statistical analysis

The crude rate (CR), standardized mortality rate (SMR), age-standardized rate by world population (WSR), age-standardized rate by Chinese standard population (CASR) were used in the statistical analysis. The Segi's world population standard and the 1982 Chinese standard population were used for age adjusting.

Methods

Cancer incidence and mortality rates were calculated based on the national registered data of female malignant tumors from 1991 to 2011. The calculation allowed us to evaluate the dynamic changes in SMR of breast cancer,

identify the change of distributions by population, time and place (three-dimension distribution), and estimate the trend over the next few years.

Trend surface analysis was used to demonstrate the geographic distributions of breast cancer mortalities and related factors in China. The world standardized mortality rates of breast cancer in China from 2003 to 2008 and in 37 registered cities/towns (these geographical locations were registered more than twice during the nearly five years) were used for our analysis. To overview the trend of geographical distribution of SMR, we tried to fit the first to fourth order regression equations. The dependent variables of the equations were longitude (x) and latitude (y), and the independent one (z) was the SMR of various cities/towns. Four different methods, including the R-square test, F-test, goodness of fit order by order test, and a subjective judgment method based on geographical epidemiology of breast cancer, were applied to select the order of trend surface modeling. Trend-surface analyses and distribution map drawings were conducted using SAS release 9.0.

Our analysis aimed to estimate the trend of breast cancer mortality in China from the period of 1991 to 2011, and to predict the trend in the ensuing 5 years. With curve estimation, time series modeling, gray modeling (GM) and joinpoint regression, we could predict epidemic trends of BC that could be used to establish an early warning system for breast cancer. The information could provide public health agencies with a scientific basis to implement disease prevention and management. Statistical analysis was performed by SPSS15.0, DPS 7.05 and Joinpoint 3.5.3. Data that described distributions were plotted Sigmplot 11.0 to present figures.

The curve estimation routine in SPSS was used to compare linear, logarithmic, inverse, quadratic, cubic, power, compound, S-curve, logistic, growth, and exponential models based on their relative goodness of fit for models where a single dependent variable was predicted by a single independent variable or by a time variable. Before selecting a more complex model, we should first consider if a transformation of the data might enable a simpler one to be used, even linear regression. Thus in this investigation, x stands for the time (year) and y stands for SMR. Models are types of linear and nonlinear curves which may be fitted to the data. In this way curve estimation not only can aid in model selection as an exploratory tool, prior to exploring the model with an appropriate statistical procedure which supports multivariate analysis and which has more input and output options, but also can probe the available data for more information and estimate the potential trend distribution of breast cancer data.

Time series forecasting was used to collect past observations of the same variable and to develop a model that describes the underlying relationship. Autoregressive integrated moving average (ARIMA), known as the Box-Jenkins model, had the fundamental impact on the time series analysis and forecasting applications. In addition, various exponential smoothing models could be implemented by ARIMA models. Methodology in this paper includes three iterative steps of model identification, parameter estimation and diagnostic checking. Through

the repeated steps, the constructed ARIMA (Holt) was adopted for prediction. The autocorrelation function (ACF), partial autocorrelation function (PACF), mean squared error (MSE) and mean absolute deviation (MAD) are selected to be the forecasting accuracy measures. The model was then used to extrapolate the time series into the future of the SMR. This modeling approach was particularly useful when little knowledge was available on the underlying data generating process or when there was no satisfactory explanatory model that related the prediction variable to other explanatory variables.

Gray system theory uses a black-gray-white color spectrum to describe a complex system whose characteristics are only partially known or known with uncertainty. The prediction for the trend of breast cancer may concern many factors and is mechanically complicated. When information is comparatively inadequate, GM (1, 1) model in the gray system theory is adopted to predict the change of BC in China. GM (1, 1) can effectively characterize the behavior of the few outputs using fewer (at least four number) information. With DPS software, we input the number 1-21 as the time dependent variable and the SMR as the independent variable to construct models. In order to make the prediction more accurate, we also adopted the improved GM (1, 1) model group and dynamic equal dimensional number progress complement so as to avoid the deficiencies of one-direction gray model, which was easily affected by unstable information.

Joinpoint regression was used as statistical software for the analysis of trends using joinpoint models. In this analysis, several different lines were connected together at the "joinpoints". It took trend data (e.g. cancer rates) and fitted the simplest joinpoint model that the data allowed. The program started with the minimum number of joinpoints (e.g. 0 joinpoints, which is a straight line) and tested whether more joinpoints were statistically significant and should be added to the model (up to that maximum number). The models might incorporate estimated variations for each point (e.g. when the responses are SMR). In addition, the models might also be linear on the log of the response (e.g. for calculating annual percentage rate change (APC) and average annual percent change (AAPC)). Thus, we fitted a joinpoint model to find out the estimated tendency and to get the APC and AAPC of BC in China.

Results

Time-dependent changes in Mortality Rates of Female Breast Cancer

Based on the increased mortality rate among Chinese women in recent decades, it can be found that breast cancer is the second leading cancer-related cause of death among women. Breast cancer is currently the sixth most common cause of overall death in Chinese women, compared to the ninth cause from 1970s to 1990s. There is a steady increase in the standardized mortality of breast malignancy, rising from 24.24‰ from 1973 to 2004, to 32.89‰ in 2000. This corresponds to an increase from 1.49/105 in 1990 to 1.98/105 in 2000. Among the causes of cancer death in the

female reproductive system, breast cancer has ascended to first with a ratio of 7%. The increment of the mortality rates is alarming.

Age characteristics of female breast cancer mortality

Breast cancer usually occurs post puberty, and its incidence increases slowly from 30 years-old, reaching a peak at the ages of 40~60, and then falling (vv 1). Consequently, it may be logical that the mortality has increased significantly as the population ages. With regard to urban women, it is interesting that the mortality rate increased with two peak times. The first peak age for death in 21st century appears at age 55, compared to 45 in 1990s, while the second peak has been delayed from age 80, in 1990s, to age 85 in the 21st century. From these results, it is clear that the mortality rate of breast cancer has advanced in urban areas whereas, over the past ten years, the mortality of breast cancer has generally declined in rural women. There are three peak ages for death: 45, 60, and 80 in 1990s; as well as 55, 75, and 85 from 2002 to 2011. The data also show that the peak age for death was also delayed by 10-15 years. Over the past decade, all peak ages for death by breast cancer have been delayed comparing with 1990s, and the first death peak occurred at 55 to 65 years of age in urban and rural areas.

Difference between the urban and rural breast cancer mortality

Comparing the mortality rates between rural and urban women, those from the urban areas had significantly higher rates than those from the rural areas (especially in the age group over 45 years-old) (Figure 1). Urban data

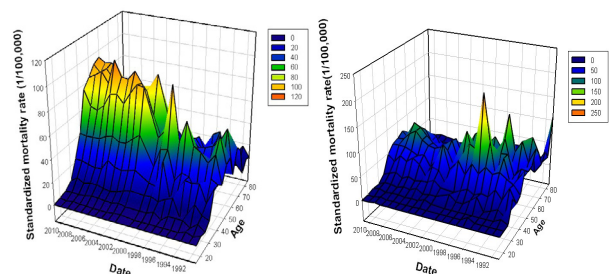


Figure 1. Trends in Age-Specific Mortality of Female Breast Cancer by Area in China From 1991-2011 (1/10⁵)

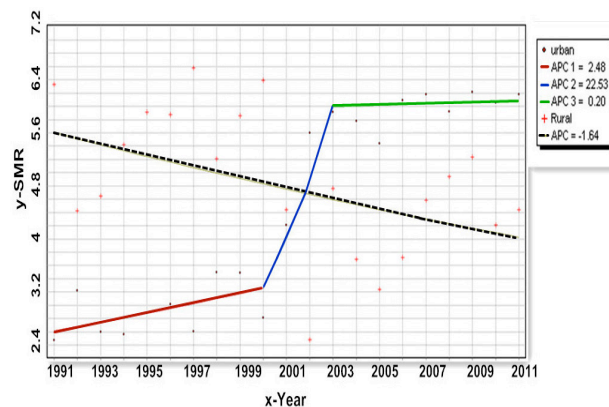


Figure 2. Trends in the Mortality of Female Breast Cancer by Joinpoint Analysis by Area in China From 1991-2011 (1/10⁵)

Table 1. The Modeled Mortalities of Female Breast Cancer by 4 Models in China from 1991 to 2011 (1/10⁵)

Year (X)	Observed WASMR ^a (Y)	Cubic		ARIMA (Holt)		GM (1,1)		Joinpoint	
		Modeled WASMR	Fitted error (%)	Modeled WASMR	Fitted error (%)	Modeled WASMR	Fitted error (%)	Modeled WASMR	Fitted error (%)
1991	4.40	4.04	-8.24	3.89	-11.59	4.14	-5.94	2.62	-40.45
1992	3.82	4.07	6.44	4.01	4.97	3.72	-2.60	2.68	-29.84
1993	3.63	4.10	12.99	4.07	12.12	3.95	8.76	2.75	-24.24
1994	3.99	4.14	3.84	4.10	2.76	4.43	11.06	2.81	-29.57
1995	4.40	4.19	-4.76	4.17	-5.23	4.62	5.03	2.88	-34.55
1996	4.45	4.24	-4.63	4.26	-4.27	4.47	0.45	2.95	-33.71
1997	4.59	4.30	-6.26	4.35	-5.23	4.34	-5.49	3.02	-34.20
1998	4.35	4.37	0.36	4.44	2.07	4.14	-4.92	3.10	-28.74
1999	4.67	4.43	-5.06	4.51	-3.43	4.25	-9.08	3.17	-32.12
2000	4.60	4.51	-2.05	4.60	0.00	4.11	-10.69	3.25	-29.35
2001	4.32	4.58	6.06	4.67	8.10	4.11	-4.76	4.01	-7.18
2002	4.04	4.66	15.37	4.72	16.83	4.48	10.77	4.94	22.28
2003	5.34	4.74	-11.17	4.73	-11.42	5.19	-2.76	6.10	14.23
2004	4.73	4.83	2.08	4.86	2.75	4.69	-0.91	5.98	26.43
2005	4.34	4.92	13.27	4.92	13.36	4.87	12.22	5.86	35.02
2006	4.90	5.01	2.15	4.94	0.82	5.52	12.72	5.74	17.14
2007	5.38	5.10	-5.27	5.01	-6.88	5.70	5.90	5.63	4.65
2008	5.43	5.19	-4.44	5.12	-5.71	5.47	0.81	5.52	1.66
2009	5.72	5.28	-7.65	5.22	-8.74	5.28	-7.62	5.41	-5.42
2010	5.13	5.38	4.79	5.34	4.09	4.89	-4.69	5.30	3.31
2011	5.31	5.47	3.01	5.39	1.51	5.17	-2.61	5.20	-2.07

Overall Models

Fitted		Cubic	ARIMA (Holt)	GM (1,1)	Joinpoint
Median	Interquartile Range	0.36	0.82	-2.6	-7.18
Error (%)	10.59	10.59	10	12.54	40.42
95%CI	(-2.69, 3.72)	(-2.69, 3.72)	(-3.04, 3.70)	(-2.90, 3.44)	(-19.97, 0.28)

^aWASMR- world age-standardized mortality; ^bND-No data

Table 2. The Predicted Mortalities of Female Breast Cancer by 4 Models in China During 2012-2016 (Predicted WASMRsa, 1/10⁵)

Year	Cubic	ARIMA (Holt)	Grey GM (1, 1)	Joinpoint	Overall	
					$\bar{x}\pm SD$	95%CI
2012	5.564	5.460	5.371	5.304	5.425±0.113	(5.314, 5.535)
2013	5.657	5.530	5.448	5.198	5.458±0.194	(5.268, 5.648)
2014	5.749	5.610	5.526	5.094	5.495±0.283	(5.218, 5.772)
2015	5.841	5.680	5.626	4.992	5.535±0.373	(5.169, 5.900)
2016	5.930	5.750	5.687	4.892	5.565±0.460	(5.114, 6.016)
$\bar{x}\pm SD$	5.75±0.145	5.61±0.115	5.53±0.128	5.10±0.163		
95%CI	(5.621, 5.875)	(5.505, 5.707)	(5.419, 5.644)	(4.953, 5.239)		

**WASMRs- world age-standardized mortality rates

showed lower standardized mortality than rural data in the 1990s, but then interchanged to become rapidly higher from the year of 2000. Mortality in the rural areas grew largely in late 1990s, but gradually dropped in nearly 1999, and rose again when the year of 2002. Thus, we have a similar conclusion of the trend between urban and rural breast cancer mortality: both standardized mortality incidences increased for both, revealing mortality being stabilized at high levels in urban areas while being volatile in rural areas (Figure 2). With joinpoint regression analysis, the average annual percent change (AAPC) of the standardized mortality rate in urban areas was 4.1% more than that in rural areas from 2002-2011 (Table 3).

Geographical distribution of the mortality

Four different methods, including the R-square test, F-test, goodness-of-fit order by order test, and

subjective judgment method based on geographical epidemiology of breast cancer, were used to select the order of trend surface modeling. The fourth-order trend surface equation was optimal to show the spatial distribution of breast cancer mortalities in China ($R^2=0.544$, $F=2.39$, $p=0.03$). The fourth-order surface equation is: $z=-35681.0867+742.4855*x+1594.0297*y-4.5285*x*x-30.9920*x*y-19.9228*y*y+0.0071*x*x*x+0.1436*x*x*y+0.4779*x*y*y-0.1698*y*y*y-0.0024*x*x*y*y+0.0009*x*y*y*y+0.0005*y*y*y*y$, where z stands for the standardized mortality ratio of breast cancer for various cities/towns, x stands for longitude of the cities/towns, and y stands for latitude.

The model can fit goodness as 54.4% of the death variation of breast cancer in Chinese women, suggesting several geographic distribution characteristics. The contour maps of breast cancer mortality rates drawn by

the mathematical models showed a unique breast cancer geographic distribution pattern in China. There appeared to be two changing tendencies: one developing step by step from southwest to northeast like a half concentric circle with the southwest (Fusui, Chongqing) reaching the minimum and the northeast (Harbin, Shenyang) holding the maximum, and another tendency from the west inland to the east and the southeast coastal areas (such as Tianjin, Shanghai, and Guangzhou) (Figure 3).

Estimation and forecasting

Up-to-date data is usually in small sample sets, and it is risky to assume the derived distribution, so we attempted to build several predictive models with different statistical methods and compared the results to find a suitable trend for mortality of breast cancer in future years. We assumed the society, the economy, the environment and the lifestyle had no dynamic and changeable characteristics. This made previous data of breast cancer mortality from 1991–2011 suitable for building a predictive model. The error value

(ERR) and the 95% Confidence Interval (CI) are selected to be the forecasting accuracy measures.

Curve estimation: We found the cubic curve model fitted the trend best ($R^2=0.654$, $F=10.701$, $p<0.001$) (Tables 1 and 2). The equation is: $y=4.016+0.018 * x +0.004* x^2+6.021* x^3$, where x stands for the year, and y stands for mortality rate.

Time series model: Depending on the above mortality data, the constructed Holt model was adopted for prediction ($R^2=0.613$, $p=0.151$) (Tables 1 and 2).

Gray model (GM): According to the theory and principle of the gray model, X (i) means the standardized mortality rate of BC, t means the year. We chose the GM (1, 1) model to perform the forecast, with fitting parameters: $a=0.0232$, $b=0.9093$. The equation is: $X(t+1)=-38.44273e-0.02324t+39.12615$ ($C=0.0949$, $p=1.000$, $Qmin=-0.81156$) (Tables 1 and 2).

Joinpoint regression: To fit the model, dependent variable X is the year, and independent variable y is the mortality rate, and we used joinpoint regression analysis to identify points where a statistically significant change over time in linear slope of the trend occurred, and found out the estimated average annual percent change (AAPC) of the standardized mortality rate was 0.6% in China during 2002–2011 (Tables 1, 2 and 3).

Table 3. APC a and AAPC b of Age-Standardized Mortality Rates from Female Breast Cancer in China From 1991-2011

Joinpoint Model				
Trends	APC ^a /AAPC ^b	Urban	Rural	Overall
Segment 0	Years	ND ^d	ND	ND
	APC(95%CI)			
Segment 1	Years	1991-2000	1991-2011	1991-2000
	APC(95%CI)	2.5 (0.5)	-1.6(-3.3,0)	2.4(-0.1,5.1)
Segment 2	Years	2000-2003	ND	2000-2003
	APC(95%CI)	22.5 (-6.3,60.3)		23.3(-6.5,62.6)
Segment 3	Years	2003-2011	ND	2003-2011
	APC(95%CI)	0.2 (-2.7,3.2)		-2.0(-4.9,1.0)
Comparing the AAPC differences in urban and rural areas				
Last5 Obs	AAPC (95%CI)	0.2(-2.7,3.2)	-1.6(-3.3,0)	-2.0(-4.9,1.0)
(2007-2011)	AAPC difference (95%CI)		1.8(-1.2,5.0) ^c	ND
Last10 Obs	AAPC (95%CI)	2.5(-1.2,3.2)	-1.6(-3.3,0)	0.6 (-3.1,4.3)
(2002-2011)	AAPC difference (95%CI)		4.1(0.2,8.0) ^c	ND

^aAPC- annual percentage change; ^bAAPC- average annual percentage change; ^cSignificantly different from zero at alpha=0.05(p<0.05).; ^dND- No data.

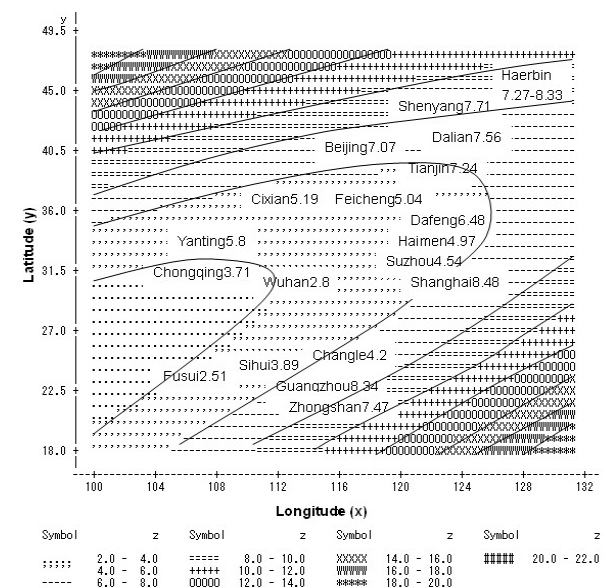


Figure 3. Geographic Distribution of the World Age-Standardized Mortality Rates of Female Breast Cancer in China (1/10⁵)

Discussion

At present, breast cancer is the most common female cancer and is the major cause of cancer deaths. Based on our research, we found that the SMR of breast cancer in China has been steadily rising and the up trend is predicted to continue in the future years. This situation will result in a serious health issue in China. Therefore, we should focus on the prevention and management of breast cancer. Mortality rates generally parallel incidence. Therefore the high incidence rate should result in high mortality, making it important to explore breast cancer etiology to reduce the risk factors and then to reduce the incidence and mortality. The known risk factors for breast cancer include genetic factors, social factors, environmental factors and life-style related factors (Gao et al., 2000; Li et al., 2008).

We find that the mortality rates in urban areas are higher than those in rural areas. The risk factors mentioned above might take effect on the high morbidity and mortality. Also, adaptation of a western lifestyle, such as high-fat diets, less sport exercise, delayed childbearing and low birth rate, etc., has been postulated as being some of the main reasons (Robles et al., 2002). The etiology of breast cancer remains unknown. Due to the lack of strong evidence, primary preventive strategies for breast cancer have commanded little attention. Thus, early detection of tumors by mammography and advances in medical treatment (surgical, radio-therapy, hormonal and chemotherapeutic measures) play a very important role in improving prognosis (outcome) and survival for women developing breast cancer (Shapiro et al., 1998).

Age-adjusted patterns of breast cancer mortality varied largely in all age groups in both city and country from 1990 to 2011, and the differences are particularly significant at the time of menopause. The SMR of breast

cancer show an increase for age groups over 35 years-old and keep markedly rising for age groups 50~55 and 60~65, until a peak appears at 85 years of age. Although the peak age for death by breast cancer was delayed for 10 years over the past decade, the reason may be improvement of prognosis and advances in medical treatment, and it may also be changes in the main cause of death for all ages.

In developed countries, screening has been responsible for a 20% to 30%, and adjuvant therapy for an additional 5 to 10% reduction in mortality (Lee et al., 2002; Vervoort et al. 2004; Cox et al., 2008). Chinese women with breast cancer may benefit even more by adequately tailored screening programs and increased access to effective therapy. Such programs should be accompanied by adequate health education strategies to ensure that all Chinese women are aware of the benefits of mammographic screening, and early breast cancer recognition and treatment. Therefore, breast cancer screening programs need to be launched and X-ray mammography or B-ultrasound need to be provided to women aged 35-65 who are at high-risk and who are in menopause. Besides, it is well known that estrogen receptor positivity is essential for breast cancer development, and the age-incidence curve is dependent on how many cases have the receptor in the population (Anderson et al., 2003). Advance study on receptors would help us improve the medical treatment and life quality. A novel observation from our study shows an increasing trend of breast cancer in young women, particularly in rural areas. It is very important for clinicians to pay more attention to this phenomenon. Young women should become one of the focus groups of prevention and treatment.

Different cancer patterns are found in urban and rural areas according to breast cancer mortality rate: rural areas had relatively higher mortality rates than urban areas in 1990s, but are lower in the early 21st century. In the 1990s, the higher mortality rate in rural areas was likely due to scarcity of medical resources, and poor cancer diagnosis and treatment conditions. Reversal of the rates in the early 21st century may be due to major changes in life style activities and environmental pollution in the urban areas. For the city development, a lot of people from rural areas started to move into urban areas in the early 21st century, and this might also cause the mortality change.

Using trend surface analysis, one of the most widely used global surface-fitting procedures, we find the mapped data are approximated by a polynomial expansion of the geographic coordinates of the control points, and the coefficients of the polynomial function are found by the method of least squares, insuring that the sum of the squared deviations from the trend surface is a minimum. Each original observation is considered to be the sum of a deterministic polynomial function of the geographic coordinates plus a random error. The two general classes of techniques for estimating a regular grid of points on a surface from scattered observations are methods called "global fit" and "local fit" (Wen, 1991). As the name suggests, global-fit procedures calculate a single function describing a surface that covers the entire map area. The function is evaluated to obtain values at the grid nodes. In contrast, local-fit procedures estimate the surface at

successive nodes in the grid using only a selection of the nearest data points. "Global fit" and "local fit" can provide important clues for the geographical distribution of both diseases and risk factors.

Trend-surface analysis on the registries shows that the Chinese breast cancer death rate is in a geographical distribution of a half-concentric circle. In addition, death rates of breast cancer in China show two tendencies, the first major trend increased from southwest to northeast, in a geographical distribution for half of the concentric circles; the second trend increased from the west inland to the east and southeast coastal area. Different spatial patterns in mortality are most likely the result of different underlying processes stemming from demographic, socio-economic, health behaviors, and relevant risk factors. Most of these areas with high mortality are developed economic regions in China where adoption of Western life-style of the diet and use of cars is prevalent. Except for social economy and educational factors, environmental factors also have major influences on the rising death rates. Environmental pollution from the rapid increase of vehicle exhaust emission, industrialization and urbanization construction could increase BC incidence and mortality. Some hypotheses point out that N-nitroso compound intake in the coastal area of China was higher, and N-nitroso compounds are risk factors of carcinogenesis (Lin et al., 2002; 2009). There may be potential environmental factors and dietary habits affecting this particular population in the coastal areas of the southeast, and the northeast and southeast regions in China are the key regions for the prevention and control of breast cancer.

In conclusions, in summary, breast cancer is the most common cancer among women in China. The mortality rate of breast cancer is increasing, and will continue to steadily rise in future years to become one of the most serious public health issues in China. Disease control centers in China should draw more attention and implement measures for women's health care, such as advocating a healthy lifestyle, developing women's self-health care, and providing instruction on self-examination. Regular medical screening, especially for young women, is very important. Early detection of tumors by mammography and advances in medical treatment should be improved for survival and quality of life. Encouraging women aged 40 years and older to have annual mammography scans and a clinical breast examination is the single most important step that clinicians can take to reduce suffering and death from breast cancer. Clinicians should also ensure that patients at high risk for breast cancer are identified and are offered appropriate screening and follow-up.

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References

Anderson WF, Chu KC, Chang S (2003). Inflammatory breast carcinoma and noninflammatory locally advanced breast

- carcinoma: distinct clinicopathologic entities. *J Clin Oncol*, **21**, 2254-59.
- Bambhroliya AB, Burau KD, Sexton K (2012). Spatial analysis of county-level breast cancer mortality in Texas. *J Environ Public Health*, 959343.
- Cancer incidence in five continents. Volume IX (2008). *IARC Sci Publ*, 1-837.
- Chen JG, Zhu J, Parkin DM, et al (2006). Trends in the incidence of cancer in Qidong, China, 1978-2002. *Int J Cancer*, **119**, 1447-54.
- China health statistics yearbook (2007). Beijing: Peking Union Medical College Publication House.
- China health statistics yearbook (2009). Beijing: Peking Union Medical College Publication House.
- China health statistics yearbook (2010). Beijing: Peking Union Medical College Publication House.
- China health statistics yearbook (2011). Beijing: Peking Union Medical College Publication House.
- Cox B (2008). The effect of service screening on breast cancer mortality rates. *Eur J Cancer Prev*, **17**, 306-11.
- Curado MP. (2011). Breast cancer in the world: incidence and mortality. *Salud Publica Mex*, **53**, 372-84.
- Ferlay J, Shin HR, Bray F, et al (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*, **127**, 2893-917.
- Franco-Marina F, Lazcano-Ponce E, Lopez-Carrillo L (2009). Breast cancer mortality in Mexico: an age-period-cohort analysis. *Salud Publica Mex*, **51**, 157-64.
- Gao YT, Shu XO, Dai Q, et al (2000). Association of menstrual and reproductive factors with breast cancer risk: results from the Shanghai Breast Cancer Study. *Int J Cancer*, **87**, 295-300.
- Lee CH. (2002). Screening mammography: proven benefit, continued controversy. *Radiol Clin North Am*, **40**, 395-407.
- Li CI, Malone KE, Daling JR (2003). Differences in breast cancer stage, treatment, and survival by race and ethnicity. *Arch Intern Med*, **163**, 49-56. v
- Li CI, Malone KE, Daling JR, et al (2008). Timing of menarche and first full-term birth in relation to breast cancer risk. *Am J Epidemiol*, **167**, 230-9.
- Kun Lin, Wenying Shen, Zhongying Shen. (2002). Dietary exposure and urinary excretion of total N-nitroso compounds, nitrosamino acids and volatile nitrosamine in inhabitants of high- and low-risk areas for esophageal cancer in southern China. *Int J Cancer*, **102**, 207-11.
- Kun Lin, Yongning Wu, Wenying Shen. (2009). Interaction of total N-nitroso compounds in environment and in vivo on risk of esophageal cancer in the coastal area, China. *Environ Int*, **35**, 376-81.
- Robles S C, Galanis E. (2002). Breast cancer in Latin America and the Caribbean. *Rev Panam Salud Publica*, **11**, 178-85.
- Roy R, Chun J, Powell SN (2012). BRCA1 and BRCA2: different roles in a common pathway of genome protection. *Nat Rev Cancer*, **12**, 68-78.
- Shapiro S, Coleman EA, Broeders M, et al (1998). Breast cancer screening programmes in 22 countries: current policies, administration and guidelines. international breast cancer screening network (IBSN) and the european network of pilot projects for breast cancer screening. *Int J Epidemiol*, **27**, 735-42.
- Smigal C, Jemal A, Ward E, et al (2006). Trends in breast cancer by race and ethnicity: update 2006. *CA Cancer J Clin*, **56**, 168-83.
- Vervoort MM, Draisma G, Fracheboud J, et al (2004). Trends in the usage of adjuvant systemic therapy for breast cancer in the Netherlands and its effect on mortality. *Br J Cancer*, **91**, 242-7.
- Huanxin W, Nan H (1991). Trend-surface analysis was applied to the study of the geographic distribution for LBWI in China. *Chinese J Hlth Stat*, **8**, 12.
- Whelan SL, Ferlay J (1992). Cancer incidence in five continents. Age-specific and standardized incidence rates. *IARC Sci Publ*, 178-861.
- Yang L, Li L, Yude C (2005). Cancer incidence and mortality estimates and prediction for year 2000 and 2005 in China. *Chinese J Hlth Stat*, **22**, 218-31.
- Zhao P, Chen WC (2008). Chinese Cancer Registry Annual Report, 2004. Beijing: Peking Union Medical College Publication House.
- Zhao P, Chen Wc (2009). Chinese Cancer Registry Annual Report, 2008-Cancer Incidence And Mortality In Chinese Cancer Registration Areas In 2005. Beijing: Military Medical Science Press.
- Zhao P, Chen Wc (2010). Chinese Cancer Registry Annual Report 2009-Cancer Incidence And Mortality In Chinese Cancer Registration Areas In 2006. Beijing: Military Medical Science Press.
- Zhao P, Chen Wc (2011). Chinese Cancer Registry Annual Report 2010-Cancer Incidence And Mortality In Chinese Cancer Registration Areas In 2007. China, Beijing: Military Medical Science Press.
- Zhao P, Chen Wc (2012). Chinese Cancer Registry Annual Report, 2011. Beijing, China: Military Medical Science Press.
- Zhu Chen, (2008). The Third National Mortality Retrospective Sampling Survey Report. Beijing: Peking Union Medical College Publication House.