Increasing Breast Cancer Incidence in China: The Numbers Add Up

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In this issue of Journal, Linos et al. (1) have combined data on the distribution of breast cancer risk factors from a representative survey of Chinese women aged 35–49 years in 2001 (2) with a breast cancer cumulative incidence model (3,4) to estimate the number of women in the survey population and, by extension, among the 130 million Chinese women aged 35–49 years in 2001 who would develop breast cancer over the next 20 years. They project nearly 2.5 million breast cancer cases in China by 2021 in this cohort and suggest some changes in lifestyle that might reduce an impending epidemic of breast cancer.

Two complementary approaches can be used to project cancer rates. One method is based on models, such as the Rosner–Colditz log incidence breast cancer model (3,4) used in Linos et al. (1). This model was developed in the Nurses’ Health Study (5), calibrated to the Shanghai Women’s Health Study (SWHS) (6), and then applied to a representative sample of Chinese women aged 35–49 years who were interviewed in the Chinese National Family Planning and Reproductive Health Survey (NFPRHS) (2) to predict age-specific breast cancer incidence rates for these Chinese women in 2021 [table 2 in (1)]. The second method involves extrapolation of observed secular trends in cancer rates. This approach requires representative data on incidence rates over time and assumptions on the nature of the extrapolation curve. Unfortunately, such incidence data are not available for all of China. However, time series for selected urban and rural locations, such as Shanghai and Qidong County, respectively (7), can be constructed from publications such as the CANCERMondial Statistical Information System (8,9). We compared the modeling approach of Linos et al., which depends on several assumptions, with simple extrapolations of empirical data for urban Shanghai and rural Qidong County.

A critical assumption made by Linos et al. (1) was that the calibration of the Rosner–Colditz model for urban Shanghai would apply equally well to all of China. Using prevalence data on breast cancer risk factors from SWHS, Linos et al. found that their model overestimated the number of breast cancer cases in this Shanghai cohort by 43% (1). They subsequently adjusted the model by changing the intercept term but not the coefficients for the individual risk factors. This correction of the intercept ensured that the new model would fit the observed numbers of cases in SWHS perfectly; however, it was unclear if this correction was appropriate for the rest of China, especially the rural regions. As Linos et al. point out, the Rosner–Colditz model, which was originally developed for US white women, may not have fit the data for Shanghai women because of differences between the two populations in adiposity, height, physical activity, diet, endogenous hormones, and genetic susceptibility. A second important assumption made by Linos et al. was that the NFPRHS survey was representative of all Chinese women aged 35–49 years. However, 74% of the women selected for the NFPRHS survey were from rural areas, whereas the National Bureau of Statistics, People’s Republic of China, reported that in 2001 only 62% of the Chinese population lived in rural areas (10).

To compare the projections of Linos et al. with estimates from observed trends for Shanghai and Qidong County that were derived from CANCERMondial (8,9), we standardized the age-specific incidence rates for women aged 35–69 years using the world standard population (11). The age-standardized breast cancer incidence rate predicted by Linos et al. for China in 2021 among women aged 35–69 years was 85.3 per 100000 woman-years, which we derived from table 2 in (1) (Figure 1). Next, we plotted the age-standardized rates for Shanghai and Qidong, with their extrapolation lines, on a logarithmic–linear scale, as described in detail in Figure 1. Our extrapolated projection for the breast cancer incidence rate in Shanghai in 2021 was 161.8 per 100000 woman-years, compared with a rate of only 42.4 per 100000 woman-years for Qidong County. We then combined these rates with 38% weight on Shanghai and 62% weight on Qidong County, to reflect the urban–rural mix reported by the Chinese National Bureau of Statistics for 2001 (10), and obtained an estimated breast cancer incidence rate of 87.8 per 100000 woman-years for all of China (Figure 1), which agrees remarkably well with the projection of 85.3 per 100000 woman-years derived from Linos et al. (1). If we had weighted the empirical results for Shanghai and Qidong County by 26% and 74%, respectively, to correspond to the NFPRHS survey data used by Linos et al., we would have obtained a lower rate for China of 73.4 per 100000 woman-years, which suggests that the risk model calibrated for Shanghai might have overestimated breast cancer risk in rural Chinese populations. Nonetheless, the excellent agreement between the model-based and empirical extrapolation approaches gives us confidence that breast cancer incidence in China will increase to roughly 85 per 100000 woman-years by 2021 if current trends continue, which is still well below the most recent Surveillance, Epidemiology, and End Results (SEER) rate of 208.1 per 100000 woman-years for the United States in 2005 (12) (Figure 1). Indeed, SEER rates for
breast cancer incidence in the United States have been greater than 85 per 100,000 woman-years for about two decades (12).

We congratulate Linos et al. for highlighting the increasing incidence of breast cancer in China. The current increase in breast cancer incidence among Chinese women was presaged by breast cancer patterns in Chinese migrants to the United States. By the mid-1980s, incidence rates of breast cancer in the migrating generation were approximately double those in Shanghai and Tianjin, while rates in Chinese Americans born in the United States were approaching the US rate for white women (13). Breast cancer incidence in third-generation Chinese Americans, although based on small numbers, seemed to have surpassed that in US white women (13). Such migrant studies suggested that the sixfold difference in breast cancer incidence between Asia and the West (8) were due primarily to modifiable lifestyle factors and not genetics. Similar conclusions are now being drawn from secular trends in Hong Kong (14), Singapore (15), Japan (16), and China itself (17). Linos et al. also used the calibrated Rosner–Colditz model to estimate the impact on breast cancer incidence of changes in modifiable risk factors, including parity, adult weight gain, postmenopausal hormone use, and alcohol intake. Risk factor prevalence for rural and urban women was either derived from individual data collected in the NFPRHS (2), if available, or imputed from other sources if not. Although the intercept of the Rosner–Colditz model was calibrated to fit the SWHS data (6), neither the individual risk factors and their interactions nor the corresponding relative risks were modified. Linos et al. cite studies among Chinese women in Shanghai and Singapore that document relative risks for accepted menstrual, reproductive, and anthropometric breast cancer risk factors that are qualitatively similar to those found in US white women. Nonetheless, differences between Chinese women and US white women—in genetics, endogenous hormone metabolism, growth patterns, or diet—may alter some of these relative risks quantitatively. Thus, estimates of the impact of changes in modifiable risk factors on breast cancer incidence in China may be more uncertain than sensitivity analyses (1) suggest.

In addition, further study is needed to determine whether programs to encourage behavioral changes will have their intended effects on risk factor prevalence and breast cancer incidence. For example, individual responses to national family planning policy are complex and difficult to predict. The net impact on fertility patterns of encouraging earlier childbirth and shorter spacing between pregnancies remains to be determined.

A more comprehensive survey in China to clarify the current status of breast cancer incidence and begin to assemble representative incidence series would lead to more accurate extrapolations. If such a survey also collected data on risk factor prevalence, it could be used to calibrate the Rosner–Colditz model in rural as well as urban settings, possibly leading to improved model-based projections of breast cancer incidence and the impact of lifestyle and policy changes.

The fact that the Rosner–Colditz model, which was developed for US white women, overestimated breast cancer risk in Shanghai by 43%, and perhaps even more in rural Chinese communities, poses a challenge to, and perhaps an opportunity for, etiologic research. Part of this overestimation is due to more extensive breast cancer screening in the United States than in China. Understanding the other part might offer new etiologic insights and opportunities for prevention.

References

Figure 1. Age-standardized breast cancer incidence rates among women. Age-standardized breast cancer incidence rates, based on age-specific rates for women aged 35–69 years and adjusted to the world standard population (18), were plotted on a logarithmic–linear scale by calendar year so that a slope of 10° represented a rate change of 1% per year (19). Surveillance, Epidemiology, and End Results (SEER) data (open circles) for breast cancer cases newly diagnosed from 1978 through 2005 were obtained from the National Cancer Institute’s SEER database (12). Data for Shanghai from 1978 through 2002 (open squares) and Qidong County from 1983 through 1987 (open diamonds) were provided by the CANCERMonial Statistical Information System (8,9). Regression lines were fitted by weighted least squares to the data from Shanghai and Qidong County. The weights were r/Var(r), where r is the direct standardized rate for a given time period; these weights represent inverse variance weighting for the logarithm of the incidence rate. The lines used for extrapolation were 3.8120 + 0.0315(year – 1980.5) for Shanghai and 3.1673 + 0.0143(year – 1980.5) for Qidong County. By substituting 2021 for year, calculating the estimated logarithm of the rate, and exponentiating, we obtained extrapolated breast cancer incidence rates (per 100,000 woman-years) of 161.8 for Shanghai and 42.4 for Qidong. A weighted average of these results with weights for Shanghai and Qidong of 0.38 and 0.62, respectively, which correspond to Chinese National Bureau of Statistics estimates of the proportions of urban and rural populations in China in 2001 (10), yielded the weighted extrapolated estimate of 87.8 per 100,000 woman-years (open triangle). The standardized rate from the age-specific rates in table 2 of Linos et al. (1) was 85.3 per 100,000 woman-years (solid triangle).

Notes
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