



# Treating breast cancer patients in China

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A national group of Chinese oncologists has offered a detailed and comprehensive set of guidelines for the treatment of women with early-stage and late-stage breast cancer in China (1). China has the greatest number of new breast cancer cases per year at 367,900—which represents approximately 18% of the world's total (2). Of these, 12.5% are diagnosed under age 40 and 37% are diagnosed under age 50.

Despite the high number of cases, the annual *per capita* incidence rate in China is relatively low at 36 per 100,000 per year. In contrast, the incidence of breast cancer among Chinese women in the United States is much higher at 83 per 100,000 per year and the incidence among white women in the USA is even higher at 134 per 100,000 per year (3) (*Table 1*).

It has been documented that by international standards, Chinese breast cancer patients have relatively poor survival. In China, 27% of women with a diagnosis with breast cancer will die of their disease, compared to 13% of Chinese patients in the USA. According to the National Central Cancer Registry of China, between 2003–2005 the 5-year survival for all women with breast cancer was 73.0% and was much lower than the crude survival of women with breast cancer in Australia (89%), Europe (82%), Hong Kong (85.2%) or the United States (90%) (2,4–6).

At first glance this would suggest that the treatment offered to Chinese women, or access to treatment, is inadequate. The guidelines issued by CSCO are very comprehensive and detailed and the treatments are not substantially different from those recommended in Canada, the United States or the United Kingdom. What is not

clear is the basis for the historical survival difference. It may be that the Chinese women present with more advanced disease than their American counterparts. Perhaps Chinese women may not be receiving optimum care—so the guidelines are a welcome tool to help bridge this gap.

To be fair, we must consider not just case-fatality but mortality rates as well. Despite the relatively poor survival, population-based mortality rates for Chinese women and Chinese-American women are similar, with a slight edge to China. If we restrict the comparison to Chinese women, then we need not entertain the notion that ethnic differences account for biologic differences in aggressivity or response to treatment.

Some would say that lifestyle issues account for the much lower incidence of breast cancer in China than in the USA (36 versus 83 per 100,000 per year) but better treatment leads to a survival advantage for American Chinese (13% versus 27%) (*Table 1*). This explanation is in vogue in western universities. As women migrate from China to the United States, they adopt a western lifestyle and raise their risk of breast cancer. All said it evens out—and the mortality rate is about the same. It is also possible that the observed survival differences may reflect differences in underlying comorbid illnesses (e.g., obesity, diabetes and cardiovascular disease).

We should consider an alternative scenario whereby the difference in incidence is due to early detection (screening) and that this is largely ineffective in reducing mortality. In other words, screening greatly increases the number of new cancer diagnoses, but does little or nothing to reduce the number of cancer deaths.

**Table 1** Comparison of incidence, mortality and case-fatality rates of Chinese versus white with breast cancer

Variables	Mortality [per 100,000 per year (ref)]	Incidence [per 100,000 per year (ref)]	Case-fatality [% of cases that died of breast cancer (ref)]
China	8.8 [2018] (2)	36.1 [2018] (2)	27.0% [1997–2001] (2)
Chinese USA	9.9 [2003–2011] (4)	82.8 [2009–2011] (5)	12.9% [2004–2015] (3)
White USA	23.3 [2003–2011] (4)	134.4 (5)	16.4% [2004–2015] (3)

The guidelines do not provide data on the actual number of cases of breast cancer in China for whom the treatment received is optimal—in other words, for what percentage of patients is treatment in accordance with the guidelines? It would be worthwhile to study if in the real world Chinese women were receiving the recommended treatment. And if not, why not? Does treatment vary by city, by urban versus rural residence, etc.? We are not told by the committee whether or not the recommended treatments are available to all patients in the context of national public health program. If some women are not being treated with the up-to-date care, is this because of access to care, poor patient compliance, provider knowledge or issues around cost? Are there other social factors at play which make it difficult for some Chinese women to access and comply with the care plan?

The guidelines focus on chemotherapy. We should also consider ovarian ablation in the mix. In some settings, ovarian ablation by surgical or by medical means offers benefit to women with premenopausal breast cancer and this may be additive or superior to standard anti-hormonal therapies (i.e., SERMS) (7). The topic is worth exploring.

Another relevant issue that is not discussed here is the value of genetic testing at time of diagnosis. Yuntao Xie and his colleagues (8) have shown through a number of large surveys in Beijing that a significant proportion of women with breast cancer, in particular with early-onset breast cancer or triple-negative breast cancer, harbor a mutation in BRCA1 or BRCA2 and that these cannot reliably be identified by triaging patients based on family history. In the most recent study, germline pathogenic variants in the *BRCA1/2* genes were sought in 9,505 unselected Chinese Han breast cancer patients (8). Four hundred and seventy-one (5.0%) breast cancer patients carried a pathogenic variant in BRCA1 or BRCA2 mutation in this cohort. There were 25 mutations which were found on four or more occasions (8 in BRCA1 and 17 in BRCA2). The Beijing group also showed that among women with a

BRCA1 or BRCA2 mutation, the addition of cisplatin to neoadjuvant chemotherapy improved both recurrence-free survival and overall survival (9). Elsewhere, we have shown that personalised treatments of breast cancer in women with a BRCA mutations may include bilateral mastectomy (10), oophorectomy (11,12) and platinum-based adjuvant chemotherapy (13). In recent studies, we have shown that salpingo-oophorectomy in the year post-diagnosis will reduce mortality from breast cancer in both BRCA1 and BRCA2 carriers (14,15).

Another issue not discussed by the committee is the management of DCIS. The treatment of DCIS is contentious and there are no clear recommendations. In the United States, the favored treatment for *in situ* breast cancer is breast conserving surgery plus radiotherapy. However, if the goal is to reduce the local invasive recurrence as much as possible, the best treatment seems to be mastectomy. This also frees up the patient from the necessity of arranging multiple return visits to the clinic for radiotherapy and later for follow-up screening.

The treatment plans outlined by the CSCO in their guidelines are reasonable and as far as I can tell, they do not differ substantially from the treatment options and recommendations for Canadian women and American women.

There is little literature on the effectiveness of these chemotherapy regimens on Chinese women versus white women and few studies are conducted in China or have a substantial number of Chinese women to form a subgroup for analysis. In particular, the lower mortality in Chinese women with early stage breast cancer may mean that some of them might forego chemotherapy. It would also be helpful to study the value of the OncotypeDx tests in Chinese women to see if it is equally predictive.

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