

Perspective

"Westernizing" Women's Risks? Breast Cancer in Lower-Income Countries

Peggy Porter, M.D.

Recent media reports have highlighted the increasing incidence of breast cancer in lowand middle-income countries. Although the disease continues to be most prominent in affluent countries,

the risks of both breast cancer and death due to breast cancer are clearly increasing worldwide (see maps). Some 45% of the more than 1 million new cases of breast cancer diagnosed each year, and more than 55% of breast-cancer–related deaths, occur in low- and middleincome countries.¹ Such countries now face the challenge of effectively detecting and treating a disease that previously was considered too uncommon to merit the allocation of precious health care dollars.

One hindrance to any discussion of global breast-cancer incidence is the limited data available for many countries. Incidence figures are based on data from small geographic areas that are often pooled and extrapolated to large regions. Reported rates may reflect only the women who are easiest to reach or who have the highest standard of living. Thus, current global figures cannot truly reflect the underlying economic and cultural diversity driving increased incidence and related mortality.

Nevertheless, the trends are clear enough to warrant concern and action. Registry data show that breast-cancer incidence has been increasing in virtually all regions since 1973.¹ Although East Asian women still have the lowest rates (about 21 per 100,000, as compared with 101 per 100,000 in the United States and 85 per 100,000 in Western Europe), countries with the most developed registries have documented increases: rates in Japan, Singapore, and Korea have doubled or tripled in the past 40 years, and China's urban registries document 20 to 30% increases in the past decade. India reports similar trends, with increases concentrated in urban areas.

In Africa, the trends are difficult to evaluate, given the general lack of large registries and accurate population data. However, it is certain that the incidence of breast cancer in African countries (reported to be 23 per 100,000) is lower than overall rates in North America or Western Europe, as well as lower than rates among black women residing in these Western countries. Local registries in Africa report a doubling of rates over the past 40 years, but the degree to which these figures represent real increases, as opposed to changes in disease tracking and reporting, is unclear.

213

The New England Journal of Medicine

Downloaded from nejm.org on November 9, 2012. For personal use only. No other uses without permission.





Estimated Age-Standardized Rates of Breast Cancer (Top Panel) and Death Due to Breast Cancer (Bottom Panel), 2002. Data are from GLOBOCAN 2002, International Agency for Research on Cancer.

The most widely cited reason for the global increase in breast cancer is the "Westernization" of the developing world. The term encompasses generally desirable changes (socioeconomic improvements that increase life expectancy and allow women reproductive control) as well as the adoption of less desirable habits (dietary changes, decreased exercise), all of which could increase breast-cancer risk. In affluent Western countries, women have relatively high social status, tend to delay childbearing, have relatively few children and, until recently, commonly used hormone-replacement therapy (HRT). Some such behavioral factors delayed childbearing, lower parity, and reduced breast-feeding — are becoming more prevalent in lowerincome countries. The challenge is understanding how these reproductive risk factors, which are primarily associated with an increased risk of postmenopausal breast cancer, relate to incidence and mortality in lower-income countries, where rates of postmenopausal breast cancer are much lower than in Western countries. The cancers apparently

N ENGLJ MED 358;3 WWW.NEJM.ORG JANUARY 17, 2008

The New England Journal of Medicine

Downloaded from nejm.org on November 9, 2012. For personal use only. No other uses without permission.

causing the most deaths in lowerincome countries may not be those influenced by such factors; more data are needed to clarify their true effect in poorer countries.

Risk factors related to diet, obesity, and exercise are also often blamed for increasing breastcancer rates. Migration studies have revealed increases in breastcancer incidence following migration from low-incidence countries to higher-incidence countries, but it is difficult to pinpoint the individual contributing factors. High fat intake, low vegetable intake, and low soy intake have all been implicated, but the data have not been consistent or conclusive. In China, an aggregate "meat-sweet" diet has been shown to increase risk.² Risk of postmenopausal (but not premenopausal) breast cancer is increased among obese women, and physical exercise probably decreases the risk of postmenopausal breast cancer.3 Early age at menarche, another important reproductive risk factor for breast cancer, is associated with a Western diet and a Western exercise and body-mass profile, and the trend toward decreasing age at menarche seen in Western countries is now being observed in lower-income countries. It will be important to understand early-in-life changes in exercise and dietary habits to completely understand the increasing incidence of breast cancer in developing countries.

In some of the lowest-income African countries, the overwhelming reality of breast cancer is the high burden of mortality in the setting of relatively low incidence. The ratio of the mortality rate to incidence is 0.69 in Africa, as compared with 0.19 in North America. This high ratio results partly from incomplete reporting of disease but largely reflects the high proportion of women who present with late-stage disease, which is not curable even in wealthy countries.

Although disparities in mortality are predominantly due to marginal health care, low awareness of breast cancer, and cultural barriers to care, there are also ongoing efforts to understand the genetic and biologic differences that might affect disease outcomes in lower-income countries. The presence or absence of estrogenreceptor (ER) expression in breast tumors is central to their behavior and treatment, and a predominance of early-onset and aggressive ER-negative breast cancers may partially account for the high breast-cancer mortality in developing countries. ER testing is a luxury in most developing countries, so data on the prevalence of ER-negative disease are limited. U.S. studies have identified postmenopausal onset and HRT as risk factors for ER-positive breast cancer and have found associations between ER-negative breast cancer and both young age at diagnosis and black race. These relationships might predict a higher burden of ER-negative breast cancer in lower-income countries where a younger average age at onset, limited use of HRT, and black race predominate. It is also possible that the lack of active screening programs in lowerincome countries might result in high rates of ER-negative tumors, since mammography tends to identify the smaller ER-positive tumors.

The need for global data about genetic and biologic influences on breast cancer is supported by recent studies in black American women revealing a higher frequency of aggressive "triple-negative" tumors (tumors that don't express ER, progesterone receptor, or the oncogene *c-erbB2*/HER2) than that among white women. In white women, such tumors are associated with inherited mutations in the breast-cancer gene BRCA1, and genetic determinants in African women may predipose them to high-risk tumors. Although cancer-predisposing BRCA1 and BRCA2 founder mutations occur at high frequencies in various populations (such as Ashkenazi Jews), such mutations seem to occur with similar frequency among white and black Americans. Ongoing studies will help elucidate the genetic and biologic contributions to breast-cancer risk in African women.

Research and health care efforts to understand and alter the trends in incidence and mortality are under way. The challenge is knowing whether the successful strategies refined in predominantly white, affluent populations (early detection through mammography, targeted hormonal and anti-HER2 therapies, and improvements in chemotherapy) will be effective, or even possible, in lower-income countries with different racial, ethnic, and cultural makeups. The need for data is great. For instance, breast self-examination would be expected to improve detection and mortality statistics in a country with no other screening program. However, in a trial involving nearly 300,000 women in Shanghai, practicing self-examination did not result in reduced breast-cancer mortality.4 China has since initiated a "million women" screening effort to determine the best imaging method for early detection in a relatively young population with mammographically dense breasts.

The causes of increasing breastcancer incidence and mortality in low-income countries are com-

N ENGLJ MED 358;3 WWW.NEJM.ORG JANUARY 17, 2008

The New England Journal of Medicine

Downloaded from nejm.org on November 9, 2012. For personal use only. No other uses without permission.

plex, and solutions will be country-specific. Recognizing that a practical approach is required, the Breast Health Global Initiative is developing guidelines for breast care that are "evidence-based, economically feasible, and culturally appropriate."⁵ Certainly, early detection must be a primary goal worldwide: given that we cannot effectively treat metastatic breast cancer in the United States, there is little hope that we'll do so in developing countries.

As more countries modernize, more women will enter an increasingly sedentary workforce, delay childbearing, exert control over their reproductive lives, live longer, and eat a more Westernized diet. Their breast-cancer rates will no doubt increase. It is crucial that women's awareness of their risk and their expectations of their government and the medical community regarding detection and treatment increase at a similar rate.

No potential conflict of interest relevant to this article was reported.

1. Curado MP, Edwards B, Shin HR, et al., eds. Cancer incidence in five continents. Vol. IX. Lyon, France: International Agency for Research on Cancer, 2007. (IARC scientific publications no. 160.) (Accessed December 27, 2007, at http://www-dep.iarc.fr/.)

2. Cui X, Dai Q, Tseng M, Shu X-O, Gao Y-T, Zheng W. Dietary patterns and breast cancer risk in the Shanghai Breast Cancer Study. Cancer Epidemiol Biomarkers Prev 2007;16: 1443-8.

3. World Cancer Research Fund, American Institute for Cancer Research. Food, nutrition, physical activity, and the prevention of cancer: a global perspective. Washington, DC: American Institute for Cancer Research, 2007.

4. Thomas DB, Gao DL, Ray RM, et al. Randomized trial of breast self-examination in Shanghai: final results. J Natl Cancer Inst 2002;94:1445-7.

5. Anderson BO, Shyyan R, Eniu A, et al. Breast cancer in limited-resource countries: an overview of the Breast Health Global Initiative 2005 guidelines. Breast J 2006;12: Suppl 1:S3-S15.

Copyright © 2008 Massachusetts Medical Society.

A Bridge to Nowhere — The Troubled Trek of Foreign Medical Graduates

Ranjana Srivastava, F.R.A.C.P.

Tt is a typical day in my Mel-Lbourne clinic, with missing files, scans gone astray, and patients overwhelmed by their diagnoses. Though a mountain of dictation remains, the day's end appears promisingly close . . . but for a scheduled tutorial. Biting into lukewarm leftovers, I am sorely tempted to cancel it. After all, I reason, it is volunteer work, squeezed in among other pressing commitments. The students will surely understand and perhaps even be grateful for the reprieve on a balmy summer evening.

Maybe the time has come to give up the tutorials, I muse. I have taught since I was a resident. Now, busy workdays added to new motherhood fill my plate; many days, the planning and patience required for the tutorial seem beyond my reach. Soon my musings turn to resentment, resentment to self-righteous justification. Surely, it is someone else's turn to assume the mantle. The hospital is filled with doctors — someone must have spare time. Seizing on this thought, I reach for the phone. But before I finish dialing, I receive a page: "Doctor, don't worry if you are late. We will wait."

My conscience pricks me. I rush through the dictation and climb the stairs to meet my students, silently rehearsing my farewell speech.

Six expectant, eager faces greet me.

"I'm sorry I'm late."

"That's OK! We thought we

would have to miss the tutorial altogether, so we are lucky!" There is a nodding of heads, shuffling of chairs and books as the students get into position.

"What a beautiful day!" I enthuse.

"To us, all the days seem the same," a glum voice says.

"What's new?" I ask.

"No one got a spot for next month's exam."

"Oh, I am sorry to hear that. What happened?" I already know the answer.

"There were too many people and too few spots." Disappointment and resignation hang in the air.

My students are foreign-trained doctors taking a "bridging" course to earn medical credentials in

The New England Journal of Medicine

Downloaded from nejm.org on November 9, 2012. For personal use only. No other uses without permission.

Dr. Porter is a cancer biology researcher at the Fred Hutchinson Cancer Research Center and a professor of pathology at the University of Washington School of Medicine — both in Seattle.