

Breast Cancer Leads Mortality Drop in U.S., U.K.

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — Total cancer mortality among middle-aged women in the United States and United Kingdom has declined markedly since 1990—and an unprecedented drop in breast cancer mortality is the biggest reason why, Sir Richard Peto, Ph.D., said at the San Antonio Breast Cancer Symposium.

Indeed, through a series of moderate gains in survival achieved via breast screening plus incremental advances in endocrine therapy, chemotherapy, and radiotherapy, breast cancer mortality in women aged 35-69 years in the United States and United Kingdom has been almost halved since 1990.

"No other common cancer can claim such success. Hodgkin's disease, yes. Testicular cancer, yes. Childhood leukemia, yes. But this absolute gain in breast cancer survival is far bigger than the absolute gain from eliminating any of those diseases," said Dr. Peto, professor of medical statistics and epidemiology at the University of Oxford (England).

A new analysis by Dr. Peto and colleagues at the Oxford-based Early Breast Cancer Trialists' Collaborative Group (EBCTCG) demonstrates how several advances in chemotherapy, each of only moderate impact, have together over the course of three decades added up to a massive survival benefit.

The bottom line of this analysis, based upon data on roughly 80,000 patients with early breast cancer randomized in chemotherapy trials, is: "If you give effective chemotherapy to women with or without estrogen receptor-positive disease, you'll reduce their mortality by about one-third if they're old, and by about one-half if they're young," he said.

"These are lovely results."

The full EBCTCG database now includes 350,000 breast cancer patients in close to 400 randomized clinical trials worldwide. The world's trialists, who have met to share their updated data every 5 years since 1985, will do so next in 2010.

The first wave of chemotherapy trials compared cyclophosphamide, methotrexate, and 5-fluorouracil (CMF) regimens with no chemotherapy. Those studies demonstrated that CMF-treated patients younger than age 50 experienced a 44% reduction in the risk of recurrence, and a 32% decrease in breast cancer mortality during the first 4 years of follow-up. Women aged 50-69 years had a 25% reduction in recurrence and a 9% decrease in mortality.

Not enough women aged 70 years or older have been enrolled in randomized chemotherapy trials to draw conclusions about the treatment's effect in that age group.

The second wave of trials compared anthracycline-based regimens with CMF regimens. The relative risk of recurrence was reduced by a further 16% with anthracycline regimens, compared with CMF, in women younger than 50, and by 11% in those aged 50-69. Mortality resulting from breast cancer was reduced by 19% in anthracycline-treated patients younger than age 50, and by 10% in those aged 50-69.

The third wave involved 20,000 participants in randomized trials of taxane- versus anthracycline-based regimens. Taxane-based therapy in women younger than age 50 conferred a 16% reduction in



recurrence risk, compared with anthracycline-based regimens, and a 14% reduction in breast cancer mortality through the first 4 years of follow-up. In 50- to 69-year-olds, taxane regimens brought an 18% decrease in recurrences and a 16% reduction in breast cancer mortality, compared with anthracycline regimens.

There haven't been trials directly comparing taxane-based regimens with no chemotherapy, but the effect can be gauged by multiplying the three event-rate ratios together. That yields a projected 62% reduction in recurrence through 4 years in women younger than age

50 who were treated with taxane regimens, compared with those getting no chemotherapy, and a 48% reduction in older patients. The reduction in breast cancer mortality works out to 54% in younger taxane-treated patients and a 33% reduction in patients aged 50-69 years, compared with those who got no chemotherapy, he continued.

Another point: The EBCTCG data convincingly show that chemotherapy is equally effective in women with estrogen receptor (ER)-positive breast cancer—the most common type of the disease—and ER-poor breast cancer. For example, women younger than age 50 who were randomized to chemotherapy had a 49% reduction in recurrence risk through 4 years if they were ER-positive, and a similar 43% reduction if they were ER-poor.

"ER status is irrelevant. The relative risk for recurrence and mortality is the same in ER-poor and ER-positive patients," Dr. Peto noted.

That being said, the size of the absolute risk reduction depends upon prognosis. And the prognosis for ER-positive disease treated with endocrine therapy is already so good—a halving of recurrence risk through 4 years—that the further absolute gain achievable with effective chemotherapy is considerably smaller than in ER-negative disease.

Acknowledging that newer targeted therapies make chemotherapy less necessary for a growing number of patients, Dr. Peto said, "I'm not making any treatment recommendations. Look at the prognosis, discuss the side effects, discuss the costs, and decide what to do."

Aside from the sharp decrease in mortality resulting from breast cancer since 1990, the biggest contributor to declining overall cancer deaths among middle-aged women in the United States and United Kingdom has been the drop in lung cancer deaths.

"Deaths due to intestinal cancer, uterine cancer, stomach cancer—they're all going down, too. These are good times to be a statistician," Dr. Peto noted.

Conference codirector Dr. C. Kent Osborne said in an interview that although there is nothing in the overview analysis that is likely to lead physicians to change how they manage patients today, the report makes an important point regarding the nature of progress in breast cancer therapy.

"There's unlikely to be a single discovery that by itself has a major impact on mortality. In fact, there have been a lot of baby steps over the last 30 years, and [those baby steps], when added up, have been shown to have a major impact," said Dr. Osborne, director of the Dan L. Duncan Cancer Center and professor of medicine and cellular and structural biology at Baylor College of Medicine, Houston. ■

Weight Gain After Breast Cancer Diagnosis Ups Mortality Risk

BY KERRI WACHTER
Senior Writer

Weight gain following a diagnosis of breast cancer significantly increases a woman's risk not only of breast cancer mortality but also of all-cause mortality over a 6-year follow-up period, results of a large study suggest.

"We found that a weight gain of 5 kg [11 pounds] increased the risk of death due to breast cancer and other causes by 14%," study investigator Hazel B. Nichols, an epidemiology doctoral student at Johns Hopkins University in Baltimore, reported at a press briefing. The briefing was held in conjunction with the annual international conference of the American Association for Cancer Research.

The findings suggest that efforts to prevent postdiagnosis weight gain could improve breast

cancer survival.

Ms. Nichols and her colleagues analyzed data from a cohort of 4,021 women, who had previously participated in consecutive population-based, case-control studies of incident breast cancer in Wisconsin, Massachusetts, and

New Hampshire. In the initial studies, women aged 20-70 years with a definitive diagnosis of invasive breast cancer between 1988 and 2001 were identified through state registries. Women were included in the studies once they had completed a structured

telephone interview with information on height and weight, reproductive and menstrual factors, lifestyle characteristics, family and personal history of breast cancer, and demographics.

During 1998-2001, all surviving women from the original case-control studies were mailed a follow-up questionnaire, which addressed postdiagnosis weight, weight gain, physical activity, diet, medication history, alternative therapies, and quality of life. Vital status was obtained by linkage through 2005. The researchers identified 121 breast cancer deaths and 428 non-breast cancer deaths after an average follow-up of 6 years (see graphic).

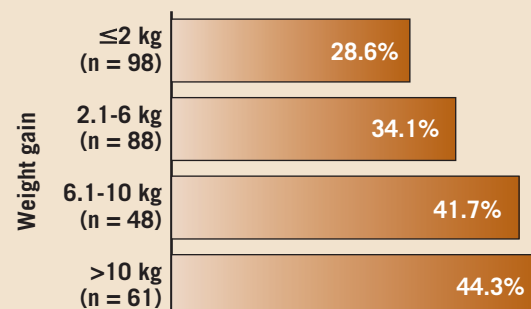
The researchers controlled for age, state of enrollment, time from breast cancer diagnosis to completion of the follow-up questionnaire, family history of breast cancer, menopausal status, and

stage of disease. Women with metastatic disease at diagnosis were excluded from the analysis to avoid the influence of disease on postdiagnosis body weight.

Obesity, regardless of weight before diagnosis, also increased a woman's risk of breast cancer and all-cause death. Women with a body mass index greater than 30 kg/m² were more than twice as likely to die of breast cancer (HR 2.36) than were women with a normal BMI (18.5 kg/m² to 24.9 kg/m²). Likewise, obese women had an almost 50% greater risk of dying from any cause (HR 1.46) than did women with a normal BMI.

Ms. Nichols cautioned that the women may have had other medical conditions that could have confounded the results, but the researchers did not have access to this information. The researchers plan to look next at the effect of postdiagnosis weight loss. ■

Percentage of Breast Cancer Deaths Increased With Weight Gain After Diagnosis



Note: Based on data for overall mortality during 6-year follow-up.
Source: Ms. Nichols