

Modeling the Incidence of Breast Cancer in China

Although breast cancer incidence in China is currently low compared with that in Western countries, the distribution of breast cancer risk factors among Chinese women is changing rapidly. To predict future trends in the incidence of breast cancer in China associated with changes in demographic and reproductive factors, **Linos et al. (p. 1352)** validated and calibrated the Rosner–Colditz log-incidence breast cancer model in Chinese women who participated in the Shanghai Women’s Health Study and then applied the validated model to Chinese national survey data. Breast cancer incidence in China is expected to increase from the current estimated rate of 10–60 cases per 100,000 women to more than 100 cases per 100,000 women aged 55–69 years by 2021. The modeling predicts 2.5 million cases of breast cancer by 2021 among Chinese women who were 35–49 years old in 2001. Modest reductions in hormone and alcohol use and weight maintenance are predicted to prevent approximately 10% of these cases.

In an editorial, **Ziegler et al. (p. 1339)** discuss the assumptions made by Linos et al., and compare this modeling approach with simple extrapolations of empirical breast cancer incidence data for rural and urban regions of China. They also discuss why the estimates of the impact of changes in modifiable risk factors on breast cancer incidence in China may be more uncertain than analyses suggest.

Hormone Therapy and *BRCA1* Mutation Carriers

Use of combination (estrogen plus progestin) hormone therapy to alleviate symptoms of menopause may be associated with an increased risk of breast cancer. The possibility of increased breast cancer risk is especially important to women with *BRCA1* mutations who undergo prophylactic oophorectomy at a young age to reduce their higher risk of breast cancer. To compare the risks of breast cancer among *BRCA1* mutation carriers who did and did not take hormone therapy, **Eisen et al. (p. 1361)** performed a case-control study of 472 postmenopausal women with *BRCA1* mutations. Surprisingly, use of hormone therapy among mutation carriers was associated with a reduced risk of breast cancer compared with no use. When analyses were stratified by type of therapy, the inverse association was observed with estrogen-only therapy but the association with

combination therapy was not statistically significant. The authors conclude that in this population of postmenopausal women with *BRCA1* mutations, hormone use was associated with a reduced risk of breast cancer.

In an editorial, **Chlebowski and Prentice (p. 1341)** highlight the limitations in the design of the study by Eisen et al. and put their findings in context with the current literature on hormone therapy, breast cancer risk, and *BRCA1* mutations. They write that caution should still be used before prescribing hormone therapy to women with *BRCA1* mutations who are at high risk for breast cancer.

Late Mortality in Long-term Survivors of Childhood Cancers

Improvements in treatment have led to better survival of individuals with childhood and adolescent cancer, and as the rate of survival increases it has become even more important to understand the specific health risks faced by survivors. To investigate temporal patterns in cause-specific mortality, **Mertens et al. (p. 1368)** analyzed data on more than 20,000 five-year survivors of childhood cancer who were members of the Childhood Cancer Survival Study cohort and had been followed for as long as 32 years. The members of the cohort had increased risks of death from subsequent malignancies, cardiac disease, pulmonary disease, and other causes compared with the general population; recurrences accounted for more than half of the deaths. The increased mortality risk persisted long after diagnosis; 15 years after diagnosis, the relative mortality rate was approximately five times higher than that in the general population.

Posttreatment Characteristics and Breast Cancer Outcomes

Postmenopausal women who are treated with neoadjuvant endocrine therapy prior to surgery for estrogen receptor (ER)-positive breast cancers are at risk for recurrence. To predict the outcomes of these patients, **Ellis et al. (p. 1380)** developed a preoperative endocrine prognostic index (PEPI) model using posttreatment tumor characteristics of postmenopausal women who participated in a breast cancer clinical trial. They validated the PEPI model using tumors from a different group of postmenopausal women who participated in another clinical trial. In the PEPI model, posttreatment tumor stage, nodal status, proliferating antigen Ki67 levels, and ER status were independently associ-

ated with relapse-free and overall survival. The PEPI model showed that postmenopausal women with breast cancers that were stage 1 or 0, were still ER-positive, and had low Ki67 levels after adjuvant endocrine therapy were at very low risk of relapse and therefore were unlikely to benefit from additional chemotherapy.

A Genetically Altered Bacterium for Pancreatic Cancer Therapy

Clostridium perfringens is an anaerobic bacterium that is a dangerous human pathogen, but with carefully engineered mutations and under controlled conditions, it might someday be used to kill the hypoxic cores of tumors. **Li et al. (p. 1389)** report the construction of a mutant strain of these bacteria that is less toxic and more effective at killing tumors compared with previous strains. They demonstrate that spores of the mutant bacteria can kill murine pancreatic tumors grown in mice. However, further mutation and testing will need to be done before clinical trials with similar oncopathic bacteria will be possible.

Gene Copy Number and Bladder Cancer Detection

Aneuploidy resulting from chromosome mis-segregation is a common change in neoplasia. The Aurora kinase A (*AURKA*) gene, which encodes a key regulator of mitosis, is frequently amplified and/or overexpressed in cancer cells, and the level of *AURKA* amplification is associated with chromosome mis-segregation and aneuploidy. **Park et al. (p. 1401)** examined the levels of *AURKA* amplification and overexpression in human bladder tumor samples and bladder cancer cell lines, the effect of overexpression of *AURKA* in human urothelial cells, and whether fluorescence in situ hybridization (FISH) detection of *AURKA* copy number in urine sediments could be used to detect bladder cancer. Forced overexpression of *AURKA* in urothelial cells induced amplification of centrosomes, chromosome missegregation, and aneuploidy. Natural overexpression of *AURKA* was detectable in in situ lesions from patients with bladder cancer. The FISH test for *AURKA* gene copy number in exfoliated cells from urine specimens yielded a specificity of 96.6% and sensitivity of 87%. *AURKA* copy number may be a promising biomarker for the noninvasive detection of bladder cancer.

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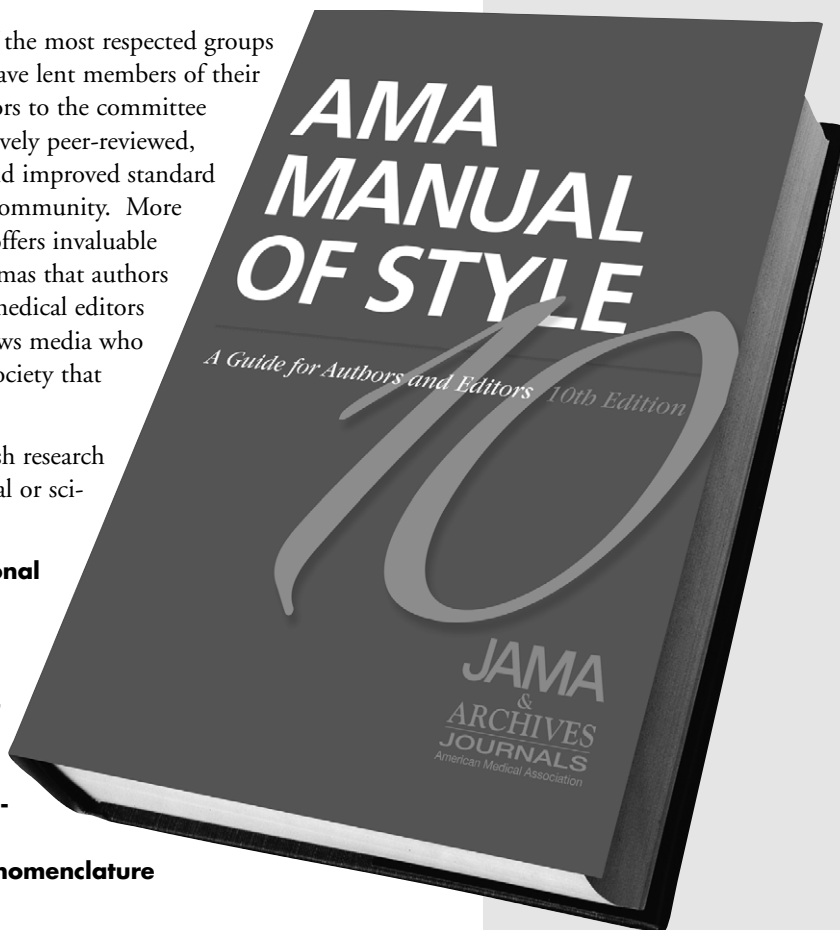
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