

CORRESPONDENCE

Re: Risk/Benefit Assessment of Tamoxifen to Prevent Breast Cancer—Still a Work in Progress?

We agree with the main contention of the editorial by Taylor et al. (1) that risk/benefit assessments of tamoxifen are very uncertain in black women and other minorities, a point repeatedly stressed by Gail et al. (2). We did want to clarify some factual issues, however.

Gail et al. (2) used relative risks associated with tamoxifen from the Breast Cancer Prevention Trial (BCPT) as well as baseline risks of various outcomes in the absence of tamoxifen derived from studies in the general population. As to the relative risks from tamoxifen, if one is willing to infer from the BCPT data, derived principally from white women, that tamoxifen lowers the risk of breast cancer in minority women by the relative risk factor observed in the BCPT, it seems reasonable to assume that tamoxifen's effects on other health outcomes, such as pulmonary embolism, in minority populations should also reflect the BCPT experience. This was the approach used by Gail et al. (2).

It is not a valid criticism that general population sources, rather than the BCPT, were used to estimate baseline risks in the absence of tamoxifen for women in the general population. The BCPT was a selected population whose health experience, while relevant for participants in other prevention trials, underestimates the risk of stroke, for example, in the general population. Gail et al. (2) present estimates based on both general population rates [see Table 10 and Table 11 in (2)] and on the selected BCPT experience [Table 12 in (2)].

Data for endometrial cancer in black women were obtained directly from Surveillance, Epidemiology, and End Results (SEER)¹ incidence tables for black women. The only multiplier used was a correction for the prevalence of hysterectomy.

Taylor et al. (1) criticize the use of black/white mortality ratios for stroke and for pulmonary embolism to estimate

baseline incidence rates in black women in the absence of tamoxifen. Although there are hypothetical reasons for thinking that mortality ratios need not equal incidence ratios, in fact, three stroke incidence studies cited by Gail et al. show that the black/white mortality ratio was indistinguishable from the black/white incidence ratios. Another point, brought out by Rosamund et al. (3), is that statistical adjustment for age, sex, hypertension, diabetes, location, education, smoking, and coronary artery disease reduces the black/white stroke incidence ratio to 1.4 but not to 1.0.

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- (2) Gail MH, Costantino JP, Bryant J, Croyle R, Freedman L, Helzlsouer K, et al. Weighing the risks and benefits of tamoxifen treatment for preventing breast cancer. *J Natl Cancer Inst* 1999;91:1829-46.
- (3) Rosamond WD, Folsom AR, Chambless LE, Wang CH, McGovern PG, Howard G, et al. Stroke incidence and survival among middle-aged adults: 9-year follow-up of the Atherosclerosis Risk in Communities (ARIC) Cohort. *Stroke* 1999;30:736-43.

NOTES

¹*Editor's note:* SEER is a set of geographically defined, population-based, central cancer registries in the United States, operated by local non-profit organizations under contract to the National Cancer Institute (NCI). Registry data are submitted electronically without personal identifiers to the NCI on a biannual basis, and the NCI makes the data available to the public for scientific research.

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RESPONSE

We recognize the importance of the work by Gail et al. (1) in beginning to assess the risk to benefit ratio for tamoxifen as a preventive strategy for women at higher risk for breast cancer, and we do not disagree with the conceptual model used by Gail et al. as it applies to the population studied. Thus, for white women, this model may provide important guidelines for breast cancer prevention. We did not criticize the use of the Breast Cancer Prevention Trial (BCPT) and general population databases to estimate tamoxifen's risk in the general population. Our concern was that, because of the unforgivably small number of minority women in the BCPT, these data are definitive for white women but are not definitive for minority women. Therefore, regardless of the sophistication of the analytic methodology, the guidelines for providing or withholding tamoxifen preventive therapy in minority women simply are not supported by data from an inadequate sample size of minority women. In their letter, Gail et al. state "if one is willing to infer from the BCPT data, derived principally from white women, that tamoxifen lowers . . . it seems reasonable to assume that tamoxifen's effects on other health outcomes. . . ." What is "reasonable to assume" as opposed to what is supported by data has, throughout the history of medicine, been all too often distressingly divergent. There are multiple examples of substantial ethnic differences in drug disposition and responsiveness (2). Thus, we are unwilling to infer that data from more than 13 000 white women, but from only 220 African-American women, and 249 women of other ethnicity will necessarily predict the effects of tamoxifen in women of African-American and other ethnicities. Rather than base guidelines for the administration of a powerful drug on inferences, we re-emphasize the need to recruit adequate numbers of minority women in important clinical trials.

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