CORRESPONDENCE

Benign Breast Disease and Breast Cancer

TO THE EDITOR: The article on the risk of cancer in patients with benign breast disease by Hartmann et al. (July 21 issue) contains some questionable assumptions. “Atypical ductal hyperplasia” and “lobular hyperplasia,” shown in Figure 1E and Figure 1F of the article, do not belong in the category of benign breast disease. Experienced pathologists know that the differentiation of the so-called atypical ductal hyperplasia from an intraductal carcinoma of the breast is extremely difficult in most cases and impossible in some.2 Lobular hyperplasia, shown in Figure 1F, is closely related to lobular carcinoma in situ, recognized for generations as a precursor lesion of breast cancer.3 Thus, these two types of lesions should be classified as precursors of mammary carcinoma, as demonstrated by a much higher rate of subsequent breast cancer in patients with these lesions than in patients with truly benign disorders. One would have expected an even higher rate of subsequent breast cancer in patients with these lesions than in patients with truly benign disorders. If this information is shared with patients, as suggested by Elmore and Gigerenzer, in the accompanying editorial.4

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TO THE EDITOR: In their editorial, Elmore and Gigerenzer offer insightful comments on the risk of risk communication. They state that risk can be communicated in terms of absolute risks, “which fosters insight” and are “clearer.” They recommend the use of the number needed to treat as a “clear” form of communication. We agree that decisions usually should be based on absolute risks, but to our knowledge, there is no evidence that absolute risk reduction or its reciprocal number needed to treat is clear or fosters insight. Rather, there is ample evidence that laypersons and professionals misunderstand number needed to treat.1-4

Elmore and Gigerenzer claim that “the use of relative risks suggests greater effects than truly exist, whereas . . . absolute risks . . . prevents this misunderstanding.” Both relative risk and absolute risk, however, are arithmetic reformulations of the same numbers and are therefore equally correct. In order to establish that one of them is more misinterpreted than the other would require a gold standard for correct interpretation. To our knowl-
edge, there is little evidence that relative risks are more misunderstood than absolute ones.

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THE AUTHORS’ REPLY: Drs. Koss and Fineberg correctly note that atypical ductal hyperplasia and atypical lobular hyperplasia form a morphologic continuum with ductal carcinoma in situ and lobular carcinoma in situ, respectively. The microscopical distinction can be difficult and is based on a number of criteria including severity of cytologic atypia, degree of alteration in architectural cellular relationships, and extent of lesions. Not all these features can be represented in a single high-power view. The epidemiologic results in our study support the accuracy of our pathological assessment. Namely, the relative risk for atypical hyperplasia in our study is 4.2, entirely consistent with other major reports.1,2 If our atypia group had included significant numbers of cases of ductal carcinoma in situ and lobular carcinoma in situ, we would expect relative risks in the range of 10 or greater.3

We do not understand the comments by Koss and Fineberg regarding precursor lesions. Many experts in the field consider atypia, especially atypical ductal hyperplasia, to be a precursor lesion to breast cancer. Our data show a slightly increased risk of ipsilateral cancer in women with atypia, compatible with the hypothesis that some atypias represent direct precursors.

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THE EDITORIALISTS’ REPLY: It should be alarming that most physicians and patients do not understand the crucial numbers that medical research provides for them. Collective innumeracy is an impediment to the efficacy of evidence-based medicine and shared decision making. Research on how to frame numbers so that physicians and patients understand them is still scarce.

Dr. Kristiansen and colleagues ask whether there is evidence that relative risks confuse people more than absolute risks or number needed to treat. In fact, several studies have shown that statements referring to relative risks make benefits appear greater to patients as well as to physicians and policymakers, whereas statements referring to absolute risks or number needed to treat make benefits appear smaller. For example, people’s willingness to accept medication or screening is substantially greater when the benefits are framed in terms of relative risks.1,2 Physicians’ treatment decisions can also be affected by the way in which research results are summarized.3 One notable study even found that health authorities were much more likely to fund a proposal for cardiac interventions and breast-cancer interventions when the benefits were framed in terms of relative risks than they were to fund an identical proposal with benefits that were framed in terms of absolute risks and number needed to treat.4

Kristiansen et al. cite studies by Sheridan et al., who conclude that discussions of absolute risks and number needed to treat may not foster insight. Yet the apparently discrepant results from Sheridan et al. might be due to the researchers’ unusual expression of these numbers.5

Physicians rarely quantify risks or benefits when talking with patients. Instead, we tend to use qualitative terms that might be ambiguous, such as “You are at increased risk of breast cancer” or “You are at high risk of breast cancer.” The way patients interpret such qualitative statements can vary widely, with a corresponding effect on the medical care that we provide. Thus we suggest using numbers along with qualitative terms to minimize ambiguity.

At issue is transparency and clarity in communications with patients. All of the foregoing enforces one conclusion: we need to overhaul our education-
al systems. Evidence-based medicine must declare war on innumeracy. Now.

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Atorvastatin in Patients with Type 2 Diabetes Mellitus Undergoing Dialysis

To the Editor: Wanner et al. (July 21 issue)1 report a lack of benefit from therapy with 20 mg of atorvastatin among patients with type 2 diabetes mellitus who were receiving hemodialysis, despite a high rate of cardiovascular events. In their discussion, the authors do not consider the possibility that this lack of benefit may have been related to a lack of appropriate exposure to statin therapy: approximately 50 percent of patients were no longer on the drug after two years of follow-up, and the rates for an average of four years of follow-up were not provided, though clearly even fewer patients would still have been receiving atorvastatin. In the 15 percent of patients who had a particularly good response to atorvastatin, with reductions in low-density lipoprotein (LDL) cholesterol levels to less than 1.3 mmol per liter (50 mg per deciliter), the dose was lowered. I would like to suggest that the lack of benefit in this important study was observed because only a minority of patients were exposed to the dose of 20 mg of atorvastatin throughout the duration of the study.

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To the Editor: It would be erroneous to conclude from the German Diabetes and Dialysis Study that atorvastatin therapy does not benefit patients with diabetes who are receiving hemodialysis. In this study, half of the deaths from cardiac causes were classified as sudden. Statin therapy would not necessarily be expected to reduce the risk of arrhythmias attributable to hemodialysis; an analysis confined to the conventional cardiac end points of fatal and nonfatal myocardial infarction, death from coronary causes, and revascularization results in a relative risk of 0.81 (95 percent confidence interval, 0.57 to 0.94) in the atorvastatin group. Furthermore, it cannot be concluded that hemodialysis attenuates the benefit of atorvastatin therapy in patients with diabetes. In the Collaborative Atorvastatin Diabetes Study,1 the relative risk of these events was 0.56 (95 percent confidence interval, 0.41 to 0.80) with atorvastatin. The pathophysiological basis for the non-significant increase in fatal and nonfatal ischemic stroke in the study by Wanner et al. is unclear. However, 32 nonfatal and fatal cardiovascular events were still prevented with atorvastatin therapy. Since the safety of atorvastatin in patients receiving hemodialysis has been established, these patients should continue to be treated according to current guidelines for cardiovascular prevention.2,3

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