

ity control and quality assurance program is more important than the type of method used to determine HER-2 status. Interpreting a HER-2 result without knowledge of reliability of test performance may sometimes be harmful to patients.

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### Frequency of Ejaculation and Risk of Prostate Cancer

**To the Editor:** In their prospective study, Dr Leitzmann and colleagues<sup>1</sup> replicated the findings of our case-control study<sup>2</sup> in regard to a protective relationship between frequency of ejaculation and risk of prostate cancer. Although the study of Leitzmann et al avoids the potential for recall bias, for both their study and ours the accuracy of ejaculation assessment was likely to be affected by problems in recall of past practice, particularly of that in early adult life. We believe that the effect of such a bias would tend to be conservative and would have thus underestimated any real effect for ejaculation.

We were puzzled by the authors' choice of men with the second lowest frequency of ejaculation as the reference category. It would be interesting to see the relative risks produced by an analysis that combined the first 2 groups together as the reference category.

Unlike many other studies, we found no effect with number of sexual partners. It would be interesting to know also if Leitzmann et al measured this variable. Our study found a particularly striking protective effect that was limited to ejaculations experienced in early adulthood.<sup>2</sup> Neither study, however, addressed the question of ejaculatory frequency during puberty, but this might prove to be particularly illuminating if appropriate questions could be included in one of the biennial follow-ups of the study of Leitzmann et al.

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**Reply:** In response to Dr Giles and colleagues, our rationale for using the category of 4 to 7 ejaculations per month as the common reference group was that that category reflects a more typical ejaculation frequency than the category of 0 to 3 ejaculations per month. In addition, the category of 4 to 7 ejaculations per month had sufficient numbers of cases across the different age groups, which ensured reasonable stability of the relative risk estimates. When we combined the first 2 groups as the reference category, the multivariate relative risks for men reporting 21 or more ejaculations per month at ages 20 to 29 years, ages 40 to 49 years, in the previous year, and across the lifespan were 0.88 (95% confidence interval [CI], 0.73-1.06), 0.69 (95% CI, 0.55-0.87), 0.42 (95% CI, 0.24-0.74), and 0.69 (95% CI, 0.52-0.91), respectively.

We did not address the association between number of sexual partners and risk of prostate cancer because we believe this variable does not represent an accurate measure of sexual function. We did examine serum testosterone levels in order to address whether the ejaculation frequency and prostate cancer relationship is mediated by androgens. The correlation between ejaculation frequency and testosterone levels in our study was low, but statistically significant ( $r=0.17$ ;  $P=.005$ ). Our finding of an inverse association between ejaculation frequency and risk of prostate cancer suggests that any androgen-related mechanism linking enhanced testosterone levels to increased risk of prostate cancer is countered by one or more nonandrogenic biological pathways.

We agree with Giles et al that evaluating ejaculation frequency during adolescence would represent an important step in determining whether the peripubertal time period is etiologically relevant regarding the association between ejaculation frequency and prostate cancer.

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