with intermediate pretest probability who are at high risk for surgical complications (*3*). They note importantly that the cost-effectiveness of various diagnostic strategies depends critically on the pretest probability of malignancy.

The strength of the evidence required before a management decision is made will vary depending on the pretest likelihood of disease and the risk of a specific intervention. As Dr. Fisher indicates, a negative predictive value of a nodule with no uptake (i.e., "definitely benign" by our criteria) is 97% and is probably acceptable for adopting a watch-and-wait strategy, but a negative predictive value of a "probably benign nodule" (estimated standardized uptake value $>$ 0.6–0.8 but $<$ 1.5–2.0) is 87% and may not be convincing enough to avoid a biopsy, especially in a patient with a smoking history and other risk factors for malignancy (*2*). Although we dichotomized the 5 confidence levels of interpretation as described for determining sensitivity and specificity, we did develop interval likelihood ratios for each level of interpretation. In this regard, with our prevalence rate of 53% malignant nodules, a patient whose nodule was rated definitely benign by PET had a posttest probability of malignancy of only 3% as pointed out by Dr. Fisher. Similarly, a patient whose nodule was rated probably benign by PET had a posttest probability of 13%. In populations with lower prevalence rates, the pretest–posttest probability decrease would be shifted even further. For example, in a population with a 20% prevalence of malignancy, the posttest probabilities would be reduced to 1% and 4% in patients with definitely benign and probably benign interpretations, respectively.

We strongly agree with Dr. Fisher about the hazards of continuing to consider a binary cutoff of 2.5 for standardized uptake value as capable of reliably distinguishing benign from malignant nodules. We would instead encourage the adoption of a visual scoring methodology with a validated, more continuous scale that relates to interval likelihood ratios, such as described in our publication. In this manner, the clinical pretest likelihood of malignancy could be incorporated into the final estimate of the posttest likelihood of a malignant or benign nodule.

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Pregnancy Outcome After ^{131}I Therapy

TO THE EDITOR: We read with interest the article by Garsi et al. (*1*) concerning the pregnancy outcome and the health of offspring of women who had received ^{131}I for differentiated thyroid cancer. In this article, the authors evaluated 2,673 pregnancies from patients treated with ^{131}I and found 10.4% miscarriages before any treatment, 20% after thyroidectomy but before ^{131}I therapy, and 19% after ^{131}I therapy. There was no significant variation according to the cumulative ^{131}I dose. The incidences of stillbirths, preterm births, low birth weight, and congenital malformations were not significantly different before and after ^{131}I therapy. The authors concluded that there was no evidence that radioiodine therapy affected the outcomes of subsequent pregnancies and offspring.

Interestingly, we have reported a relatively similar study in a smaller number of patients. Our study predominantly examined the effect of ^{131}I therapy (3,700 MBq) on menstrual cycle or pregnancy in women less than 40 y old. Specifically, we evaluated 45 women with differentiated thyroid cancer who were treated with ^{131}I therapy and compared with 83 age-matched control women. We found menstrual cycle irregularities in 13.3% of patients before ^{131}I therapy but 31.1% after treatment. However, after ^{131}I therapy there were no subsequent pregnancy abnormalities such as premature births, miscarriages, or congenital abnormalities in the 7 children who were borne of 6 of the 45 patients (*2*). Another study, of 49 pregnancies from 76 patients who received ^{131}I therapy, found 10% miscarriages, 18% induced abortions, and no congenital malformations or first-year mortality (*3*). All these findings concur that ^{131}I therapy is safe regarding subsequent pregnancy outcome. However, our results suggest an increased incidence of menstrual cycle abnormalities after ^{131}I therapy. It will be interesting to see if Garsi et al. (*1*), in their large cohort of patients, noticed any such abnormalities induced by ^{131}I therapy.

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REPLY: We were interested to see the letter of Chrissa Sioka and Andreas Fotopoulos about our article (*1*). In addition to reporting results similar to ours, showing that ^{131}I therapy is safe regarding subsequent pregnancy outcome, with no increase in the risk of miscarriage, induced abortion, or congenital malformation, they added new data showing that ^{131}I therapy probably increases the incidence of menstrual cycle abnormalities (*2*).

To confirm these results, we analyzed the responses given by women in our series to similar questions. Of 2,190 women questioned about cycle abnormalities before and after their cancer and followed at least 2 y, we excluded 36 in whom another cancer had developed before thyroid cancer, 158 in whom another malignancy later developed, 263 who received external radiotherapy for thyroid cancer, and 137 who were treated with radioiodine for distant metastases. Of the remaining 1,866 women, 1,054 were