CORRESPONDENCE

No screening yet after a negative test for the family mutation

In their interesting paper, Smith *et al*¹ postulate that after a negative test for *BRCA1* and *BRCA2*, women are still at increased risk of cancer. They therefore recommend to continue screening.

I think there are several reasons why surveillance recommendations, after a negative test for the family mutation, are premature.

(1) It should be clear how high the rest risk is. This is not really clear from this paper as DNA testing bias of breast cancer cases has played a part. When testing first-degree relatives of a *BRCA1/2* mutation carrier, it would be expected that about 50% would test positive. However, table 1 shows that 67% (376/560) tested positive. This strongly suggests preferential testing of breast cancer cases, which will also certainly increase the percentage of breast cancers in the negative tested group, without any modifying genetic factor. We have previously shown that such a DNA testing bias can

wrongfully suggest increased risks in patients who are non-*BRCA1/2*.^{2,3} To exclude this bias, only the cancer incidence after the DNA test should be taken into account.

(2) In order to recommend screening, it should be known at which age the possible rest risk may be expected. Certainly, screening should not continue from age 25–30 onwards as in carriers, if the increased risk possibly occurs mainly above age 50. Screening with mammography at age 25–40 years has too low a sensitivity, may cause too many false-positive results and could possibly induce breast cancer, so it is not justified for only a slightly increased risk.⁴

(3) As the results came from families with a high caseload, it is not known whether such modifying genes will be present in families with *BRCA1/BRCA2*, with fewer cancers.

When many breast and ovarian cases test negative for the family mutation, a second gene mutation or risk from the untested side of the family may need to be investigated.

M M A Tilanus-Linthorst

Correspondence to: Department of Surgery, Erasmus MC, Rotterdam, The Netherlands; m.tilanus-linthorst@erasmusmc.nl

References

- 1 Smith A, Moran A, Boyd MC, Bulman M, Shenton A, Smith L, Iddenden R, Woodward ER, Lalloo F, Maher ER, Evans DGR. Phenocopies in *BRCA1* and *BRCA2* families: evidence for modifier genes and implications for screening. *J Med Genet* 2007;44:10–15.
- 2 Tilanus-Linthorst MMA, Bartels K, Alves C, Bakri B, Crepin E, van den Ouweland A, Klijn JGM, Eggermont AM, meijers-Heijboer H, Brekelmans CTM. Selection bias influences reported contralateral breast cancer incidence and survival in high risk non-*BRCA1/BRCA2* patients. *Breast Cancer Res Treat* 2006;95:117–23.
- 3 Tilanus-Linthorst MMA, Alves C, Seynaeve C, Menke-Pluymers MBE, Eggermont AMM, Brekelmans CTM. Contralateral recurrence and prognostic factors in familial non-*BRCA1/2* associated breast cancer. *Br J Surg* 2006;93:961–8.
- 4 Griebsch I, Brown J, Boggis C, Dixon A, Dixon M, Easton D, Eeles R, Evans DG, Gilbert FJ, Hawnaur J, Kessar P, Lakhani SR, Moss SM, Nerurkar M, Padhani AR, Poinon LJ, Potterton J, Thompson D, Turnbull LW, Walker LG, Warren R, Leach MO. Cost-effectiveness of screening with contrast enhanced magnetic resonance imaging vs. X-ray mammography of women at a high familial risk of breast cancer. *Br J Cancer* 2006;95:801–10.