Letter to the Editor

Study design and statistics in the epidemiology of breast cancer

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British Journal of Cancer (2006) 95, 1301. doi:10.1038/sj.bjc.6603370 www.bjcancer.com
 Published online 3 October 2006
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Sir,

Your recent article by García-Closas *et al* (2006) raises interesting discussion points regarding tumour behaviour in Poland. If correct, these results may have implications for health care in Poland, but we disagree that the findings can be generalised to other populations, particularly when the reported ER negativity was 41%. There were several flaws in the study design and analysis that make such a conclusion unsafe. Firstly, we understand mammographic screening is not routine in Poland (reflected in the low incidence (6%) of DCIS). The authors should have made clear whether mammography was in fact offered to equal numbers in the study and control groups. It is possible that the results were biased by differential access to and uptake of mammography between the groups; perhaps, better educated women were both more likely to take HRT and seek mammograms. Indeed, the absolute differences

for better education between the two arms (10%, unadjusted OR = 1.89) and history of a previous mammogram (8%, unadjusted OR = 1.39) support this suggestion.

Another potential error lies in the histology. The rate of agreement between the original Polish and the subsequent American analysis varied from 18 to 80%, depending on tissue type. However, nearly one in five ($n = 428$) did not benefit from an American review, yet were still included in the study. With such high rates of discordance, it was hazardous to assume the original diagnosis was correct in the nonreviewed group. If the ratios for error are the same as the reviewed group, then at least 4.9% of all samples would have been misclassified, thus challenging many of the statistical results (see Table 1).

Analysis of data from studies of this kind is fraught with difficulties and such statistical methods are not always illuminating. We believe there is a great potential for over interpretation.

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Lukaszek S, Sherman ME (2006) Established breast cancer risk factors by clinically important tumour characteristics. *Br J Cancer* 95: 123–129, doi:10.1038/sj.bjc.6603207

Table 1 Analysis of potential misclassification in nonreviewed histology

	% of reviewed histology	Reported discordance (%)	Projected number of nonreviewed cases	Projected misclassification in nonreviewed cases	Proportion to total sample (%)
Ductal	58	20	428*58% 248 cases	248*20% 50 cases	2.2
Lobular	16	32	428*16% 69 cases	68*32% 22 cases	0.9
Mixed	12	82	428*12% 51 cases	51*82% 42 cases	1.8
Other	14	No data: Assume = 0	428*14% 60 cases	0 cases	—
Total	100	—	428 cases	114 cases	4.9

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 Published online 3 October 2006