been discussed in detail elsewhere.[3-5] Particularly, it has long been noted that misclassification of a covariate can substantially alter the stratum-specific odds ratios even if it is nondifferential, i.e. of same magnitude in cases and controls. I would like to illustrate the point with some of the data presented by Morabia and Flandre. Among others, the association between age at first livebirth (≥ 25 years versus <25 years) with breast cancer was assessed stratified by a menses-based definition of menopause using as cutpoint 24 months between last menses and diagnosis of breast cancer. From Table 1 in the paper by Morabia and and Flandre, an unadjusted odds ratio of

$$(100 \times (238-66))/((208-100) \times 66) = 2.41 \text{ and}$$
$$(114 \times (321-126))/((219-114) \times 126) = 1.68$$

can be derived for this association among premenopausal and postmenopausal women, respectively.

An age-based classification scheme of menopause using as cutpoint age 55 was estimated to have sensitivity of only about 71% in cases and about 54% in controls and almost perfect specificity in both cases and controls compared with this menses-based classification criterion (Table 4 of reference 1). This is a clear example for differential misclassification. If the misclassification had been nondifferential rather than differential with 60% sensitivity and perfect specificity in both cases and controls, the expected unadjusted odds ratio would have been

$$((100+0.4\times 114)\times(238+0.4\times 321-66-0.4\times 126)/$$
$$((208+0.4\times 219-100-0.4\times 114)\times(66+0.4\times 126)$$
$$= 2.08$$

among premenopausal women, and hence would have been considerably lower than the estimate derived from the menses-based data. The expected odds ratio among postmenopausal women would still be 1.68 in this example, but would also be biased in situations in which the specificity is also imperfect.[5]

In summary, while it is meritorious to point out and quantify the potential role of differential misclassification of menopausal status in studies on risk factors for breast cancer, there is no justification for the message of assurance that covariate misclassification may be irrelevant in other studies where it can be assumed to be nondifferential.

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Authors' response

From ALFREDO MORABIA AND PHILIPPE FLANDRE

Sir—We are grateful to Dr H Brenner for having identified a truncated sentence in our paper. The point of the paragraph was that a nondifferential misclassification bias of menopausal status would not affect the relative odds away from the null hypothesis, as shown in the example given by Dr Brenner. However, because, in our study, misclassification of menopausal status is differential between cases and controls, relative odds can be biased either away from or towards the null hypothesis. This differential misclassification bias may therefore explain part of the contradictory reports on menopausal status being an effect modifier of the relationships of reproductive factors and breast cancer. We also agree with Dr Brenner that we should have referred to the specific literature on misclassification bias related to inaccurate measurement of a covariate rather than inaccurate measurement of only outcome or exposure.

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