The recent report by Lovely et al. (1) on their investigation of the association between nonlymphocytic leukemia and appliance use appears to contain some confusion regarding appropriate analytic methods for their data. In their discussion of methods, the authors first indicate that cases and controls were matched by age and sex and then go on to state that "[I]nitially, unadjusted odds ratios were calculated as this method required the fewest assumptions and allowed for a direct test of the a priori hypothesis under investigation" (1, p. 512). (Unadjusted odds ratios are presented in their tables 1 and 4.) This violates a fundamental principal of epidemiologic analysis mentioned in standard textbooks (2, 3), namely that matching in a case-control study needs to be accounted for in the analysis, since "[a]nalyzing matched data as if they were unmatched will generally lead to biased estimates of the odds ratio" (2, p. 178). Fortunately, in this particular case, such bias does not seem to have occurred (based on the sex-specific results presented in their tables 2 and 3). Nevertheless, this does not justify the authors' assertion that their initial crude analysis "required the fewest assumptions" (1, p. 512) since it required the major assumption that there was no confounding and no effect modification attributable to the matching variables, which would have obviated the need for matching in the first place.

The authors further justify their use of crude odds ratios in the dose-response analysis (table 4) in their discussion section, stating that it was the "small number of observations attendant to stratification that largely dictated the calculation of unadjusted odds ratios to test the a priori hypothesis under investigation" (1, p. 516). This is precisely the type of situation in which the Mantel-Haenszel summarization procedures cited in their paper are advantageous, and it would be useful to know whether adjustment for the matching variables as well as smoking habits using these procedures (or alternatives, such as logistic regression) was weakly associated with increased leukemia risk..." (1, p. 516). Since there was an estimated threefold increase in the incidence rate of leukemia among both men and women who used massage units compared with nonusers (tables 2 and 3), it would seem to have been more appropriate to indicate that the evidence for an association was weak (or, more accurately, preliminary), rather than that the association itself was weak.

References

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THE AUTHORS REPLY

The analysis by Sussman and Kheifets (1) of findings we reported (2) raises an important issue that reliance on proxy responding for cases, but not for controls, carries with it the attendant risk of bias due to differential misclassification. As the authors and others (3) note, proxy reporting is more likely to be accurate for questions regarding ever/never use than for duration of use. Clearly, this is not the case in our study; Sussman and Kheifets show that the odds ratios for ever/never use are as biased as are the odds ratios for duration of use, although both analyses (1, 2) are based on small numbers. That the reported odds ratios might be totally attributable to reporting bias even for ever/never use is particularly surprising given that 62 percent of the proxy respondents were spouses of deceased cases (2) and would be expected to know the correct response to ever/never use questions. The analysis by Sussman and Kheifets further suggests that while proxy reporting was biased, it was apparently even more so for male proxy respondents. Their findings are important, and they 1) underscore the potential weakness inherent in relying on large numbers of proxy respondents in case-control studies, and 2) suggest that it would be worthwhile to conduct further methodological studies that shed light on the reasons (for differential misclassification by proxy respondents in case-control studies, and 3) persuade us that our report (1) of a weak association between electric razor use and adult leukemia is not the most parsimonious interpretation of the data.

O'Dowd (4) points out that the frequency matching on age and sex carried out by the original investigators (5) should have been taken into consideration in our analytic plan, with which we concur. It is also noted that in this case the sex-specific results shown in our tables 2 and 3 indicate that bias was not the basis of the observed association. As Sussman and Kheifets (1) point out, a quite different and apparently large bias existed in all the data because of the use of proxy respondents (Sussman, SS, Kheifets, LI. Electric Power Research Institute, personal communication, 1995, indicating that a similar bias due to proxy responding accounted for the lower odds ratios reported for hair dryer use). In light of their findings, further discussion of whether other observed association(s) were "weak (or, more accurately, preliminary)" would appear to be a moot point.

Finally, the hypothesis that use of select personal appliances might be associated with some cancers should be tested with appropriate respondent data since use of some personal appliances may well be a significant source of exposure to magnetic fields (2, 6, 7).

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