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Reply to "Evolution of Epidemiologic Evidence on Magnetic Fields and Childhood Cancers"

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We concur with Dr. Poole that issues of control selection must be considered in evaluating the results from case-control studies of electromagnetic field-cancer relations (1). However, we do not agree with his implication that the issue is unique to random digit dialing or that the success of this method hinges on the adequacy of analytic control for socioeconomic status. Virtually all of the sampling frames typically used for control selection in population-based case-control studies (e.g., households with telephones, birth certificates, town lists, motor vehicle licensing records, Health Care Financing Administration files) are to some extent an incomplete accounting of the population study base from which cases typically are ascertained. When completeness varies inversely by socioeconomic status, restricting cases to those who are part of the sampling frame reduces the potential for bias. Since we used random digit dialing as the source of controls, we excluded cases who did not have a residential telephone, thus reducing substantially the likelihood of bias due to severe discordance in socioeconomic status of the respective source populations.

With respect to nonconcurrent selection of controls, our study is similar to that of Preston-Martin et al. (2) in that our cases were diagnosed from 1984 to 1990, while enrollment of controls did not begin until 1989. In our study (3), we minimized the potential bias arising from partial nonconcurrence of control selection by requiring that a control, like a case, be a resident of the study area at the time of his or her assigned reference date. Even so, Dr. Poole correctly states that bias could still arise because some children who were residents of the study area during the case diagnosis period could not have been selected for our study because they had moved (or, far less likely, had died). For bias to have occurred, the exposure characteristics of the children who migrated out of the area must have differed meaningfully from that of the sampled control group, and the relative proportion of the population at risk that is missing due to migration must have been fairly substantial. If, however, this proportion was small (as we suspect it was for the Seattle-Puget Sound region), even marked exposure differences between residents who migrated out and residents who remained in the study area are unlikely to have much impact on our results.

We believe that in most population-based case-control studies the key potential problem with control selection, whether by random digit dialing or some other method, is bias that may arise due to differential nonparticipation (4). Although measuring and adjusting adequately for socioeconomic status can control for confounding among recruited subjects, only measurement of the exposure characteristics of the nonparticipants provides information about the impact of this source of potential selection bias (5). In addition, methodological studies such as we have conducted also can help address control nonparticipation bias concerns by providing reasonable bounds on the extent of the problem (6). The results of our methodological study showed that differential nonparticipation of persons from low-income households is unlikely to result in substantial bias from the inverse relation that exists between household income level and high exposure wire code category in the Seattle area (6).

Furthermore, selection bias due to nonparticipation depends not only on exposure differences between participating and nonparticipating controls, but also on exposure differences between participating and nonparticipating cases. In our study, we measured wire code configurations in a sample of both the nonparticipating cases and controls (3). Inclusion of these data yielded estimates for the five-level wire code scheme that were similar to those for participants alone, with one notable exception: the odds ratio relating brain tumor occurrence to the highest exposure category (very high current configuration) was 0.5 among the participants, but increased to 0.9 when nonparticipants were included. Although based on small numbers, this substantial change in the association for this wire code category occurred because 13.2 percent of nonparticipating cases were exposed to very high current configuration, compared with 3.3 percent of the participating cases; for nonparticipating and

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participating controls, the proportions were 5.5 and 6.7 percent, respectively. These findings illustrate the need to pay careful attention to limitations in both case and control selection when evaluating case-control studies of electromagnetic fields and cancer (or any hypothesized association).

Finally, Dr. Poole is concerned that the lack of association between wire codes and brain tumor incidence in our study is difficult to interpret without evidence regarding variability in magnetic field measurements across wire code levels (1). In the absence of mean magnetic flux densities for each wire code category, our a priori choice to analyze the data according to the five-level and the collapsed two-level Wertheimer-Leeper code was made to provide maximum comparability with earlier research on this topic (7, 8). As we mention in the last paragraph of our report (3), previous work (9) for an electromagnetic field-cancer study (10) showed a clear positive correlation between wire code categories and magnetic flux density ($r = 0.41$) in the Seattle area; this work was conducted during the case-diagnosis period of our current study. However, whether or not the degree of exposure variability that has been empirically observed in our study area, as well as in others (11–13), has any biologic relevance to the occurrence of cancer is a question that has yet to be answered and needs to be the focus of electromagnetic field research in the immediate future.

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