CORRESPONDENCE

Re: Recruiting Minorities Into Clinical Trials: Toward a Participant-Friendly System

The special article in the December 6 issue of the Journal (*1*) is described by the authors as a summary of the "state of the art in recruiting participants for clinical trials" and the "collective knowledge about methods of recruitment of diverse populations into clinical trials." After an extensive review of the literature that begins with cancer trials, the authors recommend that 20 specific steps to enhance minority recruitment be "routinely included in the recruitment phase of any clinical trial." With these claims and conclusions, readers may conclude that the problem of minority recruitment is critical and universal.

Thus, I must point out that nearly 95% of U.S. children with cancer receive their care at institutions affiliated with the Childrens Cancer Group (CCG) or the Pediatric Oncology Group (POG), pediatric cooperative clinical trial organizations sponsored by the National Cancer Institute (NCI) (*2,3*). More than 50% of these patients are entered into one or more clinical trials (*2*). Moreover, the racial distribution of these patients is representative of the populations served. In a recent survey (*2*), 29 859 entries of patients younger than 20 years of age in CCG and POG clinical trials between January 1, 1991, and June 30, 1994, were compared with all patients of the same age in the United States who should have been diagnosed to have cancer (*2*). The latter was predicted from the crude incidence data of the NCI Surveillance, Epidemiology, and End Results (SEER) Program[1] applied to the 1990 U.S. census. The CCG and POG had 29 090 (97.4%) of the entries. Of these entries, 11.8% of the participants were reported to be Hispanic; 10.3% were African-American; and 4.6% were Asian, American-Indian, and other racial groups. The expected values were 9.1%, 10.7%, and 4.3%, respectively, and the higher rates in the CCG and POG trials were generally statistically significant. Thus, despite the comprehensive analysis reported in the special article by Swanson and Ward, the national pediatric cancer clinical trial cooperative groups appear to have been overlooked in their accomplishment to provide equal access to clinical trials for U.S. children regardless of race or ethnicity. Because this experience is opposite to that contended in the special article, the data are being prepared for publication as a full article.

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(*3*) Ross JA, Severson RK, Robison LL, Pollock BH, Neglia JP, Woods WG, et al. Pediatric cancer in the United States. A preliminary report of a collaborative study of the Childrens Cancer Group and the Pediatric Oncology Group. Cancer 1993;71(10 Suppl):3415-21.

Note

[1]*Editor's note:* SEER is a set of geographically defined, population-based central tumor registries in the United States, operated by local nonprofit organizations under contract to the NCI. Each registry annually submits its cases to the NCI on a computer tape. These computer tapes are then edited by the NCI and made available for analysis.

Response

The issues concerning subject recruitment in pediatric and adult clinical trials are quite different; therefore, our special article was focused entirely on adult clinical trials.

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Re: Randomized Trial of Intake of Fat, Fiber, and Beta Carotene to Prevent Colorectal Adenomas

In their randomized, partially double-blinded, placebo-controlled study, MacLennan et al. (*1*) assessed whether colorectal adenomas can be prevented or can be reduced in size through multi-pronged dietary intervention. The investigators stated that the study design involved changes (for the patients studied) that would not affect other household members. Such qualification is an obvious handicap for significant dietary alterations. That these changes did, in fact, not lead to a reduction of total fat intake to 25% of total calories is rather clear, since the authors also stated that "the absence of substantial weight loss in this group suggests that this figure [the observed 19-g-day decrease in fat intake] exaggerates the true decline." Yet, even with this modest dietary modification, the size of colorectal polyps was seemingly decreased.

The point of this comment is to raise the question as to what the optimal decrease in fat intake needs to be to achieve an optimal response, i.e., in this case, the prevention of colorectal polyps. Ornish (*2*) has shown that a reduction of fat intake to 10% of total calories was needed to observe a regression of femoral atherosclerosis. In the ongoing Women's Intervention Nutrition Study, it is our goal to reduce the total fat intake to 15% of total calories among postmenopausal women with stage I or stage II breast cancer who have had standard therapy (*3,4*). Such a drastic reduction requires significant changes in one's diet, needs to be guided by an experienced nutritionist, and demands very close follow-up to achieve and measure compliance.

Epidemiologic data from rural China and from Japan in the 1950s indicate that we must reduce dietary fat to 15% of total caloric intake if we are serious about preventing the formation of colorectal polyps, especially in short-term dietary interventions that are instituted relatively late in life. Ideally, to achieve maximum effectiveness, this type of dietary intervention should take place with high intensity early in life.

We should learn from medical practitioners that the success of medical or surgical intervention depends in each case on the proper dose. To administer the proper or optimal dose requires (*a*) committed individuals (and persons with a disease are likely to be more compliant), (*b*) intensive intervention by experienced and caring individuals, and (*c*) monitoring of food records, body weights, and biomarkers of food intake (such as blood lipid profiles and bile acids in the stools) for the duration of a study.

Unless these points are consistently followed, intervention studies with respect to dietary fat and fiber may give misleading and certainly less than optimal results. As in therapeutic trials with drugs, it is the dose that makes for a successful outcome. Those researchers who deal with the prevention of smoking or of drug abuse or those who deal with dietary intervention need to learn this fundamental lesson from colleagues in the therapeutic fields. Even if, in principle, the therapy itself is effective, an insufficient dose of it will not lead to the optimal effect of healing. Giving an insufficient dose of a therapeutic agent or of an intervention means wasting time and funds. Let all interventionists, therefore, make sure that the strength of any preventive measure that we apply is the appropriate dose.

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(*2*) Ornish D. Can lifestyle changes reverse coronary heart disease? World Rev Nutr Dietet 1993;72:38-48.
(*3*) Chlebowski RT, Blackburn GL, Buzzard IM, Rose DP, Martino S, Khandekar JD, et al. Adherence to a dietary fat intake reduction program in postmenopausal women receiving therapy for early breast cancer. The Women's Intervention Nutrition Study [*see* comment citation in Medline]. J Clin Oncol 1993;11: 2072-80.
(*4*) Cohen LA, Rose DP, Wynder EL. A rationale for dietary intervention in postmenopausal breast cancer patients: an update. Nutr Cancer 1993;19:1-10.

Response

The patients in our trial met the three criteria listed by Wynder: All patients were committed individuals at increased risk of colorectal neoplasia, intensive intervention on a one-to-one basis was undertaken by experienced dietitians, and food intake (including records), body weights, and blood lipid profiles were monitored at intervals throughout the study. The progression of small adenomas to large adenomas and carcinomas may occur within a short time frame, since the rates of colorectal cancer rapidly increase among migrants to Australia (*1*), suggesting that the adult diet increases risk. We chose to reduce fat to below the level recommended at the time (*2*); although this did not decrease the development of small adenomas, in our reported intention-to-treat analysis, there was a statistically significant reduction of large adenomas. We suggest that the formation of small adenomas may be determined largely by genetic susceptibility, but our data indicate that their progression to large, high-risk lesions can be substantially influenced by the level of fat reduction/wheat bran supplementation achieved in the trial. In our study, the reduction in fat intake needed to reduce this progression, when combined with increased fiber, was less than the "drastic" reductions, quoted by Wynder, which attempt to affect established disease. But this is not inconsistent with our conceptual model of colorectal neoplasia, where high-intensity intervention early in life is not necessary for the prevention of colorectal cancer.

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Note

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