Improving power with repeated measures

Dear Sir:

In their study, Marshall et al (1) found a significant relation between serum LDL cholesterol and saturated fat intake when random-effects models for longitudinal data were used. The model parameters were estimated by using data on 928 participants from the San Luis Valley of southern Colorado. Nutritional intakes were measured by the 24-h recall method; 2 observations were available for LDL cholesterol and nutrient intakes for most subjects. The models controlled for sex, age, body mass index, and energy intakes. The authors emphasized that significant associations were observed only in the 2 cases (models C and D) in which the statistical procedures took into account individual specific random effects.

The earliest studies by Keys et al (2, 3) emphasized the importance of the role of cholesterol intakes on serum cholesterol concentrations. Because of the poor fit of the model, intakes of saturated and polyunsaturated fats were also introduced; functional forms were empirically selected. In a subsequent study of 46 adults in the Boston area, Kushi et al (4) reported significant partial correlations between serum cholesterol and intakes of dietary cholesterol and saturated fat. Thus, a natural starting point for the statistical models estimated by Marshall et al would have been to also include intakes of dietary cholesterol and polyunsaturated fat in their regression models. Furthermore, because cholesterol intakes exhibit high within-subject variation (5), and because the authors relied on 24-h dietary recalls for measuring nutrient intakes, it is plausible that the reported coefficients of saturated fat intakes were not robust to changes in model specification. The authors should have reported results for a model that included saturated and polyunsaturated fat and cholesterol intakes as regressors. It would be interesting to see whether the results with such a model would support results obtained with the Keys equation, which is often used for approximating serum cholesterol concentrations in groups of individuals. From an estimation standpoint, it seems preferable to treat fat intakes as continuously measured variables. The estimated coefficients from the expanded model would show the relative importance of saturated fat and cholesterol intakes for serum LDL.

Second, because approximately half of cholesterol is endogenously produced, an individual’s current serum cholesterol concentration is likely to depend heavily on the measurement in the previous period. Dynamic models, which allow the dependent variable (serum cholesterol) to depend on its previous value, can be estimated by the principle of maximum likelihood in the presence of time-varying covariates (6–8). These models also take into account individual specific random effects that are assumed to be multivariate and normally distributed; equation 2 in Marshall et al’s article is a special case of the general formulation. Dynamic models and the “static” formulations used by Marshall et al are potentially useful for modeling serum cholesterol. However, because of the endogenous production of cholesterol, the underlying biological relations are perhaps better suited to dynamic modeling. With only 2 time observations available in the data used by Marshall et al, the empirical results from dynamic and static models are likely to be close. However, the model parameters have been interpreted differently. For example, it seems somewhat unlikely that serum LDL will decline immediately by 0.14 mmol/L after a 20-g decrease in saturated fat intakes on the day of a 24-h recall survey. Rather, there are complex delays underlying the relation between dietary intakes and serum LDL. One might be able to analyze these relations more systematically by using data from studies such as the Women’s Health Trial Vanguard Study (9) and the Women’s Health Trial Feasibility Study in Minority Populations (10), from which multiple observations on serum cholesterol and 4-d food records are available for relatively shorter time intervals.

Last, Marshall et al state that “parameter estimates for age were so different in models A and B than in models C and D” (models A and B did not allow for individual specific random effects). The authors attributed these differences to the underlying differences in LDL-cholesterol concentrations in different age cohorts. However, an alternative explanation would be that the subject-specific random effects partially reflected the age distribution of the sample. Because the authors apparently used discrete groups to represent age, the random effects are likely to further detect age differences in serum LDL cholesterol. This in turn would decrease the magnitude of the coefficient of age in models that include random effects. Evidently, this is the case when one compares the estimated coefficients of age in models A and B with those in models C and D in Table 3 (1).

Alok Bhargava

Department of Economics
University of Houston
Houston, TX 77204–5882
E-mail: bhargava@uh.edu

REFERENCES

Reply to A Bhargava

Dear Sir:

Our study focused on the added power of random-effects models and we chose to use saturated fat for the purpose of illustration (1). Bhargava suggests that when serum cholesterol is modeled, results from models incorporating polysaturated fat and cholesterol intakes be reported. We used the Key’s index as one indicator of an atherogenic diet in descriptive studies of this population (2) and we previously evaluated the relation of the index’s components as predictors of serum lipid concentrations (3). We chose to use saturated fat because it was the strongest predictor and was relatively easy to interpret. When polysaturated fat and cholesterol intakes were added to model D, neither variable was significant and there was no improvement in the −2 log likelihood. Similarly, when saturated fat was replaced by the Key’s index in model D, the index was a significant predictor, but again there was no improvement in the model. Dietary fat intake was treated continuously in all models.

Bhargava further suggests that dynamic models that adjust for prior serum lipid concentrations by adding a lag variable be explored. We agree that this procedure is unlikely to improve the model fit with the length of follow-up (4 y), it is unlikely that age differences in models A and B compared with models C and D explain these results. When age is separated into its cross-sectional and longitudinal components (4), serum LDL concentrations increase across age cohorts and decrease within subjects over time. This finding is consistent with patterns seen in national surveys collected over time (5). We appreciate Bhargava’s analysis of our article and his effort to promote discussion.

Julie A Marshall
Richard H Jones

Department of Preventive Medicine and Biometrics
University of Colorado Health Sciences Center
Campus Box C-245
Denver, CO 80262
E-mail: julie.marshall@uchsc.edu

REFERENCES

Nutritional status and energy metabolism in Crohn disease

Dear Sir:

We read with great interest the paper by Geerling et al (1) and the related editorial (2) regarding the usefulness of a comprehensive assessment of nutritional status in patients with inactive Crohn disease (CD). In Geerling et al’s study, patients with inactive CD were found to have fat and fat-free mass contents (assessed by anthropometry and dual-energy X-ray absorptiometry) similar to those of control subjects. Our group previously reported the importance of studying CD patients during a remission phase because intercurrent factors related to inflammation can severely affect data measurement (3, 4). We found steroid treatment; the presence of clinical symptoms such as diarrhea, abdominal pain, and nausea; and the exclusion of patients who had undergone intestinal resection to be factors of primary importance for a correct evaluation of nutritional status in patients with inflammatory bowel disease (IBD). In addition, we suggested that the measurement of energy balance provides valuable information (5). We showed that CD patients with inactive disease had peculiar metabolic and body-composition features with respect to both control subjects and patients affected by ulcerative colitis.