Global Livestock CRSP

Statistical Methods for the Kenya Feeding Intervention Trial

Robert Weiss, Donald Guthrie, Li-Jung Liang,
and Susan Alber
Child Nutrition Project

Research Brief 02-02-CNP May 2002

The Child Nutrition Project in Embu was a randomized controlled feeding intervention study to test if there was a causal relationship between the intake of animal source foods, both of meat and of milk and micronutrient status, cognitive function, behavior and physical activity, physical growth, and morbidity. To better understand the findings, this Brief explains the approach used for statistical analyses, modeling, and the results. The study is a longitudinal study over a 2 year period related to a clinical trial. The primary goal of data analyses has been to compare rates of change across children and feeding groups. A Hierarchical Random Effects Model was used to examine the changes in slopes of the intervention groups and one control group over time. The rate of change for each outcome is estimated for each child. The variability in slopes is assigned to:

Fixed Conditions: feeding type, age, sex

Random Conditions: classroom, school, and child components

This is a nested design with schools within feeding groups, children within schools, and longitudinal measures within children. SAS PROC Mixed Program is utilized.

Background

The purpose of this brief is to outline the statistical methods used to analyze and interpret the Kenya Feeding Intervention Trial (KenFIT). The field data collection methods led to complex data structures, and we have developed analysis methods to address these complexities. While it may appear that simple statistical methods could be applicable, these methods cannot represent the data adequately. We outline some shortcomings of simple methods below.

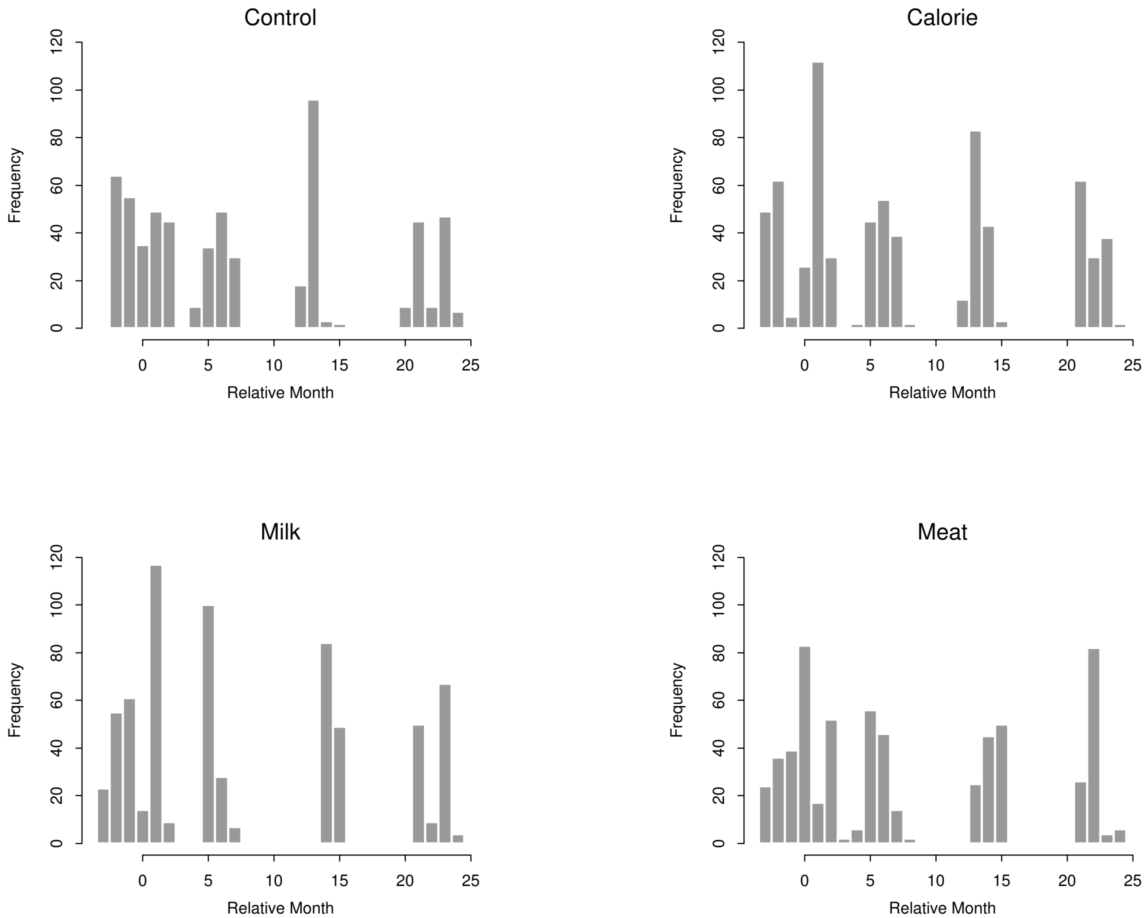
Data have been collected over a period of a few years. Once schools were randomized to one of four intervention groups (control, calorie, milk, and meat) data collection began with baseline measurements, then continued as the school snack intervention was initiated. Cognitive measures were planned for once per term, later every second term. Cognitive measurements, while recorded during a single term, were spread out over a period of months. Figure 1 shows a histogram of the dates that data was collected. Times before 0 are baseline measures taken before the intervention was initiated. Most children were measured on five occasions, but a number had fewer measures (see Table 1).

Statistical Approach

In addition to the basic outcome measures, the project collected a variety of concomitant data for use as statistical covariates in the interpretation of results. These covariates fall into two broad categories, subject-specific and time-dependent. Subject-specific covariates are those values that do not change during the study; examples include the child's gender, or family SES. Time-dependent covariates are those that are likely to change, e.g. morbidity and blood chemistry profiles. Certain outcome measures might well appear as covariates in analysis of other outcome measures.

The measured outcomes have been divided into six classes of responses – cognitive, playground and classroom activity, anthropometry, morbidity, food intake, and serum measures. Data on these have necessarily been gathered at different time intervals, and while we have attempted to maintain complete data for every child, that has not been entirely possible and some imputation will be needed. Many of the raw data values need substantial processing to convert them to more readily applied measures. For example, family SES is estimated from a very complicated formula including numbers of goats and tractors as well as number of languages spoken and education. We developed a covariate to assess child's morbidity. This involved defining approximately 20 different syndromes from our data, identifying them as mild or severe, and then checking whether each child at each morbidity assessment visit had no (level=0), mild (level=1) or severe morbidity (level=2). To create a general time invariant

Figure 1. Histogram of Cognitive Measures (Months)



Source: C: Kenya_Cognitive_cog3hist.ssc by LJL on Sat Apr 27 13:47:50 2002

morbidity covariate, we averaged this across all measurements for a given child.

Conventional repeated-measures analysis of variance (ANOVA) is frequently used to analyze longitudinal data. This method became popular because of its computational simplicity and because it provided a closed-form maximum likelihood approach to a specific model. There are, however, certain very restrictive assumptions (no missing data, equal covariances among all measurement intervals, equally spaced time points, lack of provision for time-dependent covariates, etc.) that make its use infeasible in the present context. While certain approximations have been used to overcome some of these shortcomings, during the past two decades computation methods and power have evolved, and statisticians have extended maximum likelihood methods to address more general data models. We have exploited these approaches in our analysis.

Methods

Our primary method has involved a Mixed General Linear Model (MGLM), a method that has received broad application since the exposition by Laird and Ware (1982). These models have also appeared in Littell et al. (1996) and Gibbons et al. (1993). The assumptions are simply described as follows. (1) Each child is assumed to follow a unique random linear (in time) development course (called a *slope*), but with variations at each measured time due to measurement error and random variation; (2) the slopes are assumed to be drawn from a population of slopes, with the population means depending on the child's feeding group membership; (3) a similar representation is applied to the child's general level (analogous to a regression *intercept*), and (4) there may be a random additive effect attributed to school-to-school variation.

These methods may be illustrated with application to the measurement of cognitive skills, but they are clearly

Table 1. Subjects in each feeding group that completed all five rounds of data collection, the number that were missing at least one measurement (round) and the total number of subjects in each feeding group.

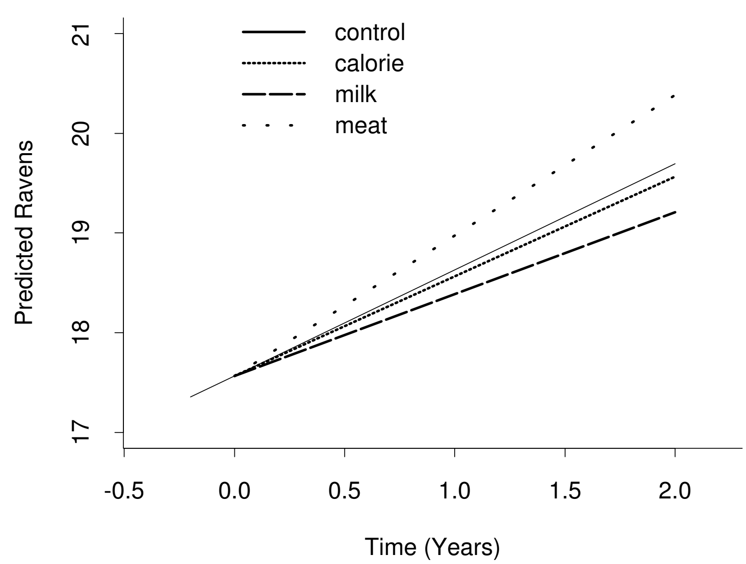
	Calorie	Control	Milk	Meat	Totals
Completed All Five Rounds	127	112	126	110	475
Missing at least One Round	21	17	18	24	80
Totals	**148**	**129**	**144**	**134**	**555**

applicable to the other measures as well. First, recall the experimental design. Twelve schools were assigned randomly to the four feeding groups (Meat, Dairy, Calorie, Control), three schools to each group. All eligible children in each school were given the feeding intervention for that school. Next, in measuring development we must allow for differences among children, we must admit that some children will learn to read faster than other children aside from the effect of feeding intervention. Statistically, this implies that there is natural variability in children's developmental courses. Thus, the study may be described as having a nested, or hierarchical (see Bryk and Raudenbush, 1992) design–-there are schools within feeding groups, children within schools, and longitudinal measurements within children. The primary goal of our data analyses has been to compare the rates of change across children and feeding groups.

Given all these assumptions, we use standard statistical software, SAS PROC MIXED (Littell et al., 1996) to compute estimates and standard errors for two types of parameters (1)–*fixed effects* including the mean intercepts and slopes for the four feeding groups, and (2) *random effects* including the intercepts and slopes of the individual children and school effects. Following these analyses, we confirm the validity of the models using standard statistical methods. We also repeat the analyses including covariates as needed for interpretation.

Figure 2 illustrates the results for one of the cognitive measures, the Raven's test (Whaley et al 2002). Detailed substantive interpretation appears elsewhere (see Whaley et al 2002). The four lines are labeled as representing the four feeding groups. At the onset, during the baseline period, the developmental course is the same for all groups since the feeding intervention has not been given (see for example Muthén et al 2000). After onset of the intervention, the mean slope trajectories diverge showing the differences among the estimated mean slopes. Maximum likelihood statistical tests may be used to assess the significance of the differences. In the complete data analysis, we have estimated how these conclusions might be affected by consideration of various subject-specific and time-dependent covariates.

Figure 2. Raven's Test



Practical Implications

Our statistical approach to data analysis is quite sophisticated and time consuming as befits a carefully collected complex data set. It takes roughly 3 months of time for a half time statistically sophisticated computer literate person before formal modeling can start. This includes time for data management, variable and problem definition, and for producing exploratory analyses.

At no stage of the analysis is the analysis automatic. It then takes approximately another three months for each analysis to be produced, and then several more months for the analysis to be written up. Each stage requires supervision by a PhD Statistician and interactions with senior project team members. During the writing stage, further final analyses must be performed, final definitions of the population under study are created, and publication quality graphs and tables are constructed.

References and Further Reading

Bryk A. and S. Raudenbush. 1992. *Hierarchical Linear Models*. Newbury Park, CA: Sage Publications.

Gibbons, R.D., D. Hedeker, I. Elkin, C. Waternaux, H.C. Kraemer, J.B. Greenhouse, M.T. Shea, S.D. Imber, S.M. Sotsky, and J.T. Watkins. 1993. "Some conceptual and statistical issues in analysis of longitudinal psychiatric data: application to the NIMH Treatment of Depression Collaborative Research Program data set." *Archives of General Psychiatry* 50:739-750.

Laird, N.M. and J.H. Ware. 1982. "Random-Effects Models for Longitudinal Data." *Biometrics*, 38:963-974.

Littell, R.C., G.A. Milliken, W.W. Stroup, and R.D. Wolfinger. 1996. *SAS System for Mixed Models*. Cary, NC: SAS Institute Inc.

Muthén, B., C.H. Brown, K. Masyn, B. Jo, S.T. Khoo, C.C. Yang, C.P. Wang, S. Kellam, J. Carlin, and J. Liao. 2000. "General growth mixture modeling for randomized preventive interventions." *Biostatistics*. In press.

Whaley, S. E., M. Sigman, C. Neumann, N. Bwibo, D. Guthrie, R.E. Weiss and S.A. Alber. 2002. "The Impact of Dietary Intervention on the Cognitive Development of Kenyan Schoolchildren." Submitted for Publication.

About the Authors: Robert Weiss, Ph.D. is an Associate Professor of Biostatistics at the University of California, Los Angeles (UCLA), School of Public Health with expertise in modeling of longitudinal data. He can be contacted at the University of California, Los Angeles, School of Public Health, Department of Biostatistics, Los Angeles, CA 90095. Telephone: (310) 206-9626. Fax: (310) 267-2113. Email: robweiss@ucla.edu.

Donald Guthrie, Ph.D. is an Emeritus Professor of Psychiatry and Biobehavioral Science in the UCLA School of Medicine. Li-Jung Liang and Susan Alber are doctoral students in the Department of Biostatistics in the UCLA School of Public Health.

The GL-CRSP Child Nutrition Project (CNP) was established in 1997 and is built on a decade of research conducted by the Nutrition CRSP (USAID) in the 1980s. The Child Nutrition Project research addresses food-based approaches to micronutrient deficiencies, particularly of children with respect to both the quantity and quality of food intake. The study is centered on a controlled intervention feeding trial of school children in Embu, Kenya. The project is directed by Dr. Charlotte Neumann and Professor Nimrod Bwibo as Principal Investigators and Suzanne Murphy, Marion Sigman, Shannon Whaley, and Lindsay Allen as Co-Investigators. Email contact for Dr. C. Neumann is: cneumann@ucla.edu.

The Global Livestock CRSP is comprised of multidisciplinary, collaborative projects focused on human nutrition, economic growth, environment and policy related to animal agriculture and linked by a global theme of risk in a changing environment. The program is active in East Africa, Central Asia and Latin America.

This publication was made possible through support provided in part by US Universities, host country institutions and the Office of Agriculture and Food Security, Global Bureau, United States Agency for International Development, under Grant No. PCE-G-00-98-00036-00 to University of California, Davis. The opinions expressed herein are those of the authors and do not necessarily reflect the views of USAID.

Design by Susan L. Johnson