Department of Nutrition and Health
Research Institute of Child Nutrition
Rheinische Friedrich-Wilhelms-Universität Bonn
Heinstück 11
44225 Dortmund
Germany
E-mail: buyken@fke-do.de

REFERENCES

Reply to AE Buyken et al

My colleagues and I thank Dr Buyken and her colleagues for their comments on the Promotion of Breastfeeding Intervention Trial (PROBIT). They claim that our study "addresses only the effect of prolonging the duration of exclusive breastfeeding." That is inaccurate, however, because the breastfeeding promotion intervention we randomly assigned (based on the WHO/UNICEF Baby-Friendly Hospital Initiative) was designed to increase both the duration of any breastfeeding and the exclusivity of breastfeeding in the first 6 mo of life. Both of those goals were achieved in the experimental group in our trial.

Buyken et al also comment that we “did not provide information on the mean number of weeks for which children in the intervention and control groups had been breastfed.” Given the left truncation and skewed distribution of breastfeeding duration, “mean number of weeks” is not a very useful metric. In fact, our earlier article, published in JAMA (1), describing breastfeeding and health outcomes in the first year of follow-up, provided detailed information on the proportion of infants breastfeeding at all weeks in the first year, as well as the proportion exclusively breastfeeding at both 3 and 6 mo.

These data were summarized in our recent AJCN article summarizing the anthropometric and blood pressure outcomes at the 6.5-y follow-up (2).

Buyken et al express their “particular concern” that “imprecise measurements may well have masked the likely modest effects of breastfeeding prolongation on the health outcomes assessed” at 6.5 y. Although random measurement errors and inter-polyclinic differences certainly did reduce the precision of the trial group differences for the triceps skinfold-thickness and blood pressure measurements, null effects with extremely narrow CIs were observed for body mass index (BMI; in kg/m²) and subcapsular skinfold thickness. In an individual-subject data meta-analysis of observational studies, Owen et al (3) were able to control for confounding by socioeconomic status, maternal BMI, and maternal smoking during pregnancy in 11 studies. After such control, they found no significant reduction in mean BMI (–0.01; 95% CI: –0.05, 0.03) between breastfed and formula-fed infants, a result that is entirely consistent with our results comparing 2 randomly assigned groups differing in breastfeeding duration and exclusivity. Although my colleagues and I agree that our results cannot address the potential benefits of any breastfeeding, compared with no breastfeeding, in the first weeks of life, the results of the systematic review of Owen et al, comparing any breastfeeding with formula feeding, cast serious doubt on any claim of a “programming” effect of early breastfeeding that confers long-term protection against obesity.

Finally, my colleagues and I urge researchers and other readers to be skeptical about all reports of conditional effects. Many biostatisticians and clinical trialists have cautioned against subgroup analysis, even in properly randomized controlled trials (4, 5). In the face of an overall null result, it is inevitable that post hoc stratification by some baseline factor (even a factor such as an astrological sign) will yield a statistically significant result. Unless such conditional (subgroup) effects are hypothesized a priori and are replicated in other studies, however, they are highly likely to reflect type I errors—ie, chance findings. Thus, the observation by Buyken et al from an observational (nonrandomized) study that breastfeeding was protective only in boys of overweight mothers should be regarded with skepticism unless and until such results are reported in other studies.

The author had no personal or financial conflict of interest.

Michael S Kramer

Departments of Pediatrics and of Epidemiology and Biostatistics
McGill University Faculty of Medicine
Montreal Children’s Hospital
2300 Tupper Street (Les Tournelles)
Montreal, PQ H3H 1P3
Canada
E-mail: michael.kramer@mcgill.ca

REFERENCES
Dear Sir:

We read with great interest the article by Yamada et al (1), entitled “Simplified nutritional screening tools for patients on maintenance hemodialysis.” In view of the high prevalence of malnutrition in hemodialysis patients and the important prognostic implications of nutritional management in such a population (2–4), the authors tested the accuracy of several nutritional screening tools (all those proposed between 1985 and 2005) to validate the potential application of at least one of them in routine evaluation. Of these, the geriatric nutritional risk index (GNRI) showed the highest accuracy according to the malnutrition-inflammation score (MIS), and a cutoff of <91.2 has been proposed (1). This article might have interesting implications in clinical practice; therefore, we believe that additional focus should be provided.

Reliable evaluation of nutritional status unfortunately still requires a multidisciplinary approach. In this respect, simple, feasible, and alternative assessment tools have been proposed to overcome limitations, such as time consumption, laborious measurements, costs, and the need for specific skills. In agreement with Yamada et al, we support the efforts of those seeking to validate such instruments. However, a common problem is the choice of reference standard to use, and in this case the MIS was used because of its better predictivity in hemodialysis patients (1).

With the exception of the initial study by Bouillanne et al (5), no validation study of GNRI as a screening tool has been conducted; its use has only been suggested, particularly when observing the significant association with a wide range of anthropometric and biochemical variables (6). In fact, the GNRI was introduced, and subsequently investigated, as a “nutrition-related” risk index and not as an index of malnutrition for elderly patients. This means that the GNRI can be used to classify patients according to a risk of complications in relation to pathologies often associated with malnutrition (5–10). This highlights clearly the prognostic meaning of this instrument. On the other hand, in math of nutrition, finding a tool that reliably describes both nutritional status and risk of complications is a key task (6). In this scenario, the study by Yamada et al represents the first attempt to validate GNRI as a screening instrument. Unfortunately, the authors tested its accuracy in an age-mixed population. Thus, its use, as well as that of the identified cutoff (GNRI < 91.2), should be suggested and applied with caution. Interestingly, patients scored as being at risk (MIS ≥ 6 and GNRI ≤ 91.2) were significantly older than those scored as normal (MIS ≤ 5 and GNRI > 91.2). Moreover, with particular regard to the cutoff proposed, some issues should be considered. We agree with Yamada et al when they discuss the usual lower threshold values of albumin (<35 g/L) and body mass index (<18.5 kg/m²) defined for hemodialysis patients. Alternatively, we also remark that the interpretation of these variables must take into consideration the normal biological changes seen with aging (11, 12). In fact, albumin possibly decreases slightly with age, ≈0.8 g/L per decade in persons older than 60 y (11). Thus, it is reasonable to argue that the weight given to albumin in GNRI’s formula has been set accordingly. Additionally, we suppose that threshold values for elderly hemodialysis patients are probably slightly lower than 35 g/L. Also, body weight decreases gradually with age in both sexes (≈0.6 kg/y in men and ≈0.5 kg/y in women). Moreover, because of the increased frailty of elderly patients and the general tendency to lose more lean body mass than adipose tissue with aging, the BMI cutoff has been set to a higher level (22–23 kg/m²) for the elderly than for the general population (<18.5 kg/m²) (12). Accordingly, we report 2 important considerations. First, the proposed cutoff (GNRI < 91.2) obviously fits to an all-age (middle + elderly) cohort of patients, and we hypothesize that in hemodialysis patients aged >65 y the threshold value might be lower. Second, it would be of interest to test the GNRI in a population in which the age effect seems to be avoided a priori when structuring the formula. We cannot exclude that this would result in improved accuracy and thus a more efficient index, at least for elderly hemodialysis patients.

Finally, we also want to strengthen the results produced by Yamada et al by additionally facing the main limitation highlighted in the discussion. We recognize that the lack of examination of GNRI on the basis of the outcomes did not allow a full validation of this instrument as a screening tool, particularly when it is considered the aim for which the index was proposed. In this respect, we report that further demonstrations of the prognostic value of the GNRI were provided (7–10) after the initial submission by Yamada et al. Particularly, significant associations have been shown with mortality, infections, bedsores, and muscle dysfunction by handgrip strength evaluation, which in turn have been shown to be independently correlated with all-cause and cardiovascular disease mortality in a similar series of patients (4). Unfortunately, most of our studies have been performed in institutionalized patients; only one study was conducted in acutely hospitalized elderly patients. The validation of screening tools is usually done in the general population, but it is nevertheless important that the validation of these tools also be conducted in select populations. Preliminary data on the GNRI appear promising but setting- and population-specific studies and cross-validations with different reference standards are clearly suggested to propose the routine use in clinical settings. Finally, nutrition intervention studies in those screened as at risk would probably allow full confirmation of the usefulness of the GNRI.

The authors certify that there were no affiliations with or involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed herein.

Emanuele Cereda
International Center for the Assessment of Nutritional Status
University of Milan
via Botticelli 21
21033 Milan
Italy

Carlo Pedrolli
Dietetic and Clinical Nutrition Unit
Trento Hospital
Trento
Italy
E-mail: carlo.pedrolli@apss.tn.it

References