Letters to the Editor

Correspondence re: A. M. Hutchins *et al.*, Flaxseed Influences Urinary Lignan Excretion in a Dose-dependent Manner in Post-menopausal Women. Cancer Epidemiol. Biomark. Prev., *9:* 1113–1118, 2000

Letter

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In their article, Hutchins *et al.* (1) claim that, referring to Table 2, there were no significant differences in total, energy or carbohydrate intake between the control and the 10-g flaxseed feeding period. This is based on the ANOVA, which they used to compare the means.

The difficulty with the ANOVA is that it assumes that the variances of the normal distributions of the means being compared are equal, though unknown. Because there is no reason why unknown variances should be homogeneous, this is a source of error with the ANOVA. The SD are not equal, giving no reason why the variances should be expected to be equal. Thus, the ANOVA is not a generally valid method of comparing normal means with unknown variances. This has already been pointed out (2).

The problem of comparing the means of normal populations at exact significance levels (in the frequent sense) when their variances are unknown is the well-known Behrens-Fisher problem, and this has been solved by Tsakok (3). Using the software General Statistical Package, which implements the Tsakok technique, it is found that, between the control and the 10-g flaxseed feeding periods, there are significant differences in the intakes of energy (kcal) and carbohydrate (CHO, g) at 0.02 significance level (2 d.p.).

Another cause for suspicion arises from the use of a logarithmic scale to correct for non-normality in urinary lignan excretion analyses (1). No justification is given, and it is not generally true that a logarithmic scale can correct for non-normality. It is known that a multiplicative model can be transformed to a linear model through a logarithmic transformation, but that does not necessarily make it normally distributed. The original data should be made available for a correct analysis, using the article by Tsakok (4), which enable exact UMPU tests to be constructed to investigate non-normal data.

Thus, the conclusions of Hutchins *et al.* (1) need to be reassessed.

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The Tsakok techniques are reprinted (5) with additional results.

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Reply

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We appreciate the comments by A. D. Tsakok on our paper in *Cancer Epidemiology, Biomarkers & Prevention*, 2000, *9:* 1113–1118. This study used a crossover design, and so the ANOVA used repeated measures, not a two-sample comparison as in the Behrens-Fisher problem. Although the variances were unknown, they were quite close in size, and the ANOVA is known to be robust to minor differences in group SD. To answer the second question, several variables with skewed distributions were analyzed on the logarithmic scale, where the sample distributions were closer to the normal curve.

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Correspondence re: A. H. Wu *et al.*, A Meta-Analysis of Soyfoods and Risk of Stomach Cancer: The Problem of Potential Confounders. Cancer Epidemiol. Biomark. Prev., *9:* 1051–1058, 2000

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We read with interest the article by Wu *et al.* (1) on a meta-analysis of 14 studies examining the link between soyfoods and risk of stomach cancer. Their analysis yielded an excess risk associated with high intake of fermented soyfoods and a reduced risk with high intake of nonfermented soyfoods. The authors postulated, however, that these observations might be confounded by other dietary variables known to be related to stomach cancer risk, particularly salt intake with fermented soyfoods, and fresh fruits and vegetables with nonfermented soyfoods. To evaluate this issue, we conducted additional analyses on the effects of soyfoods, adjusting for fresh fruits and vegetables, salted foods, and salt preference in our population-based study of stomach cancer conducted in Shanghai, China (2), the largest case-control study included in the meta-analysis.

In our study, 1124 patients that were newly diagnosed with stomach cancer (aged 20–69 years), and 1451 randomly selected population controls were interviewed in person with regard to dietary practices and other exposures. After adjusting for age, income, education, and (men only) smoking and alcohol drinking, we found that the intake of fermented bean curd was not related to risk among men (*P* for trend, 0.58) but was positively associated with risk among women (*P* for trend, 0.008). As shown in Table 1, further adjustment for intake of salted foods and salt preference tended to reduce the OR[2] slightly in both sexes, with the trend no longer being significant among women (*P* for trend, 0.18). In contrast, intake of nonfermented soyfoods was inversely related to risk among men (*P* for trend, 0.0001) but not among women (*P* for trend 0.51). Further adjustment for intake of fresh fruits and vegetables did not substantially alter the associations in either men (*P* for trend, 0.02) or women (*P* for trend, 0.83). In addition, only a weak correlation was found in our study controls between intake of fermented bean curd and salted foods (Pearson correlation coefficient, r, 0.28 for men and 0.32 for women), as well as between intake of nonfermented soyfoods and fruits (*r*, 0.11 for men and 0.01 for women) or vegetables (*r*, 0.29 for men and 0.25 for women).

Although the relationships in our study between soyfoods and gastric cancer varied by gender, there was little evidence that the risks were confounded by salt intake or by fruits and vegetables. Because gastric cancer risk was generally increased with high intake of fermented soyfoods and reduced with high intake of nonfermented soyfoods in the studies reviewed by Wu *et al.* (1), it would seem important to further explore the potential effects of soyfood components in gastric carcinogenesis.

References

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[2] The abbreviation used is OR, odds ratio.

Table 1 Adjusted ORs[a] and 95% confidence intervals (CIs) for stomach cancer in relation to fermented and nonfermented soyfoods, Shanghai, China (1988–1989)

Soyfood intake[b]	Men			Women		
	Controls	Cases	OR (95% CI)	Controls	Cases	OR (95% CI)
Fermented bean curd (frequency/month)						
0	270	275	1.00	226	113	1.00
≤2	232	237	1.01 (0.75–1.36)	197	118	1.36 (0.90–2.05)
2.1–4.9	162	168	0.93 (0.66–1.31)	113	72	1.19 (0.79–1.80)
5+	155	138	0.76 (0.53–1.10)	96	76	1.45 (0.91–2.32)
P for trend			0.17			0.18
Nonfermented soyfoods[c] (frequency/month)						
<6	142	183	1.00	160	96	1.00
6.0–9.9	242	288	0.94 (0.70–1.26)	191	122	1.13 (0.79–1.62)
10.0–19.9	229	188	0.74 (0.54–1.01)	128	86	1.29 (0.87–1.92)
20.0+	206	159	0.72 (0.52–1.00)	153	75	1.00 (0.67–1.49)
P for trend			0.02			0.83

[a] ORs adjusted for age, income, education, and (men only) cigarette smoking and alcohol drinking, with additional adjustment for salted foods and salt preference (fermented soyfoods) and fresh fruits and vegetables (nonfermented soyfoods).
[b] The cut points for intake levels were based on approximate distributions among all of the controls.
[c] Nonfermented soyfoods include soybean curd, soybean milk, and other soybean products.

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