Dear Sir:

The meta-analysis of Althuis et al (1) examining the effect of supplemental chromium on insulin, glucose, and glycated hemoglobin in controlled studies may be viewed as cogent evidence that functionally significant dietary chromium deficiency is uncommon in the United States. Most of the cited studies used doses of ≥ 200 μg Cr/d, which is roughly 7 times the average chromium intake of healthy Americans; one would certainly think that such a dose, consumed over several months, would be sufficient to correct a baseline dietary deficiency, and yet the results of most chromium supplementation studies have been paltry, at best.

However, an overview of the data is quite consistent with the possibility that high doses of well-assimilated organic forms of chromium may indeed have clinical utility in selected populations. In a study by Anderson et al (2) in which Chinese subjects with diabetes were supplemented with ≤ 1000 μg Cr (as chromium picolinate)/d—the largest controlled study yet done with supplemental chromium, but omitted from the meta-analysis because it introduced heterogeneity into the data—glycated hemoglobin fell significantly, by an average of 30%, in those receiving the 1000-μg dose, and the reductions in fasting and postprandial glucose in that group were nearly as large. The fact that the response in the group receiving the 200-μg dose for 4 mo was equivocal, with no significant improvement in either fasting or postprandial glucose relative to the control subjects, strongly suggests that correction of a baseline dietary chromium deficiency was not responsible for the marked improvement in the 1000-μg dose group, and indeed there is no evidence that chromium nutrition is poorer in China than in the United States. (Whether some other reason—e.g., genetics, body size, or diet macronutrient profile—might predispose Chinese diabetics to be more responsive to chromium than are their American counterparts remains to be seen.)

Using the same dose and form of chromium in middle-aged overweight US subjects who had first-degree relatives with diabetes, Cefalu et al (3) reported a significant increase of nearly 50% in insulin sensitivity, quantified by the minimal model method, during 4–8 mo of supplementation. Concurrent reductions of 20–25% in fasting and postprandial insulin were not statistically significant, possibly because of the small number of subjects (n = 15). Two other, somewhat shorter, controlled studies of older American subjects failed to observe an effect on insulin metabolism of 1000 μg Cr as chromium picolinate (4, 5).

The available data are thus consistent with the possibility that supranutritional doses of well-assimilated forms of chromium may indeed have useful efficacy in at least some target populations. This view is buttressed by several recent rat studies in which chromium picolinate had substantial metabolic effects (6–8); the control rats in these studies were fed normal (not chromium-depleted) diets, so it cannot be maintained that the observed responses reflected correction of dietary deficiency. It might be added that the chromium doses used in these studies, if corrected for relative body surface area, would be larger than the largest dose used in the Chinese clinical study. A supraphysiologic concentration of chromium picolinate (1 μmol/L) likewise can influence cellular function in vitro (9, 10).

The efficacy of supplemental chromium may prove to be analogous to that of vitamin E. In subjects who are not overtly vitamin E deficient, a nutritional dose of this vitamin will have no discernible effect on the oxidizability of LDL, whereas a megadose (eg, 800 IU) may have a substantial effect. The all-too-common presumption that nutrients can do nothing more than correct deficiency states is clearly wrong. The rodent and tissue culture studies cited above suggest that the physiologic effect of chromium is not always maximized at ordinary tissue concentrations; because we still do not know how chromium functions at the level of molecular biology, there are no firm grounds for assuming otherwise. In light of the fact that oral trivalent chromium has been proven to be safe in animals at any dose tested, future clinical studies with chromium should evaluate a range of daily doses of ≥ 1 mg, while attempting to identify those groups most apt to respond to high-dose chromium.

Note that my remarks pertain to dietary chromium deficiency. It is an open possibility that tissue deficiencies of chromium, attributable to metabolic perturbations that disrupt chromium transport, may be a contributory factor in various disorders. However, there is no reason to assume that ordinary dietary intakes of chromium could correct such tissue deficiencies.

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REFERENCES
Dear Sir:

The article by Althuis et al (1) in a recent issue of the Journal appears to be an imbalanced review of the publications to date regarding the potential benefit of chromium picolinate in persons with type 2 diabetes. Among the current published works, there are at least 9 noteworthy reports of clinical trials that show the relative efficacy of this mineral, nor should we dismiss consumer sup-

Clinicians cannot dismiss the current body of work that indicates chromium picolinate is indicated. However, we as scientists and face area is indicated.

In any event, with the relative safety and inexpensiveness of chromium picolinate, there seems to be no reason for it not to be used in people who have poor blood sugar control or insulin resistance syndrome (11, 12). The benefit-to-risk ratio favors benefit. Continued research on the positive effects of chromium picolinate on biomarkers of blood glucose or on insulin regulation in subjects with type 2 diabetes or in persons with induced diabetes. The major fault in the conclusions of Althuis et al is that no studies of persons with diabetes were included in their final analysis.

In reading the 9 reports, it is easy to see that 1349 total subjects were studied over the past 10 y. With such a large number of subjects having participated in single- and double-blind trials, the findings are consistent: chromium picolinate has a positive effect on fasting insulin values and on hemoglobin A1C. The data also indicate that, when used with standard treatments, chromium picolinate improves clinical results (eg, those for biguanides, sulfonylureas, or metformin alone) (10). Additional benefits have been found with chromium picolinate supplementation for coronary disease risk profiles [ie, lipids and lipoprotein(a)] that are important in the diabetic and nondiabetic communities. It is agreed that the dose for clinical benefit has not been universal, ranging from 200 to 1000 µg, but this only shows that “one size does not fit all,” and thus a dose that is dependent on body surface area is indicated.

In any event, with the relative safety and inexpensiveness of chromium picolinate, there seems to be no reason for it not to be used in people who have poor blood sugar control or insulin resistance syndrome (11, 12). The benefit-to-risk ratio favors benefit. Continued research on the positive effects of chromium picolinate on biomarkers of blood glucose or on insulin regulation in subjects with type 2 diabetes is indicated. However, we as scientists and clinicians cannot dismiss the current body of work that indicates the efficacy of this mineral, nor should we dismiss consumer support for this product as being without merit.

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REFERENCES

Reply to DS Kalman, MF McCarty, and V Juturu and JR Komorowski

Dear Sir:

We thank the authors of the letters for their comments on our article. Our review and meta-analysis summarized randomized clinical trials (RCTs) designed to assess glucose and insulin responses to dietary chromium supplements (1). We limited our review to RCTs to avoid the potential for bias inherent in nonrandomized studies. We attempted to include every RCT in the literature.

The letters by Kalman and by Juturu and Komorowski cite several studies they say our review omitted (2–11). Our review in fact included 4 of these studies (2–5); the other 6 studies they mentioned (6–11) were not RCTs and therefore were not eligible for inclusion. Specifically, 1 of the 4 RCTs cited as being omitted was both discussed in the review and combined analytically in the meta-analysis (3). In addition, we discussed in detail the findings from the other 3 RCTs although they were not included in the meta-analysis (2, 4, 5). One of these RCTs (4) was excluded from the meta-analysis because the study population—women with gestational diabetes—was not a focus of our review; one of the others was excluded simply because data presented in the original report were insufficient for abstraction, and updated data were not available from the investigators (5).