intake or consumption of foods with higher sodium content. That we observed only a small and nonsignificant rise in 24-h urinary sodium excretion in the United States between 1957 and 2003 (3) despite the increase in energy intake could be due to a modest decrease in the sodium content of food over this period that was sufficient to compensate for the increase in energy intake. It is also possible that the available data were not sufficient to detect a modest increase in sodium excretion. Our data were not compatible with a substantial reduction in sodium intake.

We did not control for changes in energy intake in our analysis because this could have been one of the factors contributing to changes in sodium intake, but had this variable been available it could have provided additional insight into the reasons for change, or lack of change, in sodium excretion. Because obesity is not a direct cause of sodium excretion, but rather a consequence of energy imbalance, adjusting for it in a multivariate model could have masked a true rise in sodium intake and led to a misleading conclusion.

We thank Strazzullo et al for pointing out the successes of Portugal and Finland in reducing population sodium intake, which refute the notion that important reductions are not possible. Similar reductions in the United States are achievable with strong, concerted efforts.

There were no conflicts of interest to report.

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doi: 10.3945/ajcn.110.009597.

Will vitamin D reduce insulin resistance? Still a long way to go

Dear Sir:

We read with interest the article by Alvarez et al (1), which aimed to investigate the relations of circulating 25-hydroxyvitamin D [25(OH)D] and parathyroid hormone (PTH) concentrations with direct measurements of insulin sensitivity, after robust measures of body composition and fat distribution were accounted for. We would like to express our opinion and a different interpretation of the data provided by authors, with the hope that other points for discussion are brought up.

In a very recent publication, Alvarez et al (2) provided novel findings suggesting that dietary vitamin D is independently associated with insulin sensitivity in African Americans (AAs) but not in European Americans (EAs). Interestingly, the 2 groups were identical for hepatic insulin sensitivity [homeostatic model assessment (HOMA)], whereas S_i, a method for measuring insulin sensitivity that encompasses both hepatic and peripheral tissues, was lower in AAs, therefore suggesting a pivotal role for insulin resistance in skeletal muscle [especially in the presence of identical body mass index (BMI)] in correlation with 25(OH)D. In the present article, the authors suggest that 25(OH)D and PTH concentrations are independently associated with whole-body insulin sensitivity and suggest that these variables may influence insulin sensitivity through independent mechanisms. In fact, multiple linear regression analysis indicated that 25(OH)D and PTH concentrations were independently related to S_i after adjustment for age, race, and intraabdominal adipose tissue. It is well known, however, that adipose tissue is the natural reservoir for lipo-soluble 25(OH)D. The higher BMI and the higher subcutaneous fat content found in AAs (although the latter difference was not statistically significant) could therefore explain the differences in 25(OH)D concentration, as well as in HOMA index, found by the authors.

We examined (3) the effect of 25(OH)D on insulin sensitivity in obese subjects and found a linear correlation between them, which is apparently in agreement with Alvarez et al. Obesity, however, is not invariably associated with insulin resistance, because normal insulin sensitivity can be present in some obese subjects. If 25(OH)D concentration influences insulin sensitivity independently of obesity, it should be found to be low in insulin-resistant obese subjects and high in insulin-sensitive obesity. We divided our obese population into 2 subgroups, according to their insulin sensitivity (low and high). The 2 groups were similar in BMI, age, and sex but did not show any difference in 25(OH)D concentration, thus confirming the hypothesis that 25(OH)D concentrations are not influenced by the degree of insulin resistance but mainly by the adipose tissue's reservoir, at least in our EA participants. Unfortunately, in the present-studied population (1) but not in the previous one (2), AAs had higher BMI (and HOMA) and the actual role of these variables in determining hypovitaminosis D was not ruled out.

In conclusion, we are certain that 25(OH)D concentration mainly reflects body fat mass, either subcutaneous or visceral; the reduction of fat mass, rather than vitamin D supplementation (4, 5), is the best route for the prevention and treatment of insulin resistance and diabetes.

None of the authors declared a conflict of interest.

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doi: 10.3945/ajcn.110.009068.

Reply to G Muscogiuri et al

Dear Sir:

We sincerely thank Muscogiuri et al for their insight and valuable comments regarding our study published in the Journal that investigated the independent relations of 25-hydroxyvitamin D [25(OH)D] and parathyroid hormone with insulin sensitivity (1).

In contrast to our finding that 25(OH)D was related to whole-body insulin sensitivity, independent of dual-energy X-ray absorptiometry (DXA)–derived percentage body fat and computed tomography (CT)–derived intraabdominal adipose tissue (IAAT), Muscogiuri et al refer to data suggesting that the relation between 25(OH)D and insulin sensitivity is mediated by body mass index (BMI) (2). There are differences, however, between the 2 studies that may be driving the conflicting results, including the study populations and the methodology used. Our study population consisted of African American (AA) and European American (EA) pre- and postmenopausal women (1). The population studied by Muscogiuri et al (2) consisted of EA men and women. In addition to differences in sex and ethnic group composition, the population of Muscogiuri et al was generally obese (2), whereas ours was generally overweight (1) [mean (±SD) BMI (in kg/m^2): 30.1 ± 5.4 compared with 26.4 ± 4.7]. It is entirely possible that, in obese conditions, influences of adiposity-induced factors, such as elevated free fatty acids and inflammation, take precedence over influences of low 25(OH)D on insulin sensitivity. Muscogiuri et al evaluated insulin sensitivity by using a hyperinsulinemic euglycemic clamp method (2), whereas we used an intravenous glucose tolerance test (IVGTT) and minimal modeling (1). Although the hyperinsulinemic euglycemic clamp is considered the gold-standard technique, one might argue that the IVGTT provides a more dynamic, physiologic measure of insulin sensitivity than do clamp-derived measures (3). Furthermore, Muscogiuri et al used BMI as a surrogate for adiposity, whereas our use of DXA and CT measurements are more direct indicators of general and localized adiposity.

Muscogiuri et al also suggest that the higher BMI and higher subcutaneous adipose tissue in our AA participants could explain ethnic differences in 25(OH)D concentrations and in the homeostatic model assessment of insulin resistance (HOMA-IR). Unpublished analyses of our data reveal that 25(OH)D remains significantly lower ($P < 0.001$) and HOMA-IR remains significantly higher ($P = 0.01$) in AA compared with EA individuals despite statistical adjustment for BMI, percentage body fat, IAAT, and subcutaneous abdominal adipose tissue. We should also note that 25(OH)D was not significantly associated with any measure of adiposity in our study population (**Table 1**); thus, it is unlikely that adiposity was a confounder in this study.

TABLE 1
Partial correlations of 25-hydroxyvitamin D [25(OH)D] and parathyroid hormone with adiposity measures, adjusted for ethnicity[1]

Adiposity measure	25(OH)D[2]
Weight	−0.09 (0.53)
BMI	−0.17 (0.26)
Percentage fat	−0.16 (0.28)
Total fat	−0.16 (0.27)
Waist circumference	−0.11 (0.49)
IAAT[2]	−0.05 (0.73)
SAAT	−0.06 (0.70)

[1] All values are *r* correlations; *P* values in parentheses. $n = 25$ African American and 25 European American women. IAAT, intraabdominal adipose tissue; SAAT, subcutaneous abdominal adipose tissue.
[2] Log_{10}-transformed for analyses.

Given the differences in the populations and methodologies used across the vitamin D and insulin sensitivity literature (1, 2, 4), it is difficult to establish the true relation between 25(OH)D and insulin sensitivity by using cross-sectional studies. Inconsistency in the effects of vitamin D supplementation on insulin sensitivity, either positive (5, 6) or null (7, 8), further the inability establish clear relations. There is much to be investigated regarding the role of vitamin D in the regulation of insulin sensitivity, and the confounding effects of adiposity highlighted by Muscogiuri et al should certainly be teased out.

The authors had no conflicts of interest to disclose.

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