rate as predictors of mortality in type 1 diabetes. *Ann Epidemiol* 12:331–337, 2002
3. Orchard TJ, Olson JC, Erbey JR, Williams K, Forrest KY, Smithline Kinder L, Ellis D, Becker DJ: Insulin resistance-related factors, but not glycemia, predict coronary artery disease in type 1 diabetes: 10-year follow-up data from the Pittsburgh Epidemiology of Diabetes Complications Study. *Diabetes Care* 26:1374–1379, 2003
4. Dabelea D, Kinney G, Snell-Bergeon JK, Hokanson JE, Eckel RH, Ehrlich J, Garg S, Hamman RF, Rewers M: Effect of type 1 diabetes on the gender difference in coronary artery calcification: a role for insulin resistance? The Coronary Artery Calcification in Type 1 Diabetes (CACTI) Study. *Diabetes* 52:2833–2839,2003
5. Orchard TJ, Chang Y, Ferrell R, Petro N, Ellis D: Nephropathy in type 1 diabetes: a manifestation of insulin resistance and multiple genetic susceptibilities? Further evidence from the Pittsburgh Epidemiology of Diabetes Complication Study. *Kidney Int* 62:963–970, 2002
6. Williams KV, Erbey JR, Becker D, Arslanian S, Orchard TJ: Can clinical factors estimate insulin resistance in type 1 diabetes? *Diabetes* 49:626–632, 2000
7. Carey DG, Cowin GJ, Galloway GJ, Jones NP, Richard JC, Biswas N, Doddrell DM: Effect of rosiglitazone on insulin sensitivity and body composition in type 2 diabetic patients. *Obes Res* 10:1008–1015, 2002 [erratum in *Obes Res* 10:following TOC, 2002]

The Effect of Rosiglitazone on Overweight Subjects With Type 1 Diabetes

Response to Orchard

Our report (1) on the effect of rosiglitazone on overweight subjects with type 1 diabetes showed that rosiglitazone-treated subjects with a BMI $\geq$30 kg/m^2 experienced significantly greater improvements in HbA_{1c} (A1C) levels than those with a BMI $<$30 kg/m^2 (-1.4 vs. -0.4%, $P = 0.032$). In addition, regression analysis showed that BMI, total daily insulin dose, and total, LDL, and HDL cholesterol levels were predictors of improvement in A1C (1). In his letter (2), Orchard raises the intriguing possibility that an estimate of insulin sensitivity (eGDR), which is based on waist-to-hip ratio, hypertension status, and A1C (3), could be an identifier of type 1 diabetic individuals who might benefit from thiazolidinedione therapy. We calculated eGDR in our subjects and found that in the rosiglitazone-treated subjects, eGDR was significantly related to change in A1C level ($P = 0.003$, $r = 0.575$). No such relationship was found in the placebo-treated subjects. However, a regression analysis incorporating BMI; total daily insulin dose; total, LDL, and HDL cholesterol; and eGDR showed that eGDR was not a significant predictor of improvement in A1C ($P = 0.155$) in the rosiglitazone-treated subjects.

Waist-to-hip ratios were the same in both the rosiglitazone and placebo groups at baseline (0.91 ± 0.06) and at the end of the study (0.93 ± 0.06), which is consistent with the observation that weight gain with thiazolidinediones is mainly peripheral rather than central. Orchard (2) noted that blood pressure but not lipids improved in our rosiglitazone-treated type 1 diabetic subjects. This result was somewhat surprising since we had observed the opposite results in our studies of troglitazone in combination with insulin in type 2 diabetic subjects (4,5). It is important to keep in mind that these studies were not designed to evaluate the effect of thiazolidinedione therapy on blood pressure; all of our subjects were treated with antihypertensive medications in an effort to normalize blood pressure levels. In addition, baseline blood pressure and history of hypertension were not related to change in A1C and were not significant predictors of improvement in A1C level in our rosiglitazone-treated type 1 diabetic subjects. Triglyceride levels also were not related to change in A1C. On the other hand, markers of insulin resistance in the type 1 diabetic subjects, such as BMI, total daily insulin dose, and cholesterol levels, were related to improvement in glycemic control when rosiglitazone treatment was used. Therefore, we do not believe that we can draw any firm conclusions from our data about the relative linkage of blood pressure versus lipid levels to insulin resistance.

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References
1. Strowig SM, Raskin P: The effect of rosiglitazone on overweight subjects with type 1 diabetes. *Diabetes Care* 28:1562–1567, 2005
2. Orchard TJ: The effect of rosiglitazone on overweight subjects with type 1 diabetes (Letter). *Diabetes Care* 29:746–747, 2006
3. Williams KV, Erbey JR, Becker D, Arslanian S, Orchard TJ: Can clinical factors estimate insulin resistance in type 1 diabetes? *Diabetes* 49:626–632, 2000
4. Strowig SM, Avilés-Santa ML, Raskin P: Comparison of insulin monotherapy and combination therapy with insulin and metformin or insulin and troglitazone in type 2 diabetes. *Diabetes Care* 25:1691–1698, 2002
5. Strowig SM, Avilés-Santa ML, Raskin P: Improved glycemic control without weight gain using triple therapy in type 2 diabetes. *Diabetes Care* 27:1577–1583, 2004

Comparison of the Effects of Vitamins and/or Mineral Supplementation on Glomerular and Tubular Dysfunction in Type 2 Diabetes

Response to Farvid et al.

Recently, Farvid et al. (1) reported on the effects of dietary supplementation of physiologic doses of vitamins and/or minerals on urinary albumin excretion rate (UAER)/urinary protein excretion rate (UPER), blood pressure, and lipid profile. Although not mentioned in the article, data on blood pressure and lipids have previously been reported elsewhere (2,3).

The main finding is a significant reduction in UAER of ~66% in the group receiving both minerals and vitamins. Although Farvid et al. claimed this to be the primary end point, it was only measured once as albumin-to-creatinine ratio in morning spot urine at baseline and after 3 months. Repeated measurements (usually at least three) are always required to obtain valid data and correct diagnosis of persistent micro- and macroalbuminuria due to a coefficient of variation of 30–50%. There is a marked discrepancy be-

tween the level of UAER (30 mg/g creatinine), suggesting microalbuminuria, and the level of UPER (1–2 g/g creatinine; equal to overt nephropathy). An inconsistent effect of mineral and vitamin supplementation on UAER and UPER was reported, suggesting a chance finding.

Furthermore, mean diastolic blood pressure in the minerals and vitamins group before treatment dropped from 94 (Table 1 in Farvid et al.) to 83 (Table 6) mmHg after exclusion of 2 of the 19 patients; this indicates an error in one of the tables, as it would only be possible if the two excluded patients had a mean diastolic blood pressure of 187 mmHg. The technique for blood pressure measurement was not stated. The conditions for the power calculation were not stated, but according to their previous reports, it was powered to detect changes in HDL cholesterol (2) and blood pressure (3).

It is claimed that the UAER findings are in accordance with the literature (refs. 14–16 in Farvid et al.). However, pharmacological doses of vitamins C and E had no or minimal effect (19%) on UAER (refs. 14,15). In contrast, a 50% reduction in UAER was reported in nine patients, applying pharmacological doses of vitamin C (ref. 16).

In conclusion, the study was not powered for realistic changes in UAER/UPER, insufficient methods for valid characterization of UAER/UPER were applied, and the effect of minerals and vitamins on UAER/UPER was not consistent, clearly suggesting a type 1 error or chance finding.

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References

1. Farvid MS, Jalali M, Siassi F, Hosseini M: Comparison of the effects of vitamins and/or mineral supplementation on glomerular and tubular dysfunction in type 2 diabetes. *Diabetes Care* 28:2458–2464, 2005
2. Farvid MS, Siassi F, Jalali M, Hosseini M, Saadat N: The impact of vitamin and/or mineral supplementation on lipid profiles in type 2 diabetes. *Diabetes Res Clin Pract* 65:21–28, 2004
3. Farvid MS, Jalali M, Siassi F, Saadat N, Hosseini M: The impact of vitamins and/or mineral supplementation on blood pressure in type 2 diabetes. *J Am Coll Nutr* 23:272–279, 2004

Comparison of the Effects of Vitamins and/or Mineral Supplementation on Glomerular and Tubular Dysfunction in Type 2 Diabetes

Response to Rossing et al.

We thank Rossing et al. (1) for their interest in our article (2) and agree that one measurement of albumin-to-creatinine ratio in morning spot urine at baseline and after 3 months is a potential limitation to our study. This limitation is described in detail in our discussion section. Although we did not obtain multiple spot urine samples or a 24-h urine collection to assess microalbuminuria, the random microalbumin-to-creatinine ratio has high reported sensitivity and specificity compared with 24-h urine microalbumin testing (3). The ratio of protein or albumin to creatinine in an untimed urine specimen has replaced protein excretion in a 24-h collection as the preferred method for measuring proteinuria. Using a ratio corrects for variations in urinary protein concentration due to hydration and is far more convenient than timed urine collections. The ratio of protein or albumin to creatinine in an untimed urine sample is an accurate estimate of the protein or albumin excretion rate (4). Also, it should be noted that after 3 months of supplementation, significant decreases in our vitamins group and minerals and vitamins group for albumin-to-creatinine ratio were observed from baseline and when compared with the placebo group. There were no significant changes in the other two groups. If the results were related to chance, microalbuminuria would have decreased in the other two groups.

We acknowledge Rossing et al. for drawing our attention to an error in Table 1. The diastolic blood pressure in the minerals and vitamins group should be amended to 84 ± 11 mmHg. Blood pressure was recorded semiautomatically using a Dinamap recorder (Critilzon, Tampa, FL). Before the study, the calculated sample size was 18 patients in each group, having 80% power to detect the postulated differences in HDL cholesterol, blood pressure, and microalbuminuria with an α error of 5%. But, after the supplementation, the calculated power for albumin-to-creatinine ratio was 0.7.

In conclusion, we do not agree with the concerns of Rossing et al. that our study was inadequately powered for detecting realistic changes in urinary albumin/protein excretion rate, that insufficient methods for valid characterization of urinary albumin/protein excretion rate were applied, and that the effect of minerals and vitamins on urinary albumin/protein excretion rate was inconsistent, which would suggest a type 1 error or a chance finding. In view of this, we believe our conclusions are valid.

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References

1. Rossing P, Cooper ME, Parving H-H: Comparison of the effects of vitamins and/or mineral supplementation on glomerular and tubular dysfunction in type 2 diabetes (Letter). *Diabetes Care* 29:747–748, 2006
2. Farvid MS, Jalali M, Siassi F, Hosseini M: Comparison of the effects of vitamins and/or mineral supplementation on glomerular and tubular dysfunction in type 2 diabetes. *Diabetes Care* 28:2458–2464, 2005
3. Zelmanovitz T, Gross JL, Oliveira JR, Paggi A, Tatsch M, Azevedo MJ: The receiver operating characteristics curve in