

SUPPLEMENTARY DATA

Supplementary Table 1. Baseline Characteristics* of the two treatment groups

	Placebo (N = 53)	Vitamin D (N = 56)
Age (years)	52.5 ±7.0	52.3 ±8.0
Sex (females)	71%	64%
Latino	83%	91%
BMI (weight/[height] ²)	32.9 ±4.3	32.1 ±4.7
FPG (mg/dL)	97.5 ± 9.4	98.7 ±8.7
2-hour glucose (mg/dL)	162 ±18	158 ± 22
HbA1c (%)	6.1 ± 0.4	6.1 ± 0.3
serum 25-OHD (ng/mL)	22.0 ± 4.8	22.0 ± 4.5

*Means ± SD

Supplementary Table 2. Association of Vitamin D Levels with Insulin Sensitivity and Insulin Secretion

	Positive	Negative
Insulin Sensitivity	References 1-11, 12*, 13 [†] ,14 [‡] , 15 [§]	References 14 [‡] , 15 [§] , 16
Insulin Secretion	References 9, 11	References 3, 5, 6, 15

*Negative when adjusted for adiposity; †Negative when adjusted for physical activity; ‡Positive in obese African-American youths but negative when adjusted for adiposity, negative in obese White youths; §Positive in Mexican-Americans and Whites but not in African-Americans; ||Negative when adjusted for BMI

Supplementary Table 3. Effects of Vitamin D Supplementation on Insulin Secretion and Insulin Sensitivity

Reference	Population	Vitamin D Dose & Duration	Outcomes	25-OHD Level (ng/mL)	Results
1	14 men with IGT and no 25-OHD deficiency	2 µg 1 alpha OH D3 per day x 18 months; No placebo	IVGTT Euglycemic clamp	Not reported	Sensitivity – no change; Secretion –transient increase
13	NGT and low 25-OHD	20,000 IU D3 PO twice a week; 45 Placebo; 49 D3	Hyperglycemic clamp	Placebo 16.1* →17.1;25-OHD 16.1* →57.1; *mean of both groups	Sensitivity – no difference; Secretion –no difference
20	Men aged 61-65 years; 56 IGT; 9 type 2 DM treated with diet	0.75 µg 1 alpha (OH)-D3 twice a day x 3 months;32 Placebo; 33 D3	IVGTT	Placebo 37 →42; Vitamin D 39 → 54	Sensitivity – no difference; Secretion – no difference
21	Non-diabetic and IFG	700 IU D3 per day x 3 years; 114 Placebo-(NFG); 108 D3 (NFG); 47 Placebo (IFG); 45 D3 (IFG)	HOMA-IR	Placebo (NFG) 28.2 → 27.8; 25-OHD (NFG) 32.6 → 44.4; Placebo (IFG) 32.5 →	Sensitivity - no change in NFG; increased in IFG

SUPPLEMENTARY DATA

				35.6; 25-OHD (IFG) 28.5 → 41.0	
22	33 NGT; 12 IGT	2 doses of 100,000 IU D3 PO every 2 weeks; No placebo	OGTT (2 weeks after 2 nd dose); HOMA-IR QUICKI	16.0 → 36.1	Sensitivity – no change by HOMA-IR, QUICKI or Avignon’s or Gutt’s modeling of OGTT
23	23 young healthy volunteers with low 25-OHD	300,000 IU/month IM x 3 (specific preparation not specified; No placebo	OGTT HOMA-IR	8.2 → 46.8	Sensitivity – no change by HOMA-IR or Matsuda’s modeling of OGTT; Secretion – no change in insulin AUC
24	42 IFG/IGT; 4 type 2 DM treated with diet	2,000 IU D3 per day x 4 months; No placebo	FSIVGTT	24.4 → 30.8	Sensitivity - no change; Secretion – increased
19	Healthy centrally obese Asian Indian men	120,000 IU D3 per 2 weeks PO x 3 weeks; 35 Placebo; 36 D3	3-hr OGTT HOMA-IR QUICKI	Placebo 12.2 → 12.5; 25-OHD 14.6 → 28.6	Sensitivity – no difference in HOMA-IR or QUICKI but increased with Mari’s modeling of OGTT
18	Insulin resistant South Asian women	4,000 IU D3 per day x 6 months; 35 Placebo; 42 D3	HOMA-IR HOMA-B	Placebo 7.6 → 11.6; 25-OHD 8.4 → 32.0	Sensitivity – increased; Secretion - no difference
17	8 IFG with 25-OHD deficiency	10,000 IU D3 per day x 1 month; No placebo	FSIVGTT	20.6 → 44.8	Sensitivity – increased; Secretion – acute insulin response decreased
25	Type 2 DM treated with metformin & bedtime insulin (withheld night before study)	4,000 IU D3 per week PO x 6 months; 16 Placebo; 16 D3	HOMA-IR HOMA-B	Placebo 23.4 → 22.9; 25-OHD 24.0 → 67.3	Sensitivity – no difference; Secretion – no difference
26	Asian Indian type 2 DM treated with diet or oral drugs not changed during study	300,000 IU D3 per week IM x 4; 14 Placebo; 14 D3	OGTT HOMA-IR	Placebo 16.7 → <30; 25-OHD 14.9 → 41.6	Sensitivity – no difference; Secretion – no difference in insulin AUC
27	4 patients with osteomalacia stated to have 25-OHD deficiency	2,000 IU D3 per day x 6 months	OGTT	Not reported	Secretion – increased insulin AUC
28	14 non-obese type 2 DM	2 µg 1 alpha-OH D3 per day x 3 weeks; 7 Control; 7 D3	OGTT	Not reported	Secretion increased insulin AUC
29	10 type 2 DM women treated with oral drugs not changed during study	1332 IU D3 per day x 1 month; No placebo	IVGTT HOMA-IR	14.1 → 25.3	Sensitivity – no change; Secretion small but significant increase in 1 st phase and no change in 2 nd phase

SUPPLEMENTARY DATA

AUC – area under the curve; DM – diabetes mellitus; FSIVGTT – frequently sampled intravenous glucose tolerance test; HOMA-B – reflects insulin secretion; HOMA-IR – reflects insulin sensitivity; IFG – impaired fasting glucose; IGT – impaired glucose tolerance; IM –intramuscular; IU – international units; IVGTT – intravenous glucose tolerance test; NFG – normal fasting glucose; NGT – normal glucose tolerance; OGTT – oral glucose tolerance test; PO – per oral; QUICKI – reflects insulin sensitivity, D2–ergocalciferol, D3–cholecalciferol

1. Lind L, Pollare T, Hvarfner A, Lithell H, Sorensen OH, Ljunghall S. Long-term treatment with active vitamin D (alphacalcidol) in middle-age men with impaired glucose tolerance; effects on insulin secretion and sensitivity, glucose tolerance and blood pressure. *Diabetes Res* 1989;11(3):141-147.
2. Lind L, Hanni H, Hvarfner A, Sorensen OH, Ljunghall S. Vitamin D is related to blood pressure and other cardiovascular risk factors in middle-aged men. *Am J Hypertens* 1995;8(9):894-901.
3. Kamycheval E, Jorde R, Figenschau Y, Haug E. Insulin sensitivity in subjects with secondary hyperparathyroidism and the effect of a low serum 25-hydroxyvitamin D on insulin sensitivity. *J Endocrinol Invest* 2007;30(2):126-132.
4. Clifton-Bligh RJ, McElduff P, McElduff A. Maternal vitamin D deficiency, ethnicity and gestational diabetes. *Diabet Med* 2008;25(6):678-684.
5. Ashraf A, Alvarez J, Saenz K, Gower B, McCormick K, Franklin F. Threshold for effects of vitamin D deficiency on glucose metabolism in obese female African-American adolescents. *J Clin Endocrinol Metab* 2009;94(9):3200-3206.
6. Chiu KC, Chu A, Go VLW, Saad M. Hypovitaminosis D is associated with insulin resistance and β cell dysfunction. *Am J Clin Nutr* 2004;79(5):820-825.
7. Lu L, Yu Z, Pan A et al. Plasma 25-hydroxyvitamin D concentration and metabolic syndrome among middle-aged and elderly Chinese individuals. *Diabetes Care* 2009;32(7):1278-1283.
8. Gannage-Yared M-H, Chedid R, Khalife S, Azzi E, Zoghbi F. Vitamin D in relation to metabolic risk factors, insulin sensitivity and adiponectin in a young Middle-Eastern population. *Eur J Endocrinol* 2009;160(6):965-971.
9. Kanayanil S, Vieth R, Retnakaran R, et al. Association of vitamin D with insulin resistance and β -cell dysfunction in subjects at risk for type 2 diabetes. *Diabetes Care* 2010;33(6):1379-1381.
10. Zhao G, Ford ES, Li C. Associations of serum concentrations of 25-hydroxyvitamin D and parathyroid hormone with surrogate markers of insulin resistance among U.S. adults without physician-diagnosed diabetes: NHANES, 2003-2006. *Diabetes Care* 2010;33(2):344-347.
11. Gulseth HL, Gjelstad IMF, Tierney AC, et al. Serum vitamin D concentration does not predict insulin action or secretion in European subjects with the metabolic syndrome. *Diabetes Care* 2010;33(4):923-925.
12. Cheng S, Massaro JM, Fox CS et al. Adiposity, cardiometabolic risk, and vitamin D status: the Framingham Heart Study. *Diabetes* 2010;59(1):242-248.
13. Grimnes G, Figenschau Y, Almas B, Jorde R. Vitamin D, insulin secretion, sensitivity, and lipids: results from a case-control study and a randomized controlled trial using hyperglycemic clamp technique. *Diabetes* 2011;60(11):2748-2757.
14. Rajakumar K, Heras JDL, Lee S, Holick MF, Arslanian SA. 25-hydroxyvitamin D concentrations and in vivo insulin sensitivity and β -cell function relative to insulin sensitivity in black and white youth. *Diabetes Care* 2012;35(3):627-633.
15. Scragg R, Sowers MF, Bell C. Serum 25-hydroxyvitamin D, diabetes, and ethnicity in the Third National Health and Nutritional Examination Survey. *Diabetes Care* 2004;27(12):2813-2818.
16. de Boer IH, Tinker LF, Curb JD, et al. Calcium plus vitamin D supplementation and the risk of incident diabetes in the Women's Health Initiative. *Diabetes Care* 2008;31(4):701-707.

SUPPLEMENTARY DATA

17. Nazarian S, St. Peter JV, Boston RC, Jones SA, Mariash CN. Vitamin D3 supplementation improves insulin sensitivity in subjects with impaired fasting glucose. *Transl Res* 2011;158(5):276-281.
 18. Von Hurst PR, Stonehouse W, Coad J. Vitamin D supplementation reduces insulin resistance in South Asian women living in New Zealand who are insulin resistant and vitamin D deficient – a randomized, placebo-controlled trial. *Br J Nutr* 2010;103(4):549-455.
 19. Nagpal J, Pande JN, Bhartia A. A double-blind, randomized, placebo-controlled trial of the short-term effect of vitamin D₃ supplementation on insulin sensitivity in apparently healthy, middle-aged, centrally obese men. *Diabet Med* 2009;26(1):19-27.
 20. Ljunghall S, Lind L, Lithell H, et al. Treatment with one-alpha-hydroxycholecalciferol in middle-aged men with impaired glucose tolerance -- a prospective randomized double-blind study. *Acta Med Scand* 1987;222(4):361-367.
 21. Pittas AG, Harris S, Stark PC, Dawson-Hughes B. The effects of calcium and vitamin D supplementation on blood glucose and markers of inflammation in nondiabetic adults. *Diabetes Care* 2007;30(4):980-986.
 22. Tau K, Need AG, Horowitz, Chapman IM. Glucose tolerance and vitamin D: effects of treating vitamin D deficiency. *Nutrition* 2008;24(10):950-956.
 23. Tarcin O, Yavuz DG, Ozben B, et al. Effect of vitamin D deficiency and replacement on endothelial function in asymptomatic subjects. *J Clin Endocrinol Metab* 2009;94(10):4023-4030.
 24. Mitri J, Dawson-Hughes B, Hu FB, Pittas AG. Effects of vitamin D and calcium supplementation on pancreatic β cell function, insulin sensitivity, and glycemia in adults at high risk of diabetes: the Calcium and Vitamin D for Diabetes Mellitus (CaDDM) randomized controlled trial. *Am J Clin Nutr* 2011;94(2):486-494.
 25. Jorde R, Figenschau Y. Supplementation with cholecalciferol does not improve glycaemic control in diabetic subjects with normal serum 25-hydroxyvitamin D levels. *Eur J Nutr* 2009;48(6):349-354.
 26. Parekh D, Sarathi V, Shivane VK, Bandgar TR, Menon PS, Shah NS. Pilot study to evaluate the effect of short-term improvement in vitamin D status on glucose tolerance in patients with type 2 diabetes mellitus. *Endocr Pract* 2010;16(4):600-608.
 27. Gedik O, Akalin S. Effects of vitamin D deficiency and repletion on insulin and glucagon secretion in man. *Diabetologia* 1986;29(3):142-145.
 28. Inomata S, Kadowaki S, Yamatani T, Fukase M, Fujita T. Effect of 1 alpha (OH)-vitamin D₃ on insulin secretion in diabetes mellitus. *Bone Miner* 1986;1(3):187-192.
- Borissova AM, Tankova T, Kirilov G, Dakovska I, Kovacheva R. The effect of vitamin D₃ on insulin secretion and peripheral insulin sensitivity in type 2 diabetic patients. *Int J Clin Pract* 2003;57(4):258-261.