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EFFECT OF HIGH-DOSE VITAMIN D REPLETION ON GLYCEMIC CONTROL IN AFRICAN AMERICAN MEN WITH PREDIABETES AND HYPOVITAMINOSIS D

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Abstract

Objective—This double blind, randomized, controlled trial evaluated 12 months high dose vitamin D2 supplementation for improving insulin sensitivity, secretion and glycemic status.

Methods—African American men with prediabetes (A1C 5.7 – 6.4%), hypovitaminosis D (25OHD 5 – 29 ng/ml), and prevalent medical problems were supplemented with vitamin D3 (400 IU/day) and then randomized to weekly placebo or vitamin D2 (50,000 IU). The primary outcome was the change in oral glucose insulin sensitivity (OGIS, from oral glucose tolerance test) after 12 months of treatment. Secondary outcomes included other glycemic indices, A1C and incident diabetes.

Results—Baseline characteristics were similar in vitamin D-supplemented (n = 87) and placebo (n = 86) subjects completing the trial with average concentrations 14.4 ng/ml, 362 and 6.1% for 25OHD, OGIS and A1C, respectively. After 12 months vitamin D-supplemented group had a change in serum 25OHD +35 vs +6 ng/ml for placebo, $p<0.001$; OGIS +7.8 vs −16.0 for placebo, $p = 0.026$; and A1C −0.01 vs +0.01% for placebo, $p = 0.66$; while 10% in both groups progressed to diabetes. A post hoc analysis of participants with baseline impaired fasting glucose showed that more subjects in the vitamin D subgroup (31.6%) than placebo (8.3%) returned to normal glucose tolerance, but the difference did not reach significance ($p=0.13$).

Conclusion—The trial does not provide evidence that 12 months of high-dose D2 repletion improves clinically relevant glycemic outcomes in subjects with prediabetes and hypovitaminosis D (NCT01375660).

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Keywords

Vitamin D supplement; prediabetes; African American

INTRODUCTION

Vitamin D deficiency contributes to health disparities and disease burden in African American men (AAM) but controversy remains on whether repletion improves outcomes. African Americans have increased risk for type 2 diabetes (T2DM) and hypovitaminosis D with the prevalence of 18% and 30% for diabetes and vitamin D deficiency, respectively, compared to 8.3% and 8.1%, respectively, in the US general population (1,2). African American men are ordinarily underrepresented in clinical trials (3,4). Addressing disparities in health care is one of the missions of the Veterans Health Administration (VHA). The VHA is America's largest integrated health care system, with more than 1,700 sites of care that delivers state of the art health care and serves clinical, educational and scientific missions (5). Prevention of diabetes constitutes one of the priorities for the VHA. Lifestyle modification is the best existing approach to diabetes prevention but is difficult to achieve and maintain over long term (6).

The search for novel approaches to prevent diabetes continues (7) and among them vitamin D supplements may play a role (8–10). A recent meta-analysis of 35 randomized controlled trials (43,407 patients, mixed populations) has shown no overall effect of vitamin D3 on glucose homeostasis or diabetes prevention (11). The Institute of Medicine has recommended a conservative approach to vitamin D supplementation and called for more research especially randomized clinical trials (12).

None of the previous longer-term trials used high dose vitamin D2 (ergocalciferol), enrolled participants with prevalent medical problems or substantial number of African American men (10,11). The objective of this randomized trial was to determine the efficacy and safety of 12 months treatment with vitamin D2 for improving glucose homeostasis in AAM veterans with dysglycemia and hypovitaminosis D. We dedicated the study to the population underrepresented in clinical trials (i.e. AAM) and used convenient weekly vitamin D2 supplement.

METHODS

Study Design and Subjects

This was a double blind randomized placebo-controlled trial "*D* vitamin *I*ntervention in *V*eteran *A*dministration (DIVA)". The primary objective was to determine whether high dose of vitamin D supplementation (designed to raise 25OHD into normal range) would improve oral glucose insulin sensitivity in African American men with dysglycemia and hypovitaminosis D. The eligible participants were randomized to placebo or vitamin D (1:1 ratio) with stratification according to age, 35–65 or 66–85 years, and presence of medical and psychiatric conditions to avoid possible age- and medical condition-related differences in primary outcome. The participants came for initial assessment including 3-hour oral

glucose tolerance test (OGTT), for follow-up every 3 months and final 3-hour OGTT after 12 months of treatment. The study was approved by the University of Illinois Institutional Review Board and by the Jesse Brown VA Medical Center (JBVAMC) Research and Development Committee. The study was registered at clinicaltrials.gov as NCT01375660.

We recruited subjects among AAM veterans coming for medical care to JBVAMC in Chicago using flyers, information sheets, prescreening of electronic medical records, and letters to JBVAMC patients and doctors. The main inclusion criteria were as follows: AAM veteran, age 35–85 years, BMI 28–39 kg/m^2, fasting glucose 95–125 mg/dl and/or A1C 5.7 – 6.4% (38.8 – 46.5 mmol/mol), 25OHD 5.0 – 29 ng/ml. The criteria for the diagnoses of prediabetes and diabetes were based on the American Diabetes Association recommendations (6). Participants who were diagnosed with diabetes during screening or intervention (A1C 6.5 – 6.9% or 47.5 – 51.9 mmol/mol) were allowed in the study if they did not need to take anti-diabetic medications and A1C remained <7% (<53 mmo/mol). The main exclusion criteria were as follows: diabetes and medical conditions that would be expected to interfere with the study or increase risk to the subject, such as kidney stones, hyperparathyroidism, sarcoidosis, hypercalcemia, and chronic kidney disease beyond stage 3a (eGFR <45 mls/min/1.73m^2). Additional recorded diagnoses included hypertension, hyperlipidemia, arthritis, cardiovascular disease, cancer and psychiatric problems as well as medications. The age-adjusted Charlson index, a validated index of chronic disease prognosis was calculated based on the previously published formula (13) and included one point for myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic obstruction pulmonary disease, connective tissue disease, peptic ulcer disease, uncomplicated diabetes and mild liver disease; two points for complicated diabetes, moderate to severe chronic kidney disease, hemiplegia, leukemia, lymphoma, solid tumor without metastasis; three points for moderate to severe liver disease and 6 points for metastatic solid tumors or AIDS. Age adjustment added 1 point for every 10 years above age 40. Total 2,067 subjects were prescreened, 205 randomized, and 173 had final OGTT (Fig. 1). The subjects provided written informed consent prior to participation.

All subjects received supplementation with cholecalciferol (D3) 400 IU as multiple vitamins from JBVAMC pharmacy since it was regarded unethical to withhold supplementation from those with hypovitaminosis D. In addition, the subjects were instructed to take either weekly ergocalciferol (D2) 50,000 IU (Pliva Co) or identically looking soy oil-containing placebo (both encapsulated by the research pharmacy). The research pharmacist randomized the subjects using a computer-generated code, adjusted doses and was the only person who knew the allocation and serum 25OHD during the study. Dose adjustments were done at 3, 6, and 9-month visits to maintain serum 25OHD concentrations of 40 – 100 ng/mL and serum calcium within normal range. Compliance was monitored by pill count at each visit. The subjects were advised to maintain their usual diet and physical activity. Season of serum 25OHD sampling was not taken into account since the study lasted 12 months.

The 3-hour OGTT was performed after an overnight fast. A baseline and post-Glucola (75g glucose) venous blood samples were obtained at 10, 20, 30, 60, 90, 120, 150 and 180 minutes for glucose, insulin, and C-peptide measurements. Glucose tolerance status was defined using the ADA criteria for normal and impaired tolerance including normal glucose

tolerance (NGT), impaired fasting glucose (IFG), impaired glucose tolerance (IFG), both (IFG and IGT), and diabetes (14).

Blood samples were used for measuring A1C, 25OHD, glucose, calcium, insulin, and C-peptide and chemistry in the clinical laboratory applying laboratory standards of care and references. The analytical methods included ion-exchange high performance liquid chromatography (TOSOH G8 analyzer) for A1C, hexokinase and spectrophotometric assay (Siemens Vista 1500 Chemistry analyzer) for glucose and calcium, chemiluminescent immunoassay (Siemens ADVIA Centaur XP Chemistry analyzer) for insulin, immunochemiluminometric assay (ICMA, DiaSorin LIAISON analyzer) for 25OHD, and chemiluminescent immunoassay (Siemens Immulite 2000 analyzer) for C-peptide.

Calculations of glycemic indices

Calculations for glycemic indices were based on OGTT under dynamic, i.e. postprandial conditions. Insulin sensitivity was assessed by two methods: 1) Oral Glucose Insulin Sensitivity (OGIS, the primary outcome) based on modeling provided online http://webmet.pd.cnr.it/ogis/ in $ml*min^{-1*}m^{-2}$ (15) and 2) Matsuda composite based on formula 10^4/Square Root of [(fasting glucose × fasting insulin) × (mean glucose × mean insulin)] (16). Insulin secretion was assessed by two methods: 1) Insulinogenic index-30 [(insulin at 30 min – fasting insulin)/(glucose at 30 min – fasting glucose)] (17,18) and 2) C-peptidogenic index-30 [(C-peptide at 30 min – fasting C-peptide)/(glucose at 30 min – fasting glucose)] (18–20). All formulas had been validated against the glucose clamp with and without tracers (15,16,18–22).

Statistical Analyses

The sample size for the study was calculated according to general recommendations and previously published data to achieve 80% power and significance level (alpha) of 0.050 using a two-sided two-sample unequal-variance t-test (23). Before statistical analysis, normal distribution and homogeneity of the variances were tested. Baseline characteristics were compared with independent t tests for continuous variables or chi-square tests for categorical variables. Between-group changes (final minus baseline) were analyzed for each outcome variable by two-way ANOVA with treatment (between), time (within) and treatment × time interaction used as independent variables. Efficacy of vitamin D supplementation was analyzed as the intention-to-treat (ITT) based on original random assignment of the groups. To verify primary analysis secondary analysis was performed using data from participants with vitamin D deficiency (25OHD <20ng/ml) and those with prediabetes. Hypotheses were specified a priori, therefore, adjustments for multiple comparisons were not made (24).

Association between main outcome OGIS and clinically relevant vitamin D-related characteristics (25) was evaluated for the whole group by simple linear and stepwise multiple linear regression analyses with OGIS response (final minus baseline) as the dependent variable and important predictors as the independent variables (baseline age, BMI, A1C, fasting glucose, insulin, C-peptide, 25OHD, OGIS, 2-hour glucose, and group assignment). Values were represented as means and standard deviations (SD) unless

specified. The significance was determined at p <0.05 (two tailed). All statistical analyses were performed using SAS 9.2 statistical software (SAS Institute, NC).

RESULTS

The data on screening, randomization, attrition and completion rates are reviewed in Fig. 1. The baseline characteristics were similar in placebo vs vitamin D group (Table 1). Likewise, baseline characteristics were similar between 173 subjects who completed and 32 subjects who discontinued the study (data not shown). Compliance was similar in both groups (77% and 76% in placebo and vitamin D groups, respectively, p=0.736). Disease burden was relatively high, average number of medical conditions was 4 (range 0 – 8) and average number of medications was 6.5 (range 0 – 17) per person. The mean [SD] dose of D2 was 62,762 [10,772], range 50,000 – 88,460 IU per week. There was a rise of serum 25OHD in both groups and at 12 months 76% of vitamin D group subjects reached 25OHD of 30 ng/dl or higher, range 12 – 109 ng/dl) (Table 1).

Table 2 summarized results for comparisons within the groups (final vs baseline) and between the groups (placebo vs vitamin D) for measured glycemic indices. Changes in body weight, BMI, blood pressure, circulating glucose, insulin, and C-peptide were not different within or between the groups (data not shown). There was no difference between the groups in A1C, incident diabetes or reversal to normal glycemia despite of improved insulin sensitivity in vitamin D group compared to placebo. The analysis of subjects with baseline 25OHD <20 ng/ml or prediabetes (n = 146) did not change the results. A post hoc analysis of participants with baseline impaired fasting glucose showed that more subjects in the vitamin D subgroup (31.6%) than placebo (8.3%) returned to normal glucose tolerance, but the difference did not reach significance (p=0.13) (Table 2). Similarly, in the subgroup with baseline impaired fasting glucose and reverting to normal glucose tolerance at study completion, insulin secretion appeared improved in vitamin D-supplemented vs placebo group. The changes in Insulinogenic Index-30 and C-peptidogenic index-30 were (mean [SD]) as follows: +4.1 [4.8] vs −0.12 [1.12] (p=0.06) and +76.3 [67.8] vs −5.4 [16.4] (p=0.016) in vitamin D-supplemented vs placebo subgroups, respectively, suggesting possibility of vitamin D contribution to improvement of insulin secretion in early stages of dysglycemia.

The univariate regression analysis for the whole group (n = 173) showed positive correlation between changes in OGIS (Δ-OGIS) and several baseline characteristics including fasting glucose (r=0.18, p=0.017), glucose at 2-hour of OGTT (r=0.19, p=0.013), group assignment (r=0.16, p=0.037) and negative correlation of Δ-OGIS with baseline OGIS (r=−0.45, p<0.001). The stepwise multiple linear regression analysis showed that baseline OGIS was the only independent predictor of OGIS response (Δ-OGIS) and the model accounted for 20% of OGIS response variance (Table 3).

There was no side effects deemed related to vitamin D treatment. One subject was diagnosed with hypercalcemia (10.2 mg/dl) at three months after initiation of treatment, was dropped from the study and subsequently revealed to belong to a placebo group. At final visit three

subjects (one in placebo and two in vitamin D group) had elevated calcium while 25OHD was in normal range (serum calcium 10.2 – 10.4 with reference range 8.5 − 10.1 mg/dl).

Based on the results that the primary outcome of the study (i.e. OGIS) improved and a secondary but more clinically relevant outcome (A1C) did not improve, we calculated the sample size based on our data for Δ-A1C. Calculation showed that 1502 subjects for each group were needed to achieve 80% power to reject the null hypothesis of equal means based on the population mean difference μ1 – μ2 = (0.01 − [−0.01]) = 0.02, standard deviations of 0.21 for group 1 and 0.18 for group 2, and a significance level (alpha) of 0.050 using a two-sided two-sample unequal-variance t-test.

DISCUSSION

The results showed that high-dose vitamin D2 supplementation for a year did not improve A1C or prevents diabetes in subjects with prediabetes. The results were in line with previously reviewed (10) and recently published trials and a meta-analysis (11،26،27). Two of published trials were using high dose vitamin D3 (≥20,000 IU/week) for 1 year in subjects with prediabetes (26،27). Both demonstrated no effect of vitamin D3 supplementation on insulin sensitivity and secretion or A1C. Similarly, the present study revealed no effect of D2 on A1C despite small but significant improvement of insulin sensitivity measured by OGIS. The OGIS index using physiological principles for empirical compartment-based modeling was validated against intravenous glucose clamp (15). Since introduction in 2001 OGIS was utilized in observational studies and randomized controlled trials (22،23،28‒32). It performed the best in comparison to other indices of insulin sensitivity (i.e. HOMA-IR, QUICKI, Matsuda composite, Stumvoll, and Gutt) (23،28) conceivably contributing to the discordance in the results of the present and previous studies. The differences in the demographic characteristics and comorbidities, all well-known determinants of glycemic status (1،6،10،14،25), might have added to the inconsistencies in the results. Furthermore, a novel approach for localizing the association of vitamin D status with insulin resistance to one region of the circulating 25OHD was suggested (25). The concept of “sensitivie range” was based on the expectation that the effect of vitamin D on glycemic control was small (about 2%), easily obscured by other factors (e.g. obesity) and, as for other nutrients, to be sigmoidal in shape, with response reaching a plateau at some point within the plausible intake range. By analyzing data from 4,116 subjects with 25OHD ranging 4 – 144 ng/ml, the authors concluded that the “sensitive range” for 25OHD was 16 – 36 ng/ml. In this response region, the absolute magnitude of interactions between vitamin D and metabolic parameters was 2 to 7 times greater than those observed for the wider range (25). Corroborating these results, we observed small effect of vitamin D supplementation with the response of OGIS about 2% (mean Δ-OGIS was 8 in vitamin D-supplemented group while population mean OGIS was 350 $ml*min^{-1*}m^{-2}$).

There were several strengths of the trial. The trial addressed disparity of health research by being dedicated to African American men with prevalent chronic conditions. The trial was of long duration, used convenient weekly D2 dosing and measured validated sensitive dynamic glycemic indices. Lastly, the results generated the hypothesis that vitamin D supplementation might be predominantly efficacious in early stages of dysglycemia, i.e.

impaired fasting glucose. There were several limitations of the study. The study enrolled a single race and gender, used surrogate markers of glucose homeostasis, was underpowered to show changes in A1C or diabetes prevention, and although the subjects were randomized, possible residual confounding by diet, physical activity, and medical problems could remain.

CONCLUSION

In conclusion, the trial does not provide evidence that 12-month high-dose D2 repletion improves clinically relevant glycemic outcomes in subjects with prediabetes and hypovitaminosis D. Further trials powered for diabetes prevention and identifying populations that can benefit from vitamin D supplementation are warranted.

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The authors' responsibilities were as follows – EB designed the study, researched the literature, obtained institutional review board approval, carried out the study, wrote the paper; BM, AA, YE, and IC: conducted research including participant recruitment, testing, data and sample collection, and analyses; SK: helped designing the study and writing the paper; EB had primary responsibility for final content.

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Abbreviations

A1C	glycosylated hemoglobin
AUC	area under the curve
BMI	body mass index
D2	ergocalciferol
D3	cholecalciferol
eGFR	estimated Glomerular Filtration Rate
HOMA-IR	Homeostatic model assessment-insulin resistance
IGT	impaired glucose tolerance
IFG	impaired fasting glucose
NGT	normal glucose tolerance
OGIS	oral glucose insulin sensitivity index
OGTT	oral glucose tolerance test
QUICKI	Quantitative Insulin-Sensitivity Check Index

VHA	Veterans Health Administration
25OHD	serum 25-hydroxyvitamin D concentration

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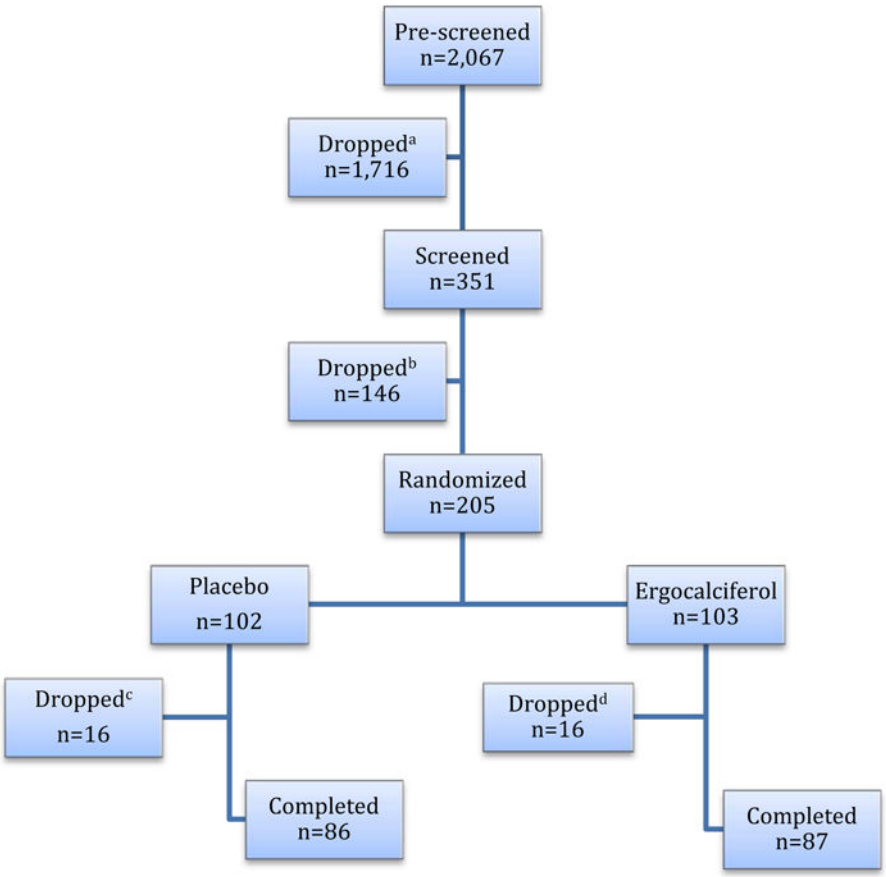

Fig. 1.

Flow diagram of the trial. [a]Ineligible n=1716: 927 T2DM, 309 BMI<28 or >40 kg/m^2, 86 A1C<5.7%, 86 GFR<45 ml/min/1.73m^2, 120 on vitamin D supplements, 137 advanced chronic conditions, 51 ineligible sex or race; [b]Dropped n=146: 17 ineligible: 5 A1C<5.7%, 5 A1C>6.9%, 3 GFR<45 ml/min/1.73m^2, 4 poor venous access, and 129 lost interest; [c]Dropped n=16: 6 personal issues and lost interest, 2 moved out of state, 2 could not be reached, 6 medical issues (3 depressive disorder and/or substance dependence, 1 hypercalcemia, 1 tumor of the bladder, 1 angioedema due to ACE inhibitor); |[d]Dropped n=16: 4 personal issues and lost interest, 3 moved out of state, 1 could not be reached, 8 medical issues (3 depressive disorder and/or substance dependence, 1 newly diagnosed T2DM requiring medications, 2 liver problems, 1 congestive heart failure, 1 hypokalemia).

Table 1

Baseline Characteristics and 25OHD Change over 12-month Trial Period[1]

Characteristics	Placebo, n=86	Vitamin D, n=87	P value
Baseline Characteristics			
Age (y)	59.8 ± 6.0	58.2 ± 6.0	0.204
Body weight (kg)	101.2 ± 9.3	102.6 ± 10.2	0.428
BMI (kg/m^2)	31.5 ± 2.4	32.4 ± 2.9	0.072
SBP (mmHg)	133 ± 13	136 ± 13	0.272
DBP (mmHg)	78 ± 11	80 ± 9	0.408
Creatinine (mg/dl)	1.2 ± 0.2	1.1 ± 0.2	0.192
Fasting glucose (mg/dl)	97.7 ± 10.3	98.3 ± 9.3	0.772
2-hour glucose (mg/dl)	129.7 ± 34.6	131.9 ± 31.8	0.749
Fasting insulin (μU/ml)	18.4 ± 9.4	19.5 ± 10.7	0.685
Fasting C-peptide (ng/ml)	3.0 ± 1.2	2.8 ± 1.0	0.335
25OHD status, n [%]			
25OHD <10 ng/ml	24 [27.9]	20 [22.7]	0.687
25OHD 10–19 ng/ml	51 [59.3]	52 [59.1]	0.912
25OHD 20–29 ng/ml	11 [12.8]	15 [18.2]	0.798
Glycemic status			
Based on A1C			
Prediabetes	77 [89.5]	69 [79.3]	0.875
Diabetes	9 [10.5]	18 [20.7]	0.068
Based on OGTT			
NGT	48 [55.7]	35 [40.2]	0.088
IFG	12 [14.0]	19 [21.8]	
IGT	6 [7.0]	16 [18.4]	
IFG & IGT	11 [12.8]	9 [10.4]	
Diabetes	9 [10.5]	8 [9.2]	
Medical problems, n [%]			
Hypertension	59 [68.6]	61 [69.3]	0.873
Hyperlipidemia	51 [59.3]	43 [48.9]	0.543
Cardiovascular[2]	11 [12.8]	15 [17.1]	0.465
Arthritis	34 [39.5]	31 [35.2]	0.784
Cancer	9 [10.5]	14 [15.9]	0.367
Psychiatric[2]	66 [76.7]	64 [72.7]	0.769
All co-morbidities/person	3.8 [1.4]	4.0 [1.6]	0.459
Number of meds/person	5.9 [3.0]	6.8 [2.9]	0.119
Charlson index[3]	2.1 [1.1]	2.3 [1.2]	0.251
25OHD change (ng/ml)			
Baseline	14.0 ± 4.8	14.7 ± 4.7	0.393
3 mo	22.0 ± 6.5	35.3 ± 10.0	<0.001

Characteristics	Placebo, n=86	Vitamin D, n=87	P value
6 mo	20.3 ± 6.1	40.0 ± 11.7	<0.001
9 mo	21.7 ± 6.9	43.3 ± 13.7	<0.001
12 mo (final)	19.9 ± 7.3	48.1 ± 18.4	<0.001

Abbreviations: A1C, glycosylated hemoglobin; DBP, diastolic blood pressure; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; NGT, normal glucose tolerance; OGTT, oral glucose tolerance test; SBP, systolic blood pressure; 25OHD, serum 25-hydroxyvitamin D.

[1] Values are Mean ± SD or n [%]; P values from independent t tests (continuous) or chi-square tests (categorical) between groups.

[2] Cardiovascular problems: coronary artery disease, stroke, peripheral vascular disease and congestive heart failure and Psychiatric problems: depression, post-traumatic stress disorder, substance use and other psychiatric conditions.

[3] Charlson index of chronic disease

Table 2

Comparison of baseline, final and change (final minus baseline) measures of main outcomes within placebo and vitamin D treatment groups, and between groups[1]

Index	Placebo, n=86	Vitamin D, n=87	P value[2]
Insulin sensitivity			
OGIS			
Baseline	369.00 ± 66.27	355.55 ± 64.10	0.277
Final	353.00 ± 63.67[3]	363.37 ± 58.60	0.455
Change (final – baseline)	−16.00 ± 55.83	7.82 ± 56.02	0.026
Matsuda composite			
Baseline	3.15 ± 1.38	2.99 ± 1.45	0.596
Final	3.28 ± 1.69	3.43 ± 1.83	0.694
Change (final – baseline)	0.13 ± 1.43	0.44 ± 1.51	0.389
Insulin secretion			
Insulinogenic index-30			
Baseline	2.06 ± 1.16	1.70 ± 0.96	0.134
Final	2.02 ± 1.24	1.98 ± 1.42	0.894
Change (final – baseline)	−0.03 ± 1.10	0.26 ± 1.03	0.340
C-peptidogenic index-30			
Baseline	37.59 ± 16.83	32.55 ± 14.43	0.148
Final	37.19 ± 18.03	38.01 ± 22.90	0.876
Change (final – baseline)	−0.64 ± 15.84	5.32 ± 17.47	0.220
A1C (%)			
Baseline	6.08 ± 0.20	6.14 ± 0.26	0.142
6 mo	6.14 ± 0.28	6.12 ± 0.31	0.707
Change (6 mo – baseline)	0.05 ± 0.20	−0.03 ± 0.18	0.031
Final 12 mo	6.09 ± 0.26	6.14 ± 0.30	0.356
Change (12 mo – baseline)	0.01 ± 0.21	−0.01 ± 0.18	0.663
Glycemic status change from baseline to 12 mo (n [%])			
Based on A1C			
Incident diabetes	9 [10.5]	9 [10.2]	0.869
From prediabetes to normal	6 [7]	8 [9.1]	0.786
Based on OGTT			
Incident diabetes	3 [3.9]	3 [3.8]	0.878
From IFG to NGT	1 [8.3]	6 [31.6]	0.132
From IGT to NGT	2 [33.3]	5 [31.3]	0.848

[1] Values are Mean ± SD or n [%]. Abbreviations: OGIS, oral glucose insulin sensitivity; NGT, IFG, IGT as in Table 1.

[2] P values from independent t tests (continuous) or chi-square tests (categorical) between 2 groups

[3] P=0.036 from independent t tests (continuous) for within the group comparison.

Table 3

Predictors of oral glucose insulin sensitivity (OGIS) response (final minus baseline)[1]

Predictors[2]	Regression coefficient	SE	95% CI	P value
Body weight	−0.027	0.411	−0.839, 0.786	0.948
A1C	−10.69	18.69	−47.61, 26.21	0.568
Fasting glucose	0.023	0.389	−0.745, 0.791	0.953
2-hour glucose	−0.137	0.127	−0.388, 0.114	0.284
OGIS	−0.445	0.081	−0.604, −0.286	<0.0001
Group[3]	17.08	9.741	−2.154, 36.31	0.081

[1] The stepwise multiple linear regression analysis for the whole group (n = 173). Adjusted R^2 for the model 0.20.

[2] Predictors are values at baseline.

[3] Group: placebo vs vitamin D-supplemented group