

Baseline characteristics of the vitamin D and type 2 diabetes (D2d) study: A contemporary prediabetes cohort

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BACKGROUND

- D2d is the largest trial to test the effect of vitamin D supplementation for prevention of diabetes.
- D2d is also the largest modern U.S. study to have assembled a cohort of people at risk for diabetes, defined as meeting at least two of the 2010 ADA criteria for prediabetes.

DESIGN AND METHODS

- Eligible participants met at least 2-of-3 2010 ADA glycemic criteria for prediabetes:
 - Fasting plasma glucose (FPG): 100-125 mg/dL
 - 2-hour glucose post-75g oral glucose load(2hPG): 140-199 mg/dL
 - Hemoglobin A1c (HbA1c): 5.7-6.4%
- Participants self-reported demographics and use of dietary supplements. Other measures were assessed using standard techniques.
- All glucose measures were run in a central laboratory:
 - HbA1c was measured using an ion-exchange HPLC method.
 - Plasma glucose was measured using a hexokinase method.

Table 1. Diabetes risk factors, glycemic profile, and vitamin D supplementation by sex

	Overall (n=2423)	Men (n=1337)	Women (n=1086)	p-value
Diabetes Risk Factors				
Self-reported family history of diabetes, No. (%)	1514 (62.5)	774 (57.9)	740 (68.1)	<0.01
Self-reported gestational diabetes, No. (%) women	NA	NA	81 (7.4)	NA
Glycemic testing , mean (SD)				
Fasting plasma glucose, mg/dL	107.9 (7.4)	108.8 (7.4)	106.9 (7.3)	<0.01
2-hour post-load plasma glucose, mg/dL	137.2 (34.3)	135.3 (35.9)	139.7 (32.1)	<0.01
Hemoglobin A1c, %	5.9 (0.2)	5.9 (0.2)	5.9 (0.2)	0.23
Pre-diabetes categories , N (%)				<0.01
iA1c + IFG	1184 (48.9)	687 (51.4)	497 (45.8)	
IFG + IGT	152 (6.3)	83 (6.2)	69 (6.4)	
IGT + iA1c	231 (9.5)	103 (7.7)	128 (11.8)	
iA1c + IFG + IGT	856 (35.3)	464 (34.7)	392 (36.1)	
Vitamin D supplement use at baseline				
Participants taking vitamin D, No. (%)	1033 (42.6)	506 (37.9)	527 (48.5)	<0.01
Vitamin D intake among all participants, IU/day, mean (SD)	311 (397)	264 (369)	369 (422)	<0.01

IFG, impaired fasting glucose defined as FPG 100-125 mg/dL (5.6-6.9 mmol/L)
IGT, impaired glucose tolerance defined as 2hPG 140-199 mg/dL (7.8-11.0 mmol/L)
iA1c, impaired A1c defined as HbA1c 5.7-6.4% (39-47 mmol/mol)

Table 2. Diabetes risk factors and glycemic profile by race

	White (N=1616, 66.7%)	Black (N=616, 25.4%)	Asian (N=130, 5.4%)	Other (N=61, 2.5%)	p-value
Diabetes Risk Factors					
Self-reported family history of diabetes, No. (%)	962 (59.5)*	420 (68.1)*	86 (66.2)	46 (75.4)	<0.01
Self-reported gestational diabetes, No. (%) women	66 (9.2)*	6 (2.0) *	5 (10.9)	4 (14.3)	<0.01
Glycemic testing , mean (SD)					
Fasting plasma glucose, mg/dL	108.8 (7.3)*	105.8 (7.4)*	107.3 (7.1)	107.3 (6.7)	<0.01
2-hour post-load plasma glucose, mg/dL	137.7 (35.0)	135.7 (32.5)	140.5 (33.7)	135.3 (35.4)	0.41
Hemoglobin A1c, %	5.9 (0.2)*	6.0 (0.2)* §	5.9 (0.2) §	5.9 (0.2)	
Pre-diabetes categories , No. (%)					<0.01
iA1c + IFG	768 (47.5)*	323 (52.4)*	64 (49.2)	29 (47.5)	
IFG + IGT	126 (7.8)*	17 (2.8)*	6 (4.6)	3 (4.9)	
IGT + iA1c	119 (7.4)*	91 (14.8)*	14 (10.8)	7 (11.5)	
iA1c + IFG + IGT	603 (37.3)*	185 (30.3)*	46 (35.4)	22 (36.1)	

Difference between White and Black significant at p<0.05
§ Difference between Black and Asian significant at p<0.05
|| Difference between Black and other significant at p<0.05

RESULTS

Table 3. Key baseline characteristics of D2d vs. other large prediabetes trials

Study Start Date [country] (Intervention, N)	D2d 2013 [US] (Vitamin D ₃ , N=2,423)	SCALE 2011 [worldwide] (Liraglutide, N=2,254)	Navigator 2002 [worldwide] (Nateglinide and/or valsartan, N=9,518)	DREAM 2001 [worldwide] (Ramipril and/or rosiglitazone, N=5,269)	DPP 1996 [US] (Metformin or lifestyle, N=3,234)	STOP-NIDDM 1995 [worldwide] (Acarbose, N=1,429)	ACE 2009 [China] (Acarbose, N=6,522)
Inclusion criteria for prediabetes	At least 2-of-3 2010 ADA criteria*	At least 1-of-3 2010 ADA criteria*	2hPG 140-199 mg/dL and FPG 95-125 mg/dL	2hPG 140-199 mg/dL or FPG 110-125 mg/dL	2hPG 140-199 mg/dL and FPG 95-125 mg/dL	2hPG 140-199 mg/dL and FPG 101-139 mg/dL	2hPG 140-199 mg/dL
Age, years, mean	59.4	47.4	63.8	54.7	50.6	54.5	64.3
Women, %	45	76	51	59	68	51	27
BMI, kg/m ² , mean	32.0	38.9	30.5	30.9	34.0	31	25.4
Waist circumference, cm, mean	105.0	116.6	101	Not reported	105.1	101	91.2
White race, %	66.7	83	83.1	Not reported	55	98	0
FPG, mg/dL mean	107.9	99.0	109.6	104.4	106.5	112.0	99.0
2hPG, mg/dL, mean	137.25	133.2	164.9	156.6	164.6	166.7	167.4
HbA1c, %, mean	5.9	5.8	5.8	NR	5.9	NR	5.9
Duration of follow-up, years, mean	3 (estimated)	3.0	5.0	3.0	2.8	3.3	5.0

* 2010 ADA criteria for pre-diabetes: 2hPG 140-199 mg/dL; FPG 100-125 mg/dL; HbA1c 5.7-6.4%

- 2,423 participants (45% women, 33% non-White) were randomized.
- More women than men reported a family history of diabetes (Table 1).
- Mean FPG was lower while mean 2hPG was higher in women than men; HbA1c concentrations did not differ (Table 1).
- More Black than white participants reported a family history of diabetes (Table 2).
- Black participants had higher HbA1c and lower FPG concentration than other races; 2hPG concentration did not differ by race (Table 2).
- Hispanics were more likely to have a family history of diabetes (69% vs 62%) but similar glycemic concentrations compared to non-Hispanics (data not shown).
- The D2d cohort generally has lower 2hPG but similar HbA1c and FPG concentrations than previous prediabetes cohorts (Table 3).

DISCUSSION

- The D2d cohort has a glycemic profile that closely matches that of contemporary prediabetes patients.
- D2d is well positioned to examine how the ADA criteria predict incident diabetes and how risk varies by age, sex, race, and ethnicity.
- Black participants had higher HbA1c despite lower FPG and similar 2hPG concentrations, which suggests that HbA1c overestimates mean glycemia in Black individuals compared with those of other races.

CONCLUSIONS

- In a contemporary cohort of U.S. adults at risk for diabetes, D2d is expected to address two important knowledge gaps:
 - Whether vitamin D supplementation prevents diabetes
 - How the 2010 ADA criteria may impact the prevalence of prediabetes and the progression to diabetes among those at high risk for prediabetes (having at least 2-of-3 ADA criteria).
- The answers to these questions may have implications for the many U.S. adults at risk for diabetes.

Acknowledgements

- Grant funding support provided by NIDDK (grant U01DK098245) and ADA (grant 1-14-D2d)
- Thank you to the D2d participants for their ongoing dedication to the study.

