

Supplemental Table 1. Screening, Run-in Schedule and Collection of Measurements and Assessments

	Screening	Final Run-in	Baseline
HbA1c	Local	Central	
Oral Glucose Tolerance Test (OGTT)			Central
Hematocrit	Local		
Liver Function Tests (ALT)	Local		
Serum Creatinine/eGFR	Local	Central	
Albumin:Creatinine (urine)			Central
Fasting Lipids			Central
Blood, Urine Samples			Central
Stool Samples			Central
DNA			Central
History (events-medications)	Local		Local
Physical Assessment (BP, Weight)	Local		Local
Height			Local
Waist and Hip Circumference			Local
Peripheral Neuropathy			Local
Study Drug Adherence		Local	Local
ECG			Local (read centrally)
Cognitive Battery			Local (read centrally)
QOL Assessments (SF-36, QWB, Treatment Satisfaction)			Local

Supplemental Table 2. Physical and laboratory measurements of GRADE cohort by age group: <45, 45 to <55, 55 to <65, 65 years and older.

	<45	45-<55	55-<65	65+	P
N total	623	1,436	1,778	1,210	
<b>Measurements of Adiposity</b>					
Weight (kg)	104.2±26.1	102.1±23.5	99.7±21.6	95.6±18.8	<0.001
BMI (kg/m <sup>2</sup> )	36.2±8.0	35.2±7.2	34.1±6.4	32.5±5.5	<0.001
BMI (kg/m <sup>2</sup> )					<0.001
<18.5	0 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)	
18.5-<25.0	24 (3.9%)	49 (3.4%)	71 (4.0%)	78 (6.5%)	
25.0-<30.0	115 (18.5%)	303 (21.1%)	445 (25.1%)	360 (29.8%)	
30.0+(obese)	483 (77.7%)	1,084 (75.5%)	1,255 (70.8%)	770 (63.7%)	
Waist Circumference (cm)	113.4±18.1	112.4±16.1	112.4±15.5h	111.7±14.5	0.170
Hip Circumference (cm)	115.1±16.0	114.2±14.9	113.8±14.2	110.7±12.4	<0.001
Waist hip ratio	0.986±0.084	0.985±0.079	0.989±0.085	1.010±0.083	<0.001
<b>Blood Pressure</b>					
Systolic BP (mmHg)	124.4±12.8	127.1±14.1	129.6±15.4	130.0±15.0	<0.001
Systolic BP					<0.001
<120	241 (38.7%)	437 (30.5%)	473 (26.6%)	298 (24.6%)	
120-<140	305 (49.0%)	736 (51.3%)	873 (49.1%)	600 (49.6%)	
140+	77 (12.4%)	262 (18.3%)	431 (24.3%)	312 (25.8%)	
Diastolic BP (mmHg)	78.9±9.4	79.2±9.8	77.4±9.8	74.0±9.3	<0.001
Diastolic BP					<0.001
<80	339 (54.4%)	756 (52.7%)	1,057 (59.5%)	891 (73.6%)	
80-<90	199 (31.9%)	480 (33.4%)	556 (31.3%)	271 (22.4%)	
90+	85 (13.6%)	199 (13.9%)	164 (9.2%)	48 (4.0%)	
Optimal BP (<140 SBP and < 90 DPB)	503 (80.7%)	1104 (77.0%)	1310 (73.7%)	883 (73.0%)	<0.001
<b>Measurements of Glycemia</b>					
HbA1c at baseline (%)	7.6±0.5	7.5±0.5	7.5±0.5	7.4±0.5	<0.001
HbA1c at baseline (mmol/mol)	59.1±5.4	58.9±5.4	58.1±5.2	57.8±5.1	<0.001

### Lipids and Cardiovascular Risk Measures

Total Cholesterol (mg/dL)	171.1±36.0	169.2±38.3	163.1±38.2	154.6±35.3	<0.001
HDL (mg/dL)	41.2±9.3	42.9±10.4	44.3±10.9	43.8±10.6	<0.001
LDL (mg/dL)	97.6±30.2	95.3±32.3	89.9±31.8	82.5±29.6	<0.001
LDL < 100 mg/dL	328 (56.3%)	784 (57.6%)	1,148 (66.6%)	891 (75.6%)	<0.001
Triglycerides (mg/dL)	174.8±157.1, 134.0 [92.0, 197.8]	160.9±122.8, 127.0 [87.0, 195.5]	147.9±122.3, 122.0 [86.0, 178.0]	143.9±93.0, 124.0 [88.0, 172.0]	<0.001
hs-CRP* (mg/dL)	5.8±6.9, 3.8 [1.8, 8.0]	5.1±8.1, 3.2 [1.6, 6.2]	4.3±6.3, 2.3 [1.2, 4.8]	3.5±5.3, 2.1 [1.0, 4.2]	<0.001
ASCVD Score	4.2±4.5, 2.5 [1.3, 5.5]	9.0±7.1, 7.0 [3.9, 11.7]	16.9±9.2, 15.2 [10.1, 22.1]	32.3±11.8, 31.4 [23.8, 39.5]	<0.001
Framingham score†	8.8±5.9	16.8±10.2	25.5±13.6	36.6±15.6	<0.001

### Measures of Kidney Function

eGFR (mL/min/1.73m <sup>2</sup> )	113.5±12.4	101.2±14.0	91.9±13.9	82.1±13.6	<0.001
Serum creatinine (mg/dL)	0.7±0.2	0.8±0.2	0.8±0.2	0.9±0.2	<0.001
ACR (mg/g)	34.0±145.7, 7.0 [3.3, 18.3]	30.3±175.8, 5.7 [2.9, 14.8]	29.5±107.7, 6.0 [3.0, 16.2]	34.4±128.1, 7.5 [3.4, 20.4]	0.749
ACR (mg/g)					0.472
<30	526 (84.6%)	1216 (84.9%)	1505 (84.7%)	993 (82.1%)	
30-<300	83 (13.3%)	197 (13.8%)	243 (13.7%)	193 (16.0%)	
300+	13 (2.1%)	19 (1.3%)	28 (1.6%)	24 (2.0%)	
CKD Stage					<0.001
1	525 (84.4%)	1,209 (84.5%)	1,478 (83.3%)	934 (77.2%)	
2	84 (13.5%)	202 (14.1%)	266 (15.0%)	233 (19.3%)	
3	13 (2.1%)	19 (1.3%)	31 (1.7%)	41 (3.4%)	
4	0 (0.0%)	1 (0.1%)	0 (0.0%)	2 (0.2%)	
CKD Score	1.2±0.4	1.2±0.4	1.2±0.4	1.3±0.5	<0.001

### Other Measures

SF36 physical function domain score (%)	82.7±23.1	78.2±25.4	74.7±25.4	72.9±23.7	<0.001
MNSI score	1.4±1.8	1.7±1.9	1.8±1.9	1.9±2.0	<0.001

Cell counts and column percentages for categorical variables. Mean ± SD (and median, interquartile ranges for skewed variables) for continuous variables. Pearson's Chi-squared test and ANOVA Type III F test p-values for categorical and continuous variables, respectively. †We calculated the Framingham General Cardiovascular Risk Score for estimating the 10-year cardiovascular risk. The score is derived from a sex specific Cox proportional hazards model with the following covariates: age (years), total cholesterol (mg/dL), HDL cholesterol (mg/dL), systolic blood pressure (mmHg), antihypertensive medication use, current smoking, and diabetes status. \*hs-CRP results are reported for n=1736 participants.

## GRADE Research Group (April 30, 2021)

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