

ONLINE SUPPLEMENT

METHODS

Risk Factor Assessment and Definition

The methods of risk factor measurement in the Framingham Heart Study have been previously described.¹ At each examination, participants underwent a routine physical examination including height and weight measurements, medical history interview, and laboratory tests. Body mass index (BMI) was defined as weight (kilograms) divided by the square of height (meters). An individual was considered to be a current smoker if they reported smoking ≥ 1 cigarette per day on average for the past year.

Hypertension was defined as a systolic blood pressure (SBP) of ≥ 140 mm Hg or diastolic blood pressure (DBP) of ≥ 90 mm Hg or treatment with an antihypertensive medication. If a participant had diabetes, hypertension was defined as a SBP of ≥ 130 mm Hg or DBP of ≥ 80 mm Hg or treatment with an antihypertensive medication.² The proportion of individuals treated for hypertension was calculated by dividing the number of participants receiving antihypertensive medication by the total number of individuals with hypertension. The proportion of individuals with controlled hypertension was calculated by dividing the number of participants with SBP $< 140/90$ mm Hg ($< 130/80$ mm Hg for individuals with diabetes²) by the total number of individuals with hypertension.

Total and low-density lipoprotein (LDL) cholesterol were measured after an overnight fast. Elevated LDL was defined as ≥ 130 mg/dL among those without diabetes and ≥ 100 mg/dL among those with diabetes or treatment with a lipid lowering medication. The proportion of individuals treated for high LDL cholesterol was calculated by dividing the number of participants receiving lipid lowering medication by the total number of individuals with high LDL. The proportion of individuals with controlled LDL levels was calculated by dividing the number of participants with LDL < 130 mg/dL (< 100 mg/dL for individuals with diabetes²) by the total number of individuals with high LDL cholesterol.

Diabetes Status Assessment

Participants were diagnosed as having type 2 diabetes if they had a fasting plasma glucose level of ≥ 126 mg/dL (Offspring and Third Generation cohorts), a casual plasma glucose level of ≥ 200 mg/dL (Original cohort) or if they reported treatment with insulin or an oral hypoglycemic agent. Participants with type I diabetes, as determined by chart review, were excluded from the analysis.

REFERENCES

- (1) Cupples LA, D'Agostino RB, Sr. Section 34. Some risk factors related to the annual incidence of cardiovascular disease and death in pooled repeated biennial measurements: Framingham Heart Study, 30-year follow-up (NIH publication no. 87-2703.). In: Kannel WB, Wolf PA, Garrison RJ, editors. *The Framingham Study: an epidemiological investigation of cardiovascular disease*. National Heart, Lung, and Blood Institute, 1987.
- (2) Standards of medical care in diabetes--2008. *Diabetes Care* 2008;31 Suppl 1:S12-S54.

Online Supplemental Table 1. Change in cardiovascular risk factor levels per decade among participants with and without diabetes in the Framingham Heart Study (1970-2005), after adjustment for sex and body mass index.

Risk Factor	No Diabetes		Diabetes	
	Beta* (SE)	P-value	Beta* (SE)	P-value
Age 50				
Total Cholesterol, mg/dL	-7.59 (0.58)	<0.001	-15.8 (3.58)	<0.001
LDL Cholesterol, mg/dL	-7.72 (0.53)	<0.001	-14.7 (3.26)	<0.001
Systolic Blood Pressure, mm Hg	-3.70 (0.24)	<0.001	-4.88 (1.38)	<0.001
Diastolic Blood Pressure, mm Hg	-2.51 (0.14)	<0.001	-3.47 (0.75)	<0.001
Age 60				
Total Cholesterol, mg/dL	-9.94 (0.79)	<0.001	-14.1 (2.91)	<0.001
LDL Cholesterol, mg/dL	-10.1 (0.71)	<0.001	-14.0 (2.56)	<0.001
Systolic Blood Pressure, mm Hg	-4.68 (0.31)	<0.001	-5.91 (1.13)	<0.001
Diastolic Blood Pressure, mm Hg	-3.03 (0.16)	<0.001	-3.01 (0.63)	<0.001

Abbreviations: SE, standard error

^aSample size is 4,195 (3,990 non-DM, 205 DM) for age 50 analysis and 3,495 (3,178 non-DM, 317 DM) for age 60 analysis.

^bAll beta coefficients are adjusted for sex and body mass index (kg/m²).

* Beta represents the change in risk factor level per 10 years.

Online Supplemental Table 2. Difference in cardiovascular risk factor levels per decade among participants with and without diabetes in the Framingham Heart Study, among individuals free of prevalent CVD.

Risk Factor	No Diabetes		Diabetes		P-value for interaction**
	Beta* (SE)	P-value	Beta* (SE)	P-value	
Age 50					
Body mass index, kg/m ²	0.38 (0.07)	<0.001	2.47 (0.45)	<0.001	<0.001
Total cholesterol, mg/dL	-7.24 (0.58)	<0.001	-16.6 (3.23)	<0.001	0.001
LDL cholesterol, mg/dL	-7.23 (0.54)	<0.001	-14.2 (2.89)	<0.001	0.009
Systolic blood pressure, mm Hg	-3.37 (0.25)	<0.001	-3.66 (1.33)	0.007	0.89
Diastolic blood pressure, mm Hg	-2.28 (0.15)	<0.001	-2.58 (0.73)	<0.001	0.70
Age 60					
Body mass index, kg/m ²	0.57 (0.08)	<0.001	1.53 (0.36)	<0.001	0.002
Total cholesterol, mg/dL	-9.78 (0.79)	<0.001	-14.4 (2.85)	<0.001	0.08
LDL cholesterol, mg/dL	-10.1 (0.71)	<0.001	-14.0 (2.50)	<0.001	0.10
Systolic blood pressure, mm Hg	-4.07 (0.32)	<0.001	-6.06 (1.17)	<0.001	0.04
Diastolic blood pressure, mm Hg	-2.71 (0.17)	<0.001	-2.72 (0.64)	<0.001	0.64

Abbreviations: SE, standard error

^aSample size is 4,094 (3,897 non-DM, 197 DM) for age 50 analysis and 3,264 (2,995 non-DM, 269 DM) for age 60 analysis.

^bAll beta coefficients are adjusted for sex.

* Beta represents the change in risk factor level per 10 years.

**P-value for diabetes by calendar year interaction.