

SUPPLEMENTARY DATA

Supplementary Table 1. Characteristics of all the EDC participants at the 18-year Clinical Exam Compared to the Subsample Participating in the Skin Intrinsic Fluorescence (SIF) Substudy, %, mean, or median (IQR).

Characteristics	Total population participating in 18-year follow-up	SIF substudy population at 18-year follow-up	18-year follow-up participants not in SIF substudy	p-value*
Age (years)	45.0 (7.5)	46.5 (7.0)	44.2 (7.6)	0.01
Duration (years)	36.8 (7.1)	37.5 (6.9)	36.5 (7.2)	0.24
Sex (female)	51.5	54.9	50.0	0.40
Race (White)	98.4	97.1	99.0	0.20
HbA1c (%)	7.9 (1.7)	7.6 (1.5)	8.0 (1.8)	0.03
Updated mean HbA1c (%)	8.7 (1.1)	8.4 (1.0)	8.6 (1.1)	0.04
BMI (kg/m <sup>2</sup> )	27.1 (4.5)	26.1 (4.4)	27.6 (4.5)	0.006
Serum creatinine (mg/dL)**	1.0 (0.90-1.2)	1.0 (0.90-1.1)	1.0 (0.90-1.2)	0.75
HDLc (mg/dL)	58.7 (16.3)	59.9 (17.8)	58.0 (15.5)	0.35
Non-HDLc (mg/dL)	117.0 (36.4)	109.9 (28.4)	120.5 (39.5)	0.008
SBP (mm Hg)	116.8 (16.5)	114.2 (14.4)	118.1 (17.4)	0.04
DBP (mm Hg)	66.3 (10.8)	64.3 (10.4)	67.3 (10.9)	0.02
Hypertension medication use	25.4	18.6	28.8	0.05
ACE medication use	54.1	55.9	53.2	0.65
Autonomic neuropathy	57.7	59.8	56.6	0.59
Confirmed distal symmetrical polyneuropathy	57.7	64.7	54.2	0.08

\*Difference between SIF participants and SIF non-participants at 18-year clinical exam

\*\*Natural logarithmically transformed before analyses

HDLc=high density lipoprotein cholesterol

SBP=systolic blood pressure

DBP=diastolic blood pressure

ACE=angiotensin converting enzyme

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**Supplementary Table 2. Relationship of Skin Intrinsic Fluorescence with the Clinical Characteristics of the EDC Population**

Characteristic	r	OR (95% CI)	p-value
Autonomic neuropathy		3.43 (1.97-5.97)	<0.0001
Confirmed distal symmetrical		3.10 (1.82-5.26)	<0.0001
Age (years)	0.42		<0.0001
Duration (years)	0.37		<0.0001
Sex (female)		1.17 (0.81-1.69)	0.41
Height (m)	-0.16		0.11
Pulse (beats/min)	0.06		0.55
R-R interval*	-0.47		<0.0001
Toe vibratory threshold*	0.50		<0.0001
BMI (kg/m <sup>2</sup> )	-0.07		0.50
HbA1c (%)	0.13		0.19
Updated mean HbA1c (%)	0.26		0.006
Albumin excretion rate (µg/min)*	0.36		0.0003
Serum creatinine (mg/dL)*	0.32		0.0006
Systolic blood pressure (mm Hg)	0.31		0.001
Diastolic blood pressure (mm Hg)	-0.09		0.37
Blood pressure medication use		1.75 (1.06-2.89)	0.03
High density lipoprotein cholesterol (mg/dL)	0.08		0.40
Non-high density lipoprotein cholesterol	-0.08		0.42
ACE medication use		1.53 (1.03-2.29)	0.04
History of smoking	1.58	(1.02-2.46)	0.04

\*Natural logarithmically transformed before analysis.

**Supplementary Table 3. Mean Skin Intrinsic Fluorescence Level (AU)\* by Autonomic Neuropathy and Confirmed Distal Symmetrical Polyneuropathy Status and Time Interval since Last Clinical Exam in the EDC Study**

	Case	Non-case	p-value
<b>Autonomic Neuropathy</b>			
≤Median follow-up time from last visit	0.01	0.008	0.002
> Median follow-up time from last visit	0.009	0.007	0.0002
<b>Confirmed Distal Symmetrical Polyneuropathy</b>			
≤Median follow-up time from last visit	0.01	0.007	0.002
> Median follow-up time from last visit	0.009	0.008	0.0002

AU=arbitrary units \*Natural Logarithmically transformed before analysis

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**Supplementary Table 4. Characteristics of MedStar Study Participants by Distal Symmetrical Polyneuropathy Status**

Characteristics	MedStar (Type 1 Diabetes Participants)		
	cases (n=16)	noncases (n=42)	p-value
Skin intrinsic fluorescence (AU)*	0.0077 (0.0016)	0.0066 (0.0019)	0.07
Age (yrs)	53.6 (12.9)	47.9 (9.3)	0.07
Diabetes duration (yrs)	34.3 (9.7)	26.2 (12.2)	0.02
Sex (female)	43.8 (7)	50.0 (21)	0.67
HbA1c (%)	8.0 (1.1)	7.8 (1.0)	0.62
Updated mean HbA1c (%)	8.1 (0.78)	7.8 (0.99)	0.30
Body mass index (BMI (kg/m <sup>2</sup> ))	26.6 (3.1)	26.4 (4.3)	0.84
Height (cm)	166.3 (14.0)	172.7 (8.6)	0.12
Heart rate (beats/min)	78.6 (7.9)	76.4 (9.3)	0.45
Serum creatinine (mg/dl) *	1.2 (0.71)	0.93 (0.20)	0.25
HDL cholesterol (mg/dl)	64.4 (20.4)	64.7 (19.6)	0.96
Non-HDL cholesterol (mg/dl)*	111.2 (34.1)	107.7 (33.3)	0.66
Systolic blood pressure (mm Hg)	127.1 (19.2)	121.6 (12.8)	0.30
Diastolic blood pressure (m Hg)	71.6 (8.7)	72.4 (9.3)	0.78
Coronary artery disease	6.3 (1)	7.1 (3)	1.00**
Overt nephropathy	26.7 (4)	2.4 (1)	0.02
Proliferative retinopathy	43.8 (7)	11.9 (5)	0.01
Autonomic neuropathy	37.5 (6)	11.9 (5)	0.06
Lower extremity arterial disease	6.3 (1)	0.0 (0)	<0.0001
Hypertension medication use	68.8 (11)	52.4 (22)	0.26
A history of smoking	25.0 (3)	21.2 (7)	0.29

\*Natural logarithmically transformed before analyses. \*\*Fisher's exact test