Online-Only Supplementary Material

Brain Structure among Middle-aged and Older Adults with Longstanding Type 1 Diabetes in the DCCT/EDIC Study

This document presents supplementary materials cited in the text of the main manuscript.

Additional Materials

Supplementary Table S1. Characteristics of all surviving EDIC participants at the time of the MRI study and EDIC participants enrolled in the MRI study (2018-2019)

Supplementary Table S2. MRI outcomes among EDIC participants and controls without diabetes further adjusted for sex, alcohol use, and BMI

Supplementary Table S3. MRI outcomes EDIC participants, by DCCT treatment group assignment

Supplementary Table S4. Association of traditional glycemic and non-glycemic risk factors and micro- and macrovascular complications with MRI outcomes among EDIC participants, adjusted for intracranial volume, age, and scanner (n=416)

Supplementary Table S5. Association of MRI measures with cognitive domains among controls (n=94)

Supplementary Figure S1. Flow chart of participants in the EDIC MRI study.

Supplementary Figure S2. Example images from MRI scans. Cases were selected to better visualize the nature of the findings. T1 axial images from A) a 65 year old male control participant in the top decile for total brain volume and B) a 66 year old male EDIC participant in the bottom decile for total brain volume. There is a difference in ventricular volume as well as subtle enlargement in cerebral sulci in the EDIC participant compared to the control (arrows). Axial FLAIR images from C) a 67 year old male control participant near the median for white matter hyperintensity volume and D) a 67 year old male EDIC participant with high white matter hyperintensity volume (>95th percentile). White matter hyperintensity are seen as areas of white signal intensity most commonly in periventricular regions (arrows). The EDIC participant has enlarged cerebral ventricles compared to the control.

Supplementary Figure S3. Scatterplots of age by A) total brain volume, B) ventricles, and C) white matter hyperintensity for EDIC participants (n=415) vs. controls (n=99). The scatterplots illustrate the partial association of each MRI outcome with age, adjusting for intracranial volume and scanner. Each plot includes a regression line for participants and controls separately. There were no significant age by group (participant vs. control) interactions (p=0.0924, p=0.1132, and p=0.3079, respectively).

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Additional Materials

Evaluations, Risk Factors, and Coexisting Complications

A detailed medical history including demographic factors, medications, and medical outcomes and a physical examination with measurements of height, weight, body mass index (BMI), sitting blood pressure, and pulse rate were obtained [1, 2]. Laboratory studies included fasting lipids, albumin excretion rates (AER), HbA1c measured by high performance liquid chromatography, and, for EDIC participants, serum creatinine. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or having medically documented hypertension or using anti-hypertensive medication. Hyperlipidemia was defined as low-density lipoprotein cholesterol ≥130 mg/dl or lipid-lowering medication use.

Among EDIC participants, severe hypoglycemia was defined as the cumulative number of events leading to coma or seizure within the 3-months prior to each DCCT/EDIC study visit based on self-report. Estimated glomerular filtration rates (eGFR) were calculated from serum creatinine and estimated with the Chronic Kidney Disease Epidemiology Collaboration equation. Kidney disease was defined as an AER ≥30 mg/24 hr on ≥2 consecutive visits or eGFR <60 mL/min/1.73m^2 [3], at any time during the DCCT/EDIC study. Proliferative diabetic retinopathy was defined by neovascularization observed on standardized stereoscopic seven-field fundus photography grading or evidence of scatter photocoagulation, and clinically-significant macular edema was defined using fundus photography grading for evidence of macular thickening or the presence of focal photocoagulation scars, at any time during the DCCT/EDIC study [4]. Neurologic evaluations, nerve conduction studies, and cardiac autonomic testing were conducted periodically [5, 6]. All cardiovascular disease (CVD) events were adjudicated and classified by a committee masked to DCCT treatment group assignment and HbA1c levels [7].

Cognitive Protocol

Psychomotor and mental efficiency was evaluated using Verbal Fluency, Digit Symbol Substitution Test, Trail Making Part B, and the Grooved Pegboard. Immediate memory scores were derived from the Logical Memory subtest of the Wechsler Memory Scale and the Wechsler Digit Symbol Substitution Test. Delayed recall was assessed by recall of Logical Memory stories after a 10 to 15-minute delay.

References

1. EDIC Research Group, *Epidemiology of Diabetes Interventions and Complications (EDIC). Design, implementation, and preliminary results of a long-term follow-up of the Diabetes Control and Complications Trial cohort.* Diabetes Care, 1999. **22**(1): p. 99-111.
2. DCCT Research Group, *Implementation of treatment protocols in the Diabetes Control and Complications Trial.* Diabetes Care, 1995. **18**(3): p. 361-76.
3. Perkins, B.A., et al., *Risk Factors for Kidney Disease in Type 1 Diabetes.* Diabetes Care, 2019. **42**(5): p. 883-890.
4. Hainsworth, D.P., et al., *Risk Factors for Retinopathy in Type 1 Diabetes: The DCCT/EDIC Study.* Diabetes Care, 2019. **42**(5): p. 875-882.
5. Albers, J.W., et al., *Effect of prior intensive insulin treatment during the Diabetes Control and Complications Trial (DCCT) on peripheral neuropathy in type 1 diabetes during the Epidemiology of Diabetes Interventions and Complications (EDIC) Study.* Diabetes Care, 2010. **33**(5): p. 1090-6.
6. Pop-Busui, R., et al., *Effects of prior intensive insulin therapy on cardiac autonomic nervous system function in type 1 diabetes mellitus: the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications study (DCCT/EDIC).* Circulation, 2009. **119**(22): p. 2886-93.
7. DCCT/EDIC Study Research Group, et al., *Intensive diabetes treatment and cardiovascular disease in patients with type 1 diabetes.* N Engl J Med, 2005. **353**(25): p. 2643-53.

Supplementary Table S1. Characteristics of all surviving EDIC participants at the time of the MRI study and EDIC participants enrolled in the MRI study (2018-2019)

	All Surviving EDIC Participants	**EDIC Participants Enrolled in MRI Study**
N	**1,085**	**416**
Demographic		
Age (years)	59.3 ± 6.7	59.6 ± 6.4
Age [median (range)]	59 (43-75)	60 (44-74)
Female sex (%)	47.4	44.2
College graduate (%)	63.0	64.2
Professional or technical occupation (%)	55.3	58.7
Married or remarried (%)	78.6	81.9
Behavioral		
Current cigarette smoker (%)	7.1	8.0
Occasional or regular alcohol use (%)	50.0	53.5
Physical		
Body mass index (kg/m^2)*	27.4 ± 4.1	26.6 ± 3.7
Waist circumference (cm)	96.6 ± 15.3	94.7 ± 13.9
Blood pressure		
Systolic blood pressure (mm Hg)*	119.2 ± 8.2	118.6 ± 8.1
Diastolic blood pressure (mm Hg)*	73.1 ± 5.0	73.0 ± 5.1
Any treated hypertension (%)	87.1	86.5
Pulse rate (bpm)*	71.6 ± 6.8	70.8 ± 6.6
Lipids (mg/dl)		
Total cholesterol*	178.9 ± 23.1	177.9 ± 23.2
Triglycerides*	81.5 ± 39.1	77.5 ± 36.5
HDL cholesterol*	57.0 ± 13.5	57.8 ± 14.2
LDL cholesterol*	105.5 ± 19.6	104.6 ± 19.8
Any treated hyperlipidemia (%)	88.0	86.0
Glycemia		
HbA1c (%)*	7.9 ± 0.9	7.8 ± 0.8

Complications		
Sustained AER ≥30 mg/24 hr (%)‡	31.0	24.0
eGFR <60 mL/min/1.73 m^2 (%)‡	13.5	9.0
PDR (%)‡	26.5	23.3
CSME (%)‡	31.1	27.4
Peripheral neuropathy (%)‡	30.7	28.0
Cardiovascular autonomic neuropathy (%)‡	43.0	39.7
Cardiovascular disease (%)‡	14.1	13.0

Data are mean ± SD or percent.
* Risk factors were characterized by the time-weighted mean values of all follow-up values since DCCT baseline up to the MRI study visit.
† Severe hypoglycemia was defined as the cumulative number of events leading to coma or seizure documented by self-report for the 3-month period prior to each visit.
‡ Any report between DCCT baseline and the MRI study visit.

Supplementary Table S2. MRI outcomes among EDIC participants and controls without diabetes further adjusted for sex, alcohol use, and BMI

	EDIC Participants	Controls	p-value	Cohen's *d*	Equivalent Years of Age
N	**416**	**99**			
Total Brain Volume (cm^3)	1207 ± 1.7	1230 ± 3.5	<0.0001	-0.68	7.4
Gray Matter (cm^3)	647 ± 1.7	660 ± 3.4	0.0004	-0.39	4.8
White Matter (cm^3)	538 ± 1.5	549 ± 2.8	0.0004	-0.36	---
Ventricles (cm^3)	34 ± 0.8	26 ± 1.5	<0.0001	0.51	8.6
Subarachnoid CSF (cm^3)	197 ± 1.6	181 ± 3.3	<0.0001	0.48	6.9
White Matter Hyperintensity (cm^3)*	2.66 ± 0.17	2.16 ± 0.28			
White Matter Hyperintensity asinh (cm^3)*	1.37 ± 0.04	1.04 ± 0.08	0.0003	0.45	8.1
White Matter Mean FA†	0.409 ± 0.001	0.413 ± 0.002	0.0829	-0.19	5.9

Data are least square means ± standard errors from linear mixed models with adjustment for intracranial volume, age, scanner, sex, alcohol use, and BMI. Cohen's *d* effect size was calculated by taking the difference in means between EDIC participants and controls and dividing by the pooled standard deviation. We estimated the additional number of years of age that would yield the same difference in each MRI outcome as the difference between controls without diabetes and the T1DM participants by taking the ratio of the beta coefficient estimate for subject group (1= participant, 0=control) to that for age from a linear mixed model including both factors. The equivalent years of aging is not presented for WM volume since age was not a significant factor in the model.

* White matter hyperintensity was assessed in N=381 EDIC participants and N=82 controls; an inverse hyperbolic sine transformation was used to normalize the distribution (asinh).

† White matter mean FA was assessed in N=363 EDIC participants and N=80 controls and was not adjusted for intracranial volume.

Supplementary Table S3. MRI outcomes EDIC participants, by DCCT treatment group assignment

	Intensive	**Conventional**	**p-value**
N	**214**	**202**	
Total Brain Volume (cm^3)	1207 ± 2.5	1210 ± 2.5	0.4103
Gray Matter (cm^3)	648 ± 2.4	650 ± 2.5	0.5518
White Matter (cm^3)	538 ± 2.1	539 ± 2.1	0.7208
Ventricles (cm^3)	34 ± 1.1	34 ± 1.1	0.9120
Subarachnoid CSF (cm^3)	199 ± 2.3	196 ± 2.4	0.3544
White Matter Hyperintensity (cm^3)*	3.01 ± 0.25	2.41 ± 0.25	
White Matter Hyperintensity asinh (cm^3)*	1.43 ± 0.05	1.32 ± 0.05	0.1570
White Matter Mean FA†	0.410 ± 0.002	0.409 ± 0.002	0.7727

Data are least square means ± standard errors from analysis of covariance models with adjustment for intracranial volume, age, and scanner.
* White matter hyperintensity was assessed in N=381 participants (196 intensive and 185 conventional); an inverse hyperbolic sine transformation was used to normalize the distribution (asinh).
† White matter mean FA was assessed in N=363 participants (186 intensive and 177 conventional) and was not adjusted for intracranial volume.

Supplementary Table S4. Association of traditional glycemic and non-glycemic risk factors and micro- and macrovascular complications with MRI outcomes among EDIC participants, adjusted for intracranial volume, age, and scanner (n=416)

	Total Brain Volume (cm^3)				**Gray Matter (cm^3)**				**Ventricles (cm^3)**			
	β	**SE**	**t**	**p-value**	**β**	**SE**	**t**	**p-value**	**β**	**SE**	**t**	**p-value**
Demographic Characteristics												
Sex (men vs. women)	-1.96	4.76	-0.41	0.6802	7.18	4.60	1.56	0.1193	0.75	2.09	0.36	0.7203
Education (per 1 year)	1.02	0.96	1.06	0.2881	1.09	0.93	1.18	0.2406	1.08	0.42	2.58	0.0101
Risk Factors												
Glycemic												
HbA1c (per 1 %)*	-1.80	2.12	-0.85	0.3964	-2.43	2.05	-1.18	0.2372	1.13	0.93	1.21	0.2253
Severe hypoglycemia												
Cumulative (≥1 vs. 0 events)†	-4.04	3.57	-1.13	0.2584	0.16	3.47	0.05	0.9625	-1.69	1.57	-1.08	0.2812
1-5 vs. 0 events	-3.10	3.83	-0.81	0.4184	0.84	3.72	0.22	0.8223	-1.86	1.68	-1.11	0.2678
>5 vs. 0 events	-7.71	6.42	-1.20	0.2305	-2.45	6.24	-0.39	0.6941	-1.02	2.82	-0.36	0.7186
Non-glycemic												
Body mass index (per 1 kg/m^2)*	1.13	0.48	2.33	0.0202	0.84	0.47	1.79	0.0745	-0.05	0.21	-0.22	0.8255
Waist circumference (per 5 cm)	0.81	0.67	1.20	0.2304	1.00	0.65	1.55	0.1225	-0.22	0.30	-0.76	0.4503
Blood pressure (per 5 mm Hg)*												
Systolic	-1.93	1.13	-1.71	0.0876	-1.46	1.09	-1.33	0.1835	1.22	0.49	2.47	0.0138
Diastolic	-3.43	1.80	-1.91	0.0571	-3.39	1.74	-1.95	0.0519	1.42	0.79	1.80	0.0729
Any treated hypertension (yes vs. no)	-6.90	5.27	-1.31	0.1909	-7.65	5.10	-1.50	0.1341	2.79	2.31	1.21	0.2274
Pulse rate (per 1 bpm)*	-0.21	0.28	-0.76	0.4487	0.42	0.27	1.57	0.1179	0.20	0.12	1.67	0.0960

Plasma lipids*												
HDL/LDL ratio (per 0.1)	-2.03	0.90	-2.24	0.0253	-1.39	0.87	-1.59	0.1122	0.44	0.40	1.09	0.2774
Triglycerides (log)	2.94	4.71	0.62	0.5325	5.52	4.53	1.22	0.2234	0.79	2.08	0.38	0.7038
Any treated hyperlipidemia (yes vs. no)	7.82	5.17	1.51	0.1311	3.11	5.02	0.62	0.5356	0.89	2.27	0.39	0.6961
Complications												
Kidney Disease												
Sustained AER ≥30 mg/24 hr (yes vs. no)‡	-0.82	4.21	-0.19	0.8463	4.20	4.04	1.04	0.2995	1.46	1.85	0.79	0.4297
eGFR <60 mL/min/1.73 m^2 (yes vs. no)‡	-3.28	6.27	-0.52	0.6013	-8.73	6.03	-1.45	0.1489	4.77	2.74	1.74	0.0824
Retinopathy												
PDR (yes vs. no)‡	0.83	4.18	0.20	0.8420	3.03	4.05	0.75	0.4544	5.22	1.82	2.87	0.0044
CSME (yes vs. no)‡	1.98	3.98	0.50	0.6190	3.74	3.85	0.97	0.3326	2.86	1.74	1.64	0.1019
Neuropathy												
Peripheral neuropathy (yes vs. no)‡	-2.62	4.00	-0.66	0.5121	8.74	3.85	2.27	0.0237	3.08	1.75	1.76	0.0793
Cardiovascular autonomic neuropathy (yes vs. no)‡	-3.36	3.69	-0.91	0.3632	-2.88	3.57	-0.81	0.4206	2.81	1.62	1.74	0.0832
Cardiovascular												
Cardiovascular disease (yes vs. no)‡	2.96	5.31	0.56	0.5767	-3.78	5.14	-0.74	0.4618	0.87	2.33	0.37	0.7101

Data are beta coefficients, standard errors, t-values, and p-values from individual linear regression models evaluating the association of each covariate of interest (independent) with each MRI outcome (dependent), with adjustment for intracranial volume, age, and scanner. Beta estimates are equal to the difference in means between groups or the slope of the association (e.g. increase or decrease in MRI outcome for every unit change in the covariate). The signed t-value corresponds to the magnitude and directionality of the association. HDL denotes high-density lipoprotein, LDL low-density lipoprotein, AER albumin excretion rate, eGFR estimated glomerular filtration, PDR proliferative diabetic retinopathy, and CSME clinically-significant macular edema.

* Risk factors were characterized by the time-weighted mean values of all follow-up values since DCCT baseline up to the MRI study visit.

† Severe hypoglycemia was defined as events leading to coma or seizure documented by self-report for the 3-month period prior to each visit.

‡ Any report between DCCT baseline and the MRI study visit.

Supplementary Table S4 (continued). Association of traditional glycemic and non-glycemic risk factors and micro- and macrovascular complications with MRI outcomes among EDIC participants, adjusted for intracranial volume, age, and scanner (n=416)

	White Matter Hyperintensity asinh (cm^3)				**White Matter Mean FA**			
	β	**SE**	**t**	**p-value**	**β**	**SE**	**t**	**p-value**
Demographic Characteristics								
Sex (men vs. women)	-0.06	0.10	-0.59	0.5523	0.003	0.002	1.03	0.3017
Education (per 1 year)	-0.01	0.02	-0.37	0.7105	0.001	0.001	1.51	0.1313
Risk Factors								
Glycemic								
HbA1c (per 1 %)*	0.03	0.05	0.76	0.4459	-0.003	0.001	-2.01	0.0456
Severe hypoglycemia								
Cumulative (≥1 vs. 0 events)†	0.05	0.08	0.63	0.5310	0.001	0.002	0.54	0.5879
1-5 vs. 0 events	0.05	0.08	0.62	0.5340	0.003	0.003	0.95	0.3417
>5 vs. 0 events	0.04	0.14	0.26	0.7932	-0.003	0.004	-0.67	0.5007
Non-glycemic								
Body mass index (per 1 kg/m^2)*	0.00	0.01	-0.10	0.9167	0.000	0.000	-0.76	0.4468
Waist circumference (per 5 cm)	-0.02	0.01	-1.12	0.2648	0.000	0.000	-0.46	0.6485
Blood pressure (per 5 mm Hg)*								
Systolic	0.06	0.02	2.51	0.0124	-0.002	0.001	-2.74	0.0064
Diastolic	0.09	0.04	2.32	0.0207	-0.002	0.001	-1.85	0.0648
Any treated hypertension (yes vs. no)	0.06	0.11	0.51	0.6136	-0.001	0.004	-0.15	0.8824
Pulse rate (per 1 bpm)*	0.01	0.01	1.53	0.1277	0.000	0.000	-0.73	0.4678

Plasma lipids*								
HDL/LDL ratio (per 0.1)	0.02	0.02	1.10	0.2703	-0.001	0.001	-1.00	0.3190
Triglycerides (log)	-0.11	0.10	-1.11	0.2691	0.004	0.003	1.36	0.1759
Any treated hyperlipidemia (yes vs. no)	0.11	0.11	1.02	0.3102	0.000	0.004	-0.08	0.9392
Complications								
Kidney Disease								
Sustained AER ≥30 mg/24 hr (yes vs. no)‡	0.07	0.09	0.81	0.4209	-0.006	0.003	-2.06	0.0399
eGFR <60 mL/min/1.73 m^2 (yes vs. no)‡	0.01	0.14	0.04	0.9670	-0.009	0.004	-2.10	0.0362
Retinopathy								
PDR (yes vs. no)‡	0.22	0.09	2.48	0.0137	0.000	0.003	-0.08	0.9367
CSME (yes vs. no)‡	0.08	0.09	0.91	0.3635	-0.004	0.003	-1.59	0.1124
Neuropathy								
Peripheral neuropathy (yes vs. no)‡	0.11	0.09	1.25	0.2135	0.001	0.003	0.53	0.5985
Cardiovascular autonomic neuropathy (yes vs. no)‡	0.10	0.08	1.22	0.2249	-0.001	0.003	-0.57	0.5720
Cardiovascular								
Cardiovascular disease (yes vs. no)‡	-0.13	0.12	-1.10	0.2715	-0.005	0.004	-1.49	0.1384

Data are beta coefficients, standard errors, t-values, and p-values from individual linear regression models evaluating the association of each covariate of interest (independent) with each MRI outcome (dependent), with adjustment for intracranial volume, age, and scanner. Beta estimates are equal to the difference in means between groups or the slope of the association (e.g. increase or decrease in MRI outcome for every unit change in the covariate). The signed t-value corresponds to the magnitude and directionality of the association. White matter hyperintensity was assessed in N=381 EDIC participants; an inverse hyperbolic sine transformation was used to normalize the distribution (asinh). White matter mean FA was assessed in N=363 participants and was not adjusted for intracranial volume. HDL denotes high-density lipoprotein, LDL low-density lipoprotein, AER albumin excretion rate, eGFR estimated glomerular filtration, PDR proliferative diabetic retinopathy, and CSME clinically-significant macular edema.

* Risk factors were characterized by the time-weighted mean values of all follow-up values since DCCT baseline up to the MRI study visit.

† Severe hypoglycemia was defined as events leading to coma or seizure documented by self-report for the 3-month period prior to each visit.

‡ Any report between DCCT baseline and the MRI study visit.

Supplementary Table S5. Association of MRI measures with cognitive domains among controls (n=94)

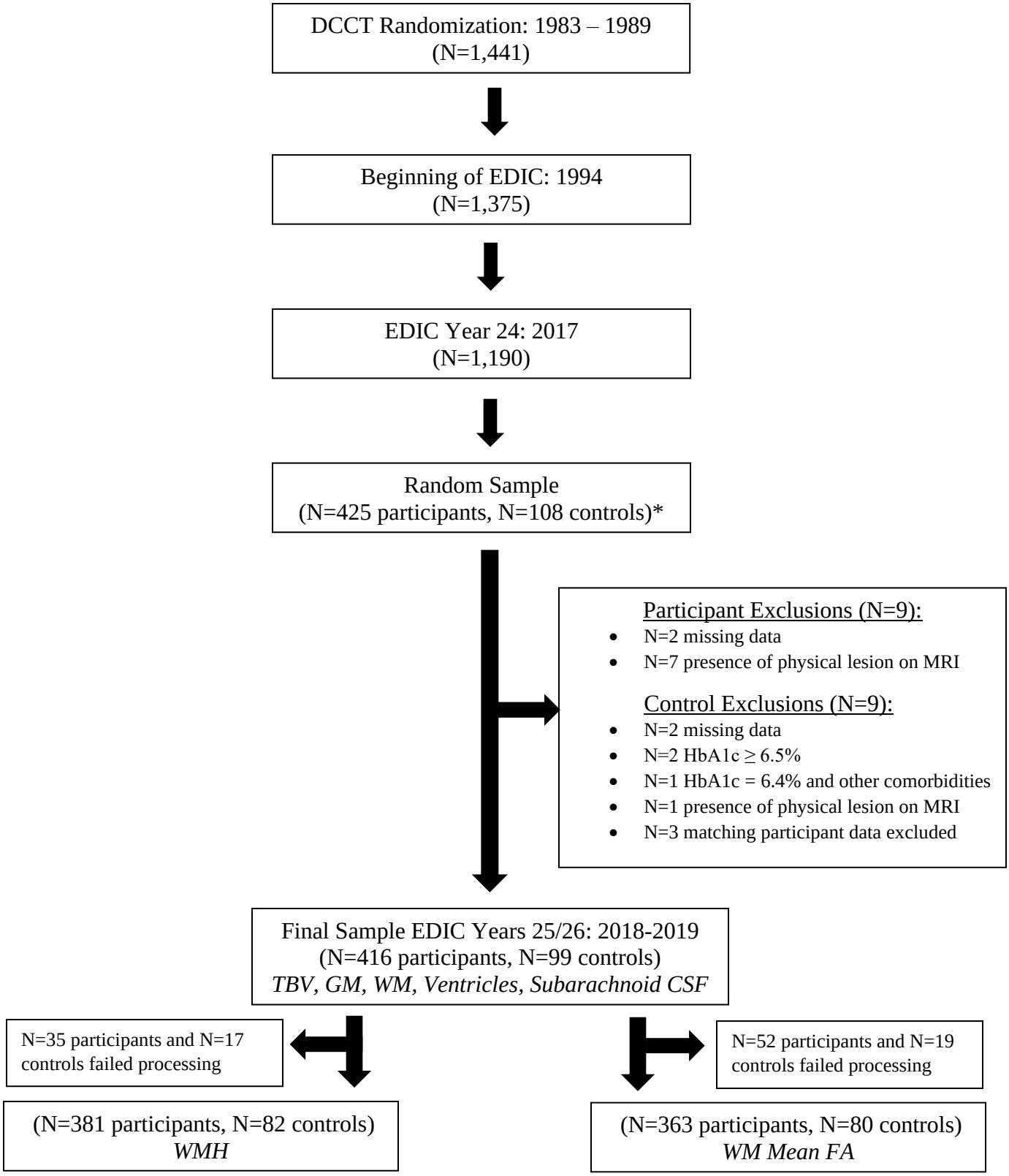
	Immediate Memory				Delayed Recall				Psychomotor and Mental Efficiency			
	β	**SE**	**t**	**p-value**	**β**	**SE**	**t**	**p-value**	**β**	**SE**	**t**	**p-value**
Total Brain Volume (per 10 cm^3)	0.031	0.039	0.80	0.4274	0.033	0.041	0.80	0.4251	0.002	0.003	0.55	0.5824
Gray Matter (per 10 cm^3)	0.028	0.038	0.74	0.4600	0.038	0.039	0.96	0.3396	-0.002	0.003	-0.57	0.5717
White Matter (per 10 cm^3)	0.005	0.041	0.11	0.9108	-0.006	0.043	-0.13	0.8950	0.004	0.003	1.31	0.1943
Ventricles (per 10 cm^3)	0.167	0.112	1.50	0.1376	0.168	0.117	1.43	0.1554	0.007	0.009	0.79	0.4346
Subarachnoid CSF (per 10 cm^3)	-0.056	0.041	-1.38	0.1720	-0.058	0.043	-1.36	0.1782	-0.003	0.003	-0.86	0.3936
Hippocampus (per 1 cm^3)	-0.036	0.176	-0.20	0.8401	-0.013	0.184	-0.07	0.9458	-0.037	0.147	-0.25	0.8038
White Matter Hyperintensity asinh (per 1 cm^3)*	-0.048	0.187	-0.26	0.7987	-0.064	0.189	-0.34	0.7354	-0.243	0.146	-1.67	0.0991
White Matter Mean FA (per 0.01 unit)†	-0.026	0.056	-0.47	0.6415	0.033	0.059	0.56	0.5769	-0.049	0.046	-1.06	0.2948

Data are beta coefficients, standard errors, t-values, and p-values from individual linear regression models evaluating the association of each MRI measure (independent) with each cognitive domain (dependent), with adjustment for intracranial volume, age, sex, years of education, and scanner. Beta estimates are equal to the slope of the association (e.g. increase or decrease in cognitive domain for every unit change in the covariate). The signed t-value corresponds to the magnitude and directionality of the association.

* White matter hyperintensity was assessed in N=78 controls; an inverse hyperbolic sine transformation was used to normalize the distribution (asinh).

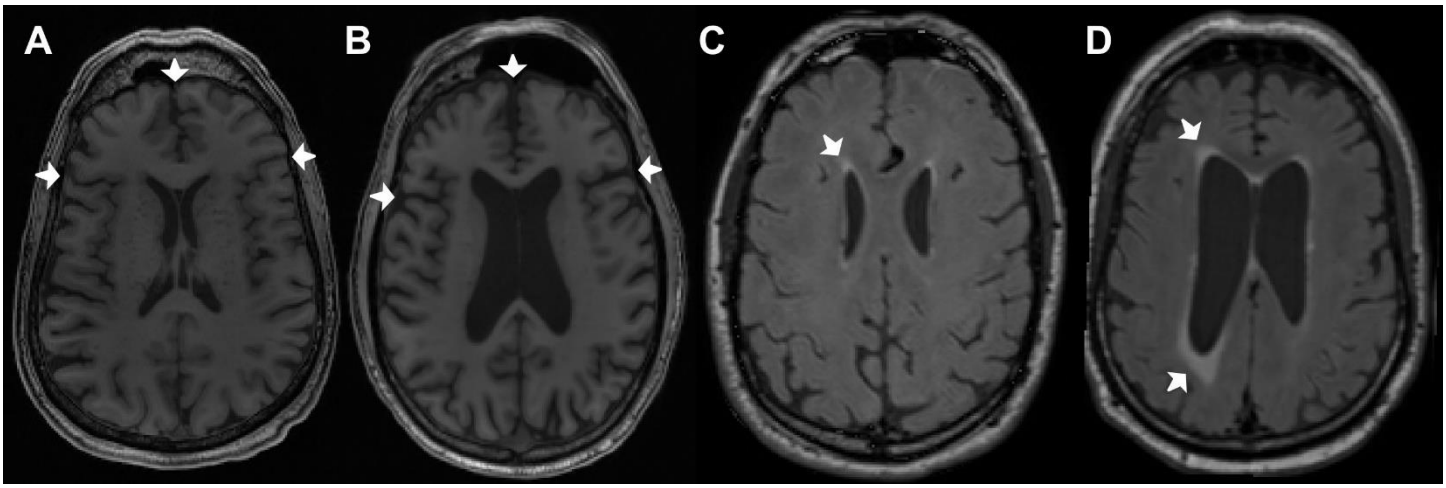
† White matter mean FA was assessed in N=79 controls and was not adjusted for intracranial volume.

Supplementary Figure S1.

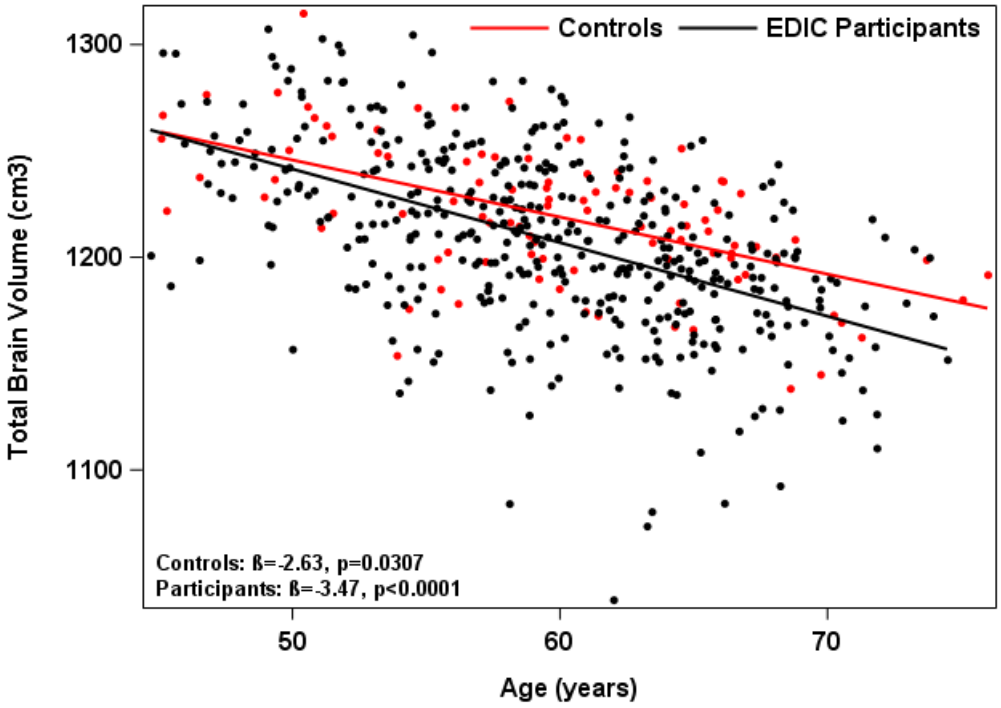


*Randomly selected replacement participants were sampled as needed due to participant ineligibility.

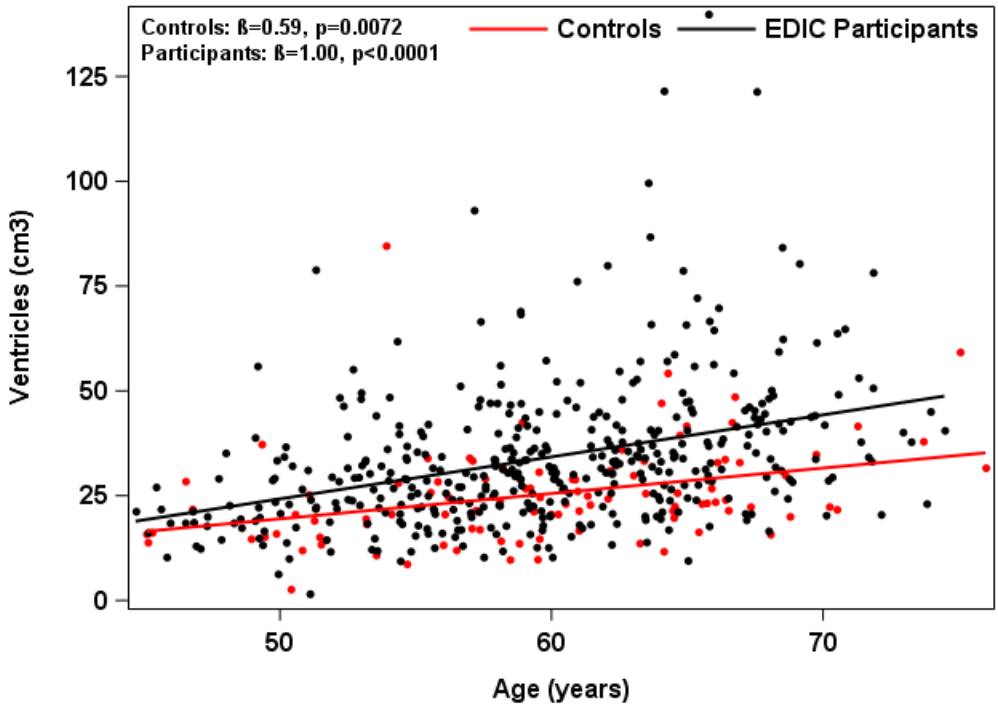
Supplementary Figure S2.



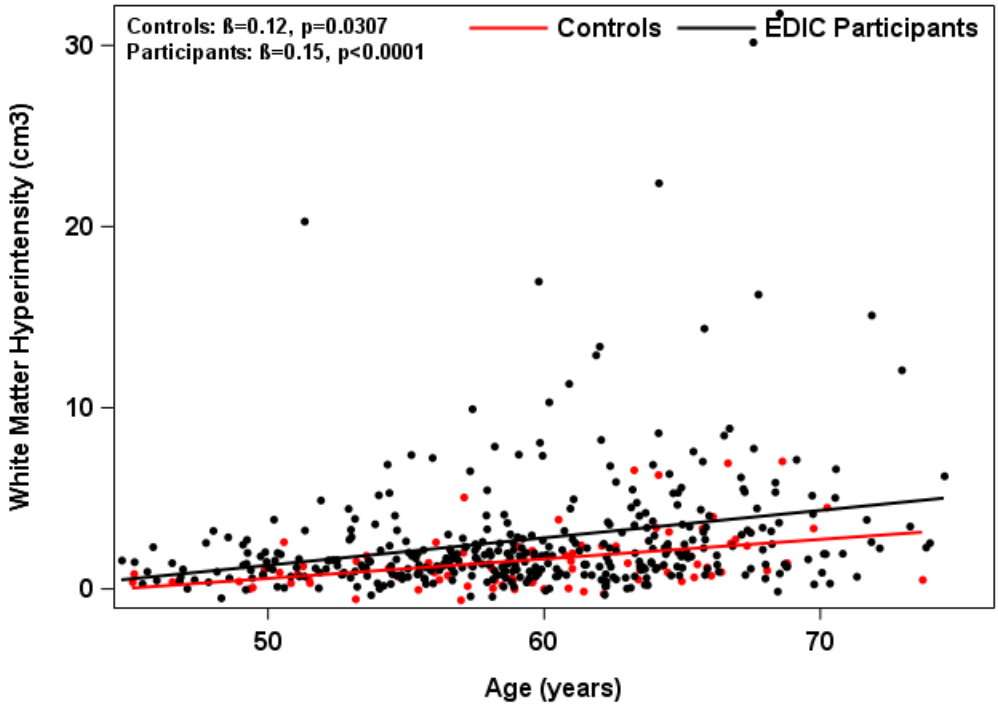
Supplementary Figure S3.



A)



B)


Controls: ß=0.12, p=0.0307
Participants: ß=0.15, p<0.0001
Controls
EDIC Participants
White Matter Hyperintensity (cm3)
30
20
10
0
50
60
70
Age (years)

C)

DCCT/EDIC Research Group

Study Chairpersons – D.M. Nathan (chair), B. Zinman (vice-chair); *Past*: O. Crofford; *Deceased*: S. Genuth

Editor, EDIC Publications – D.M. Nathan

Clinical Centers

Case Western Reserve University – *Current*: R. Gubitosi-Klug, L. Mayer, J. Wood, D. Miller, A. Nayate, M. Novak, S. Pendegast, L. Singerman, D. Weiss, H. Zegarra; *Past*: E. Brown, P. Crawford, M. Palmert, P. Pugsley, J. Quin, S. Smith-Brewer; *Deceased*: W. Dahms, S. Genuth, J. McConnell

Weill Cornell Medical College – *Current*: N.S. Gregory, R. Hanna, R. Chan, S. Kiss, A. Orlin, M. Rubin; *Past*: S. Barron, B. Bosco, D. Brillon, S. Chang, A. Dwoskin, M. Heinemann, L. Jovanovic, M.E. Lackaye, T. Lee, B. Levy, V. Reppucci, M. Richardson; *Deceased*: R. Campbell

Henry Ford Health System – *Current*: A. Bhan, J.K. Jones, D. Kruger, P.A. Edwards, H. Remtema; *Past*: E. Angus, A. Galprin, M. McLellan, A. Thomas; *Deceased*: J.D. Carey, F. Whitehouse

International Diabetes Center – *Current*: R. Bergenstal, S. Dunnigan, M. Johnson, A. Carlson, ; *Past*: R. Birk, P. Callahan, G. Castle, R. Cuddihy, M. Franz, D. Freking, L. Gill, J. Gott, K. Gunyou, P. Hollander, D. Kendall, J. Laechelt, S. List, G. Matfin, W. Mestrezat, J. Nelson, B. Olson, N. Rude, M. Spencer, L. Thomas; *Deceased*: D. Etzwiler, K. Morgan

Joslin Diabetes Center – *Current*: L.P. Aiello, E. Golden, P. Arrigg, R. Beaser, L. Bestourous, J. Cavallerano, R. Cavicchi, O. Ganda, O. Hamdy, T. Murtha, D. Schlossman, S. Shah, G. Sharuk, P. Silva, P. Silver, M. Stockman, J. Sun, E. Weimann; *Past*: V. Asuquo, A. Jacobson, R. Kirby, L. Rand, J. Rosenzwieg, H. Wolpert

Massachusetts General Hospital – *Current*: D.M. Nathan, M.E. Larkin, M. Cayford, A. deManbey, L . Gurry, J. Heier, A. Joseph, F. Leandre, K. Martin, C. Shah, C. Stevens, N. Thangthaeng; *Past*: E. Anderson, H. Bode, S. Brink, M. Christofi, C. Cornish, D. Cros, S. Crowell, L. Delahanty, K. Folino, S. Fritz, C. Gauthier-Kelly, J. Godine, C. Haggan, K. Hansen, P. Lou, J. Lynch, C. McKitrick, D. Moore, D. Norman, M. Ong, E. Ryan, C. Taylor, D. Zimbler

Mayo Clinic – *Current*: A. Vella, A. Zipse, A. Barkmeier; *Past*: B. French, M. Haymond, J. Mortenson, J. Pach, R. Rizza, L. Schmidt, W.F. Schwenk, F.J. Service, R. Woodwick, G. Ziegler; *Deceased*: R. Colligan, A. Lucas, B. Zimmerman

Medical University of South Carolina – *Current*: H. Karanchi, L. Spillers, J. Fernandes, K. Hermayer, S. Kwon, K. Lee, M. Lopes-Virella, T. Lyons, M. Nutaitis; *Past*: A. Blevins, M. Bracey, S. Caulder, J. Colwell, S. Elsing, A. Farr, D. Lee, P. Lindsey, L. Luttrell, R. Mayfield, J. Parker, N. Patel, C. Pittman, J. Selby, J. Soule, M. Szpiech, T. Thompson, D. Wood, S. Yacoub-Wasef

Northwestern University – *Current*: A. Wallia, M. Hartmuller, S. Ajroud-Driss, P. Astelford, A. Degillio, M. Gill, L. Jampol, C. Johnson, L. Kaminski, N. Leloudes, A. Lyon, R. Mirza, D. Ryan, E. Simjanoski, Z. Strugula; *Past*: D. Adelman, S. Colson, M. Molitch, B. Schaefer

University of California, San Diego – *Current*: S. Mudaliar, G. Lorenzi, O. Kolterman, M. Goldbaum; *Past*: T. Clark, M. Giotta, I. Grant, K. Jones, R. Lyon, M. Prince, R. Reed, M. Swenson; *Deceased*: G. Friedenberg

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University of Michigan – *Current*: W.H. Herman, R. Pop-Busui, C.L. Martin, P. Lee, J. W. Albers, E.L. Feldman; *Past*: N. Burkhart, D.A. Greene, T. Sandford, M.J. Stevens; *Deceased*: J. Floyd

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University of Pennsylvania – *Current*: M. Schutta, P.A. Bourne, A. Brucker; *Past*: S. Braunstein, B.J. Maschak-Carey, S. Schwartz; *Deceased*: L. Baker

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University of Washington – *Current*: I. Hirsch, R. Fahlstrom, L. Van Ottingham, I.H. de Boer, L. Olmos de Koo; *Past*: S. Catton, J. Ginsberg, J. Kinyoun, J. Palmer

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Vanderbilt University – *Current*: M. May, J. Lipps Hagan, T. Adkins, A. Agarwal, C. Lovell; *Past*: S. Feman, R. Lorenz, R. Ramker; *Deceased*: L. Survant

Washington University, St. Louis – *Current*: N.H. White, L. Levandoski; *Deceased*: I. Boniuk, J. Santiago

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Albert Einstein – *Past*: J. Brown-Friday, J. Crandall, H. Engel, S. Engel, H. Martinez, M. Phillips, M. Reid, H. Shamoon, J. Sheindlin

Clinical Coordinating Center

Case Western Reserve University – *Current*: R. Gubitosi-Klug, L. Mayer, C. Beck, K. Farrell, P. Gaston; *Past*: S. Genuth, M. Palmert, J. Quin, R. Trail; *Deceased*: W. Dahms

Data Coordinating Center

George Washington University, The Biostatistics Center – *Current*: J. Lachin, I. Bebu, B. Braffett, J. Backlund, L. Diminick, L. El ghormli, X. Gao, S. Ho, D. Kenny, K. Klumpp, M. Lin, V. Trapani; *Past*: K. Anderson, K. Chan, P. Cleary, A. Determan, L. Dews, W. Hsu, P. McGee, H. Pan,B. Petty, D. Rosenberg, B. Rutledge, W. Sun, S. Villavicencio, N. Younes; *Deceased*: C. Williams

National Institute of Diabetes and Digestive and Kidney Disease

National Institute of Diabetes and Digestive and Kidney Disease Program Office – *Current*: E. Leschek; *Past*: C. Cowie, C. Siebert

EDIC Core Central Units

Central Biochemistry Laboratory (University of Minnesota) – *Current*: M. Steffes, A. Karger, J. Seegmiller, V. Arends; *Past*: J. Bucksa, B. Chavers, A. Killeen, M. Nowicki, A. Saenger

Central ECG Reading Unit (Wake Forest School of Medicine) – *Current*: E.Z. Soliman, M. Barr, C. Campbell, S. Hensley, J. Hu, L. Keasler, Y. Li, T. Taylor, Z.M. Zhang; *Past*: Y. Pokharel, R. Prineas

Central Ophthalmologic Reading Unit (University of Wisconsin) – *Current*: B. Blodi, R. Danis, D. Lawrence, H. Wabers; *Past*: M. Burger, M. Davis, J. Dingledine, V. Gama, S. Gangaputra, L. Hubbard, S. Neill, R. Sussman

Central Neuropsychological Reading Unit (NYU Long Island School of Medicine, University of Pittsburgh) – *Current*: A. Jacobson, C. Ryan, D. Saporito; *Past*: B. Burzuk, E. Cupelli, M. Geckle, D. Sandstrom, F. Thoma, T. Williams, T. Woodfill