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Dataset Integrity Check for the DCCT-EDIC Baseline Analysis File

As a partial check of the integrity of the DCCT-EDIC datasets archived in the NIDDK data repository, a dataset integrity check (DSIC) was performed to verify that selected published results from the DCCT-EDIC study can be reproduced using archived datasets. A small number of analyses were performed to duplicate published results on the EDIC baseline dataset reported by the DCCT-EDIC Research Group [1] in *Diabetes Care (Jan 1999, [22(1)])*. Results of the DSIC are described below.

The intent of this DSIC is to provide confidence that the data distributed by the NIDDK repository is a true copy of the study data. Our intent is ***not*** to assess the integrity of the statistical analyses reported by study investigators. As with all statistical analyses of complex datasets, complete replication of a set of statistical results should not be expected on a first (or second) exercise in secondary analysis. This occurs for a number of reasons including differences in the handling of missing data, restrictions on cases included in samples for a particular analysis, software coding used to define complex variables, etc. Experience suggests that most discrepancies can ordinarily be resolved by consultation with the study DCC, however this process is labor-intensive for both DCC and Repository staff. It is thus not our policy to resolve every discrepancy that is observed in an integrity check. Thus, we do not attempt to resolve minor or inconsequential discrepancies with published results or discrepancies that involve complex analyses unless staff of the NIDDK Repository suspect that the observed discrepancy suggests that the dataset may have been corrupted in storage, transmission, or processing by repository staff. We do, however, document in footnotes to the integrity check those instances in which our secondary analyses produced results that were not fully consistent with those reported in the target publication.

DCCT-EDIC Baseline Analysis. Table 3 of the publication (p.104) compares characteristics of 1375 participants who completed the DCCT study and were recruited into EDIC, with those of 50 DCCT participants who declined to enroll into EDIC. Table 1 of this DSIC compares the published breakdown to results obtained from the archived SAS data file. The counts, percentages, means, and standard deviations obtained from analyses of the archived data closely match the published tabulations. Likewise[a], *P*-values for tests of differences between treatment groups calculated from archived data exactly match the published results.

[a] In determining statistical significance of differences in group means or percentages, Wilcoxon rank-sum tests were used for continuous variables, and chi-square tests were used for categorical variables. These statistical methods are the same as those outlined in the footnotes in the published tables, with the exception of the comparison of event rates (see discussion under *Diabetes management of EDIC cohort during the first 2 years of EDIC,* p.7 of this DSIC).

TABLE 1. Characteristics of EDIC participants compared with nonparticipants: Top panel is calculated from Archived Data; Bottom panel contains published results (Table 3 in publication, p.104).

Characteristic	Participants	Nonparticipants	P value
N	1375	53[b]	
Age (years)	33.6 ± 7.0	31.0 ± 7.7	0.016
Sex (% female)	48	45	NS
Duration of type 1 diabetes (years)	12.2 ± 4.8	11.6 ± 4.4	NS
Treatment group during DCCT (% intensive)	50	30	0.005
HbA1c at closeout of DCCT (%)			
Intensive Group	7.4 ± 1.1	8.5 ± 1.6	0.003
Conventional group	9.1 ± 1.5	9.6 ± 1.4	0.112
Debriefed at DCCT study's end (%)	99	74	<0.0001
Care transferred to non-DCCT personnel (%)	48	79	<0.0001

Table 3—*Characteristics of EDIC participants compared with nonparticipants*

Characteristic*	Participants	Nonparticipants	*P* value
n	1,375	50	—
Age (years)	33.6 ± 7.0	31.0 ± 7.7	0.0155
Sex (% female)	48	45	NS
Duration of type 1 diabetes (years)	12.2 ± 4.8	11.6 ± 4.4	NS
Treatment group during DCCT (% intensive)	50	30	0.0048
HbA_{1c} at closeout of DCCT (%)			
Intensive group	7.4 ± 1.1	8.5 ± 1.6	0.0031
Conventional group	9.1 ± 1.5	9.6 ± 1.4	0.1123
Debriefed at DCCT study's end (%)	99	74	<0.0001
Care transferred to non-DCCT personnel (%)	48	79	<0.0001

Data are means ± SD or %. *P* values for continuous variables are from Wilcoxon's rank-sum test; *P* values for categorical variables are from the contingency-table χ^2 test.

[b] The DCC acknowledges the discrepancy between the 50 nonparticipants in published data, and the 53 nonparticipants in archived data.

Risk factors during first 2 years of EDIC. Table 4 of the publication (p.104) presents the distribution of risk factors, by gender group, for participants in the first two years of EDIC. Table 2 of this DSIC compares the published breakdown to results obtained from the archived SAS data file. The counts, percentages, means, and standard deviations obtained from analyses of the archived data closely match the published tabulations. Any differences in estimates could be attributed to rounding error. Similarly, *P*-values for tests of differences between treatment groups calculated from archived data closely match the published results.

TABLE 2. Risk factors measured during the first two years of the EDIC study, based on the most recent observation from each patient: Results on current page are calculated from Archived Data; Next page contains published results (Table 4, p.104).

Characteristic	Men	Women	P value
n (%)[c]	719 (52.4)	653 (47.6)	
Age (years)	36.4 ± 6.6	35.4 ± 7.2	0.0066
Duration of type 1 diabetes (years)	14.3 ± 4.8	14.8 ± 5.0	NS
BMI (kg/m2)	26.6 ± 3.9	26.0 ± 4.2	<0.0001
Overweight (%)	30.9	31.9	NS
Waist-to-hip ratio	0.88 ± 0.06	0.77 ± 0.07	<0.0001
Insulin dose	0.72 ± 0.25	0.70 ± 0.24	NS
HbA1c (%)	8.2 ± 1.3	8.3 ± 1.5	NS
Total cholesterol (mg/dl)	185.1 ± 35.6	188.1 ± 37.0	NS
Triglyceride (mg/dl)	96.8 ± 75.8	83.1 ± 73.3	<0.0001
HDL cholesterol (mg/dl)	49.5 ± 12.0	59.2 ± 14.0	<0.0001
<35 mg/dl (%)	8.2	1.6	<0.0001
LDL cholesterol (mg/dl)	116.4 ± 30.8	112.1 ± 30.3	0.0083
>130 mg/dl (%)	30.6	26.0	NS
Hypertension (%)	26.6	18.1	0.0002
Current cigarette smoker (%)	22.7	19.9	NS
Exercise level			<0.0001
Strenuous	10.4	2.9	
Vigorous	5.9	3.4	
Moderate	49.5	58.3	
Sedentary	34.3	35.4	
Current alcohol use (%)	47.4	32.1	<0.0001
Urinary albumin excretion (mg/24 h)	38.1 ± 118.4	41.8 ± 226.9	NS
DQOL total score	76.4 ± 9.4	75.3 ± 8.6	0.0186

[c] Three subjects – one male and two females – are identified as EDIC participants in the archived dataset, but have no EDIC data except IMT in one subject. When these subjects are removed, the gender breakdowns on archived data match published gender breakdowns.

TABLE 2, cont'd. Risk factors measured during the first two years of the EDIC study, based on the most recent observation from each patient: Published results (Table 4 in publication, p.104)

Table 4—*Risk factors measured during the first 2 years of the EDIC study, based on the most recent observation from each patient*

	Men	Women	*P* value
n (%)	719 (52.4)	653 (47.6)	—
Age (years)	36.4 ± 6.6	35.4 ± 7.2	0.0068
Duration of type 1 diabetes (years)	14.3 ± 4.8	14.8 ± 5.0	NS
BMI (kg/m^2)	26.6 ± 3.9	26.0 ± 4.2	0.0001
Overweight (%)	30.9	31.8	NS
Waist-to-hip ratio	0.88 ± 0.06	0.77 ± 0.07	<0.0001
Insulin dose (U · kg^{-1} · day^{-1})	0.71 ± 0.25	0.69 ± 0.24	NS
HbA_{1c} (%)	8.2 ± 1.3	8.3 ± 1.5	NS
Total cholesterol (mg/dl)	185.1 ± 35.6	188.1 ± 37.0	NS
Triglyceride (mg/dl)	96.8 ± 75.8	83.1 ± 73.3	0.0001
HDL cholesterol (mg/dl)	49.5 ± 12.0	59.2 ± 14.0	<0.0001
<35 mg/dl (%)	8.2	1.6	<0.0001
LDL cholesterol (mg/dl)	116.4 ± 30.8	112.1 ± 30.3	0.0083
>130 mg/dl (%)	30.6	26.0	NS
Hypertension (%)	26.6	18.1	0.0002
Current cigarette smoker (%)	22.7	19.9	NS
Exercise level			<0.001
Strenuous	10.3	2.9	
Vigorous	5.9	3.4	
Moderate	49.5	58.2	
Sedentary	34.3	35.4	
Current alcohol use (%)	47.4	32.2	<0.001
Urinary albumin excretion (mg/24 h)	38.1 ± 118.4	41.8 ± 226.9	NS
DQOL total score	76.4 ± 9.4	75.3 ± 8.6	0.0184

Data are means ± SD or %. *P* values are for men versus women. Waist-to-hip ratio is based on natural waist circumference. Hypertension is percent diagnosed as hypertensive at any time during DCCT or EDIC and is defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or use of antihypertensives. Alcohol use is percent reporting consumption of at least one alcoholic beverage per week. DQOL, Diabetes Quality of Life

Ankle-to-Arm Systolic Blood Pressure Ratio (PVD); Carotid Artery Intimal Medial Thickness (CIMT). Table 5 of the publication (p.105) presents the baseline measurements of ankle-to-arm systolic blood pressure ratio and carotid artery intimal-medial thickness, by age and gender group. Table 3 of this DSIC compares the published breakdown to results obtained from the archived SAS data file. The counts, percentages, means, and standard deviations obtained from analyses of the archived data closely match the published tabulations. Similarly, *P*-values for tests of differences between treatment groups calculated from archived data closely match the published results.

TABLE 3. PVD and CIMT: Results on current page are calculated from Archived Data; Next page contains published results (Table 5 in publication, p.105).

			Systolic blood pressure ratio of resting ankle to arm					
					Prevalence of abnormal ankle-to-arm ratio (% in any four ratios)			
Characteristic	Age decade	n[d]	Right	Left	Percent <0.8	P (0.8)	Percent >1.4[e]	Percent either
Women	20-29	154	1.08 ± 0.10	1.08 ± 0.10	2.6	0.9863	0.0	2.6
	30-39	289	1.11 ± 0.12	1.09 ± 0.13	2.8	0.1306	5.9	8.3
	40-49	202	1.10 ± 0.13	1.08 ± 0.12	3.5	0.7089	1.5	5.0
Men	20-29	117	1.07 ± 0.12	1.08 ± 0.10	2.6		2.6	5.1
	30-39	351	1.12 ± 0.13	1.10 ± 0.13	1.1		3.7	4.8
	40-49	241	1.13 ± 0.13	1.11 ± 0.14	4.2		3.7	7.9

			Maximum intimal-medial thickness of common and internal carotid artery	
Characteristic	Age decade	n	Common (mm)	Internal (mm)
Women	20-29	172	0.616 ± 0.073	0.583 ± 0.092
	30-39	278	0.657 ± 0.081	0.632 ± 0.147
	40-49	178	0.696 ± 0.079	0.719 ± 0.226
Men	20-29	125[f]	0.636 ± 0.059	0.629 ± 0.083
	30-39	350	0.684 ± 0.083	0.684 ± 0.114
	40-49	211	0.745 ± 0.104	0.806 ± 0.261

[d] Published n's for systolic blood pressure ratio are the largest n for an individual measure (right SBP ratio, left SBP ratio, prevalence of abnormal ankle-to-arm ratio)
[e] The published heading, "Percent < 1.4", is clearly a typographical error.
[f] One male DCCT subject, aged 20-29, had IMT data collected for EDIC, but died soon after. He is identified in the archived dataset as *not* an EDIC subject (IN_EDIC=0). Analyses of archived data match published results only when his IMT data are included in the sample. The DCC has confirmed that IMT was analyzed as a separate study from EDIC.

TABLE 3, cont'd. PVD and CIMT, published results (Table 5 in publication, p.105).

Table 5—*New measurements in the EDIC protocol*

		Systolic blood pressure ratio of resting ankle to arm							Maximum intimal-medial thickness of common and internal carotid artery		
					Prevalence of abnormal ankle-to-arm ratio (percent in any four ratios)						
	Age decade	*n*	Right	Left	Percent <0.8	*P* (0.8)	Percent <1.4	Percent either	*n*	Common (mm)	Internal (mm)
Women*	20–29	154	1.08 ± 0.11	1.08 ± 0.13	2.6	0.9864	0.0	2.6	172	0.616 ± 0.073	0.583 ± 0.092
	30–39	289	1.11 ± 0.12	1.10 ± 0.13	2.8	0.1307	5.9	8.3	278	0.657 ± 0.081	0.632 ± 0.147
	40–49	202	1.09 ± 0.12	1.07 ± 0.11	3.5	0.7093	1.5	5.0	178	0.696 ± 0.079	0.719 ± 0.226
Men*	20–29	117	1.07 ± 0.11	1.08 ± 0.10	2.6		2.6	5.1	125	0.636 ± 0.059	0.629 ± 0.083
	30–39	351	1.11 ± 0.12	1.10 ± 0.12	1.1		3.7	4.8	350	0.684 ± 0.083	0.684 ± 0.114
	40–49	241	1.13 ± 0.13	1.12 ± 0.14	4.1		3.7	7.9	211	0.745 ± 0.104	0.806 ± 0.261

Data are *n*, means ± SD, or %. Dorsalis pedis and posterior tibral pressures were combined using an algorithm of Hiatt et al. (51). *P* values are for men vs. women. **P* value for trend in percent <0.8: women, 0.6171; men, 0.1513. $P < 0.0001$ for both common and internal intimal-medial thickness; all are from Wilcoxon's rank-sum test after linear adjustment for covariance with age.

Diabetes management of EDIC cohort during the first 2 years of EDIC. Table 6 of the publication (p.105) presents characteristics of diabetes management in the EDIC sample in the first 24 months after DCCT closeout. Table 4 of this DSIC compares the published breakdown to results obtained from the archived SAS data file. The counts, percentages, means, and standard deviations obtained from analyses of the archived data closely match the published tabulations. Similarly, *P*-values for tests of differences between treatment groups calculated from archived data closely match the published results. Differences in event rates of hypoglycemia and/or DKA could be attributed to differences in statistical analyses methods[g].

TABLE 4. Diabetes management in EDIC during the first 2 years: Results on current page are calculated from Archived Data; Next page contains published results (Table 6 in publication, p.105) (Note: Slightly different procedures were used in these analyses; see footnote[f]).

	DCCT treatment group assignment		
Characteristic	Intensive	Conventional	P value
n	687	688	
Insulin delivery during EDIC			<0.0001
CSII	37.0	12.6	
MDI	57.6	56.9	
One or two injections/day	5.3	30.3	
Unknown	0.2	0.3	
Human insulin (% of subjects using)	91.1	90.8	NS
Insulin dose (U * kg^{-1} * day^{-1})	0.75 $\pm$ 0.28	0.67 $\pm$ 0.20	<0.0001
Self-monitored blood glucose $\geq$4/day (%)	46.4	36.4	0.0002
Hypoglycemia (rate per 100 patient-years)			
Coma/seizure	6.2	7.2	NS
Requiring assistance	24.9	26.3	NS
DKA (rate per 100 patient-years)	2.76	2.36	NS
Overweight (%)			
Men	32.5	29.7	NS
Women	38.0	25.2	0.0005

[g] Event rates were calculated by multiplying each individual daily rate -- available in the archived dataset -- by a constant (365.25) to get the yearly rate, and then taking the mean across individuals. To compare group event rates, Wilcoxon's rank sum test was used. This is in contrast to published analyses methods, where a Wald test of the log-relative, adjusted for overdispersion, was used to compare event rates. However, conclusions resulting from statistical comparisons remained the same between analyses of archived data and published results.

TABLE 4, cont'd. Diabetes management in EDIC during the first 2 years: Published results (Table 6 in publication, p.105).

Table 6—*Diabetes management of EDIC cohort during the first 2 years of EDIC*

	DCCT treatment group assignment		
	Intensive	Conventional	*P* value
n	687	688	—
Insulin delivery during EDIC			<0.0001
CSII	37.0	12.6	
MDI	57.6	56.9	
One or two injections/day	5.3	30.3	
Unknown	0.1	0.3	—
Human insulin (% of subjects using)	91.1	90.8	NS
Insulin dose ($U \cdot kg^{-1} \cdot day^{-1}$)	0.75 ± 0.28	0.67 ± 0.20	<0.0001
Self-monitored blood glucose ≥4/day (%)	46.4	36.4	0.0002
Hypoglycemia (rate per 100 patient-years)			
Coma/seizure	6.3	7.1	NS
Requiring assistance	25.4	25.7	NS
DKA (rate per 100 patient-years)	2.68	2.37	NS
Overweight (%)			
Men	32.5	29.7	NS
Women	38.4	25.2	0.0005

Data are means ± SD. *P* values are from the contingency-table χ^2 test for categorical variables, Wilcoxon's rank-sum test for continuous variables, and from a Wald test of the log-relative adjusted for overdispersion of event rates. Overweight is defined for men as BMI (kg/m^2) >27.8 from the second National Health and Nutrition Examination Survey (NHANES II) of 1976 to 1980 (50) and for women as BMI (kg/m^2) >27.3.

APPENDIX A

Full Text of Article

Epidemiology of Diabetes Interventions and Complications (EDIC) Research Group (1999). 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, 22(1):99-111.

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

EPIDEMIOLOGY OF DIABETES INTERVENTIONS AND COMPLICATIONS (EDIC) RESEARCH GROUP

OBJECTIVE — The Diabetes Control and Complications Trial (DCCT) demonstrated the powerful impact of glycemic control on the early manifestations of microvascular complications. Contemporary prospective data on the evolution of macrovascular and late microvascular complications of type 1 diabetes are limited. The Epidemiology of Diabetes Interventions and Complications (EDIC) study is a multicenter, longitudinal, observational study designed to use the well-characterized DCCT cohort of >1,400 patients to determine the long-term effects of prior separation of glycemic levels on micro- and macrovascular outcomes.

RESEARCH DESIGN AND METHODS — Using a standardized annual history and physical examination, 28 EDIC clinical centers that were DCCT clinics will follow the EDIC cohort for 10 years. Annual evaluation also includes resting electrocardiogram, Doppler ultrasound measurements of ankle/arm blood pressure, and screening for nephropathy. At regular intervals, a timed 4-h urine is collected, lipid profiles are obtained, and stereoscopic fundus photographs are taken. In addition, dual B-mode Doppler ultrasound scans of the common and internal carotid arteries will be performed at years 1 and 6 and at study end.

RESULTS — Written informed consent was obtained from 96% of the DCCT subjects. The participants, compared with nonparticipants, tended to have better glycemic control at the completion of the DCCT and were more likely to have their diabetes care provided by DCCT personnel. The EDIC baseline measurement stratified by sex delineates multiple cardiovascular disease risk factor differences such as age (older in men), waist-to-hip ratio (higher in men), HDL cholesterol (lower in men), hypertension (more prevalent in men), and maximum intimal-medial thickness of common and internal carotid arteries (thicker in men). Of the original conventional treatment group, 69% have changed to continuous subcutaneous insulin infusion or multiple daily injections. Although the mean HbA_{1c} difference between the intensive and conventional treatment groups narrowed at EDIC years 1 and 2, HbA_{1c} remained significantly lower in the intensive group. Of all expected clinic visits, 95% were completed, and the quality of EDIC data is very similar to that observed in the DCCT.

CONCLUSIONS — Although obvious problems exist in extended follow-up studies of completed clinical trials, these are balanced by the value of continued systematic observation of the DCCT cohort. In contrast to other epidemiologic studies, EDIC will provide *1*) definitive data on type 1 as distinct from type 2 diabetes; *2*) reliance on prospective rather than on cross-sectional analysis; *3*) long-term follow-up in a large population; *4*) consistent use of objective, reliable measures of outcomes and glycemia; and *5*) observation of patients from before the onset of complications.

Diabetes Care 22:99–111, 1999

Morbidity and mortality in type 1 diabetic patients derive mainly from advanced microvascular, neuropathic, and macrovascular complications, with the major clinical impact beginning 15–20 years after the onset of diabetes (1,2). The Diabetes Control and Complications Trial (DCCT) demonstrated that therapy aimed at maintaining HbA_{1c} levels as close to normal as feasible reduced the risks for the development and progression of early microvascular and neurologic complications of type 1 diabetes (3–5). While the reduction of the earlier stages of diabetic complications could reasonably be expected to slow the evolution to end-stage complications, such as loss of vision or renal failure, too few severe complications occurred during the DCCT to establish this conclusion. Similarly, although fewer intensively treated than conventionally treated patients in the DCCT experienced cardiovascular events (3,6), the numbers were too small to be conclusive and the differences were not statistically significant. Overall, relatively little is known about the development of cardiovascular disease in type 1 diabetes, although it is the major cause of mortality.

Currently available data on the evolution of long-term complications are limited by *1*) failure to separate type 1 diabetes from type 2 diabetes in study populations; *2*) reliance on cross-sectional studies that are prone to prevalence bias; *3*) studies of small, selected populations with limited generalizability; and *4*) relatively brief follow-up and significant attrition in prospective studies. Since most studies suggest that overt late-

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A complete listing of the EDIC Research Group appears in ACKNOWLEDGMENTS.

Abbreviations: CAD, coronary artery disease; CSII, continuous subcutaneous insulin infusion; DCCT, Diabetes Control and Complications Trial; DKA, diabetic ketoacidosis; ECG, electrocardiogram; EDIC, Epidemiology of Diabetes Intervention and Complications; ETDRS, Early Treatment of Diabetic Retinopathy Study; HRQOL, health-related quality of life; MDI, multiple daily injections; MI, myocardial infarction; MNSI, Michigan Neuropathy Screening Instrument; NIDDK, National Institute of Diabetes, Digestive and Kidney Diseases; PDR, proliferative diabetic retinopathy; PVD, peripheral vascular disease; WESDR, Wisconsin Epidemiologic Study of Diabetic Retinopathy.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

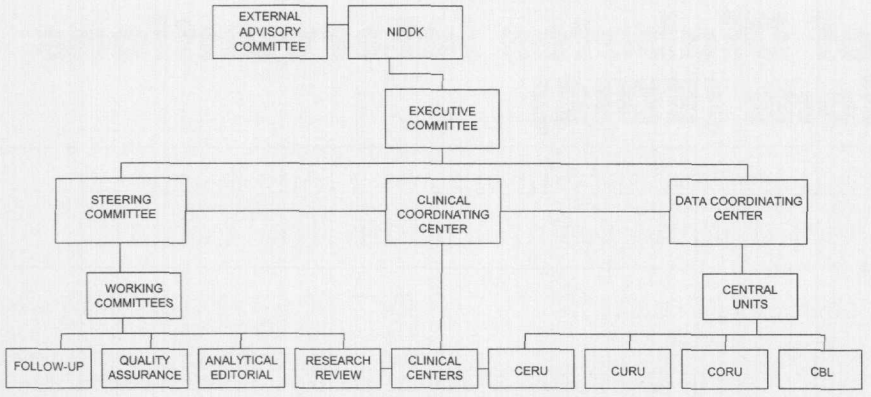

Figure 1—*Organization chart for the EDIC study. CBL, central biochemical laboratory; CERU, central ECG reading unit; CORU, central ophthalmologic reading unit; CURU, central ultrasound reading unit.*

stage complications usually occur after 15–25 years' duration of type 1 diabetes, further study of the DCCT cohort, with an average diabetes duration of 12 years at study end, would delineate the evolution of late-stage complications. In addition, the DCCT cohort offered the following advantages for a long-term follow-up study of advanced complications: *1*) the early stages of these complications had been well characterized with reliable objective outcome measurements; *2*) established and putative risk factors for cardiovascular complications had already been measured repeatedly; and *3*) all of the subjects had been strongly advised to follow intensive treatment regimens after the conclusion of the DCCT. We therefore designed a protocol to examine the DCCT cohort in a prospective multicenter 10-year observational study. The Epidemiology of Diabetes Interventions and Complications (EDIC) study began in January 1994, shortly after the closeout of the DCCT, and after approval of the EDIC protocol by the Director of the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK). The EDIC study focuses on the interactions between established and putative risk factors for long-term microvascular, neurologic, and cardiovascular outcomes of type 1 diabetes, including prior diabetes treatment and the level of glycemic control during the DCCT.

Study objectives

The major study objectives include the following:

- To describe the development and progression of cardiovascular (coronary, peripheral, and cerebral) disease in type 1 diabetes.
- To study the effects and interactions of potential risk factors for cardiovascular disease in type 1 diabetes, including those established in nondiabetic and type 2 diabetic populations.
- To examine the long-term effects of differences in prior diabetes treatment (conventional versus intensive) during the DCCT on the subsequent development and progression of cardiovascular disease.
- To examine the development of abnormal lipid and lipoprotein levels over time, their relationship to metabolic and other variables, and their contribution, both independently and in conjunction with other risk factors, to the development of macrovascular diseases.
- To relate early degrees of microalbuminuria, therapeutic interventions, and other established risk factors to the subsequent development of clinical nephropathy.
- To study the rate of development of clinically significant neuropathy and its relationship to other complications and risk factors.
- To examine the transition from background to more severe stages of retinopathy, such as proliferative diabetic retinopathy (PDR), and its relationship to established and putative risk factors, including previous treatment, ongoing level of glycemia, hypertension, and renal insufficiency.
- To examine the long-term effects of differences in prior diabetes treatment during the DCCT on the development and progression of nephropathy, neuropathy, and retinopathy, refining estimates of the risks associated with varying levels of antecedent glycemic control.
- To examine the effect(s) of putative genetic factors that may be identified in the future on the development and/or progression of all complications in type 1 diabetes and their interactions with other risk factors.
- To observe the current health care provided to EDIC patients in the U.S. and Canada, including the implementation and maintenance of intensive therapy, and the associations between different types of medical care and health outcomes.
- To study health-related quality of life (HRQOL) and the relationship between HRQOL and the development of clinically significant complications.

RESEARCH DESIGN AND METHODS

Subjects

At the completion of the DCCT, subjects were informed of the purpose, procedures, benefits, and risks of the EDIC. Written informed consent to participate in EDIC was obtained from 96% of DCCT subjects. All clinically relevant measurements obtained during follow-up would be provided to EDIC subjects and their physicians.

Organization

The organizational structure of the EDIC study is designed to coordinate the activities of the committees, laboratories, units, and review groups, and to ensure careful conduct of the study by uniform adherence to the *Protocol and Manual of Operations* (7) (Fig. 1). Of the 29 DCCT clinics, 28 opted to participate as EDIC clinical centers (1 of the 29 with relatively few patients was merged with its neighboring clinic). The organization of EDIC includes a clinical coordinating center, a data coordinating center, and four reading centers and laboratories (see ACKNOWLEDGMENTS for a listing of all EDIC participating centers, laboratories, and reading units). All study procedures and tests are performed in the EDIC clinical centers with standardized methods by trained and certified personnel. Analysis of samples and grading of eye photographs, carotid ultrasounds, and electrocardiograms (ECGs) are performed in the respective central laboratory or reading centers, using standardized quality-controlled methods.

Procedures and methods

Each subject has a standardized annual history and physical examination on the anniversary of randomization into the DCCT (Table 1). This examination is per-

Table 1—*Schedule of follow-up examinations*

Examinations (outcomes)	EDIC year 1	2	3	4	5	6	7	8	9	10
Cardiovascular (CABG, MI, angina, CHF, stroke, TIA)										
Standardized history (including family) and physical exam	X	X	X	X	X	X	X	X	X	X
ECG	X	X	X	X	X	X	X	X	X	X
Duplex carotid ultrasonography central review	X					X				X
Peripheral vascular (foot ulcer, amputation, bypass graft)										
Standardized history and physical exam	X	X	X	X	X	X	X	X	X	X
Ankle/arm index by Doppler	X	X	X	X	X	X	X	X	X	X
Lipoprotein levels (hypercholesterolemia, hypertriglyceridemia)										
Total cholesterol										
HDL cholesterol	Scheduling of visits is a function of randomization date (alternate years)									
Triglycerides										
Calculated LDL cholesterol										
Nephropathic (renal failure, transplant, dialysis, elevated serum creatinine)										
Standardized history and physical exam	X	X	X	X	X	X	X	X	X	X
Serum creatinine	X	X	X	X	X	X	X	X	X	X
Glomerular filtration										
Albumin excretion rate	Scheduling of visits is a function of randomization date (alternate years)									
4-h standard creatinine clearance										
Neuropathy										
MNSI	X	X	X	X	X	X	X	X	X	X
10-g filament examination	X	X	X	X	X	X	X	X	X	X
Retinopathic (photocoagulation, vitrectomy, blindness, vitreous hemorrhage)										
Standardized history	X	X	X	X	X	X	X	X	X	X
Ophthalmological exam*										
Visual acuity*										
Fundus photographs*	Scheduling of visits is a function of randomization date									
Hypoglycemia (mortality/morbidity)										
Standardized history	X	X	X	X	X	X	X	X	X	X
Metabolic (DKA, chronic glycemia)										
Standardized history	X	X	X	X	X	X	X	X	X	X
HbA_{1c}	X	X	X	X	X	X	X	X	X	X
Psychological										
Quality of life questionnaire (DQOL)	X		X		X		X		X	X
Health status questionnaire (SF-36)	X		X		X		X		X	X
Health care delivery										
Standardized questionnaire	X	X	X	X	X	X	X	X	X	X
Dietary										
Food frequency recall questionnaire	In conjunction with lipids									

*Ophthalmological exam, visual acuity, and fundus photographs to be done on the patient's 8th, 12th, and 16th anniversaries of randomization. CABG, coronary revascularization; CHF, congestive heart failure; DQOL, Diabetes Quality of Life; SF, short form; TIA, transient ischemic attack.

formed within 4 months of the anniversary date and includes detailed evaluation of overall health status, diabetes management, occurrence of diabetic complications, development of new diseases since the previous annual visit, and all medications used. Measures of health satisfaction and quality of life are obtained every other year.

Annual evaluations also include resting ECGs and Doppler ultrasound measurement of ankle/arm blood pressure, as well as screening for peripheral neuropathy by both 10-g filament examination (8) and administration of the Michigan Neuropathy Screening Instrument (MNSI) (9). A timed 4-h urine is collected in alternate years for measurement of albumin excretion rate and creatinine clearance; lipid profiles are obtained in the years that renal studies are not performed; and a dietary recall questionnaire is given in conjunction with the lipid assessment. Dual B-mode Doppler ultrasound scans of the common and internal carotid arteries were carried out at entry into the EDIC study and are expected to be repeated at intervals of 5 years. Table 2 lists the specific methods used in EDIC.

DNA has been obtained from peripheral blood leukocytes in all subjects and stored as a long-term resource for potential analyses.

Table 2—*Methods in EDIC*

Measurement	Method or assay
Glycosylated hemoglobin	High-performance ion-exchange liquid chromatography
Serum creatinine	Automated kinetic method with Jaffè reaction
Urine creatinine	Automated kinetic method with Jaffè reaction
Urine albumin	Solid-phase fluoroimmunoassay
Serum albumin	Thin-film adaption of a bromcresal colorimetric procedure
Serum cholesterol	Cholesterol oxidase, spectrophotometric
Serum triglyceride	Glycerol-blanked glycerol kinase/glycerol oxidase, spectrophotometric
Serum HDL cholesterol	Magnesium dextran precipitation
Calculated LDL cholesterol	Friedewald equation
12-lead resting ECG	Central reading using revised Minnesota Code
Intimal-media wall thickness	High resolution β-mode ultrasound graded centrally with standardized protocol
Fundus photograph	Central reading of seven-field stereo photographs using final ETDRS grading scale for retinopathy and macular edema
Blood pressure	
Systolic	Sitting, right arm reading with sphygmomanometer
Diastolic	
Ankle-to-arm blood pressure ratio	Resting systolic blood pressure with a Doppler ultrasonic instrument
Food frequency	Harvard Food Frequency; self-administered
Current medication	EDIC Form 004; administered by study coordinator
Hypoglycemia	Interview at annual visit
Neuropathy	MNSI
HRQOL	HRQOL (DQOL, SF-36)

DQOL, Diabetes Quality of Life; SF, short form.

Quality control

Quality control procedures in the EDIC study include those in place internally in all the laboratories and reading centers as well as those implemented as part of EDIC data collection. The local clinic procedures that require training and certification include the performance of Doppler ankle-arm index, 10-g filament test, renal studies, ECG recording, carotid ultrasound, and fundus photographs. All blood and urine tests undergo repeated assessments for analytic precision by assays of split-duplicate samples in the central laboratory. Split-duplicate analysis is also used to monitor grading of the carotid ultrasound recordings, ECGs, and fundus photographs.

Analytic procedures

General principles. Defined incident events are coded for analysis based on the measurements and evaluations noted above. Previously documented or treated events in the DCCT are risk factors and not incident events. Deaths and major morbid events will be classified by a classification committee composed of a cardiologist and two diabetologists who are masked to previous treatment assignment in the DCCT and current diabetes treatment. The definitions of these events are as follows:

- Cardiovascular disease: death secondary to cardiovascular disease or any sudden death judged not to be caused by hypoglycemia or other known reason, acute myocardial infarction (MI), silent MI appearing as a major new Q-wave abnormality on a routine ECG, initiation of thrombolytic therapy for suspected MI, coronary artery disease (CAD) requiring bypass surgery or angioplasty, or CAD confirmed by angiography or by a combination of angina and ischemia documented with noninvasive testing.
- Hypercholesterolemia: calculated LDL cholesterol ≥160 mg/dl on two occasions 24 months apart or the use of lipid-lowering medication for previously documented hypercholesterolemia as defined in the DCCT (6).
- Hypertriglyceridemia: serum triglyceride >400 mg/dl on two occasions 24 months apart or the use of lipid-lowering medication for previously documented hypertriglyceridemia as defined in the DCCT (6).
- Cerebrovascular disease: stroke or transient ischemic attack confirmed by angiography or noninvasive testing.
- Peripheral vascular disease (PVD): surgical amputation of a lower extremity necessitated by vascular disease, arterial vascular events requiring bypass or angioplasty, claudication with exercise testing or angiographic evidence of vascular disease, or an ankle-to-arm blood pressure ratio <0.8 or >1.4.
- Lower-extremity ulcer: a traumatic or nontraumatic excavation or loss of subcutaneous tissue in the foot or leg that requires medical or surgical treatment by a health professional in an office or hospital setting irrespective of whether the etiology is neuropathic, ischemic, or both.
- Hypertension: confirmed sitting systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, or the use of antihypertensive medication for previously documented hypertension.
- Microalbuminuria: urinary albumin excretion of ≥28 μg/min during the 4-h timed collection.
- Albuminuria: urinary albumin excretion ≥208 μg/min during the 4-h timed collection.
- Renal insufficiency: serum creatinine ≥2 mg/dl, glomerular filtration rate <70 ml · min^{-1} · 1.73 m^{-2}, or the need for dialysis or renal transplantation.
- Doubling of serum creatinine: doubling of centrally measured serum creatinine from DCCT baseline.
- Advanced retinopathy: PDR according to the final Early Treatment of Diabetic Retinopathy Study (ETDRS) grading scale (10).
- Blindness: loss of vision in one or both eyes, defined as visual acuity of 20/200 or worse.
- Photocoagulation: focal or panretinal for macular edema or PDR.
- Severe hypoglycemia: events that require assistance from another individual, including episodes of seizure and/or coma.
- Diabetic ketoacidosis (DKA): an event characterized by hyperglycemia (>200 mg/dl) in the presence of ketonuria and acidemia requiring treatment at a health care facility.

Baseline. The baseline data for EDIC are defined as that collected during the first two visits (to provide the full complement of data, some of which was collected biannually) to an EDIC clinical center that occurred between 1 January 1994 and 31 December 1995. Those visits were scheduled as close as possible to the subject's DCCT randomization anniversary.

Data management

Data management in the EDIC study follows the principles established in the DCCT, but specific procedures take advantage of new technical advances.

Data management and statistical analysis are conducted using SAS software (SAS Institute, Cary, NC). Incoming data forms are keyed into SAS data files for the appropriate form types, then merged into the corresponding master files after new records are edited for possible data errors by SAS application programs.

Data forms are tracked through the data coordinating center by a check-off system that is reviewed at each step (log-in, keying, editing) to ensure that no forms are lost during paper handling. Lab result reports are distributed biweekly to all clinics. This system provides a mechanism for detecting errors and explaining irregularities in the study database.

Statistical analyses

Significance level. All significance tests for the comparisons (predominantly between the groups previously assigned to intensive and conventional therapy) will be two-sided. A Bonferroni adjustment (11) will be used to control for the multiple pairwise comparisons of treatment arms and the multiple primary outcomes. All results at $P < 0.05$ will be considered significant.

Intention to treat. All hypothesis testing with regard to possible persistent effects of intensive therapy during the DCCT will adhere to the intention-to-treat approach, i.e., all data will be analyzed according to the participants' original DCCT treatment assignment regardless of subsequent treatment during EDIC. Epidemiologic analyses will use treatment assignment during the DCCT as one variable included in the study of risk factors and outcomes.

Stratification. Analyses may be stratified by retinopathy status at entry into the DCCT, duration of type 1 diabetes, HbA_{1c}, age, sex, and other relevant factors. The original DCCT cohort was stratified into a primary prevention cohort and a secondary intervention cohort based on duration of diabetes and the presence of retinopathy (3). Where similar results are obtained for the two cohorts, a single pooled analysis for all EDIC patients combined may be presented.

For outcomes collected during the EDIC follow-up period (starting with year 1 EDIC time, 1994), analyses of cumulative incidence will use standard life-table methods for grouped time intervals (12). These include the modified actuarial life table with tests of differences between groups, using the log-rank test, and analyses adjusting for other covariates, using the proportional hazards regression model (12). Some outcome measures obtained in the DCCT and also in EDIC, e.g., retinopathy, will be assessed at time points relative to the original randomization into the DCCT (i.e., DCCT time). Therefore, at any fixed point in EDIC time, DCCT time will vary from subject to subject.

When outcomes collected in DCCT time are analyzed starting from the date of initiation of the EDIC, subjects will have staggered gaps of unequal length in their periods of observation. Likewise, observations collected in EDIC time and analyzed in DCCT time will also have unequal gaps between assessments. In such cases, analyses of cumulative incidence will be performed using methods for interval-censored observations that allow for unequal intervals between visits. These include the Turnbull estimate of the survival (cumulative incidence) function (13) and the generalizations of the log-rank test and the proportional hazards regression model (14) for such interval-censored data.

In addition, longitudinal analyses of point prevalence will be conducted. Most such analyses will be conducted in DCCT time using multivariate methods for the analysis of prevalence of quantitative, ordinal, or qualitative measures. These include the Wei-Lachin test for qualitative observations (15), the method of generalized estimating equations (16), and longitudinal mixed-effects growth-curve models (17).

The incidence of single or recurrent events, such as hypoglycemia, will be summarized as a crude rate. Such rates will be presented as the number of events per 100 patient-years based on the ratio of the observed number of events to the total patient-years of exposure. The standard error for such rates will be computed allowing for overdispersion (18). The risk ratio (relative risk) will be used to summarize the difference between groups, and tests will be based on the large-sample estimate of the variance of the log of relative risk (19). To account for the effects of covariates on the incidence rate, either the Poisson regression model (18) or the multiplicative intensity model (20) will be used. Analyses that assess the association between various outcomes and a time-dependent covariate, such as the HbA_{1c} level over time, will use the appropriate regression models described above.

Power calculations

Estimates of the statistical power of intention-to-treat comparisons of cause-specific mortality between the two original DCCT treatment groups after an additional 10 years of follow-up in EDIC are given in Table A1 of APPENDIX 1. Estimates of 10-year mortality among patients randomized to conventional treatment in the DCCT were based on the weighted average of age-specific mortality rates reported in ETDRS (F. Ferris, personal communication). Since the ETDRS reported 5-year mortality, the estimate was constructed in two stages by applying the appropriate ETDRS mortality rates to the expected number of survivors at the end of the first 5-year period.

The estimated power of the EDIC to find a difference in the 10-year prevalence of combined nephropathy outcomes (death from kidney failure, kidney transplant, renal dialysis, candidacy for renal transplant or dialysis, and clinical proteinuria) is shown in Table A4 of APPENDIX 1. These estimates are based on two-sided comparisons of the original DCCT treatment groups at a significance level of 0.05. The 10-year prevalence of this outcome among subjects randomized to the DCCT conventional treatment group was also based on ETDRS data stratified by age and duration of type 1 diabetes.

RESULTS

Recruitment of DCCT subjects into the EDIC

In January 1994, the 1,425 surviving DCCT patients were invited to participate in the EDIC; 1,375 subjects (96%) agreed to participate, of whom 687 had been originally assigned to intensive treatment and 688 to conventional treatment. The major demographic and clinical characteristics of the active EDIC participants and of the 50 subjects who chose not to participate are shown in Table 3. Compared with participants, the nonparticipants tended to have worse glycemic control at the completion

Table 3—*Characteristics of EDIC participants compared with nonparticipants*

Characteristic*	Participants	Nonparticipants	*P* value
n	1,375	50	—
Age (years)	33.6 ± 7.0	31.0 ± 7.7	0.0155
Sex (% female)	48	45	NS
Duration of type 1 diabetes (years)	12.2 ± 4.8	11.6 ± 4.4	NS
Treatment group during DCCT (% intensive)	50	30	0.0048
HbA_{1c} at closeout of DCCT (%)			
Intensive group	7.4 ± 1.1	8.5 ± 1.6	0.0031
Conventional group	9.1 ± 1.5	9.6 ± 1.4	0.1123
Debriefed at DCCT study's end (%)	99	74	<0.0001
Care transferred to non-DCCT personnel (%)	48	79	<0.0001

Data are means ± SD or %. *P* values for continuous variables are from Wilcoxon's rank-sum test; *P* values for categorical variables are from the contingency-table χ^2 test.

of the DCCT, fewer had been debriefed, and the majority were no longer under the care of former DCCT personnel (Table 3).

EDIC baseline

Table 4 presents various risk factors for cardiovascular disease separately for men and women at EDIC baseline. The men and women were similar with respect to age, duration of type 1 diabetes, HbA_{1c}, and proportion who were currently smoking. As expected, the men and women differed on several risk factors. Hypertension, a low serum HDL cholesterol, and a high LDL cholesterol were more frequent in men. In Table 5, the baseline measurements of ankle-to-arm systolic blood pressure ratio (PVD) and of carotid artery intimal-medial thickness (atherosclerosis) are presented, stratified by sex and decade of age for EDIC patients. PVD, defined as ankle-to-arm systolic blood pressure ratio <0.8, although uncommon, was equally prevalent in men and women. There were no trends with age or duration of type 1 diabetes.

The average maximums of the carotid artery wall thickness for the common and internal carotid arteries were different between men and women ($P < 0.0001$). Adjusting for height reduced, but did not eliminate, the difference ($P = 0.0007$). A test of trend for maximum wall thickness over decades of age was significant in all strata ($P \leq 0.0001$). Attained duration of diabetes was associated with wall thickness in both carotid arteries in men ($r = 0.13$ and 0.12, $P < 0.01$) but only in the internal carotid artery in women ($r = 0.12$, $P < 0.01$).

Table 6 describes diabetes management in the EDIC cohort in the first 24 months after DCCT closeout. After the completion of DCCT data collection, conventionally treated subjects were offered, and strongly encouraged to accept, DCCT clinic help in implementing intensive therapy. Following this, an orderly transfer of diabetes care, either to personnel in the center (former DCCT or non-DCCT physicians) or to other care providers was effected for all subjects. This transition took place between June and December of 1993. During the first 2 years after DCCT closeout, 69% of the original conventional group were using either multiple daily injections (MDI) or continuous subcutaneous insulin injection (CSII) therapy, while 95% of those originally assigned to the intensive treatment group continued using MDI or CSII. Similar proportions of the two original DCCT treatment groups were using human insulin preparations, with the previous intensive group continuing to use more daily insulin. A higher proportion of the previous intensive group was performing ≥4 self-monitoring of blood glucose tests per day. Rates of severe hypoglycemia and DKA were comparable in the two groups, but a larger fraction of the DCCT intensive treatment cohort was classified as overweight (Table 5).

Figure 2 presents the distribution of HbA_{1c} for the intensive and conventional treatment groups at DCCT closeout and at

Table 4—*Risk factors measured during the first 2 years of the EDIC study, based on the most recent observation from each patient*

	Men	Women	*P* value
n (%)	719 (52.4)	653 (47.6)	—
Age (years)	36.4 ± 6.6	35.4 ± 7.2	0.0068
Duration of type 1 diabetes (years)	14.3 ± 4.8	14.8 ± 5.0	NS
BMI (kg/m^2)	26.6 ± 3.9	26.0 ± 4.2	0.0001
Overweight (%)	30.9	31.8	NS
Waist-to-hip ratio	0.88 ± 0.06	0.77 ± 0.07	<0.0001
Insulin dose ($U \cdot kg^{-1} \cdot day^{-1}$)	0.71 ± 0.25	0.69 ± 0.24	NS
HbA_{1c} (%)	8.2 ± 1.3	8.3 ± 1.5	NS
Total cholesterol (mg/dl)	185.1 ± 35.6	188.1 ± 37.0	NS
Triglyceride (mg/dl)	96.8 ± 75.8	83.1 ± 73.3	0.0001
HDL cholesterol (mg/dl)	49.5 ± 12.0	59.2 ± 14.0	<0.0001
<35 mg/dl (%)	8.2	1.6	<0.0001
LDL cholesterol (mg/dl)	116.4 ± 30.8	112.1 ± 30.3	0.0083
>130 mg/dl (%)	30.6	26.0	NS
Hypertension (%)	26.6	18.1	0.0002
Current cigarette smoker (%)	22.7	19.9	NS
Exercise level			<0.001
Strenuous	10.3	2.9	
Vigorous	5.9	3.4	
Moderate	49.5	58.2	
Sedentary	34.3	35.4	
Current alcohol use (%)	47.4	32.2	<0.001
Urinary albumin excretion (mg/24 h)	38.1 ± 118.4	41.8 ± 226.9	NS
DQOL total score	76.4 ± 9.4	75.3 ± 8.6	0.0184

Data are means ± SD or %. *P* values are for men versus women. Waist-to-hip ratio is based on natural waist circumference. Hypertension is percent diagnosed as hypertensive at any time during DCCT or EDIC and is defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg or use of antihypertensives. Alcohol use is percent reporting consumption of at least one alcoholic beverage per week. DQOL, Diabetes Quality of Life

Table 5—*New measurements in the EDIC protocol*

			Systolic blood pressure ratio of resting ankle to arm		Prevalence of abnormal ankle-to-arm ratio (percent in any four ratios)				Maximum intimal-medial thickness of common and internal carotid artery		
	Age decade	*n*	Right	Left	Percent <0.8	*P* (0.8)	Percent <1.4	Percent either	*n*	Common (mm)	Internal (mm)
Women*	20–29	154	1.08 ± 0.11	1.08 ± 0.13	2.6	0.9864	0.0	2.6	172	0.616 ± 0.073	0.583 ± 0.092
	30–39	289	1.11 ± 0.12	1.10 ± 0.13	2.8	0.1307	5.9	8.3	278	0.657 ± 0.081	0.632 ± 0.147
	40–49	202	1.09 ± 0.12	1.07 ± 0.11	3.5	0.7093	1.5	5.0	178	0.696 ± 0.079	0.719 ± 0.226
Men*	20–29	117	1.07 ± 0.11	1.08 ± 0.10	2.6		2.6	5.1	125	0.636 ± 0.059	0.629 ± 0.083
	30–39	351	1.11 ± 0.12	1.10 ± 0.12	1.1		3.7	4.8	350	0.684 ± 0.083	0.684 ± 0.114
	40–49	241	1.13 ± 0.13	1.12 ± 0.14	4.1		3.7	7.9	211	0.745 ± 0.104	0.806 ± 0.261

Data are *n*, means ± SD, or %. Dorsalis pedis and posterior tibral pressures were combined using an algorithm of Hiatt et al. (51). *P* values are for men vs. women. *P value for trend in percent <0.8: women, 0.6171; men, 0.1513. $P < 0.0001$ for both common and internal intimal-medial thickness; all are from Wilcoxon's rank-sum test after linear adjustment for covariance with age.

EDIC years 1 and 2. Although the difference between the treatment groups narrowed, HbA_{1c} remained significantly lower in the intensive group ($P < 0.0001$) at each time point.

Data completeness and timeliness

Of all expected clinic visits, 95% occurred, and no decline occurred between years 1 and 2. Typically, there was a 1-month interval between the collection of each sample in the clinic and the feedback report to the clinic.

Data quality

The precision of analysis of HbA_{1c} and lipids and renal function, ECGs, carotid ultrasound, and fundus photographs during the initial 2-year follow-up ranged from 0.88 (ECG) to 0.99 (HbA_{1c}, albumin excretion rate, serum cholesterol, and serum LDL cholesterol). The precision of these measurements is very similar to that observed over the 9 years of the DCCT.

CONCLUSIONS — The DCCT recruited 1,441 subjects with type 1 diabetes between 1983 and 1989 to a randomized clinical trial designed to examine the effects of intensive treatment compared with conventional treatment on the development and progression of early microvascular, neurologic, and other complications (3–6). The adherence of the subjects to the complex protocol was extraordinary, with <3% loss to follow-up and <3% non–study-mandated deviation from assigned treatment over the 10 years of the study. After the closeout of the DCCT, these subjects have continued to demonstrate their remarkable stability as a research cohort, and 96% of them are now enrolled in the EDIC study.

The generalizability of the findings in this study cohort to the population of type 1 diabetes is germane to the rationale for EDIC. A collaborative study between the DCCT and the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) compared the DCCT cohort to a population-based type 1 diabetes cohort (22,23). The EDIC cohort has a narrower age range (age at entry to EDIC is ~17–50 years vs. 16–78 in WESDR in 1994) and is healthier, with relatively few subjects having clinically significant diabetes complications. Comparisons of the conventionally treated DCCT subjects at baseline with the respective WESDR group revealed older age and older age at diagnosis, lower HbA_{1c}, and more frequent insulin injections and monitoring in the DCCT cohort, but few other substantive differences between the populations. Moreover, the 4-year progression of retinopathy and its association with baseline HbA_{1c} were similar for the two cohorts, except for a lower rate of progression in the DCCT secondary intervention cohort than in its WESDR counterpart, perhaps because of lower HbA_{1c} in the DCCT (23). Thus, the entire EDIC cohort is reasonably representative of the type 1 diabetic population, at least with respect to retinopathy.

Table 6—*Diabetes management of EDIC cohort during the first 2 years of EDIC*

	DCCT treatment group assignment		
	Intensive	Conventional	*P* value
n	687	688	—
Insulin delivery during EDIC			<0.0001
CSII	37.0	12.6	
MDI	57.6	56.9	
One or two injections/day	5.3	30.3	
Unknown	0.1	0.3	—
Human insulin (% of subjects using)	91.1	90.8	NS
Insulin dose ($U \cdot kg^{-1} \cdot day^{-1}$)	0.75 ± 0.28	0.67 ± 0.20	<0.0001
Self-monitored blood glucose ≥4/day (%)	46.4	36.4	0.0002
Hypoglycemia (rate per 100 patient-years)			
Coma/seizure	6.3	7.1	NS
Requiring assistance	25.4	25.7	NS
DKA (rate per 100 patient-years)	2.68	2.37	NS
Overweight (%)			
Men	32.5	29.7	NS
Women	38.4	25.2	0.0005

Data are means ± SD. *P* values are from the contingency-table χ^2 test for categorical variables, Wilcoxon's rank-sum test for continuous variables, and from a Wald test of the log-relative adjusted for overdispersion of event rates. Overweight is defined for men as BMI (kg/m^2) >27.8 from the second National Health and Nutrition Examination Survey (NHANES II) of 1976 to 1980 (50) and for women as BMI (kg/m^2) >27.3.

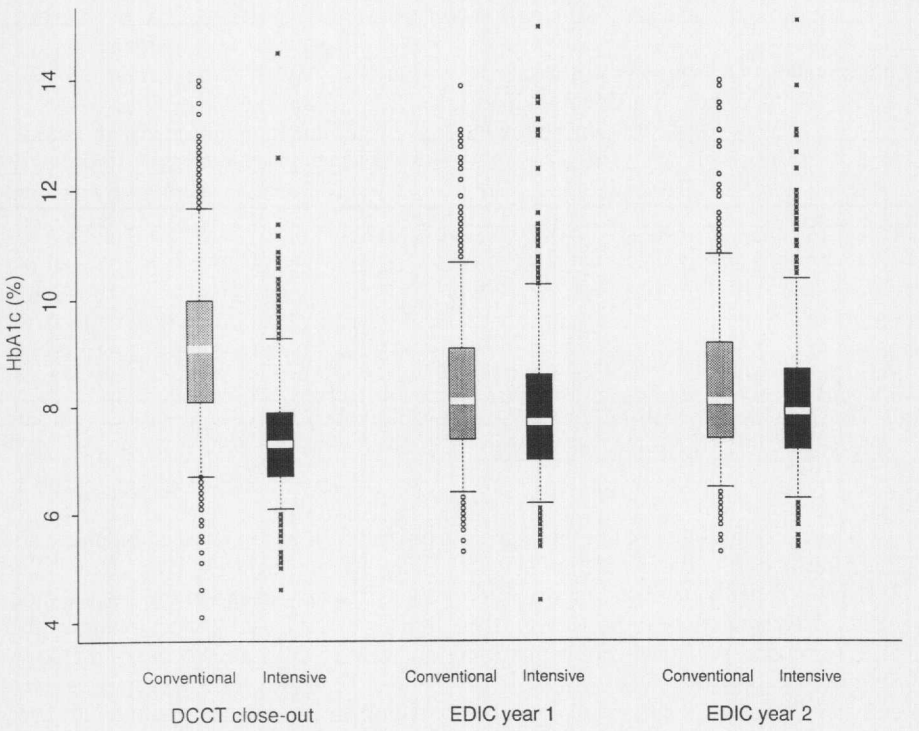

Figure 2—*Distribution of HbA_{1c} (intensive vs. conventional treatment group) at DCCT closeout and EDIC years 1 and 2. For each distribution, the median is shown by the white area with 25th and 75th percentiles shown by the boxes and 5th and 95th pecentiles shown by the bars.*

CAD

With respect to potential risk factors for macrovascular disease, the DCCT excluded patients with hypertension, nondiabetic hyperlipidemia, and known CAD (3). The EDIC cohort provides an opportunity to examine a population of type 1 diabetic patients without obvious CAD risk factors at baseline, other than their diabetes, that has had careful prospective measurement of many of the CAD risk factors established in type 2 diabetic and nondiabetic populations. The randomized interventions during the DCCT might influence the development of CAD either directly, by altering glycemia, or indirectly, by altering lipid levels (6) or by changing the development of nephropathy (5). The DCCT did not show an effect of intensive treatment on blood pressure (6). In addition, other effects of intensive therapy, such as increased weight gain, which has persisted in the EDIC cohort previously treated with intensive therapy, might alter the risk for CAD. Therefore, randomized treatment assignment and HbA_{1c} during the DCCT will be included as a covariate in analyses of CAD outcomes.

At the end of the DCCT in 1993, the entire cohort had a mean age of 33 years and mean durations of diabetes of 9 and 15 years in the primary prevention and secondary intervention cohorts, respectively. Consistent with their young age, the exclusion of patients with preexisting macrovascular risk factors, and the low incidence of nephropathy during the DCCT, only a small number of CAD events had occurred by the study's end (6). However, CAD events are likely to increase in frequency during the 10-year follow-up of the EDIC study. By study's end, the mean age of the EDIC population will approach 43 years, and mean duration of diabetes will be 19 and 25 years in the primary prevention and secondary intervention cohorts, respectively. Based on estimates derived from previous studies (24–31), the prevalence of CAD as manifested clinically and/or as detected by ECG or exercise tolerance tests is likely to be 20–40% in the DCCT secondary intervention cohort. Because age appears to be more important than duration of diabetes for the risk of CAD, only a modest downward adjustment in expected prevalence (to 15–30%) is required for the DCCT primary prevention cohort. Although clinical event rates may be further lowered by aggressive treatment with antihypertensive and hypolipidemic agents during the course of EDIC, the use of carotid ultrasound to determine intimal-medial wall thickness will enhance the sensitivity for detecting atherosclerosis. In a recent study of type 1 diabetes, patients with a 10-year history of better glycemic control exhibited significantly less arterial disease, as measured by carotid ultrasound, than poorly controlled patients (32).

PVD

PVD is also a major cause of morbidity, loss of productivity, and hospital expense and contributes to mortality in type 1 diabetes (33). The development of PVD and its relationship to potential risk factors in type 1 diabetes have not been determined definitively. Studies such as the Pittsburgh Epidemiology of Diabetes Complications Study provide data on which to base the expected prevalence of PVD in type 1 diabetes (24). As in CAD, attained age appears to be a more important predictor of PVD than duration of diabetes. For patients 18–29 years of age, PVD prevalence defined by an ankle-to-arm blood pressure ratio <0.8 is 2–4% for diabetes duration ranging from 5–9 years to 25–29 years, compared with 18% for patients aged >30 years with similar duration. A prevalence of 16% was found in a sample of type 1 diabetic patients from a Seattle, Washington, registry with a mean age of 34 years and a mean duration of diabetes of 17 years. The prevalence of PVD increased from ~12 to 40% between the ages of 34 and 45 (32). A threefold greater prevalence of PVD in women than in men has been observed, with smoking and hypertension (24) and retinopathy (34) identified as potential risk factors.

Based on these data, we estimate that the cumulative prevalence of PVD detected by ankle-to-arm blood pressure ratios at the end of EDIC will be 32% in the primary prevention cohort and 44% in the secondary intervention group of the DCCT. To ascertain accurately and objectively the development of PVD, we have implemented measurement of the ankle-to-arm blood pressure ratio, a sensitive and specific method that is relatively easy to apply and standardize in the context of a multicenter study.

Cerebrovascular disease

The relatively low frequency of stroke compounded by the previous lack of widely available sensitive noninvasive diagnostic

methods has made the study of cerebrovascular disease in type 1 diabetes problematic. Although it is assumed that cerebrovascular disease is more common in the diabetic population than in the nondiabetic population, there are few reports of its prevalence (35,36).

The 30-year-old data from the Joslin Clinic suggest that cerebrovascular disease accounts for 6.8% of deaths in diabetic patients with diabetes onset at age <20 years (37). Cerebrovascular disease also accounted for 7% of deaths among youth-onset Danish diabetic patients, a 50% higher rate than the level in similarly aged nondiabetic subjects (36). Neither study included sufficient data on vascular disease risk factors or chronic glycemia to permit analysis. More current data from the ETDRS indicate an increasing frequency of strokes with increasing age in their type 1 diabetic population (F. Ferris, personal communication). By extrapolation of the ETDRS data, the prevalence of stroke in the age range of the EDIC cohort at the end of 10-year follow-up will be ~6–8%.

This relatively low anticipated prevalence of cerebrovascular disease events may yield too few cases to analyze meaningfully. However, noninvasive measurement of the carotid artery wall thickness provides a relatively accurate and specific means of quantifying carotid atherosclerosis. High-resolution B-mode ultrasonography can be performed with standardized methods at multiple centers with a high degree of reproducibility and acceptable center-to-center variability (38). The quality of the data obtained in the EDIC cohort at baseline suggests that this method will provide a useful and reproducible measurement of carotid artery wall thickness as it changes over time (39).

Diabetic nephropathy

Because of the relatively brief duration of type 1 diabetes in the DCCT cohort and the exclusion of patients with proteinuria, the patient cohort recruited experienced only a small number of advanced renal events (clinical grade proteinuria, n = 55, and/or renal insufficiency, n = 2) by study's end. Whether the demonstrated decrease in development of microalbuminuria and clinical albuminuria with intensive therapy translates into a decrease in more advanced renal disease is a clinically important question that will be answered in the EDIC study. Previous observational studies have shown that the yearly incidence of clinical nephropathy (i.e., >500 mg proteinuria per day) begins to rise at 10 years' duration of type 1 diabetes and reaches a peak between 11 and 15 years. In the ETDRS, renal insufficiency requiring dialysis or transplantation developed within 5 years in 12.9% of subjects with duration of type 1 diabetes between 11 and 15 years at entry and in 8.7% of subjects with a duration between 15 and 20 years (F. Ferris, personal communication). Thus, 20–25% of EDIC patients who had diabetes of >11 years' duration would be predicted to develop renal insufficiency over a 10-year follow-up during the EDIC study. The implementation of preventive and therapeutic modalities, such as treatment of hypertension or the use of ACE inhibitors, will be tracked and can be adjusted for by multivariate analysis.

Advanced diabetic retinopathy

The EDIC will study the development of more advanced retinopathy in the DCCT cohort. Longitudinal and cross-sectional studies suggest a progressive increase in diabetic retinopathy from background to preproliferative to proliferative stages (22,40,41). The baseline degree of retinopathy and, in particular, the number of microaneurysms and retinal hemorrhages are high-risk factors for later development of PDR (22). Therefore, the demonstration by the DCCT of a beneficial effect of intensive insulin treatment on progression from no retinopathy to background retinopathy and ultimately to preproliferative and severe retinopathy suggests that glycemic control should have a similar protective effect in PDR with high-risk characteristics. Long-term study of the EDIC population should address this question directly. Older retrospective studies indicate that the period of most rapid development of PDR begins at 10–13 years of duration (41). At closeout, the DCCT cohort had a mean duration of 12 years. From the prospective WESDR study results, we can expect ~20% of the EDIC cohort to develop PDR (and 4–5% to reach high-risk characteristics) in each 5-year segment of the study. A higher proportion of these events would be expected to occur in the original DCCT secondary intervention group than in the primary prevention group. Other factors have been demonstrated to contribute to the risk of retinopathy progression, including higher diastolic blood pressure (42), renal insufficiency and microalbuminuria (43), and duration of diabetes (22). Certain HLA haplotypes have been reported to be associated with higher risk (44,45). Of particular interest, the DCCT has now demonstrated concordance for severity of retinopathy within multiplex families with type 1 diabetes (46). How these risk factors interact with glycemic control will be addressed in the EDIC study.

Value of extended follow-up of a clinical trial

The potential scientific gains of conducting extended observational follow-up of subjects from completed randomized clinical trials have been summarized (47,48). These include the following: *1*) additional beneficial or adverse effects of a treatment regimen on more slowly developing, but possibly more serious, consequences may be discovered (an example is the demonstration by a 9-year extended follow-up that nicotinic acid reduced coronary heart disease mortality and all-cause mortality after the original 6-year randomized clinical trial had demonstrated a decrease in MIs but not in mortality [49]); 2) particular subgroups with differential treatment benefits may be identified, generating new hypotheses and new randomized clinical trials; and 3) acquisition of up-to-date natural history data in the context of community treatment can help in the design of future intervention trials.

While there are potential problems in extended follow-up studies, EDIC may have limited, if not eliminated, them (47,48). First, the design and data to be collected are subject to bias if they are based on knowledge of results from the randomized trial itself. However, the EDIC protocol was largely developed before unmasking of the DCCT results and was, therefore, uninfluenced by them. Second, data acquired with extended follow-up may lack completeness due to subject unwillingness to undergo sufficiently frequent or rigorous examination, diminished resources, and/or long-term subject attrition. The experience of EDIC thus far suggests that subject adherence has not declined, and the study is sufficiently supported by available resources to anticipate nearly complete data collection. Third, future differences in outcomes may be blurred by treatment crossovers, by introduction of new treatments, or by withdrawal from treatments because treatment is not systematically regulated during the post-trial follow-up. The former intensive

treatment group has largely continued on that regimen, albeit with a modest increase in average HbA_{1c}. The former conventional treatment group was appropriately encouraged to cross over to intensive treatment based on the results of the DCCT. It is, therefore, possible that the narrowed differences between the two groups with regard to treatments and in the resultant mean HbA_{1c} levels may partly obscure differences in long-term outcomes over time. Multivariate analyses can help to identify such confounding (4). Estimates of the statistical power to detect differences in outcomes during extended follow-up by continuation of intention-to-treat analysis are subject to uncertainty with regard to future dropout rates, introduction of new therapies that will influence measured outcomes, or inadequacy of the natural history data that were available for the power calculations. None of these potential difficulties are likely to be limiting in EDIC. Subject dropout can be strongly influenced by the strong bonds that developed with the subjects during the DCCT (5). Moreover, our subjects realize that EDIC is a unique study and do not seem inclined to join other studies. It may be difficult to ascertain accurately the rigor with which each of two previous randomized treatments is actually used by subjects during a follow-up study. In EDIC, HbA_{1c} measurements are a reasonable surrogate for the diabetes treatment regimens themselves. Since glycemic differences were the dominant factor that generated treatment-group differences in outcomes during the DCCT, monitoring of HbA_{1c} will permit analysis of glycemia as a risk factor. The EDIC investigators and the NIDDK have concluded that the potential weaknesses of extended follow-up studies are greatly outweighed by the significant value of continued systematic observation of the DCCT cohort and that the EDIC is a valuable natural history study of a cohort previously enrolled in a controlled clinical trial.

In conclusion, the EDIC study successfully enrolled 96% of the surviving DCCT cohort in a long-term study that will focus on late-occurring more severe micro- and macrovascular complications of diabetes. EDIC has achieved a high degree of baseline data collection using reliable quality-controlled measurements. The cohort has been comprehensively characterized at baseline in terms of the presence or absence of micro- and macrovascular complications of type 1 diabetes, the major recognized risk factors for these complications, preceding and current levels of chronic glycemia, and treatment. The study is adequately powered to examine hypotheses related to progression of cardiovascular disease, nephropathy, neuropathy, and retinopathy.

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APPENDIX 1

Estimated power of mortality comparisons in the EDIC patient population

Tables A1–A3 provide estimates of the statistical power of intent-to-treat comparisons of mortality between the two randomized treatment groups of the DCCT after an additional 10 years of follow-up in the EDIC study. These estimates are based on a simple test of proportions after 10 years of observation. Survival analysis may provide a more powerful test of treatment differences, but the increase in power is difficult to estimate without making untestable assumptions about the future shapes of the respective hazard functions.

The 10-year mortality among patients randomized to conventional treatment in the DCCT was estimated as the weighted average of the age-specific mortality rates reported by the ETDRS, shown in APPENDIX 2. Since the ETDRS reported 5-year mortality, the estimate was constructed in two

Table A1—*All-cause mortality*

	Assumed treatment effect						
n	20%	25%	30%	35%	40%	45%	50%
350	0.173	0.249	0.344	0.453	0.570	0.684	0.786
400	0.191	0.278	0.384	0.504	0.627	0.741	0.837
450	0.209	0.307	0.423	0.552	0.678	0.790	0.877
500	0.227	0.335	0.461	0.596	0.724	0.831	0.908
550	0.246	0.362	0.498	0.637	0.764	0.864	0.932
600	0.264	0.389	0.532	0.675	0.799	0.892	0.950
650	0.281	0.416	0.565	0.710	0.830	0.914	0.964

The assumed combined 10-year mortality in the DCCT conventional group is 11.8%.

Table A2—*Mortality due to CAD*

	Assumed treatment effect						
n	20%	25%	30%	35%	40%	45%	50%
350	0.138	0.192	0.262	0.346	0.441	0.544	0.647
400	0.150	0.213	0.292	0.386	0.491	0.600	0.705
450	0.163	0.234	0.322	0.426	0.538	0.651	0.755
500	0.176	0.255	0.352	0.464	0.582	0.697	0.798
550	0.189	0.275	0.381	0.500	0.623	0.738	0.834
600	0.202	0.296	0.409	0.535	0.661	0.774	0.865
650	0.215	0.316	0.437	0.568	0.695	0.806	0.890

The assumed combined 10-year mortality in the DCCT conventional group is 8.7%.

Table A3—*Mortality due to stroke*

	Assumed treatment effect						
n	20%	25%	30%	35%	40%	45%	50%
350	0.060	0.066	0.074	0.083	0.095	0.109	0.126
400	0.061	0.068	0.077	0.088	0.102	0.118	0.137
450	0.063	0.070	0.080	0.093	0.108	0.127	0.148
500	0.064	0.073	0.084	0.098	0.115	0.135	0.160
550	0.065	0.075	0.087	0.103	0.122	0.144	0.171
600	0.067	0.077	0.091	0.108	0.128	0.153	0.182
650	0.068	0.080	0.094	0.113	0.135	0.162	0.194

The assumed combined 10-year mortality in the DCCT conventional group is 1.1%.

Table A4—*Combined renal outcomes*

	Assumed treatment effect						
n	20%	25%	30%	35%	40%	45%	50%
350	0.245	0.360	0.495	0.633	0.760	0.860	0.929
400	0.273	0.403	0.548	0.692	0.813	0.902	0.956
450	0.301	0.443	0.598	0.742	0.856	0.932	0.973
500	0.328	0.482	0.643	0.786	0.890	0.953	0.984
550	0.355	0.520	0.685	0.823	0.917	0.968	0.991
600	0.382	0.555	0.723	0.854	0.937	0.979	0.994
650	0.408	0.598	0.756	0.881	0.953	0.986	0.997

The assumed 10-year prevalence in the DCCT conventional group is 17.4%. Adapted from the EDIC Data Coordinating Center Manual of Operations (7).

Table A5—*The 5-year mortality in the ETDRS*

	Age at entry (years)				
	18–29	30–34	35–39	40–44	45+
n	609	262	209	132	232
Cause of death					
All causes	2.0	4.6	7.2	6.1	13.4
CAD	0.8	3.1	5.3	4.6	11.2
Stroke	0.2	0.8	0.5	0.8	0.4

Data are (%). Adapted from the EDIC Data Coordinating Center Manual of Operations (7).

Table A6—*Ages of EDIC participants at DCCT closeout*

Age range (years)	All patients	Conventional group
17–24	172	95
25–29	244	122
30–34	348	185
35–39	340	173
40–44	249	123
45+	74	32

Data are *n*.

stages by applying the appropriate ETDRS mortality rates to the expected number of survivors at the end of the first 5-year period.

Alternative hypotheses are expressed as the anticipated reduction in the risk of death associated with assignment to intensive therapy during the DCCT. It is assumed that all tests will be two-sided at the 0.05 significance level.

Estimated power of intent-to-treat comparisons of combined nephropathic outcomes in the EDIC

Table A4 describes the estimated power of the EDIC to find a difference in the combined 10-year prevalence of death from kidney failure, kidney transplant, renal dialysis, awaiting renal transplant or dialysis, and clinical proteinuria. Once again, they are based on two-sided comparisons of the original DCCT treatment groups at a significance level of 0.05. ETDRS data stratified by age and duration of type 1 diabetes were used to estimate the 10-year prevalence of this outcome among patients randomized to the conventional group of the DCCT.

APPENDIX 2 — Data on 5-year mortality in the ETDRS and the ages of EDIC participants at DCCT closeout can be found in Tables A5 and A6.

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APPENDIX B

SAS 9.1 Log for programming code submitted for the replication of results in Tables 3-6 of EDIC Baseline Paper

```
1                                          The SAS System           19:17
Wednesday, July 11, 2007

NOTE: Copyright (c) 2002-2003 by SAS Institute Inc., Cary, NC, USA.
NOTE: SAS (r) 9.1 (TS1M3)
      Licensed to RESEARCH TRIANGLE INSTITUTE, Site 0047670011.
NOTE: This session is executing on the XP_PRO  platform.



NOTE: SAS 9.1.3 Service Pack 3

NOTE: SAS initialization used:
      real time           1.62 seconds
      cpu time            0.37 seconds

1          * Filename:  EDICbsln.SAS
2            Location:
\\Rtints23\niddk2\05_Users\Sylvia\DCCT_EDIC\IntegCheck\EDIC_bsln
3            Project:   NIDDK Data Repository -- Dataset Integrity Checks
4            By:        Sylvia Tan
5            Purpose:   Analysis of integrity of EDIC Baseline archived
dataset in the NIDDK Data
5         ! Repository
6            Compare results to tables in paper published by
7            DCCT-EDIC Research Group in 1999 (Diabetes Care, [22(1)])
8            Last updated:  7/11/07 *;
9
10         options ps=500 ls=180 nonumber formchar='|----|+\---+=|-^<>*'
mprint
10        ! orientation=portrait;
11
12         libname EDICBase "C:\DATA\NIDDK\EDICbase\DSIC";
NOTE: Libref EDICBASE was successfully assigned as follows:
      Engine:        V9
      Physical Name: C:\DATA\NIDDK\EDICbase\DSIC
13         libname EDICBa_x xport
13        !
"\\Rtints23\niddk2\03_Data_And_Tools\Database\Databases\DCCT_EDIC\DCCT Old
13        ! Versions\EDIC_NEW\Phase3\Study1\edicBASE.xpt";
NOTE: Libref EDICBA_X was successfully assigned as follows:
      Engine:        XPORT
      Physical Name:
\\Rtints23\niddk2\03_Data_And_Tools\Database\Databases\DCCT_EDIC\DCCT Old
      Versions\EDIC_NEW\Phase3\Study1\edicBASE.xpt
14         libname library
"\\Rtints23\niddk2\03_Data_And_Tools\Database\Databases\DCCT_EDIC\DCCT
14        ! Old Versions\EDIC_NEW\All Formats";
NOTE: Libref LIBRARY was successfully assigned as follows:
      Engine:        V9
      Physical Name:
\\Rtints23\niddk2\03_Data_And_Tools\Database\Databases\DCCT_EDIC\DCCT Old
      Versions\EDIC_NEW\All Formats
15
16         * create SAS dataset from XPT file *;
17         proc cimport data=EDICBase.EDICbase infile=EDICBa_x; run;
```

```
NOTE: Proc CIMPORT begins to create/update data set EDICBASE.EDICbase
NOTE: Data set contains 46 variables and 1428 observations.
      Logical record length is 304

NOTE: PROCEDURE CIMPORT used (Total process time):
      real time           1.85 seconds
      cpu time            0.03 seconds


18
19         data EDICBASE; set edicbase.edicbase;
20
21         ****************************************;
22         * EDIC Baseline:  Table 3               *;
23         * compare EDIC participants vs non-part *;
24         ****************************************;
25         ods rtf file="C:\DATA\NIDDK\EDICbase\DSIC\EDICBASE_T3.rtf"
style=sasdocprinter;
NOTE: Writing RTF Body file: C:\DATA\NIDDK\EDICbase\DSIC\EDICBASE_T3.rtf
26
27         title EDIC Bsln Paper - Replicate Table 3;

NOTE: There were 1428 observations read from the data set EDICBASE.EDICBASE.
NOTE: The data set WORK.EDICBASE has 1428 observations and 46 variables.
NOTE: DATA statement used (Total process time):
      real time           2.43 seconds
      cpu time            0.46 seconds


28         proc freq; tables in_edic; run;

NOTE: There were 1428 observations read from the data set WORK.EDICBASE.
NOTE: The PROCEDURE FREQ printed page 1.
NOTE: PROCEDURE FREQ used (Total process time):
      real time           0.18 seconds
      cpu time            0.01 seconds


29         proc means maxdec=1 n mean std; var exit_age exit_dur; class
in_edic; run;

NOTE: There were 1428 observations read from the data set WORK.EDICBASE.
NOTE: The PROCEDURE MEANS printed page 2.
NOTE: PROCEDURE MEANS used (Total process time):
      real time           0.12 seconds
      cpu time            0.01 seconds


30         proc npar1way wilcoxon; var exit_age exit_dur; class in_edic; run;

NOTE: There were 1428 observations read from the data set WORK.EDICBASE.
NOTE: The PROCEDURE NPAR1WAY printed pages 3-4.
NOTE: PROCEDURE NPAR1WAY used (Total process time):
      real time           0.10 seconds
      cpu time            0.01 seconds
```

```
31
32         proc sort; by group;

NOTE: There were 1428 observations read from the data set WORK.EDICBASE.
NOTE: The data set WORK.EDICBASE has 1428 observations and 46 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.01 seconds
      cpu time            0.00 seconds


33         proc means maxdec=1 n mean std; var  hbam999; class in_edic; by
group; run;

NOTE: There were 1428 observations read from the data set WORK.EDICBASE.
NOTE: The PROCEDURE MEANS printed page 5.
NOTE: PROCEDURE MEANS used (Total process time):
      real time           0.10 seconds
      cpu time            0.00 seconds


34         proc npar1way wilcoxon; var  hbam999; class in_edic; by group;
run;

NOTE: There were 1428 observations read from the data set WORK.EDICBASE.
NOTE: The PROCEDURE NPAR1WAY printed pages 6-7.
NOTE: PROCEDURE NPAR1WAY used (Total process time):
      real time           0.14 seconds
      cpu time            0.03 seconds


35         proc freq; tables (sex group mab1 mac1)*in_edic/chisq exact; run;

NOTE: There were 1428 observations read from the data set WORK.EDICBASE.
NOTE: The PROCEDURE FREQ printed pages 8-13.
NOTE: PROCEDURE FREQ used (Total process time):
      real time           0.32 seconds
      cpu time            0.07 seconds


36
37         ods rtf close; run;
38
39         ****************************************;
40         * EDIC Baseline:  Table 4               *;
41         * Risk factors during 1st 2 yrs of EDIC *;
42         ****************************************;
43           * just EDIC participants *;
44         DATA EDICBASE_A; set edicbase;
45           if in_edic=1;
46           if smoking=3 then currsmok=1; else if smoking in (1,2) then
currsmok=0;
47
48           if age=. and yrs_iddm=. and bmi=. and hba1c=. and tchol=. and
triglyc=. and hdl=. and
49           ldl=. and aer=. and qol=. and whr=. and std_ins=.
50           and over_wt=. and low_hdl=. and high_ldl=. and ht=. and
smoking=. and currsmok=. and
```

```
51           exercise=. and obdrink1=. then NODATA=1; /* 2females and 1male
were missing all data,
51       !  except
52           IMT in one subject, take them out to match gender breakdowns in
published Table 4;
52       ! */run;

NOTE: There were 1428 observations read from the data set WORK.EDICBASE.
NOTE: The data set WORK.EDICBASE_A has 1375 observations and 48 variables.
NOTE: DATA statement used (Total process time):
      real time           0.38 seconds
      cpu time            0.03 seconds


53
54         ods rtf file="C:\DATA\NIDDK\EDICbase\DSIC\EDICBASE_T4.rtf"
style=sasdocprinter;
NOTE: Writing RTF Body file: C:\DATA\NIDDK\EDICbase\DSIC\EDICBASE_T4.rtf
55
56         title EDIC Bsln Paper - Replicate Table 4;
57         proc freq; tables sex; WHERE NODATA^=1; run;

NOTE: There were 1372 observations read from the data set WORK.EDICBASE_A.
      WHERE NODATA not = 1;
NOTE: The PROCEDURE FREQ printed page 14.
NOTE: PROCEDURE FREQ used (Total process time):
      real time           0.06 seconds
      cpu time            0.01 seconds


58         proc means n mean std maxdec=1; class sex; WHERE NODATA^=1;
59           var age yrs_iddm bmi hba1c tchol triglyc hdl ldl aer qol; run;

NOTE: There were 1372 observations read from the data set WORK.EDICBASE_A.
      WHERE NODATA not = 1;
NOTE: The PROCEDURE MEANS printed pages 15-16.
NOTE: PROCEDURE MEANS used (Total process time):
      real time           0.12 seconds
      cpu time            0.03 seconds


60         proc means n mean std maxdec=2; class sex; WHERE NODATA^=1;
61           var whr std_ins; run;

NOTE: There were 1372 observations read from the data set WORK.EDICBASE_A.
      WHERE NODATA not = 1;
NOTE: The PROCEDURE MEANS printed page 17.
NOTE: PROCEDURE MEANS used (Total process time):
      real time           0.12 seconds
      cpu time            0.01 seconds


62         proc npar1way wilcoxon; class sex; WHERE NODATA^=1;
63           var age yrs_iddm bmi whr std_ins hba1c tchol triglyc hdl ldl aer
qol; run;

NOTE: There were 1372 observations read from the data set WORK.EDICBASE_A.
```

```
      WHERE NODATA not = 1;
NOTE: The PROCEDURE NPAR1WAY printed pages 18-29.
NOTE: PROCEDURE NPAR1WAY used (Total process time):
      real time           0.17 seconds
      cpu time            0.07 seconds


64         proc freq; tables (over_wt low_hdl high_ldl ht smoking currsmok
exercise obdrink1)*sex/
65           chisq exact; WHERE NODATA^=1;
66           run;

NOTE: There were 1372 observations read from the data set WORK.EDICBASE_A.
      WHERE NODATA not = 1;
NOTE: The PROCEDURE FREQ printed pages 30-39.
NOTE: PROCEDURE FREQ used (Total process time):
      real time           0.40 seconds
      cpu time            0.14 seconds



67
68         ods rtf close; run;
69
70         ****************************************;
71         * EDIC Baseline:  Table 5               *;
72         * New measurements in EDIC protocol     *;
73         ****************************************;
74         data EDICBASE_A; set edicbase_a;
75           if low_aar=1 or high_aar=1 then lowhigh_aar=1;
76           else if low_aar=0 and high_aar=0 then lowhigh_aar=0;
77
78         ods rtf file="C:\DATA\NIDDK\EDICbase\DSIC\EDICBASE_T5.rtf"
style=sasdocprinter;
NOTE: Writing RTF Body file: C:\DATA\NIDDK\EDICbase\DSIC\EDICBASE_T5.rtf
79
80         title EDIC Bsln Paper - Replicate Table 5;

NOTE: There were 1375 observations read from the data set WORK.EDICBASE_A.
NOTE: The data set WORK.EDICBASE_A has 1375 observations and 49 variables.
NOTE: DATA statement used (Total process time):
      real time           0.67 seconds
      cpu time            0.17 seconds


81         proc means n mean std maxdec=2 data=edicbase_a; where decade not
in ('','50 plus');
82          class sex decade; var ldp_mean rdp_mean; run;

NOTE: There were 1355 observations read from the data set WORK.EDICBASE_A.
      WHERE decade not in (' ', '50 plus');
NOTE: The PROCEDURE MEANS printed page 40.
NOTE: PROCEDURE MEANS used (Total process time):
      real time           0.14 seconds
      cpu time            0.03 seconds


83         proc freq;  where decade not in ('','50 plus');
```

```
84          tables sex*(low_aar high_aar lowhigh_aar)*decade; run;

NOTE: There were 1355 observations read from the data set WORK.EDICBASE_A.
      WHERE decade not in (' ', '50 plus');
NOTE: The PROCEDURE FREQ printed pages 41-43.
NOTE: PROCEDURE FREQ used (Total process time):
      real time           0.18 seconds
      cpu time            0.01 seconds


85          proc sort data=edicbase_a; by decade;

NOTE: There were 1375 observations read from the data set WORK.EDICBASE_A.
NOTE: The data set WORK.EDICBASE_A has 1375 observations and 49 variables.
NOTE: PROCEDURE SORT used (Total process time):
      real time           0.01 seconds
      cpu time            0.00 seconds


86         proc freq; where decade not in ('','50 plus');
87          by decade; tables sex*low_aar/chisq exact; run;

NOTE: There were 1355 observations read from the data set WORK.EDICBASE_A.
      WHERE decade not in (' ', '50 plus');
NOTE: The PROCEDURE FREQ printed pages 44-49.
NOTE: PROCEDURE FREQ used (Total process time):
      real time           0.17 seconds
      cpu time            0.03 seconds


88
89           * run IMT analysis on entire dataset to get published n's (DCC:
IMT was a separate
89       ! study) *;
90         proc means n mean std maxdec=3 DATA=EDICBASE; class sex dec_imt;
var common internal;
90       ! run;

NOTE: There were 1428 observations read from the data set WORK.EDICBASE.
NOTE: The PROCEDURE MEANS printed pages 50-51.
NOTE: PROCEDURE MEANS used (Total process time):
      real time           0.10 seconds
      cpu time            0.03 seconds


91
92         ods rtf close; run;
93
94         ****************************************;
95         * EDIC Baseline:  Table 6               *;
96         * Diab mgmt during 1st two yrs of EDIC  *;
97         ****************************************;
98         ods rtf file="C:\DATA\NIDDK\EDICbase\DSIC\EDICBASE_T6.rtf"
style=sasdocprinter;
NOTE: Writing RTF Body file: C:\DATA\NIDDK\EDICbase\DSIC\EDICBASE_T6.rtf
99
100        title EDIC Bsln Paper - Replicate Table 6;
```

```
101
102        proc freq data=edicbase_a; tables group; run;

NOTE: There were 1375 observations read from the data set WORK.EDICBASE_A.
NOTE: The PROCEDURE FREQ printed page 52.
NOTE: PROCEDURE FREQ used (Total process time):
      real time           0.12 seconds
      cpu time            0.01 seconds


103        proc freq data=edicbase_a; tables (obinsreg hum_ins
sbgm_4)*group/chisq exact; run;

NOTE: There were 1375 observations read from the data set WORK.EDICBASE_A.
NOTE: The PROCEDURE FREQ printed pages 53-58.
NOTE: PROCEDURE FREQ used (Total process time):
      real time           0.21 seconds
      cpu time            0.07 seconds


104        proc means n mean std maxdec=2; var std_ins; class group; run;

NOTE: There were 1375 observations read from the data set WORK.EDICBASE_A.
NOTE: The PROCEDURE MEANS printed page 59.
NOTE: PROCEDURE MEANS used (Total process time):
      real time           0.12 seconds
      cpu time            0.01 seconds


105          proc npar1way wilcoxon; var std_ins; class group; run;

NOTE: There were 1375 observations read from the data set WORK.EDICBASE_A.
NOTE: The PROCEDURE NPAR1WAY printed page 60.
NOTE: PROCEDURE NPAR1WAY used (Total process time):
      real time           0.07 seconds
      cpu time            0.01 seconds


106
107        data EDICBASE_A; set edicbase_a;
108          pt_cs_b=365.25*pt_cs;
109          pt_ra_b=365.25*pt_ra;
110          pt_dka_b=365.25*pt_dka;
111
112          title2 mean rates per year;

NOTE: Missing values were generated as a result of performing an operation on
missing values.
      Each place is given by: (Number of times) at (Line):(Column).
      7 at 108:17   7 at 109:17   7 at 110:18
NOTE: There were 1375 observations read from the data set WORK.EDICBASE_A.
NOTE: The data set WORK.EDICBASE_A has 1375 observations and 52 variables.
NOTE: DATA statement used (Total process time):
      real time           0.37 seconds
      cpu time            0.01 seconds
```

```
113        proc means mean maxdec=2; class group; var pt_cs_b pt_ra_b
pt_dka_b; run;

NOTE: There were 1375 observations read from the data set WORK.EDICBASE_A.
NOTE: The PROCEDURE MEANS printed page 61.
NOTE: PROCEDURE MEANS used (Total process time):
      real time           0.13 seconds
      cpu time            0.03 seconds


114          proc npar1way wilcoxon; class group; var pt_cs_b pt_ra_b
pt_dka_b; run;

NOTE: There were 1375 observations read from the data set WORK.EDICBASE_A.
NOTE: The PROCEDURE NPAR1WAY printed pages 62-64.
NOTE: PROCEDURE NPAR1WAY used (Total process time):
      real time           0.09 seconds
      cpu time            0.01 seconds


115        title;
116        proc freq data=edicbase_a; tables sex*ow*group/all; run;

NOTE: There were 1375 observations read from the data set WORK.EDICBASE_A.
NOTE: The PROCEDURE FREQ printed pages 65-71.
NOTE: PROCEDURE FREQ used (Total process time):
      real time           0.28 seconds
      cpu time            0.03 seconds


117
118        ods rtf close; run;
119

NOTE: SAS Institute Inc., SAS Campus Drive, Cary, NC USA 27513-2414
NOTE: The SAS System used:
      real time           13.70 seconds
      cpu time            2.17 seconds
```

APPENDIX C

SAS 9.1 Output for programming code submitted for the replication of results in Tables 3-6 of EDIC Baseline Paper

EDIC Bsln Paper - Replicate Table 3

The FREQ Procedure

EDIC participant				
IN_EDIC	Frequency	Percent	Cumulative Frequency	Cumulative Percent
0: No	53	3.71	53	3.71
1: Yes	1375	96.29	1428	100.00

EDIC Bsln Paper - Replicate Table 3

The MEANS Procedure

EDIC participant	N Obs	Variable	Label	N	Mean	Std Dev
0: No	53	EXIT_AGE	Age (years) at DCCT Close-Out (Table 3)	51	31.0	7.7
		EXIT_DUR	Duration of IDDM (years) at DCCT Close-Out	51	11.6	4.4
1: Yes	1375	EXIT_AGE	Age (years) at DCCT Close-Out (Table 3)	1372	33.6	7.0
		EXIT_DUR	Duration of IDDM (years) at DCCT Close-Out	1372	12.2	4.8

EDIC Bsln Paper - Replicate Table 3

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable EXIT_AGE Classified by Variable IN_EDIC

IN_EDIC	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
1: Yes	1372	983836.50	976864.0	2879.12406	717.081997
0: No	51	29339.50	36312.0	2879.12406	575.284314

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	29339.5000
Normal Approximation	
Z	-2.4216
One-Sided Pr < Z	0.0077
Two-Sided Pr > |Z|	0.0155
t Approximation	
One-Sided Pr < Z	0.0078
Two-Sided Pr > |Z|	0.0156

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	5.8648
DF	1
Pr > Chi-Square	0.0154

EDIC Bsln Paper - Replicate Table 3

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable EXIT_DUR Classified by Variable IN_EDIC

IN_EDIC	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
1: Yes	1372	979027.0	976864.0	2881.48724	713.576531
0: No	51	34149.0	36312.0	2881.48724	669.588235

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	34149.0000
Normal Approximation	
Z	-0.7505
One-Sided Pr < Z	0.2265
Two-Sided Pr > |Z|	0.4530
t Approximation	
One-Sided Pr < Z	0.2265
Two-Sided Pr > |Z|	0.4531

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	0.5635
DF	1
Pr > Chi-Square	0.4529

EDIC Bsln Paper - Replicate Table 3

The MEANS Procedure

TREATMENT GROUP=EXPERIMENTAL: Intensive Treatment

Analysis Variable : HBAM999 DCCT close-out HBA1c (Table3)

EDIC participant	N Obs	N	Mean	Std Dev
0: No	16	12	8.5	1.6
1: Yes	687	685	7.4	1.1

TREATMENT GROUP=STANDARD: Conventional Treatment

Analysis Variable : HBAM999 DCCT close-out HBA1c (Table3)

EDIC participant	N Obs	N	Mean	Std Dev
0: No	37	35	9.6	1.4
1: Yes	688	687	9.1	1.5

EDIC Bsln Paper - Replicate Table 3

The NPAR1WAY Procedure

TREATMENT GROUP=EXPERIMENTAL: Intensive Treatment

Wilcoxon Scores (Rank Sums) for Variable HBAM999 Classified by Variable IN_EDIC

IN_EDIC	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
1: Yes	685	237019.50	239065.0	691.027395	346.013869
0: No	12	6233.50	4188.0	691.027395	519.458333

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	6233.5000
Normal Approximation	
Z	2.9594
One-Sided Pr > Z	0.0015
Two-Sided Pr > |Z|	0.0031
t Approximation	
One-Sided Pr > Z	0.0016
Two-Sided Pr > |Z|	0.0032

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	8.7621
DF	1
Pr > Chi-Square	0.0031

EDIC Bsln Paper - Replicate Table 3

The NPAR1WAY Procedure

TREATMENT GROUP=STANDARD: Conventional Treatment

Wilcoxon Scores (Rank Sums) for Variable HBAM999 Classified by Variable IN_EDIC

IN_EDIC	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
1: Yes	687	246439.0	248350.50	1203.33963	358.717613
0: No	35	14564.0	12652.50	1203.33963	416.114286

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	14564.0000
Normal Approximation	
Z	1.5881
One-Sided Pr > Z	0.0561
Two-Sided Pr > |Z|	0.1123
t Approximation	
One-Sided Pr > Z	0.0564
Two-Sided Pr > |Z|	0.1127

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	2.5233
DF	1
Pr > Chi-Square	0.1122

EDIC Bsln Paper - Replicate Table 3

The FREQ Procedure

Table of SEX by IN_EDIC

SEX(Gender (coded M or F)) / IN_EDIC(EDIC participant) / Frequency / Percent / Row Pct / Col Pct	0: No	1: Yes	Total
F: Female	24	655	679
	1.68	45.87	47.55
	3.53	96.47	
	45.28	47.64	
M: Male	29	720	749
	2.03	50.42	52.45
	3.87	96.13	
	54.72	52.36	
Total	53	1375	1428
	3.71	96.29	100.00

Statistics for Table of SEX by IN_EDIC

Statistic	DF	Value	Prob
Chi-Square	1	0.1133	0.7364
Likelihood Ratio Chi-Square	1	0.1135	0.7362
Continuity Adj. Chi-Square	1	0.0386	0.8442
Mantel-Haenszel Chi-Square	1	0.1132	0.7365
Phi Coefficient		-0.0089	
Contingency Coefficient		0.0089	
Cramer's V		-0.0089	

Fisher's Exact Test	
Cell (1,1) Frequency (F)	24
Left-sided Pr <= F	0.4230
Right-sided Pr >= F	0.6825
Table Probability (P)	0.1055
Two-sided Pr <= P	0.7804

Sample Size = 1428

EDIC Bsln Paper - Replicate Table 3

The FREQ Procedure

Table of GROUP by IN_EDIC

GROUP(TREATMENT GROUP) Frequency Percent Row Pct Col Pct	IN_EDIC(EDIC participant) 0: No	 1: Yes	 Total
EXPERIMENTAL: Intensive Treatment	16 1.12 2.28 30.19	687 48.11 97.72 49.96	703 49.23
STANDARD: Conventional Treatment	37 2.59 5.10 69.81	688 48.18 94.90 50.04	725 50.77
Total	53 3.71	1375 96.29	1428 100.00

Statistics for Table of GROUP by IN_EDIC

Statistic	DF	Value	Prob
Chi-Square	1	7.9844	0.0047
Likelihood Ratio Chi-Square	1	8.2152	0.0042
Continuity Adj. Chi-Square	1	7.2129	0.0072
Mantel-Haenszel Chi-Square	1	7.9789	0.0047
Phi Coefficient		-0.0748	
Contingency Coefficient		0.0746	
Cramer's V		-0.0748	

Fisher's Exact Test	
Cell (1,1) Frequency (F)	16
Left-sided Pr <= F	0.0033
Right-sided Pr >= F	0.9987
Table Probability (P)	0.0020
Two-sided Pr <= P	0.0049

EDIC Bsln Paper - Replicate Table 3

The FREQ Procedure

Statistics for Table of GROUP by IN_EDIC

Sample Size = 1428

Table of MAB1 by IN_EDIC

MAB1(Was patient debriefed?) / IN_EDIC(EDIC participant)	0: No	1: Yes	Total
1: No	13	19	32
	0.92	1.34	2.26
	40.63	59.38	
	26.00	1.39	
2: Yes	37	1346	1383
	2.61	95.12	97.74
	2.68	97.32	
	74.00	98.61	
Total	50	1365	1415
	3.53	96.47	100.00

Frequency Missing = 13

Statistics for Table of MAB1 by IN_EDIC

Statistic	DF	Value	Prob
Chi-Square	1	132.1422	<.0001
Likelihood Ratio Chi-Square	1	48.3065	<.0001
Continuity Adj. Chi-Square	1	121.2436	<.0001
Mantel-Haenszel Chi-Square	1	132.0488	<.0001
Phi Coefficient		0.3056	
Contingency Coefficient		0.2923	
Cramer's V		0.3056	

WARNING: 25% of the cells have expected counts less than 5. Chi-Square may not be a valid test.

EDIC Bsln Paper - Replicate Table 3

The FREQ Procedure

Statistics for Table of MAB1 by IN_EDIC

Fisher's Exact Test	
Cell (1,1) Frequency (F)	13
Left-sided Pr <= F	1.0000
Right-sided Pr >= F	5.541E-12
Table Probability (P)	5.335E-12
Two-sided Pr <= P	5.541E-12

Effective Sample Size = 1415
Frequency Missing = 13

Table of MAC1 by IN_EDIC

MAC1(Future diabetes care) / IN_EDIC(EDIC participant) Frequency Percent Row Pct Col Pct	0: No	1: Yes	Total
DCCT staff	10 0.74 1.46 20.83	676 49.74 98.54 51.56	686 50.48
Non-DCCT staff	38 2.80 5.65 79.17	635 46.73 94.35 48.44	673 49.52
Total	48 3.53	1311 96.47	1359 100.00

Frequency Missing = 69

Statistics for Table of MAC1 by IN_EDIC

Statistic	DF	Value	Prob
Chi-Square	1	17.4928	<.0001
Likelihood Ratio Chi-Square	1	18.5732	<.0001
Continuity Adj. Chi-Square	1	16.2851	<.0001
Mantel-Haenszel Chi-Square	1	17.4799	<.0001

EDIC Bsln Paper - Replicate Table 3

The FREQ Procedure

Statistics for Table of MAC1 by IN_EDIC

Statistic	DF	Value	Prob
Phi Coefficient		-0.1135	
Contingency Coefficient		0.1127	
Cramer's V		-0.1135	

Fisher's Exact Test	
Cell (1,1) Frequency (F)	10
Left-sided Pr <= F	1.727E-05
Right-sided Pr >= F	1.0000
Table Probability (P)	1.327E-05
Two-sided Pr <= P	2.460E-05

Effective Sample Size = 1359
Frequency Missing = 69

EDIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Gender (coded M or F)

SEX	Frequency	Percent	Cumulative Frequency	Cumulative Percent
F: Female	653	47.59	653	47.59
M: Male	719	52.41	1372	100.00

EDIC Bsln Paper - Replicate Table 4

The MEANS Procedure

Gender (coded M or F)	N Obs	Variable	Label	N	Mean	Std Dev
F: Female	653	AGE	Age at Edic Year 2 (Table 4)	652	35.4	7.2
		YRS_IDDM	Current duration of IDDM (years)	650	14.8	5.0
		BMI	Body mass index (kg/m**2)	650	26.0	4.2
		HBA1C	Last Non-Missing HbA1c During EDIC Year 1&2 (Tb4)	648	8.3	1.5
		TCHOL	Serum total cholesterol (mg/dl)	631	188.1	37.0
		TRIGLYC	Serum triglycerides (mg/dl)	631	83.1	73.3
		HDL	Serum HDL cholesterol (mg/dl)	631	59.2	14.0
		LDL	Serum LDL cholesterol (mg/dl)	627	112.1	30.3
		AER	Albumin excretion rate (mg/day)	627	41.8	226.9
		QOL	quality of life	640	75.3	8.6
M: Male	719	AGE	Age at Edic Year 2 (Table 4)	718	36.4	6.6
		YRS_IDDM	Current duration of IDDM (years)	717	14.3	4.8
		BMI	Body mass index (kg/m**2)	716	26.6	3.9
		HBA1C	Last Non-Missing HbA1c During EDIC Year 1&2 (Tb4)	715	8.2	1.3
		TCHOL	Serum total cholesterol (mg/dl)	696	185.1	35.6
		TRIGLYC	Serum triglycerides (mg/dl)	696	96.8	75.8
		HDL	Serum HDL cholesterol (mg/dl)	696	49.5	12.0
		LDL	Serum LDL cholesterol (mg/dl)	690	116.4	30.8
		AER	Albumin excretion rate (mg/day)	694	38.1	118.4
		QOL	quality of life	704	76.4	9.4

EDIC Bsln Paper - Replicate Table 4

The MEANS Procedure

Gender (coded M or F)	N Obs	Variable	Label	N	Mean	Std Dev
F: Female	653	WHR	Waist-to-hip ratio (natural waist)	648	0.77	0.07
		STD_INS	Insulin dose (units/kg/day)	651	0.70	0.24
M: Male	719	WHR	Waist-to-hip ratio (natural waist)	716	0.88	0.06
		STD_INS	Insulin dose (units/kg/day)	718	0.72	0.25

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable AGE Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	652	427074.50	446946.0	7313.31141	655.022239
M: Male	718	512060.50	492189.0	7313.31141	713.176184

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	427074.5000
Normal Approximation	
Z	-2.7171
One-Sided Pr < Z	0.0033
Two-Sided Pr > |Z|	0.0066
t Approximation	
One-Sided Pr < Z	0.0033
Two-Sided Pr > |Z|	0.0067

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	7.3830
DF	1
Pr > Chi-Square	0.0066

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable YRS_IDDM Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	650	456469.50	444600.0	7288.86263	702.260769
M: Male	717	478558.50	490428.0	7288.86263	667.445607

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	456469.5000
Normal Approximation	
Z	1.6284
One-Sided Pr > Z	0.0517
Two-Sided Pr > |Z|	0.1034
t Approximation	
One-Sided Pr > Z	0.0518
Two-Sided Pr > |Z|	0.1037

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	2.6518
DF	1
Pr > Chi-Square	0.1034

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable BMI Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	650	415002.50	444275.0	7281.26468	638.465385
M: Male	716	518658.50	489386.0	7281.26468	724.383380

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	415002.5000
Normal Approximation	
Z	-4.0202
One-Sided Pr < Z	<.0001
Two-Sided Pr > |Z|	<.0001
t Approximation	
One-Sided Pr < Z	<.0001
Two-Sided Pr > |Z|	<.0001

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	16.1624
DF	1
Pr > Chi-Square	<.0001

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable WHR Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	648	251234.50	442260.0	7264.73378	387.707562
M: Male	716	679695.50	488670.0	7264.73378	949.295391

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	251234.5000
Normal Approximation	
Z	-26.2948
One-Sided Pr < Z	<.0001
Two-Sided Pr > |Z|	<.0001
t Approximation	
One-Sided Pr < Z	<.0001
Two-Sided Pr > |Z|	<.0001

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	691.4221
DF	1
Pr > Chi-Square	<.0001

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable STD_INS Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	651	437682.0	445935.0	7305.03550	672.322581
M: Male	718	500083.0	491830.0	7305.03550	696.494429

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	437682.0000
Normal Approximation	
Z	-1.1297
One-Sided Pr < Z	0.1293
Two-Sided Pr > |Z|	0.2586
t Approximation	
One-Sided Pr < Z	0.1294
Two-Sided Pr > |Z|	0.2588

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	1.2764
DF	1
Pr > Chi-Square	0.2586

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable HBA1C Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	648	440919.50	441936.0	7254.60201	680.431327
M: Male	715	488646.50	487630.0	7254.60201	683.421678

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	440919.5000
Normal Approximation	
Z	-0.1400
One-Sided Pr < Z	0.4443
Two-Sided Pr > |Z|	0.8886
t Approximation	
One-Sided Pr < Z	0.4443
Two-Sided Pr > |Z|	0.8886

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	0.0196
DF	1
Pr > Chi-Square	0.8886

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable TCHOL Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	631	428078.0	418984.0	6971.18656	678.412044
M: Male	696	453050.0	462144.0	6971.18656	650.933908

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	428078.0000
Normal Approximation	
Z	1.3044
One-Sided Pr > Z	0.0960
Two-Sided Pr > |Z|	0.1921
t Approximation	
One-Sided Pr > Z	0.0962
Two-Sided Pr > |Z|	0.1923

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	1.7018
DF	1
Pr > Chi-Square	0.1921

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable TRIGLYC Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	631	391693.0	418984.0	6971.12271	620.749604
M: Male	696	489435.0	462144.0	6971.12271	703.211207

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	391693.0000
Normal Approximation	
Z	-3.9148
One-Sided Pr < Z	<.0001
Two-Sided Pr > |Z|	<.0001
t Approximation	
One-Sided Pr < Z	<.0001
Two-Sided Pr > |Z|	<.0001

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	15.3262
DF	1
Pr > Chi-Square	<.0001

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable HDL Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	631	510644.0	418984.0	6969.37382	809.261490
M: Male	696	370484.0	462144.0	6969.37382	532.304598

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	510644.0000
Normal Approximation	
Z	13.1518
One-Sided Pr > Z	<.0001
Two-Sided Pr > |Z|	<.0001
t Approximation	
One-Sided Pr > Z	<.0001
Two-Sided Pr > |Z|	<.0001

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	172.9706
DF	1
Pr > Chi-Square	<.0001

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable LDL Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	627	394996.0	413193.0	6892.85838	629.977671
M: Male	690	472907.0	454710.0	6892.85838	685.372464

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	394996.0000
Normal Approximation	
Z	-2.6399
One-Sided Pr < Z	0.0041
Two-Sided Pr > |Z|	0.0083
t Approximation	
One-Sided Pr < Z	0.0042
Two-Sided Pr > |Z|	0.0084

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	6.9695
DF	1
Pr > Chi-Square	0.0083

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable AER Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	627	405685.0	414447.0	6909.70218	647.025518
M: Male	694	467496.0	458734.0	6909.70218	673.625360

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	405685.0000
Normal Approximation	
Z	-1.2680
One-Sided Pr < Z	0.1024
Two-Sided Pr > |Z|	0.2048
t Approximation	
One-Sided Pr < Z	0.1025
Two-Sided Pr > |Z|	0.2050

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	1.6080
DF	1
Pr > Chi-Square	0.2048

EDIC Bsln Paper - Replicate Table 4

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable QOL Classified by Variable SEX

SEX	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
F: Female	640	413668.50	430400.0	7106.23470	646.357031
M: Male	704	490171.50	473440.0	7106.23470	696.266335

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	413668.5000
Normal Approximation	
Z	-2.3544
One-Sided Pr < Z	0.0093
Two-Sided Pr > |Z|	0.0186
t Approximation	
One-Sided Pr < Z	0.0093
Two-Sided Pr > |Z|	0.0187

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	5.5436
DF	1
Pr > Chi-Square	0.0185

EDIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Table of OVER_WT by SEX

OVER_WT(Overweight (BMI>=27.8 M, 27.3 F)(Table4))	SEX(Gender (coded M or F))		
Frequency **Percent** **Row Pct** **Col Pct**	**F: Female**	**M: Male**	**Total**
0: No	443 32.43 47.23 68.15	495 36.24 52.77 69.13	938 68.67
1: Yes	207 15.15 48.36 31.85	221 16.18 51.64 30.87	428 31.33
Total	650 47.58	716 52.42	1366 100.00

Frequency Missing = 6

Statistics for Table of OVER_WT by SEX

Statistic	DF	Value	Prob
Chi-Square	1	0.1522	0.6965
Likelihood Ratio Chi-Square	1	0.1521	0.6965
Continuity Adj. Chi-Square	1	0.1100	0.7401
Mantel-Haenszel Chi-Square	1	0.1520	0.6966
Phi Coefficient		-0.0106	
Contingency Coefficient		0.0106	
Cramer's V		-0.0106	

EDIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Statistics for Table of OVER_WT by SEX

Fisher's Exact Test	
Cell (1,1) Frequency (F)	443
Left-sided Pr <= F	0.3700
Right-sided Pr >= F	0.6732
Table Probability (P)	0.0431
Two-sided Pr <= P	0.7261

Effective Sample Size = 1366
Frequency Missing = 6

Table of LOW_HDL by SEX

LOW_HDL(HDL < 35 mg/dl (0 = no, 1 = yes))	SEX(Gender (coded M or F))		
Frequency Percent Row Pct Col Pct	F: Female	M: Male	Total
0: No	621 46.80 49.29 98.42	639 48.15 50.71 91.81	1260 94.95
1: Yes	10 0.75 14.93 1.58	57 4.30 85.07 8.19	67 5.05
Total	631 47.55	696 52.45	1327 100.00

Frequency Missing = 45

Statistics for Table of LOW_HDL by SEX

Statistic	DF	Value	Prob
Chi-Square	1	30.1157	<.0001
Likelihood Ratio Chi-Square	1	33.4845	<.0001
Continuity Adj. Chi-Square	1	28.7537	<.0001
Mantel-Haenszel Chi-Square	1	30.0930	<.0001

EDIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Statistics for Table of LOW_HDL by SEX

Statistic	DF	Value	Prob
Phi Coefficient		0.1506	
Contingency Coefficient		0.1490	
Cramer's V		0.1506	

Fisher's Exact Test	
Cell (1,1) Frequency (F)	621
Left-sided Pr <= F	1.0000
Right-sided Pr >= F	9.004E-09
Table Probability (P)	7.447E-09
Two-sided Pr <= P	1.143E-08

Effective Sample Size = 1327
Frequency Missing = 45

Table of HIGH_LDL by SEX

HIGH_LDL(LDL > 130 mg/dl (0 = no, 1 = yes))	SEX(Gender (coded M or F))		
Frequency Percent Row Pct Col Pct	F: Female	M: Male	Total
0: No	464 35.23 49.20 74.00	479 36.37 50.80 69.42	943 71.60
1: Yes	163 12.38 43.58 26.00	211 16.02 56.42 30.58	374 28.40
Total	627 47.61	690 52.39	1317 100.00

Frequency Missing = 55

Statistics for Table of HIGH_LDL by SEX

EDIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Statistics for Table of HIGH_LDL by SEX

Statistic	DF	Value	Prob
Chi-Square	1	3.3931	0.0655
Likelihood Ratio Chi-Square	1	3.4012	0.0651
Continuity Adj. Chi-Square	1	3.1715	0.0749
Mantel-Haenszel Chi-Square	1	3.3905	0.0656
Phi Coefficient		0.0508	
Contingency Coefficient		0.0507	
Cramer's V		0.0508	

Fisher's Exact Test	
Cell (1,1) Frequency (F)	464
Left-sided Pr <= F	0.9716
Right-sided Pr >= F	0.0374
Table Probability (P)	0.0090
Two-sided Pr <= P	0.0668

Effective Sample Size = 1317
Frequency Missing = 55

EDIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Table of HT by SEX

HT(History of hypertension (1 = yes)) / Frequency, Percent, Row Pct, Col Pct	SEX(Gender (coded M or F)) F: Female	M: Male	Total
0: No	535	528	1063
	38.99	38.48	77.48
	50.33	49.67	
	81.93	73.44	
1: Yes	118	191	309
	8.60	13.92	22.52
	38.19	61.81	
	18.07	26.56	
Total	653	719	1372
	47.59	52.41	100.00

Statistics for Table of HT by SEX

Statistic	DF	Value	Prob
Chi-Square	1	14.1499	0.0002
Likelihood Ratio Chi-Square	1	14.2800	0.0002
Continuity Adj. Chi-Square	1	13.6673	0.0002
Mantel-Haenszel Chi-Square	1	14.1396	0.0002
Phi Coefficient		0.1016	
Contingency Coefficient		0.1010	
Cramer's V		0.1016	

Fisher's Exact Test	
Cell (1,1) Frequency (F)	535
Left-sided Pr <= F	0.9999
Right-sided Pr >= F	1.027E-04
Table Probability (P)	4.198E-05
Two-sided Pr <= P	1.723E-04

DIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Statistics for Table of HT by SEX

Sample Size = 1372

Table of SMOKING by SEX

SMOKING(Smoking (1=never, 2=former, 3=current)) / SEX(Gender (coded M or F))	F: Female	M: Male	Total
1: Never smokers: Never or quit 1yr+	484	518	1002
	35.28	37.76	73.03
	48.30	51.70	
	74.12	72.04	
2: Former smokers: 3 mnth <quit <= 1yr	39	38	77
	2.84	2.77	5.61
	50.65	49.35	
	5.97	5.29	
3: Current smokers: Curr or quit <= 3mnth	130	163	293
	9.48	11.88	21.36
	44.37	55.63	
	19.91	22.67	
Total	653	719	1372
	47.59	52.41	100.00

Statistics for Table of SMOKING by SEX

Statistic	DF	Value	Prob
Chi-Square	2	1.7124	0.4248
Likelihood Ratio Chi-Square	2	1.7154	0.4241
Mantel-Haenszel Chi-Square	1	1.1822	0.2769
Phi Coefficient		0.0353	
Contingency Coefficient		0.0353	
Cramer's V		0.0353	

Fisher's Exact Test	
Table Probability (P)	0.0021
Pr <= P	0.4243

EDIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Statistics for Table of SMOKING by SEX

Sample Size = 1372

Table of currsmok by SEX

currsmok	SEX(Gender (coded M or F))		
Frequency Percent Row Pct Col Pct	F: Female	M: Male	Total
0	523 38.12 48.47 80.09	556 40.52 51.53 77.33	1079 78.64
1	130 9.48 44.37 19.91	163 11.88 55.63 22.67	293 21.36
Total	653 47.59	719 52.41	1372 100.00

Statistics for Table of currsmok by SEX

Statistic	DF	Value	Prob
Chi-Square	1	1.5547	0.2124
Likelihood Ratio Chi-Square	1	1.5579	0.2120
Continuity Adj. Chi-Square	1	1.3945	0.2376
Mantel-Haenszel Chi-Square	1	1.5535	0.2126
Phi Coefficient		0.0337	
Contingency Coefficient		0.0336	
Cramer's V		0.0337	

EDIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Statistics for Table of currsmok by SEX

Fisher's Exact Test	
Cell (1,1) Frequency (F)	523
Left-sided Pr <= F	0.9055
Right-sided Pr >= F	0.1188
Table Probability (P)	0.0242
Two-sided Pr <= P	0.2351

Sample Size = 1372

Table of EXERCISE by SEX

EXERCISE(Current exercise level) / Frequency / Percent / Row Pct / Col Pct	SEX(Gender (coded M or F)) F: Female	M: Male	Total
1: Very Hard	19	74	93
	1.39	5.42	6.81
	20.43	79.57	
	2.92	10.35	
2: Hard	22	42	64
	1.61	3.08	4.69
	34.38	65.63	
	3.38	5.87	
3: Moderate	379	354	733
	27.77	25.93	53.70
	51.71	48.29	
	58.31	49.51	
4: Mild	230	245	475
	16.85	17.95	34.80
	48.42	51.58	
	35.38	34.27	
Total	650	715	1365
	47.62	52.38	100.00

Frequency Missing = 7

Statistics for Table of EXERCISE by SEX

EDIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Statistics for Table of EXERCISE by SEX

Statistic	DF	Value	Prob
Chi-Square	3	37.0921	<.0001
Likelihood Ratio Chi-Square	3	39.3383	<.0001
Mantel-Haenszel Chi-Square	1	18.1121	<.0001
Phi Coefficient		0.1648	
Contingency Coefficient		0.1626	
Cramer's V		0.1648	

Fisher's Exact Test	
Table Probability (P)	1.529E-12
Pr <= P	1.738E-08

Effective Sample Size = 1365
Frequency Missing = 7

Table of OBDRINK1 by SEX

OBDRINK1(Drinks 1+ alcoholic beverage/week (2=y))	SEX(Gender (coded M or F))		
Frequency Percent Row Pct Col Pct	F: Female	M: Male	Total
1: No	442 32.29 53.90 67.90	378 27.61 46.10 52.65	820 59.90
2: Yes	209 15.27 38.07 32.10	340 24.84 61.93 47.35	549 40.10
Total	651 47.55	718 52.45	1369 100.00

Frequency Missing = 3

Statistics for Table of OBDRINK1 by SEX

EDIC Bsln Paper - Replicate Table 4

The FREQ Procedure

Statistics for Table of OBDRINK1 by SEX

Statistic	DF	Value	Prob
Chi-Square	1	33.0539	<.0001
Likelihood Ratio Chi-Square	1	33.2821	<.0001
Continuity Adj. Chi-Square	1	32.4221	<.0001
Mantel-Haenszel Chi-Square	1	33.0298	<.0001
Phi Coefficient		0.1554	
Contingency Coefficient		0.1535	
Cramer's V		0.1554	

Fisher's Exact Test	
Cell (1,1) Frequency (F)	442
Left-sided Pr <= F	1.0000
Right-sided Pr >= F	5.558E-09
Table Probability (P)	2.689E-09
Two-sided Pr <= P	8.922E-09

Effective Sample Size = 1369
Frequency Missing = 3

EDIC Bsln Paper - Replicate Table 5

The MEANS Procedure

Gender (coded M or F)	Age Decade at EDIC Year 2 (Table 5)	N Obs	Variable	Label	N	Mean	Std Dev
F: Female	20 - 29	154	LDP_MEAN	Left Ankle Arm ratio	154	1.08	0.10
			RDP_MEAN	Right Ankle Arm ratio	154	1.08	0.10
	30 - 39	289	LDP_MEAN	Left Ankle Arm ratio	287	1.09	0.13
			RDP_MEAN	Right Ankle Arm ratio	288	1.11	0.12
	40 - 49	202	LDP_MEAN	Left Ankle Arm ratio	202	1.08	0.12
			RDP_MEAN	Right Ankle Arm ratio	202	1.10	0.13
M: Male	20 - 29	117	LDP_MEAN	Left Ankle Arm ratio	116	1.08	0.10
			RDP_MEAN	Right Ankle Arm ratio	116	1.07	0.12
	30 - 39	351	LDP_MEAN	Left Ankle Arm ratio	351	1.10	0.13
			RDP_MEAN	Right Ankle Arm ratio	351	1.12	0.13
	40 - 49	242	LDP_MEAN	Left Ankle Arm ratio	241	1.11	0.14
			RDP_MEAN	Right Ankle Arm ratio	241	1.13	0.13

EDIC Bsln Paper - Replicate Table 5

The FREQ Procedure

Table 1 of LOW_AAR by DECADE

Controlling for SEX=F: Female

LOW_AAR(Ankle/arm < 0.8)	DECADE(Age Decade at EDIC Year 2 (Table 5))			
Frequency Percent Row Pct Col Pct	20 - 29	30 - 39	40 - 49	Total
0: No	150	281	195	626
	23.26	43.57	30.23	97.05
	23.96	44.89	31.15	
	97.40	97.23	96.53	
1: Yes	4	8	7	19
	0.62	1.24	1.09	2.95
	21.05	42.11	36.84	
	2.60	2.77	3.47	
Total	154	289	202	645
	23.88	44.81	31.32	100.00

Table 2 of LOW_AAR by DECADE

Controlling for SEX=M: Male

LOW_AAR(Ankle/arm < 0.8)	DECADE(Age Decade at EDIC Year 2 (Table 5))			
Frequency Percent Row Pct Col Pct	20 - 29	30 - 39	40 - 49	Total
0: No	114	347	231	692
	16.08	48.94	32.58	97.60
	16.47	50.14	33.38	
	97.44	98.86	95.85	
1: Yes	3	4	10	17
	0.42	0.56	1.41	2.40
	17.65	23.53	58.82	
	2.56	1.14	4.15	
Total	117	351	241	709
	16.50	49.51	33.99	100.00

Frequency Missing = 1

EDIC Bsln Paper - Replicate Table 5

The FREQ Procedure

Table 1 of HIGH_AAR by DECADE

Controlling for SEX=F: Female

HIGH_AAR(Ankle/arm > 1.4)	DECADE(Age Decade at EDIC Year 2 (Table 5))			
Frequency **Percent** **Row Pct** **Col Pct**	**20 - 29**	**30 - 39**	**40 - 49**	**Total**
0: No	154 23.88 24.64 100.00	272 42.17 43.52 94.12	199 30.85 31.84 98.51	625 96.90
1: Yes	0 0.00 0.00 0.00	17 2.64 85.00 5.88	3 0.47 15.00 1.49	20 3.10
Total	154 23.88	289 44.81	202 31.32	645 100.00

Table 2 of HIGH_AAR by DECADE

Controlling for SEX=M: Male

HIGH_AAR(Ankle/arm > 1.4)	DECADE(Age Decade at EDIC Year 2 (Table 5))			
Frequency **Percent** **Row Pct** **Col Pct**	**20 - 29**	**30 - 39**	**40 - 49**	**Total**
0: No	114 16.08 16.67 97.44	338 47.67 49.42 96.30	232 32.72 33.92 96.27	684 96.47
1: Yes	3 0.42 12.00 2.56	13 1.83 52.00 3.70	9 1.27 36.00 3.73	25 3.53
Total	117 16.50	351 49.51	241 33.99	709 100.00

Frequency Missing = 1

EDIC Bsln Paper - Replicate Table 5

The FREQ Procedure

Table 1 of lowhigh_aar by DECADE

Controlling for SEX=F: Female

lowhigh_aar	DECADE(Age Decade at EDIC Year 2 (Table 5))			
Frequency Percent Row Pct Col Pct	20 - 29	30 - 39	40 - 49	Total
0	150 23.26 24.71 97.40	265 41.09 43.66 91.70	192 29.77 31.63 95.05	607 94.11
1	4 0.62 10.53 2.60	24 3.72 63.16 8.30	10 1.55 26.32 4.95	38 5.89
Total	154 23.88	289 44.81	202 31.32	645 100.00

Table 2 of lowhigh_aar by DECADE

Controlling for SEX=M: Male

lowhigh_aar	DECADE(Age Decade at EDIC Year 2 (Table 5))			
Frequency Percent Row Pct Col Pct	20 - 29	30 - 39	40 - 49	Total
0	111 15.66 16.64 94.87	334 47.11 50.07 95.16	222 31.31 33.28 92.12	667 94.08
1	6 0.85 14.29 5.13	17 2.40 40.48 4.84	19 2.68 45.24 7.88	42 5.92
Total	117 16.50	351 49.51	241 33.99	709 100.00

Frequency Missing = 1

EDIC Bsln Paper - Replicate Table 5

The FREQ Procedure

Age Decade at EDIC Year 2 (Table 5)=20 - 29

Table of SEX by LOW_AAR

SEX(Gender (coded M or F)) / Frequency / Percent / Row Pct / Col Pct	LOW_AAR(Ankle/arm < 0.8) 0: No	1: Yes	Total
F: Female	150	4	154
	55.35	1.48	56.83
	97.40	2.60	
	56.82	57.14	
M: Male	114	3	117
	42.07	1.11	43.17
	97.44	2.56	
	43.18	42.86	
Total	264	7	271
	97.42	2.58	100.00

Statistics for Table of SEX by LOW_AAR

Statistic	DF	Value	Prob
Chi-Square	1	0.0003	0.9863
Likelihood Ratio Chi-Square	1	0.0003	0.9863
Continuity Adj. Chi-Square	1	0.0000	1.0000
Mantel-Haenszel Chi-Square	1	0.0003	0.9864
Phi Coefficient		-0.0010	
Contingency Coefficient		0.0010	
Cramer's V		-0.0010	

WARNING: 50% of the cells have expected counts less than 5. Chi-Square may not be a valid test.

EDIC Bsln Paper - Replicate Table 5

The FREQ Procedure

Statistics for Table of SEX by LOW_AAR

Age Decade at EDIC Year 2 (Table 5)=20 - 29

Fisher's Exact Test	
Cell (1,1) Frequency (F)	150
Left-sided Pr <= F	0.6482
Right-sided Pr >= F	0.6494
Table Probability (P)	0.2976
Two-sided Pr <= P	1.0000

Sample Size = 271

EDIC Bsln Paper - Replicate Table 5

The FREQ Procedure

Age Decade at EDIC Year 2 (Table 5)=30 - 39

Table of SEX by LOW_AAR

SEX(Gender (coded M or F)) / Frequency / Percent / Row Pct / Col Pct	LOW_AAR(Ankle/arm < 0.8) 0: No	1: Yes	Total
F: Female	281	8	289
	43.91	1.25	45.16
	97.23	2.77	
	44.75	66.67	
M: Male	347	4	351
	54.22	0.63	54.84
	98.86	1.14	
	55.25	33.33	
Total	628	12	640
	98.13	1.88	100.00

Statistics for Table of SEX by LOW_AAR

Statistic	DF	Value	Prob
Chi-Square	1	2.2848	0.1306
Likelihood Ratio Chi-Square	1	2.2926	0.1300
Continuity Adj. Chi-Square	1	1.4854	0.2229
Mantel-Haenszel Chi-Square	1	2.2813	0.1309
Phi Coefficient		-0.0597	
Contingency Coefficient		0.0596	
Cramer's V		-0.0597	

EDIC Bsln Paper - Replicate Table 5

The FREQ Procedure

Statistics for Table of SEX by LOW_AAR

Age Decade at EDIC Year 2 (Table 5)=30 - 39

Fisher's Exact Test	
Cell (1,1) Frequency (F)	281
Left-sided Pr <= F	0.1117
Right-sided Pr >= F	0.9649
Table Probability (P)	0.0766
Two-sided Pr <= P	0.1515

Sample Size = 640

EDIC Bsln Paper - Replicate Table 5

The FREQ Procedure

Age Decade at EDIC Year 2 (Table 5)=40 - 49

Table of SEX by LOW_AAR

SEX(Gender (coded M or F)) / Frequency / Percent / Row Pct / Col Pct	LOW_AAR(Ankle/arm < 0.8) 0: No	1: Yes	Total
F: Female	195	7	202
	44.02	1.58	45.60
	96.53	3.47	
	45.77	41.18	
M: Male	231	10	241
	52.14	2.26	54.40
	95.85	4.15	
	54.23	58.82	
Total	426	17	443
	96.16	3.84	100.00

Frequency Missing = 1

Statistics for Table of SEX by LOW_AAR

Statistic	DF	Value	Prob
Chi-Square	1	0.1393	0.7089
Likelihood Ratio Chi-Square	1	0.1402	0.7081
Continuity Adj. Chi-Square	1	0.0156	0.9005
Mantel-Haenszel Chi-Square	1	0.1390	0.7093
Phi Coefficient		0.0177	
Contingency Coefficient		0.0177	
Cramer's V		0.0177	

EDIC Bsln Paper - Replicate Table 5

The FREQ Procedure

Statistics for Table of SEX by LOW_AAR

Age Decade at EDIC Year 2 (Table 5)=40 - 49

Fisher's Exact Test	
Cell (1,1) Frequency (F)	195
Left-sided Pr <= F	0.7308
Right-sided Pr >= F	0.4532
Table Probability (P)	0.1840
Two-sided Pr <= P	0.8067

Effective Sample Size = 443
Frequency Missing = 1

EDIC Bsln Paper - Replicate Table 5

The MEANS Procedure

Gender (coded M or F)	Age Decade When IMT Was Taken (Table 5)	N Obs	Variable	Label	N	Mean	Std Dev
F: Female	20 - 29	172	COMMON	Average maximum thickness: Common	172	0.616	0.073
			INTERNAL	Average maximum thickness: Internal	172	0.583	0.092
	30 - 39	278	COMMON	Average maximum thickness: Common	278	0.657	0.081
			INTERNAL	Average maximum thickness: Internal	278	0.632	0.147
	40 - 49	178	COMMON	Average maximum thickness: Common	178	0.696	0.079
			INTERNAL	Average maximum thickness: Internal	178	0.719	0.226
M: Male	20 - 29	125	COMMON	Average maximum thickness: Common	125	0.636	0.059
			INTERNAL	Average maximum thickness: Internal	125	0.629	0.083
	30 - 39	350	COMMON	Average maximum thickness: Common	350	0.684	0.083
			INTERNAL	Average maximum thickness: Internal	350	0.684	0.114
	40 - 49	211	COMMON	Average maximum thickness: Common	211	0.745	0.104
			INTERNAL	Average maximum thickness: Internal	211	0.806	0.261

EDIC Bsln Paper - Replicate Table 6

The FREQ Procedure

TREATMENT GROUP

GROUP	Frequency	Percent	Cumulative Frequency	Cumulative Percent
EXPERIMENTAL: Intensive Treatment	687	49.96	687	49.96
STANDARD: Conventional Treatment	688	50.04	1375	100.00

EDIC Bsln Paper - Replicate Table 6

The FREQ Procedure

Table of OBINSREG by GROUP

OBINSREG(Current insulin regimen)	GROUP(TREATMENT GROUP)		
Frequency Percent Row Pct Col Pct	EXPERIMENTAL: Intensive Treatment	STANDARD: Conventional Treatment	Total
CSII	253 18.49 74.63 36.99	86 6.29 25.37 12.57	339 24.78
MDI	394 28.80 50.32 57.60	389 28.44 49.68 56.87	783 57.24
1-2 injections	36 2.63 14.81 5.26	207 15.13 85.19 30.26	243 17.76
Other	1 0.07 33.33 0.15	2 0.15 66.67 0.29	3 0.22
Total	684 50.00	684 50.00	1368 100.00

Frequency Missing = 7

Statistics for Table of OBINSREG by GROUP

Statistic	DF	Value	Prob
Chi-Square	3	202.9670	<.0001
Likelihood Ratio Chi-Square	3	219.3409	<.0001
Mantel-Haenszel Chi-Square	1	196.4286	<.0001
Phi Coefficient		0.3852	
Contingency Coefficient		0.3594	
Cramer's V		0.3852	

WARNING: 25% of the cells have expected counts less than 5. Chi-Square may not be a valid test.

EDIC Bsln Paper - Replicate Table 6

The FREQ Procedure

Statistics for Table of OBINSREG by GROUP

Fisher's Exact Test	
Table Probability (P)	4.931E-51
Pr <= P	5.771E-48

Effective Sample Size = 1368
Frequency Missing = 7

Table of HUM_INS by GROUP

HUM_INS(Reports using human insulin)	GROUP(TREATMENT GROUP)		
Frequency **Percent** **Row Pct** **Col Pct**	**EXPERIMENTAL: Intensive Treatment**	**STANDARD: Conventional Treatment**	**Total**
0: No	61 4.46 49.19 8.91	63 4.60 50.81 9.21	124 9.06
1: Yes	624 45.58 50.12 91.09	621 45.36 49.88 90.79	1245 90.94
Total	685 50.04	684 49.96	1369 100.00

Frequency Missing = 6

Statistics for Table of HUM_INS by GROUP

Statistic	DF	Value	Prob
Chi-Square	1	0.0388	0.8439
Likelihood Ratio Chi-Square	1	0.0388	0.8439
Continuity Adj. Chi-Square	1	0.0105	0.9182
Mantel-Haenszel Chi-Square	1	0.0387	0.8440
Phi Coefficient		-0.0053	
Contingency Coefficient		0.0053	
Cramer's V		-0.0053	

EDIC Bsln Paper - Replicate Table 6

The FREQ Procedure

Statistics for Table of HUM_INS by GROUP

Fisher's Exact Test	
Cell (1,1) Frequency (F)	61
Left-sided Pr <= F	0.4591
Right-sided Pr >= F	0.6144
Table Probability (P)	0.0736
Two-sided Pr <= P	0.8512

Effective Sample Size = 1369
Frequency Missing = 6

Table of SBGM_4 by GROUP

SBGM_4(SBGM => 4 times/day) / Frequency / Percent / Row Pct / Col Pct	GROUP(TREATMENT GROUP) EXPERIMENTAL: Intensive Treatment	STANDARD: Conventional Treatment	Total
0: No	367 26.81 45.76 53.58	435 31.78 54.24 63.60	802 58.58
1: Yes	318 23.23 56.08 46.42	249 18.19 43.92 36.40	567 41.42
Total	685 50.04	684 49.96	1369 100.00

Frequency Missing = 6

Statistics for Table of SBGM_4 by GROUP

Statistic	DF	Value	Prob
Chi-Square	1	14.1617	0.0002
Likelihood Ratio Chi-Square	1	14.1895	0.0002
Continuity Adj. Chi-Square	1	13.7517	0.0002
Mantel-Haenszel Chi-Square	1	14.1513	0.0002

EDIC Bsln Paper - Replicate Table 6

The FREQ Procedure

Statistics for Table of SBGM_4 by GROUP

Statistic	DF	Value	Prob
Phi Coefficient		-0.1017	
Contingency Coefficient		0.1012	
Cramer's V		-0.1017	

Fisher's Exact Test	
Cell (1,1) Frequency (F)	367
Left-sided Pr <= F	1.030E-04
Right-sided Pr >= F	0.9999
Table Probability (P)	3.670E-05
Two-sided Pr <= P	1.889E-04

Effective Sample Size = 1369
Frequency Missing = 6

EDIC Bsln Paper - Replicate Table 6

The MEANS Procedure

Analysis Variable : STD_INS Insulin dose (units/kg/day)

TREATMENT GROUP	N Obs	N	Mean	Std Dev
EXPERIMENTAL: Intensive Treatment	687	685	0.75	0.28
STANDARD: Conventional Treatment	688	684	0.67	0.20

EDIC Bsln Paper - Replicate Table 6

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable STD_INS
Classified by Variable GROUP

GROUP	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
EXPERIMENTAL: Intensive Treatment	685	507914.50	469225.0	7313.79782	741.481022
STANDARD: Conventional Treatment	684	429850.50	468540.0	7313.79782	628.436404

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	429850.5000
Normal Approximation	
Z	-5.2899
One-Sided Pr < Z	<.0001
Two-Sided Pr > |Z|	<.0001
t Approximation	
One-Sided Pr < Z	<.0001
Two-Sided Pr > |Z|	<.0001

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	27.9834
DF	1
Pr > Chi-Square	<.0001

EDIC BsIn Paper - Replicate Table 6
mean rates per year

The MEANS Procedure

TREATMENT GROUP	N Obs	Variable	Mean
EXPERIMENTAL: Intensive Treatment	687	pt_cs_b	6.20
		pt_ra_b	24.87
		pt_dka_b	2.76
STANDARD: Conventional Treatment	688	pt_cs_b	7.16
		pt_ra_b	26.32
		pt_dka_b	2.36

EDIC Bsln Paper - Replicate Table 6
mean rates per year

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable pt_cs_b
Classified by Variable GROUP

GROUP	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
EXPERIMENTAL: Intensive Treatment	685	467944.0	468882.50	3717.01596	683.129927
STANDARD: Conventional Treatment	683	468452.0	467513.50	3717.01596	685.874085

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	468452.0000
Normal Approximation	
Z	0.2524
One-Sided Pr > Z	0.4004
Two-Sided Pr > |Z|	0.8008
t Approximation	
One-Sided Pr > Z	0.4004
Two-Sided Pr > |Z|	0.8008

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	0.0637
DF	1
Pr > Chi-Square	0.8007

EDIC Bsln Paper - Replicate Table 6
mean rates per year

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable pt_ra_b
Classified by Variable GROUP

GROUP	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
EXPERIMENTAL: Intensive Treatment	685	468745.50	468882.50	5506.92950	684.300000
STANDARD: Conventional Treatment	683	467650.50	467513.50	5506.92950	684.700586

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	467650.5000
Normal Approximation	
Z	0.0248
One-Sided Pr > Z	0.4901
Two-Sided Pr > |Z|	0.9802
t Approximation	
One-Sided Pr > Z	0.4901
Two-Sided Pr > |Z|	0.9802

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	0.0006
DF	1
Pr > Chi-Square	0.9802

EDIC Bsln Paper - Replicate Table 6
mean rates per year

The NPAR1WAY Procedure

Wilcoxon Scores (Rank Sums) for Variable pt_dka_b
Classified by Variable GROUP

GROUP	N	Sum of Scores	Expected Under H0	Std Dev Under H0	Mean Score
EXPERIMENTAL: Intensive Treatment	685	468891.50	468882.50	2550.50866	684.513139
STANDARD: Conventional Treatment	683	467504.50	467513.50	2550.50866	684.486823

Average scores were used for ties.

Wilcoxon Two-Sample Test	
Statistic	467504.5000
Normal Approximation	
Z	-0.0033
One-Sided Pr < Z	0.4987
Two-Sided Pr > |Z|	0.9973
t Approximation	
One-Sided Pr < Z	0.4987
Two-Sided Pr > |Z|	0.9973

Z includes a continuity correction of 0.5.

Kruskal-Wallis Test	
Chi-Square	0.0000
DF	1
Pr > Chi-Square	0.9972

Table 1 of OW by GROUP

Controlling for SEX=F: Female

OW(Overweight (BMI>=27.8 M, 27.3 F)(Table6))	GROUP(TREATMENT GROUP)		
Frequency Percent Row Pct Col Pct	EXPERIMENTAL: Intensive Treatment	STANDARD: Conventional Treatment	Total
0: No	207 31.80 46.62 61.98	237 36.41 53.38 74.76	444 68.20
1: Yes	127 19.51 61.35 38.02	80 12.29 38.65 25.24	207 31.80
Total	334 51.31	317 48.69	651 100.00

Frequency Missing = 4

Statistics for Table 1 of OW by GROUP Controlling for SEX=F: Female

Statistic	DF	Value	Prob
Chi-Square	1	12.2630	0.0005
Likelihood Ratio Chi-Square	1	12.3497	0.0004
Continuity Adj. Chi-Square	1	11.6804	0.0006
Mantel-Haenszel Chi-Square	1	12.2441	0.0005
Phi Coefficient		-0.1372	
Contingency Coefficient		0.1360	
Cramer's V		-0.1372	

The FREQ Procedure

Statistics for Table 1 of OW by GROUP
Controlling for SEX=F: Female

Fisher's Exact Test	
Cell (1,1) Frequency (F)	207
Left-sided Pr <= F	3.038E-04
Right-sided Pr >= F	0.9998
Table Probability (P)	1.436E-04
Two-sided Pr <= P	5.443E-04

Statistic	Value	ASE
Gamma	-0.2902	0.0785
Kendall's Tau-b	-0.1372	0.0385
Stuart's Tau-c	-0.1278	0.0360
Somers' D C|R	-0.1473	0.0413
Somers' D R|C	-0.1279	0.0361
Pearson Correlation	-0.1372	0.0385
Spearman Correlation	-0.1372	0.0385
Lambda Asymmetric C|R	0.0946	0.0632
Lambda Asymmetric R|C	0.0000	0.0000
Lambda Symmetric	0.0573	0.0391
Uncertainty Coefficient C|R	0.0137	0.0077
Uncertainty Coefficient R|C	0.0152	0.0086
Uncertainty Coefficient Symmetric	0.0144	0.0081

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	0.5502	0.3931	0.7701
Cohort (Col1 Risk)	0.7599	0.6560	0.8802
Cohort (Col2 Risk)	1.3812	1.1394	1.6742

Effective Sample Size = 651
Frequency Missing = 4

Table 2 of OW by GROUP

Controlling for SEX=M: Male

OW(Overweight (BMI>=27.8 M, 27.3 F)(Table6))	GROUP(TREATMENT GROUP)		
Frequency Percent Row Pct Col Pct	EXPERIMENTAL: Intensive Treatment	STANDARD: Conventional Treatment	Total
0: No	237 33.01 47.88 67.52	258 35.93 52.12 70.30	495 68.94
1: Yes	114 15.88 51.12 32.48	109 15.18 48.88 29.70	223 31.06
Total	351 48.89	367 51.11	718 100.00

Frequency Missing = 2

Statistics for Table 2 of OW by GROUP Controlling for SEX=M: Male

Statistic	DF	Value	Prob
Chi-Square	1	0.6468	0.4213
Likelihood Ratio Chi-Square	1	0.6467	0.4213
Continuity Adj. Chi-Square	1	0.5235	0.4693
Mantel-Haenszel Chi-Square	1	0.6459	0.4216
Phi Coefficient		-0.0300	
Contingency Coefficient		0.0300	
Cramer's V		-0.0300	

The FREQ Procedure

Statistics for Table 2 of OW by GROUP
Controlling for SEX=M: Male

Fisher's Exact Test	
Cell (1,1) Frequency (F)	237
Left-sided Pr <= F	0.2347
Right-sided Pr >= F	0.8119
Table Probability (P)	0.0466
Two-sided Pr <= P	0.4679

Statistic	Value	ASE
Gamma	-0.0648	0.0803
Kendall's Tau-b	-0.0300	0.0373
Stuart's Tau-c	-0.0278	0.0345
Somers' D C|R	-0.0324	0.0403
Somers' D R|C	-0.0278	0.0346
Pearson Correlation	-0.0300	0.0373
Spearman Correlation	-0.0300	0.0373
Lambda Asymmetric C|R	0.0142	0.0422
Lambda Asymmetric R|C	0.0000	0.0000
Lambda Symmetric	0.0087	0.0259
Uncertainty Coefficient C|R	0.0006	0.0016
Uncertainty Coefficient R|C	0.0007	0.0018
Uncertainty Coefficient Symmetric	0.0007	0.0017

Estimates of the Relative Risk (Row1/Row2)

Type of Study	Value	95% Confidence Limits	
Case-Control (Odds Ratio)	0.8783	0.6402	1.2051
Cohort (Col1 Risk)	0.9366	0.7998	1.0967
Cohort (Col2 Risk)	1.0663	0.9100	1.2496

Effective Sample Size = 718
Frequency Missing = 2

The FREQ Procedure

Summary Statistics for OW by GROUP
Controlling for SEX

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	**Nonzero Correlation**	1	9.0075	0.0027
2	**Row Mean Scores Differ**	1	9.0075	0.0027
3	**General Association**	1	9.0075	0.0027

Estimates of the Common Relative Risk (Row1/Row2)

Type of Study	Method	Value	95% Confidence Limits	
Case-Control	Mantel-Haenszel	0.7043	0.5600	0.8859
(Odds Ratio)	Logit	0.7051	0.5600	0.8878
Cohort	Mantel-Haenszel	0.8439	0.7578	0.9399
(Col1 Risk)	Logit	0.8373	0.7520	0.9324
Cohort	Mantel-Haenszel	1.1988	1.0603	1.3553
(Col2 Risk)	Logit	1.1840	1.0476	1.3381

Breslow-Day Test for Homogeneity of the Odds Ratios	
Chi-Square	3.9513
DF	1
Pr > ChiSq	0.0468

Effective Sample Size = 1369
Frequency Missing = 6