

## Dataset Integrity Check for EDIC Carotid Intima-Media Thickness (CIMT) Analysis Dataset

As a partial check of the integrity of the EDIC Carotid Intima Media Thickness analysis (EDIC - CIMT) datasets archived in the NIDDK data repository, a set of tabulations was performed to verify that published results from the EDIC-CIMT study can be reproduced using the archived datasets. A small number of analyses were performed to duplicate published results for EDIC subjects and a matched sample of normal subjects reported by The DCCT/EDIC Research Group in 2003 in the *New England Journal of Medicine* (NEJM [1]; a copy of this article is included in Appendix A). The results of this integrity check are described below.

**Purpose.** The intent of this dataset integrity check is to provide confidence that the dataset 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 a dataset 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 dataset integrity check those instances in which our secondary analyses produced results that were not fully consistent with those reported in the target publication.

**Datasets.** The EDIC-CIMT authors report data on 1,229 subjects with Type 1 diabetes who were enrolled in DCCT and included in the EDIC followup. Carotid intima-media thickness was measured in these subjects in 1994-96 and again in 1998-2000 using B-mode ultrasonography of the internal and common carotid arteries. A primary focus of this article is comparison of the results for the 618 subjects who had been randomly assigned to receive intensive diabetes treatment in DCCT to results for 611 subjects assigned to conventional diabetes treatment. Data for these subjects is contained in the SAS file *EDICmsCuru6.sas7bdat* extracted using the SAS CIMPORT procedure from the file *edicimt6.xpt* supplied by the Data Coordinating Center for EDIC. A second file, *EDxCURU6.sas7bdat*, containing limited data<sup>1</sup> on a matched sample of normal subjects was also extracted from the same source.<sup>2</sup>

**Comparison to DCC Documentation.** As a partial check of the integrity of these datasets, we verified that the means, standard deviations, and ranges of metric variables in the datasets archived with the repository matched the documentation provided by the DCC. Similar tabulations were performed on nominal variables to insure that the distributions obtained by tabulating the archived data matched those described in the DCC's dataset documentation. As Appendix B shows, these initial analyses found that the results obtained from the archived data exactly match the results reported in the DCC's documentation.

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<sup>1</sup> IMT for common and internal carotid artery, gender, and masked ID.

<sup>2</sup> Analyses reported in this memorandum used a STATA version 8/se dataset translated from these SAS datasets using STAT/Transfer (Cricle Systems, <http://www.stattransfer.com>).

**Sample Characteristics.** Table 1 of the 2003 NEJM article on CIMT presents selected characteristics of the experimental and control groups broken down by gender. The archived data were analyzed to produce the same characteristics. Table A compares the published results to those obtained for our analysis of the archived data. It will be seen from Table A that calculations from the archived data exactly replicate the published results with the exception of two trivial differences that may reflect differences in rounding.<sup>3</sup>

**CIMT in Normal and EDIC subjects.** Figure 1 of the 2003 NEJM publication compares the median, 1<sup>st</sup>, and 3<sup>rd</sup> quartiles of the distributions for common and internal carotid artery thickness for EDIC subjects and an age-matched non-diabetic control group. These published figures are reproduced in our Figure 1b. Using the EDIC subjects (from file *EDICmsCuru6.sas7bdat*) and the age-matched normal subjects (from file *EDxCURU6.sas7bdat*) we replicated this analysis. Figure 1a is a box-and-whiskers plot of our results. Please note that the “whiskers” in Figure 1a are **not** included in the published figure (Fig. 1b). Visual inspection reveals that the calculated medians, 1<sup>st</sup>, and 3<sup>rd</sup> quartiles appear equivalent to the published results. Significance levels for the Wilcoxon rank-sum tests calculated from the archived data are identical to those reported in the publication.

**CIMT univariate associations with risk factors.** Table 3 of the 2003 NEJM publication reports univariate associations (unstandardized coefficients and standard errors) between three CIMT measurements and 8 risk factors (Treatment, BMI, Smoking, Systolic Blood Pressure, Hypertension [binary variable], LDL/HDL ratio, log AER, and HbA1c). These analyses included controls for age, sex, the ultrasonography equipment used, and Year 1 intima-media thickness. (Note that the last variable was the variable that paralleled the CIMT dependent variable, i.e., common CIMT, reciprocal of internal CIMT, and combined CIMT). Our Table B compares the results of our analyses to the published results. It will be seen that with the exception of one trivial difference, the results obtained from our analyses of the archived data are identical to the published results.

**CIMT multivariate associations with risk factors.** Table 4 of the 2003 NEJM publication reports results (unstandardized coefficients and standard errors) of multivariate linear regression analyses predicting two CIMT measurements (common and combined IMT measurements) as a function of age, sex, Year 1 IMT, systolic blood pressure, treatment, an age-by-treatment interaction variable, and control variables for the various combinations of site and type of ultrasonography equipment used to make the measurements. We repeated these analyses using the archived data. The results are presented in Table C, and they are identical to the published version with two extremely trivial discrepancies.

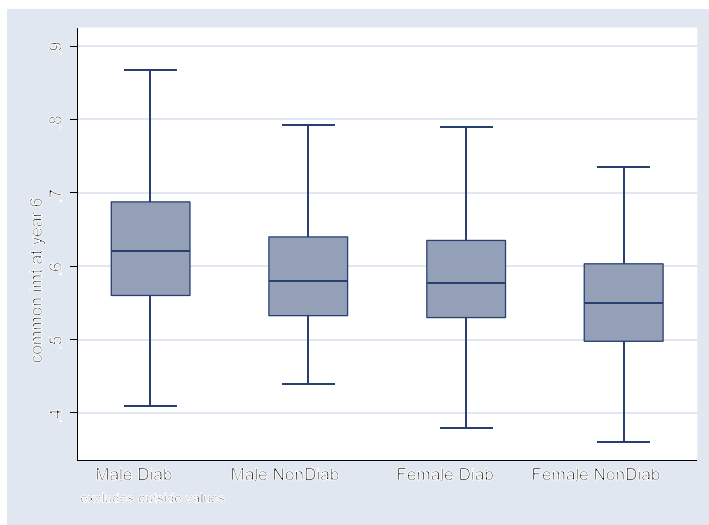
**Conclusion.** Replication of a variety of analyses reported by the DCC in its documentation and in the 2003 NEJM article produced no noteworthy discrepancies.

## References.

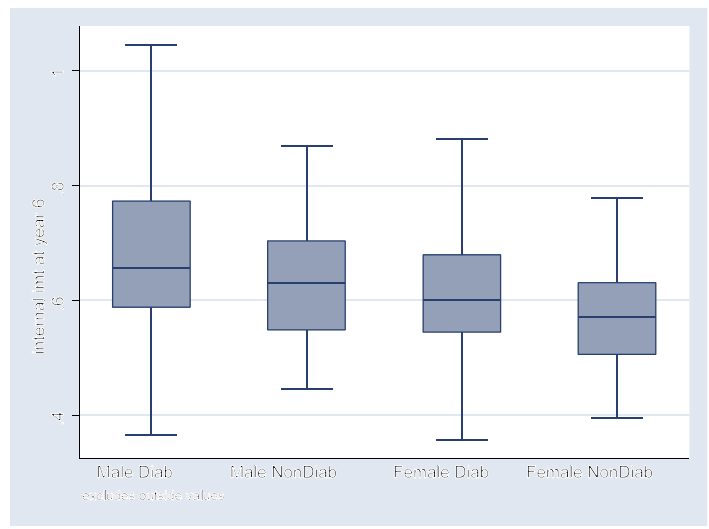
DCCT-EDIC Research Group (2003) Intensive Diabetes Therapy and Carotid Intima-Media Thickness in Type 1 Diabetes Mellitus. *New England Journal of Medicine*, 348(23):2294-2303.

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<sup>3</sup> There were a few instances in which data were unavailable in the datasets to document statements made in the text. For example, page 2297 of the NEJM article states that mean glycosylated hemoglobin in the treatment and control groups remained significantly, although minimally, different during the first four years of the EDIC study, but by year 5 they were no longer significantly different (7.9% ... vs. 8.0% ...,  $p=0.075$ ). No year-by-year HbA1c values are included in this analysis dataset.

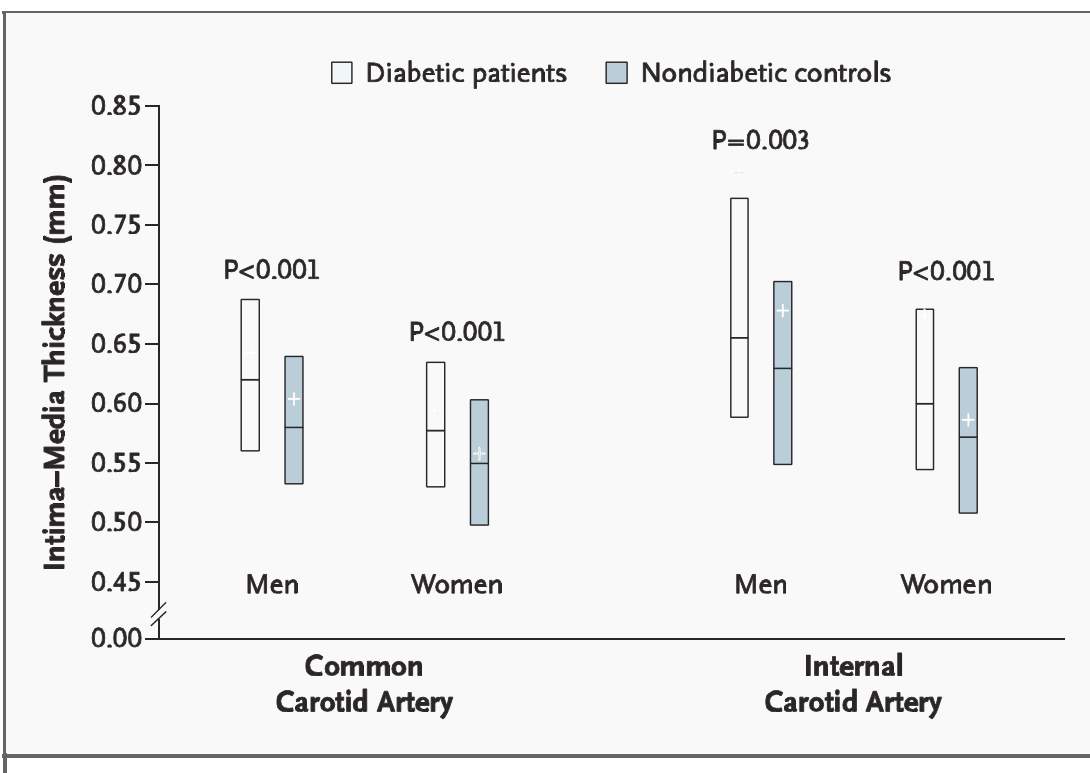


**Common Carotid Artery**  
(Calculated from archived data)



**Internal Carotid Artery**  
(Calculated from archived data)

**FIGURE 1a.** Box plots representing the median, second and third quartiles (shaded box), and ranges excluding outliers (whiskers) for intima-media thickness of common and internal carotid arteries *calculated from archived data*. P-values calculated using Wilcoxon rank-sum test are .0004 (common) for both males and females and .0028 and .0001 (internal) for males and females respectively.



**FIGURE 1b.** *Published* box plots representing the median, mean (+), second and third quartiles (shaded box) for intima-media thickness of common and internal carotid arteries. *Published* P-values are “calculated using Wilcoxon rank-sum test.”

**TABLE A.** Comparison of characteristics of sample by gender published in NEJM (2003, Table 1) and values calculated from EDIC CIMT analysis dataset deposited in NIDDK Repository.

CHARACTERISTIC	FEMALES, PUBLISHED				FEMALES, Tabulated from Archived Data			
	Intensive Treatment (N=295)		Conventional Treatment (N=289)		Intensive Treatment (N=295)		Conventional Treatment (N=289)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
<b>Demographic, year 1</b>								
Age (yr)	35	7	34	7	35.15593	7.141625	33.97232	7.249947
Current smoker %	20%		19%		20.07%		19.03%	
Duration of Diabetes (yr)	13.9	4.8	14.2	5.2	13.89802	4.817854	14.1286	5.136499
<b>Medical Year 1</b>								
BMI	26.5	4.5	25	3.5	26.47652	4.525977	25.01792	3.451216
Waist:Hip circumference	0.76	0.07	0.76	0.07	0.7592578	0.0744102	0.760481	0.0702378
Ankle:Arm BP < 0.9 (%)	8.80%		8.70%		8.84%		8.65%	
Systolic BP	114	12	114	13	114.1301	12.20347	114.2249	13.11281
Diastolic BP	74	9	72	9	73.50512	8.677487	72.2699	9.485908
Hypertension (%)	10.4%		14%		10.38%		14.04%	
<b>Lipids, year 1 or 2</b>								
Total cholestereol	188	36	188	38	187.6958	35.65963	188.1383	38.07006
HDL cholesterol	59	14	59	14	58.7972	14.3874	59.23759	14.00852
LDL cholesterol	112	29	112	30	112.0035	29.37927	112.1	30.33925
LDL:HDL ratio	2		2		2.029237	0.7722056	1.997175	0.7238223
Triglycerides	83	76	83	76	83.06294	75.84858	82.89362	75.93026
Hyperlipidemia (%)	27.1		26.8		27.10%		26.80%	
<b>AER, year 1 or 2</b>								
Value	22	67	67	330	21.8271	67.33366	67.15217	330.6526
>40mg	6.8		15.7		6.81%		15.66%	
<b>HBa1c</b>								
During DCCT	7.3	0.9	9.1	1.3	7.304381	0.9048686	9.110137	1.345111
Year 1 EDIC	7.9	1.4	8.1	1.4	7.880756	1.363606	8.148239	1.432891
<b>IM Thickness, year 1 or 2</b>								
Common carotid artery	0.566	0.077	0.557	0.076	0.5657740	0.0769705	0.5569723	0.0755307
Internal carotid artery	0.608	0.165	0.628	0.251	0.6084818	0.1646724	0.6276088	0.2506052

Table A, continued

CHARACTERISTIC	MALES, Published				MALES, Tabulated from Archived Data			
	Intensive Treatment (N=323)		Conventional Treatment (N=322)		Intensive Treatment (N=323)		Conventional Treatment (N=322)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
<b>Demographic, year 1</b>								
Age (yr)	36	7	36	7	35.77399	6.72358	35.74224	6.560907
Current smoker %	20%		17%		19.50%		17.45%	
Duration of Diabetes (yr)	13.9	4.8	13.3	4.6	13.98271	4.912048	13.27562	4.573646
<b>Medical Year 1</b>								
BMI	26.7	3.9	26	3.2	26.72371	3.911454	25.98145	3.190197
Waist:Hip circumference	0.88	0.08	0.87	0.09	0.8830098	0.0803522	0.8738495	0.0934564
Ankle:Arm BP < 0.9 (%)	4.6%		6.9%		4.64%		6.85%	
Systolic BP	119	11	120	12	119.3065	11.11552	120.3625	11.85042
Diastolic BP	77	9	77	8	76.89164	9.099725	77.29375	8.457229
Hypertension (%)	22.9%		17.9%		22.88%		17.92%	
<b>Lipids, year 1 or 2</b>								
Total cholestereol	187	35	182	36	187.3714	34.56175	182.4628	36.39514
HDL cholesterol	49	13	50	11	49.27848	12.5922	49.65049	11.47615
LDL cholesterol	119	30	114	32	119.125	29.96183	113.9643	31.79928
LDL:HDL ratio	2.6		2.4		2.577837	0.9515922	2.420564	0.8942188
Triglycerides	96	72	96	79	96.05063	71.51839	96.15534	79.39815
Hyperlipidemia (%)	35.3%		30.0%		35.3%		30.0%	
<b>AER, year 1 or 2</b>								
Value	30	118	43	117	30.02701	117.8683	42.52181	116.9985
>40mg	7.7%		16.5%		7.72%		16.45%	
<b>HBa1c</b>								
During DCCT	7.2	0.9	9	1.1	7.226603	0.8684062	8.967268	1.128859
Year 1 EDIC	7.8	1.2	8.3	1.2	7.847649	1.247079	8.345912	1.215346
<b>IM Thickness, year 1 or 2</b>								
Common carotid artery	0.597	0.082	0.604	0.097	0.5973891	0.0821517	0.6039286	0.0967217
Internal carotid artery	0.668	0.22	0.681	0.268	0.6677754	0.2204556	0.6809653	0.2675956

**TABLE B.** Comparison of published results and results calculated from archived data: Univariate associations of carotid intima-media thickness with risk factors, adjusted for age, sex, ultrasonography equipment used, and Year 1 intima-media thickness.

CIMT Measurement (Dep. Var) & Risk Factor	PUBLISHED			CALCULATED FROM ARCHIVED DATA		
	Estimate of Coefficient	S.E.	P	Estimate of Coefficient	S.E.	P
<b>Common Carotid Intima-Media Thickness, <i>commyr6</i></b>						
Treatment Group	0.0135	0.0053	0.02	0.0135	0.0053	0.012
Body Mass Index	0.0016	0.0007	0.03	0.0016	0.0007	0.028
Smoking (yes/no)	0.0247	0.0068	<.001	0.0247	0.0068	0.000
Systolic blood pressure	0.0008	0.0002	<.001	0.0008	0.0002	0.001
Hypertension (yes/no)	0.0189	0.0074	0.01	0.0189	0.0074	0.011
Low-density lipoprotein: High-density lipoprotein ratio	0.0072	0.0032	0.03	0.0072	0.0032	0.026
Log albumin excretion rate	0.0068	0.0025	0.006	0.0068	0.0025	0.006
Glycosylated hemoglobin value during DCCT	0.0065	0.0020	0.001	0.0065	0.0020	0.001
<b>Reciprocal of Internal Carotid-Media Thickness, <i>r_int6</i></b>						
Treatment Group	-0.0330	0.0183	0.07	-0.0330	0.0813	0.071
Body Mass Index	-0.0032	0.0025	0.20	-0.0032	0.0025	0.197
Smoking (yes/no)	-0.0822	0.0231	<.001	-0.0822	0.0231	<.001
Systolic blood pressure	-0.0023	0.0008	0.004	-0.0023	0.0008	0.004
Hypertension (yes/no)	-0.1105	0.0258	<.001	-0.1105	0.0258	<.001
Low-density lipoprotein: High-density lipoprotein ratio	-0.0505	0.0113	<.001	-0.0505	0.0113	<.001
Log albumin excretion rate	-0.0212	0.0084	0.01	-0.0212	0.0084	0.011
Glycosylated hemoglobin value during DCCT	-0.0193	0.0067	0.004	-0.0193	0.0067	0.004
<b>Combined Intima-Media Thickness, <i>comint6a</i></b>						
Treatment Group	0.1619	0.0669	0.02	0.1619	0.0669	0.016
Body Mass Index	0.0136	0.0089	0.13	0.0136	0.0089	0.126
Smoking (yes/no)	0.3468	0.0850	<.001	0.3468	0.0850	<.001
Systolic blood pressure	0.0088	0.0029	0.002	0.0088	0.0029	0.002
Hypertension (yes/no)	0.3016	0.0939	0.001	0.3016	0.0939	0.001
Low-density lipoprotein: High-density lipoprotein ratio	0.1427	0.0405	<.001	0.1427	0.0405	<.001
Log albumin excretion rate	0.0912	0.0308	0.003	0.0912	0.0308	0.003
Glycosylated hemoglobin value during DCCT	0.1014	0.0244	<.001	0.1014	0.0244	<.001

**NOTE.** These multiple regressions modeled Year 6 intima-media thickness as a linear, additive function of the risk factor listed in the row heading controlling for age, sex, Year 1 intima-media thickness, and dummy variables representing the multiple types of ultrasonography equipment used. (The Year 1 intima-media thickness variable used in each regression was the one that paralleled the dependent variable, i.e., (1) common, (2) reciprocal of internal, and (3) combined carotid intima-media thickness [common, *r\_int*, *comint1a*].)

**TABLE C. Multivariate associations of carotid intima-media thickness with various risk factors: Comparison of published results (NEJM, 2003, Table 4) and results calculated from archived data:**

CIMT Measurement (Dep. Var)	PUBLISHED			CALCULATED FROM ARCHIVED DATA		
	Estimate of Coefficient	S.E.	P	Estimate of Coefficient	S.E.	P
<b>Common Carotid Intima-Media Thickness, <i>commyr6</i></b>						
Age	0.0029	0.0006	<.001	0.0029	0.0006	<.001
Sex (female vs. male)	-0.0173	0.0055	0.002	-0.0173	0.0055	0.002
Year 1 intima-media thickness	0.6188	0.0361	<.001	0.6188	0.0361	<.001
Smoking (yes vs. no)	0.0265	0.0068	<.001	0.0265	0.0068	<.001
Systolic blood pressure	0.0008	0.0002	0.001	0.0008	0.0002	0.001
Ultrasonography equipment (12 combinations)	---	---	<.001	---	---	---
Treatment group (conventional vs. intensive)	-0.0453	0.0274	0.10	-0.0453	0.0274	0.099
Age X Treatment interaction	0.0017	0.0008	0.03	0.0017	0.0008	0.029
<b>R<sup>2</sup></b>	<b>40%</b>			<b>39.8%</b>		
<b>Combined Intima-Media Thickness, <i>comint6a</i></b>						
Age	0.0248	0.0071	<.001	0.0248	0.0071	<.001
Sex (female vs. male)	-0.2506	0.0689	<.001	-0.2506	0.0689	<.001
Year 1 intima-media thickness	0.5961	0.0238	<.001	0.5961	0.0238	<.001
Smoking (yes vs. no)	0.3737	0.0851	<.001	0.3737	0.0850	<.001
Systolic blood pressure	0.0092	0.0029	0.001	0.0092	0.0029	0.001
Ultrasonography equipment (12 combinations)	---	---	<.001	---	---	---
Treatment group (conventional vs. intensive)	-0.5433	0.3435	0.12	-0.5433	0.3435	0.114
Age X Treatment interaction	0.0201	0.0096	0.04	0.0201	0.0096	0.036
<b>R<sup>2</sup></b>	<b>52%</b>			<b>52.2%</b>		

NOTE. Multiple regression models used carotid artery thickness as outcome predicted by the independent variables shown in the table. (The Year 1 intima-media thickness variable used in each regression was the one that paralleled the dependent variable, i.e., (1) common, or (2) combined carotid intima-media thickness [common, *comint1a*].)

## **APPENDIX A**

DCCT-EDIC Research Group (2003) Intensive Diabetes Therapy and Carotid Intima-Media Thickness in Type 1 Diabetes Mellitus. *New England Journal of Medicine*, 348(23):2294-2303.

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## ORIGINAL ARTICLE

# Intensive Diabetes Therapy and Carotid Intima–Media Thickness in Type 1 Diabetes Mellitus

The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group\*

## ABSTRACT

The writing group of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Research Group (David M. Nathan, M.D., John Lachin, Sc.D., Patricia Cleary, M.S., Trevor Orchard, M.D., David J. Brillon, M.D., Jye-Yu Backlund, M.P.H., Daniel H. O'Leary, M.D., and Saul Genuth, M.D.) assumes responsibility for the contents of this article. Address reprint requests to DCCT/EDIC Research Group at Box NDIC/DCCT, Bethesda, MD 20892, or at dnathan@partners.org.

\*A complete list of the persons and institutions participating in the DCCT/EDIC Research Group appears in the Appendix.

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**BACKGROUND**

Cardiovascular disease causes severe morbidity and mortality in type 1 diabetes, although the specific risk factors and whether chronic hyperglycemia has a role are unknown. We examined the progression of carotid intima–media thickness, a measure of atherosclerosis, in a population with type 1 diabetes.

**METHODS**

As part of the Epidemiology of Diabetes Interventions and Complications (EDIC) study, the long-term follow-up of the Diabetes Control and Complications Trial (DCCT), 1229 patients with type 1 diabetes underwent B-mode ultrasonography of the internal and common carotid arteries in 1994–1996 and again in 1998–2000. We assessed the intima–media thickness in 611 subjects who had been randomly assigned to receive conventional diabetes treatment during the DCCT and in 618 who had been assigned to receive intensive diabetes treatment.

**RESULTS**

At year 1 of the EDIC study, the carotid intima–media thickness was similar to that in an age- and sex-matched nondiabetic population. After six years, the intima–media thickness was significantly greater in the diabetic patients than in the controls. The mean progression of the intima–media thickness was significantly less in the group that had received intensive therapy during the DCCT than in the group that had received conventional therapy (progression of the intima–media thickness of the common carotid artery, 0.032 vs. 0.046 mm;  $P=0.01$ ; and progression of the combined intima–media thickness of the common and internal carotid arteries,  $-0.155$  vs.  $0.007$ ;  $P=0.02$ ) after adjustment for other risk factors. Progression of carotid intima–media thickness was associated with age, and the EDIC base-line systolic blood pressure, smoking, the ratio of low-density lipoprotein to high-density lipoprotein cholesterol, and urinary albumin excretion rate and with the mean glycosylated hemoglobin value during the mean duration (6.5 years) of the DCCT.

**CONCLUSIONS**

Intensive therapy during the DCCT resulted in decreased progression of intima–media thickness six years after the end of the trial.

**D**IABETES MELLITUS IS ACCOMPANIED by a substantial increase in the risk of cardiovascular disease.<sup>1-5</sup> Most epidemiologic and clinical-trial data have derived from the study of type 2 diabetes, in which cardiovascular disease accounts for 70 percent of all deaths.<sup>1-3</sup> Much less is known about cardiovascular disease in type 1 diabetes. Although the absolute risk of cardiovascular disease is lower in patients with type 1 diabetes than in those with type 2 diabetes, owing in part to their younger age, the relative risk, as compared with that of nondiabetic persons of similar age, may be increased by a factor of 10.<sup>4,5</sup> Much of the risk of cardiovascular disease in patients with type 1 diabetes has been attributed to the development of renal disease.<sup>6</sup> In addition to renal disease, autonomic neuropathy, dyslipidemia, and microvascular cardiac disease have been suggested as cardiovascular risk factors.<sup>7</sup> Interestingly, glycemia has not been documented to be a risk factor for heart disease in patients with type 1 diabetes.

During the Diabetes Control and Complications Trial (DCCT), patients with type 1 diabetes were randomly assigned either to receive intensive diabetes therapy, subsequently maintaining a mean glycosylated hemoglobin value of 7.2 percent during the mean follow-up of 6.5 years, or to receive standard therapy, subsequently maintaining a mean glycosylated hemoglobin value of 9 percent.<sup>8</sup> Although intensive therapy reduced the risk of development and progression of microvascular and neuropathic complications by 35 to 76 percent, the incidence of cardiovascular disease events was not significantly different between the two treatment groups.<sup>9</sup> After completion of the DCCT, long-term follow-up of the DCCT cohort, called the Epidemiology of Diabetes Interventions and Complications (EDIC) study,<sup>10</sup> included B-mode ultrasonography to measure the thickness of the intima-media wall of the carotid artery on two occasions. Carotid intima-media thickness is a well-established index of atherosclerosis that correlates with prevalent and incident coronary heart disease<sup>11-14</sup> and stroke.<sup>12,14,15</sup> We analyzed the changes in the intima-media thickness over time and associated risk factors, according to the original intention-to-treat assignment during the DCCT.

## METHODS

### PATIENTS

The 1441 patients enrolled in the DCCT between 1983 and 1989 were 13 to 39 years old, had had type 1

diabetes for 1 to 15 years, and were in generally good health at base line.<sup>8</sup> After a mean of 6.5 years of follow-up, 1375 of the 1425 surviving members volunteered to participate in the EDIC study, an observational follow-up of the DCCT cohort.<sup>10</sup> During the EDIC study, all therapy was provided by the patients' own physicians and intensive therapy was recommended for all patients. A detailed description of the study procedures and base-line characteristics has been published.<sup>10</sup> Carotid ultrasonography was performed between June 1994 and April 1996 (1 to 2 years after the initiation of the EDIC study and approximately 8 years after the beginning of the DCCT; range, 4 to 11). It was repeated between October 1998 and November 2000 in 1229 participants, who are the subjects of this study (Table 1).

### CONTROL SUBJECTS

Healthy age- and sex-matched subjects without diabetes were recruited from each of the 28 EDIC centers to serve as contemporaneous controls to determine carotid intima-media thickening. One group of eight controls from each center was selected in 1994-1996,<sup>16</sup> and a second group of eight was selected in 1998-2000. In 1998-2000, 222 healthy volunteers with a mean ( $\pm$ SD) age of 39 $\pm$ 11 years were studied. Fifty percent were female. Mean systolic and diastolic blood pressures were 117 $\pm$ 11 and 75 $\pm$ 9 mm Hg, respectively, similar to those of the DCCT cohort. The prevalence of smoking, however, was much lower: 5.9 percent, as compared with 16.8 percent in the DCCT cohort ( $P < 0.001$ ). The mean glycosylated hemoglobin value was 5.0 $\pm$ 0.35 percent.

### ASSESSMENT OF CAROTID INTIMA-MEDIA THICKNESS

The measurement of intima-media thickness has been described in detail.<sup>16</sup> A single longitudinal lateral view of the distal 10 mm of the right and left common carotid arteries and three longitudinal views in different imaging planes of each internal carotid artery were obtained. The internal carotid artery was defined as including both the carotid bulb and the 10-mm segment distal to the tip of the flow divider that separates the internal from the external carotid artery. Studies were performed by certified technicians at the clinical centers, recorded on videotapes, and read in a central unit (Tufts University, Boston) by a single reader, who was unaware of the subjects' diagnostic groups, treatment assignments and the time of the studies (year 1 as compared with year 6).

**Table 1. Clinical Characteristics of the Epidemiology of Diabetes Interventions and Complications (EDIC) Participants, According to Sex and Treatment Assignment in the Diabetes Control and Complications Trial (DCCT).\***

Characteristic	Female Patients		Male Patients	
	Intensive Treatment (N=295)	Conventional Treatment (N=289)	Intensive Treatment (N=323)	Conventional Treatment (N=322)
Demographic, year 1				
Age (yr)	35±7	34±7	36±7	36±7
Current smoker (%)	20	19	20	17
Duration of diabetes (yr)	13.9±4.8	14.2±5.2	13.9±4.8	13.3±4.6
Medical, year 1				
Body-mass index	26.5±4.5†	25.0±3.5	26.7±3.9‡	26.0±3.2
Natural waist:hip circumference	0.76±0.07	0.76±0.07	0.88±0.08	0.87±0.09
Ankle:arm blood pressure <0.9 (%)	8.8	8.7	4.6	6.9
Systolic blood pressure (mm Hg)	114±12	114±13	119±11	120±12
Diastolic blood pressure (mm Hg)	74±9	72±9	77±9	77±8
Hypertension (%)§	10.4	14.0	22.9	17.9
Lipids, year 1 or 2				
Total cholesterol (mg/dl)¶	188±36	188±38	187±35	182±36
HDL cholesterol (mg/dl)¶	59±14	59±14	49±13	50±11
LDL cholesterol (mg/dl)¶	112±29	112±30	119±30‡	114±32
LDL:HDL ratio	2.0	2.0	2.6	2.4
Triglycerides (mg/dl)¶	83±76	83±76	96±72	96±79
Hyperlipidemia (%)**	27.1	26.8	35.3	30.0
Albumin excretion rate, year 1 or 2				
Value (mg/24 hr)	22±67††	67±330	30±118	43±117
>40 mg/24 hr (%)	6.8†	15.7	7.7†	16.5
Glycosylated hemoglobin (%)				
During DCCT	7.3±0.9†	9.1±1.3	7.2±0.9†	9.0±1.1
Year 1 EDIC	7.9±1.4‡	8.1±1.4	7.8±1.2†	8.3±1.2
Intima-media thickness, year 1 or 2 (mm)				
Common carotid artery	0.566±0.077	0.557±0.076	0.597±0.082	0.604±0.097
Internal carotid artery	0.608±0.165	0.628±0.251	0.668±0.220	0.681±0.268

\* Plus-minus values are means ±SD. All data are from EDIC year 1 or year 2 unless otherwise noted. Comparisons between intensive-treatment and conventional-treatment groups are based on the chi-square test or Wilcoxon rank-sum test. The body-mass index is the weight in kilograms divided by the square of the height in meters.

† P<0.001 for the comparison of intensive treatment with conventional treatment.

‡ P<0.05 for the comparison of intensive treatment with conventional treatment.

§ Hypertension was defined by a systolic blood pressure of at least 140 mm Hg, a diastolic blood pressure of at least 90 mm Hg, the presence of documented hypertension, or the use of antihypertensive agents.

¶ To convert the values for cholesterol to millimoles per liter, multiply by 0.02586. HDL denotes high-density lipoprotein, and LDL low-density lipoprotein.

|| To convert the values for triglycerides to millimoles per liter, multiply by 0.01129.

\*\* Hyperlipidemia was defined by an LDL cholesterol level of at least 130 mg per deciliter (3.36 mmol per liter) or by the use of lipid-lowering agents.

†† P<0.01 for the comparison of intensive treatment with conventional treatment.

**QUALITY-CONTROL PROCEDURES**

Reproducibility analysis of 50 replicate measures of year 1 and year 6 carotid studies resulted in absolute mean differences of 0.03 and 0.02 mm for the year 1 common carotid artery and internal carotid artery, respectively, and 0.03 and 0.04 mm for the year 6 common carotid artery and internal carotid artery, respectively. The respective intraclass correlations between the original and maximal wall thickness and the measurement obtained on rereading were 0.87 and 0.99 for year 1 common and internal carotid arteries and 0.99 and 0.99 for year 6 common and internal carotid arteries.

**OTHER PROCEDURES**

Each subject in the EDIC study underwent an annual history-taking, physical examination, electrocardiography, and laboratory testing, including measurements of serum creatinine and glycosylated hemoglobin, determined as they were in the DCCT.<sup>8,17</sup> Lipid profiles and four-hour urine collections for the measurement of the albumin excretion rate and creatinine clearance were obtained in alternate years during the EDIC study.<sup>10</sup>

**MEASUREMENTS**

Base-line covariates were obtained from the year 1 history and physical examination and from the laboratory data (lipid levels measured after an overnight fast and renal-function values) collected in either year 1 or year 2. The maximal intima-media thickness of the common carotid artery was defined as the mean of the maximal value for the near and far walls on both the right and left sides. The internal intima-media thickness was defined as the mean of the maximal value for anterior, lateral, and posterior views on both sides. The combined intima-media thickness was defined as the sum of the standardized intima-media measurements of the common and internal carotid arteries. The standardized intima-media thickness was defined as  $(\text{variable} - \text{mean}) \div \text{SD}$ .<sup>18</sup> The change in the thickness was defined as the difference between results for year 6 and those for year 1.

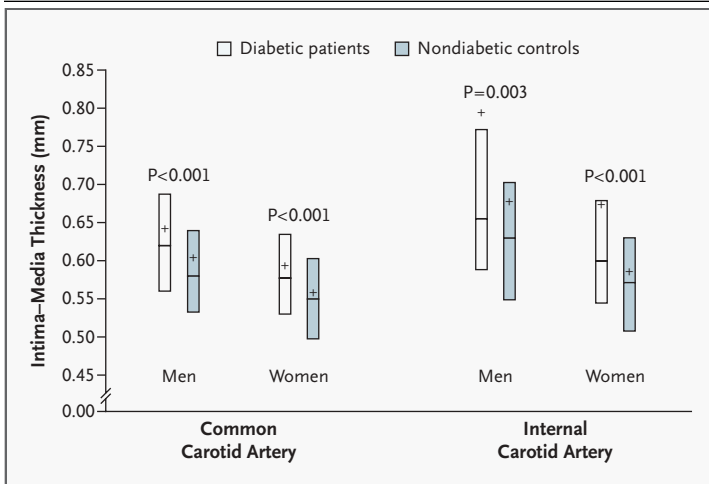
**STATISTICAL ANALYSIS**

Group differences were compared with use of the Wilcoxon rank-sum test for quantitative variables and the chi-square test for categorical variables. A paired t-test was used to test the significance of the change over time. To compare the two treatment groups, we used analysis of covariance of the change

in the intima-media thickness (year 6 minus year 1) with the year 1 thickness as an adjusting covariate. To obtain the least-squares means of the change in intima-media thickness, we fitted the model using the change in the thickness as the outcome and adjusting for the year 1 value, age, sex, and the ultrasonography equipment used (12 combinations of ultrasonography equipment were used at 28 clinical centers). A reciprocal transformation of the internal intima-media thickness was used to yield approximately normal residuals.<sup>19</sup> The association of each covariate (listed in Table 1) with each intima-media measure was assessed, with adjustment for the year 1 value, sex, attained age, and the ultrasonography equipment used. To study the risk factors, a multiple linear regression model was fitted with the use of the year 6 intima-media thickness as the outcome and the year 1 thickness as a covariate. The most significant factor for the multivariate association among similar variables (e.g., systolic and diastolic blood pressure) was selected. Only covariates known to be unaffected by the DCCT treatment group were included. All two-way interaction terms were assessed, and those nominally significant at a P level of less than 0.10 were retained.<sup>20</sup> The final model included the ultrasonography equipment used, attained age, sex, the year 1 intima-media thickness, smoking status, systolic blood pressure, treatment group, and the interaction between attained age and treatment group. The overall effect of the DCCT treatment group was assessed with the use of a general linear test with 2 degrees of freedom for both the main effect and the interaction.<sup>21,22</sup>

**RESULTS**

The clinical characteristics of the EDIC study cohort at year 1, according to sex and treatment assignment during the DCCT, are shown in Table 1. Mean blood pressure and lipid levels were not significantly different between the group that had received intensive therapy during the DCCT and the group that had received conventional treatment. On the other hand, mean glycosylated hemoglobin levels in the two groups remained significantly, albeit minimally, different during the first four years of the EDIC study; by year 5 they were no longer different (7.9 percent in the original intensive-treatment group and 8.0 percent in the conventional-treatment group,  $P=0.075$ ).<sup>23</sup> Albumin excretion rates remained significantly lower in the intensive-



**Figure 1. Intima-Media Thickness of the Common and Internal Carotid Arteries at Year 6 in Diabetic Patients and Age-Matched Nondiabetic Control Subjects.**

Box plots represent the second and third quartiles of the distribution, the center line the median, and the plus sign the mean. P values were calculated with use of the Wilcoxon rank-sum test.

treatment group than in the conventional-treatment group during the six years of EDIC follow-up, reflecting the previously described long-lasting beneficial effects of intensive therapy on diabetic nephropathy.<sup>8,24</sup> Body-mass index during the EDIC study remained significantly higher in the group that had received intensive treatment during DCCT, as it had been at the end of that study.

The intima-media measurements in the age- and sex-matched 1998–2000 nondiabetic population

were similar to published data in healthy nondiabetic subjects, with a mean intima-media thickness of  $0.58 \pm 0.10$  mm for the common carotid artery and a mean of  $0.63 \pm 0.18$  mm for the internal carotid artery.<sup>15,24</sup> Although no significant differences in thickness were demonstrable between the diabetic cohort and nondiabetic controls at year 1,<sup>16</sup> by year 6, the intima-media thickness for the common and internal carotid arteries was significantly greater in the diabetic cohort than in the nondiabetic cohort for each sex, even after adjustment for smoking status (Fig. 1).

There was less progression of the intima-media thickness of the common carotid artery from year 1 to year 6 among the patients who had received intensive treatment during the DCCT than among those who had received conventional treatment. After adjustment for sex, age, the ultrasonography equipment used, and the year 1 intima-media thickness (Table 2), the mean progression was 0.032 mm in the intensive-treatment group and 0.046 mm in the conventional-treatment group, with a difference of 0.013 mm (95 percent confidence interval for the difference, 0.003 to 0.024). The progression of the intima-media thickness of the combined common and internal carotid arteries was also less in the intensive-treatment group, where regression occurred, than in the conventional-treatment group ( $-0.155$  vs.  $0.007$ ; a difference of  $0.162$ ; 95 percent confidence interval for the difference,  $0.031$  to  $0.293$ ) (Table 2). The differences between treatment groups in the reciprocal values for the intima-media thickness of the internal carotid artery were not significant ( $P=0.07$ ). There was no significant treat-

**Table 2. Least-Squares Mean Change in the Intima-Media Thickness of the Common Carotid Artery and of the Combined Common and Internal Carotid Arteries from Year 1 to Year 6 of the Epidemiology of Diabetes Interventions and Complications Study, According to the Treatment Assignment in the Diabetes Control and Complications Trial.\***

Variable	Change in Intima-Media Thickness of Common Carotid Artery		Change in Combined Intima-Media Thickness	
	Least-Squares Mean (95% CI)	P Value	Least-Squares Mean (95% CI)	P Value
	mm		mm	
Conventional treatment	0.046 (0.023 to 0.068)		0.007 (-0.277 to 0.292)	
Intensive treatment	0.032 (0.010 to 0.055)		-0.155 (-0.440 to 0.131)	
Difference between treatment groups	0.013 (0.003 to 0.024)	0.01	0.162 (0.031 to 0.293)	0.02

\* The change in the intima-media thickness was used as the outcome to fit a general linear model, adjusted for sex, age, ultrasonography equipment used, and the year 1 thickness. CI denotes confidence interval.

ment effect according to sex. Finally, the potential effect of any differences in the use of hypolipidemic or antihypertensive agents between the two treatment groups was analyzed by including terms for medication use in the analyses in Table 2. The results were unchanged.

The intima-media thickness at year 6 of the EDIC study was associated with smoking status, systolic (but not diastolic) blood pressure, the presence or absence of hypertension, total and high-density lipoprotein cholesterol levels (data not shown), the ratio of low-density lipoprotein to high-density lipoprotein cholesterol, urinary albumin excretion rate, and the mean glycosylated hemoglobin level during the DCCT (Table 3). All of the associations were similar in magnitude and direction for the intima-media thickness of the common carotid artery and the internal carotid artery and the combined intima-media thickness and when the change in thickness was substituted for the year 6 thickness. The association of the mean glycosylated hemoglobin value during the DCCT with the year 6 intima-media thickness of the common carotid artery

remained significant ( $P < 0.001$ ) after adjustment for age, sex, year 1 intima-media thickness of the common carotid artery, and the ultrasonography equipment used.

Since many of the univariate risk factors differed between groups at year 1 of the EDIC study, reflecting the effects of treatment during the DCCT, multivariate regression modeling adjusted only for the covariates not affected by treatment at year 1 of the EDIC study. These models revealed that, for each measure, the benefits of intensive treatment increased with age (Table 4). Furthermore, the overall treatment effect with 2 degrees of freedom was significant for all these measures ( $P = 0.004$  for the intima-media thickness of the common carotid artery and  $P = 0.005$  for the combined thickness), including the reciprocal internal intima-media thickness ( $P = 0.049$ ) (data not shown). The complete model explained approximately 40 percent of the variation in the intima-media thickness of the common carotid artery and 52 percent of the variation in the combined thickness. Figure 2 shows the difference between the conventional-treatment and

**Table 3. Univariate Associations of Carotid Intima-Media Thickness, with Risk Factors Adjusted for Age, Sex, Ultrasonography Equipment Used, and Year 1 Intima-Media Thickness Measurement.\***

Risk Factor	Common Carotid Intima-Media Thickness		Internal Carotid Intima-Media Thickness (Reciprocal)		Combined Intima-Media Thickness	
	Estimate of $\beta$ Coefficient $\pm$ SE	P Value	Estimate of $\beta$ Coefficient $\pm$ SE	P Value	Estimate of $\beta$ Coefficient $\pm$ SE	P Value
	<i>mm</i>					
Treatment group (conventional vs. intensive)	0.0135 $\pm$ 0.0053	0.02	-0.0330 $\pm$ 0.0183	0.07	0.1619 $\pm$ 0.0669	0.02
Body-mass index (per unit)	0.0016 $\pm$ 0.0007	0.03	-0.0032 $\pm$ 0.0025	0.20	0.0136 $\pm$ 0.0089	0.13
Smoking (yes vs. no)	0.0247 $\pm$ 0.0068	<0.001	-0.0822 $\pm$ 0.0231	<0.001	0.3468 $\pm$ 0.0850	<0.001
Systolic blood pressure (per mm Hg)	0.0008 $\pm$ 0.0002	<0.001	-0.0023 $\pm$ 0.0008	0.004	0.0088 $\pm$ 0.0029	0.002
Hypertension (yes vs. no) <sup>†</sup>	0.0189 $\pm$ 0.0074	0.01	-0.1105 $\pm$ 0.0258	<0.001	0.3016 $\pm$ 0.0939	0.001
Low-density lipoprotein:high-density lipoprotein ratio	0.0072 $\pm$ 0.0032	0.03	-0.0505 $\pm$ 0.0113	<0.001	0.1427 $\pm$ 0.0405	<0.001
Log albumin excretion rate	0.0068 $\pm$ 0.0025	0.006	-0.0212 $\pm$ 0.0084	0.01	0.0912 $\pm$ 0.0308	0.003
Glycosylated hemoglobin value during DCCT (per 1 percentage point)	0.0065 $\pm$ 0.0020	0.001	-0.0193 $\pm$ 0.0067	0.004	0.1014 $\pm$ 0.0244	<0.001

\* The multiple regression model used the year 6 intima-media thickness as the outcome and fit the covariates one at a time after adjustment for age, sex, ultrasonography equipment used, and year 1 intima-media thickness. The  $R^2$ , based on a general linear model (PROC GLM) in which the year 6 intima-media thickness was the outcome, adjusted for age, sex, ultrasonography equipment used, and year 1 intima-media thickness, respectively, is 37.76 percent, 39.58 percent, and 50.60 percent for the common carotid, internal carotid, and combined intima-media thickness, respectively. DCCT denotes Diabetes Control and Complications Trial.

<sup>†</sup> Hypertension was defined by a systolic blood pressure of at least 140 mm Hg, a diastolic blood pressure of at least 90 mm Hg, documented hypertension, or the use of antihypertensive agents.

**Table 4. Multivariate Association of Carotid Intima–Media Thickness with Various Risk Factors.\***

Risk Factor	Common Carotid Intima–Media Thickness			Combined Intima–Media Thickness		
	Estimate of $\beta$ Coefficient $\pm$ SE	Semipartial R <sup>2</sup>	P Value	Estimate of $\beta$ Coefficient $\pm$ SE	Semipartial R <sup>2</sup>	P Value
		%			%	
Age (per year of age)	0.0029 $\pm$ 0.0006	1.32	<0.001	0.0248 $\pm$ 0.0071	0.49	<0.001
Sex (female vs. male)	-0.0173 $\pm$ 0.0055	0.50	0.002	-0.2506 $\pm$ 0.0689	0.53	<0.001
Year 1 intima–media thickness	0.6188 $\pm$ 0.0361	14.79	<0.001	0.5961 $\pm$ 0.0238	24.90	<0.001
Smoking (yes vs. no)	0.0265 $\pm$ 0.0068	0.77	<0.001	0.3737 $\pm$ 0.0851	0.77	<0.001
Systolic blood pressure (per mm Hg)	0.0008 $\pm$ 0.0002	0.61	<0.001	0.0092 $\pm$ 0.0029	0.42	0.001
Ultrasonography equipment used (12 combinations)†	—	1.64	<0.001	—	1.92	<0.001
Treatment group (conventional vs. intensive)	-0.0453 $\pm$ 0.0274	0.14	0.10	-0.5433 $\pm$ 0.3435	0.10	0.12
Interaction between age and treatment group	0.0017 $\pm$ 0.0008	0.24	0.03	0.0201 $\pm$ 0.0096	0.18	0.04
Overall treatment effect (treatment effect as a function of age)‡	§	0.57	0.004		0.42	0.005
Total R <sup>2</sup> (%)	40	0.40		52	0.52	

\* The multiple regression model used the year 6 intima–media thickness as the outcome and fit the listed covariates simultaneously.

† Eleven estimates are omitted.

‡ The overall treatment effect was determined by two regression coefficients: treatment group and the interaction between age and treatment group. The use of either coefficient alone did not reflect the overall treatment effect. The overall treatment effect was based on the general linear test with 2 degrees of freedom for the numerator.

§ For the common carotid artery,  $\beta = (-0.0453) + (0.0017) \times \text{age}$ , and the standard error =  $(7.5 \times 10^{-4}) - (4.1 \times 10^{-5}) \times \text{age} + (6.4 \times 10^{-7}) \times \text{age}^2$ .

|| For the combined value,  $\beta = (-0.5433) + (0.0201) \times \text{age}$ , and the standard error =  $(0.1180) - (0.0065) \times \text{age} + (9.2 \times 10^{-5}) \times \text{age}^2$ .

intensive-treatment groups in the change in the intima–media thickness of the common carotid artery as a function of attained age. The intensive therapy during 6.5 years of the DCCT resulted in a significantly slower rate of progression of intima–media thickness during the 6 years of the EDIC study (P=0.004).

#### DISCUSSION

We assessed the long-term effect of intensive treatment of type 1 diabetes, presumably mediated through improved glycemic control, on the thickness of the carotid-artery wall over time. Using a multivariate linear regression model incorporating important covariates that were not affected or confounded by treatment, as well as the interaction between age and treatment group, we found a significant effect of intensive therapy, as compared with conventional treatment, during the DCCT on the subsequent change in the intima–media thickness with age. The intensively treated group had a small-

er increase in the thickness with age than did the conventionally treated group. The differences in intima–media thickness between these treatment groups could be due to the less atherogenic lipid profile and decreased level of microalbuminuria seen with intensive therapy during the DCCT. However, even after adjustment for these variables in additional models, intensive therapy (and the lower mean glycosylated hemoglobin value during the DCCT) continued to be associated with a decrease in the progression of the intima–media thickness. The differences in the glycosylated hemoglobin value during the DCCT explained 96 percent of the long-term differences between groups (sum of squares) in the intima–media thickness of the common carotid artery at year 6.

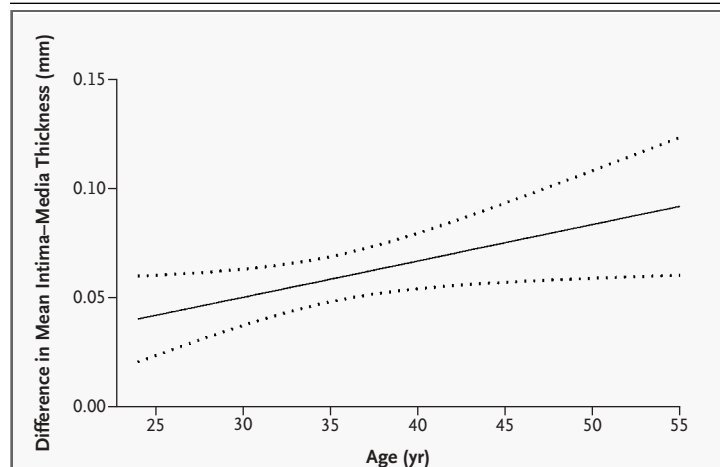
Although the rate of cardiovascular disease is increased among patients with diabetes,<sup>1,5</sup> the role of glycemia in this process remains uncertain.<sup>1,25</sup> Intervention trials achieving variable degrees of glycemic control in patients with type 1 and type 2 diabetes have found either no statistically sig-

nificant beneficial effect on cardiovascular end points<sup>9,26,27</sup> or a positive effect that was not consistent in all groups and analyses.<sup>28-30</sup> A meta-regression analysis, including predominantly patients with type 2 diabetes and subjects without diabetes, found a progressive relation between initial fasting and postprandial glucose levels and the subsequent occurrence of cardiovascular events over a 12-year period.<sup>31</sup> The increased relative risk extended to subjects with glucose levels below the threshold for the diagnosis of diabetes. These studies have generally focused on cardiovascular disease events. However, several epidemiologic analyses in patients with type 2 diabetes have shown associations between intima-media thickness — as an early indicator of atherosclerosis — and glycemia.<sup>32,33</sup>

Our results demonstrate an association between glycemia and intima-media thickness, a sensitive marker for coronary and cerebral vascular disease, in patients with type 1 diabetes. The explanation for the apparently delayed effect of diabetes interventions on intima-media thickness — at year 1 of the EDIC study there was no effect of intensive therapy and no significant associations between carotid intima-media thickness and the mean glycosylated hemoglobin value during the DCCT<sup>16</sup> — may lie in the putative pathogenic mechanism of atherosclerosis and in the demographics of the DCCT cohort. The accelerated development of atherosclerotic lesions in patients with diabetes may be the result of a gradual accumulation of advanced glycosylation end products.<sup>34,35</sup> Thus, it may take years for atherosclerosis caused by various levels of hyperglycemia to develop, especially in a relatively young population, such as the DCCT cohort.

We<sup>16</sup> and others<sup>36-38</sup> have found the conventional cardiovascular disease risk factors of hypertension, dyslipidemia, and smoking to be related to intima-media thickness in patients with type 1 diabetes. Urinary albumin excretion was also associated with atherosclerosis, as suggested in other studies.<sup>39</sup>

The differences in intima-media thickness that we observed at year 6 between the diabetic cohort and the age- and sex-matched nondiabetic controls confirm and extend the results of several earlier, smaller studies. Increased carotid intima-media thickness has been reported in 105 Japanese patients with type 1 diabetes, as compared with those in age- and sex-matched controls,<sup>40</sup> and in 60 Italian patients with type 1 diabetes.<sup>41</sup> Studies of patients with type 2 diabetes have also demonstrated



**Figure 2.** Mean Treatment-Related Difference in the Relation between the Estimated Mean Intima-Media Thickness and Age.

Dotted lines represent 95 percent confidence intervals. The overall difference (conventional treatment minus intensive treatment) was significant ( $P=0.004$ ).

a difference in intima-media thickness between diabetic patients and nondiabetic subjects<sup>32,42</sup>; however, the relevance of these findings in the generally younger patients with type 1 diabetes who have a lower burden of cardiovascular disease and risk factors for cardiovascular disease is uncertain.

Our study has some limitations. The entire EDIC cohort did not participate in the carotid ultrasonographic measurements. However, the proportion of subjects who did not participate was small (10.6 percent), and the clinical characteristics of the non-participants and participants were generally similar. The unequal prevalence of smoking in the EDIC cohort and the age-matched nondiabetic controls could account for some of the differences in carotid intima-media thickness between these two groups; however, analyses that controlled for smoking yielded similar results. Differential use between treatment groups of medications known to ameliorate risk factors for cardiovascular disease and atherogenesis might explain, or confound, these results. However, here again, analyses that controlled for medication use and elevated blood pressure or low-density lipoprotein level yielded the same results. In fact, the more frequent use of such medications by the conventional-treatment group would be expected to decrease the differences in intima-media thickness that we found.

The results for intima-media thickness in the



DCCT cohort, which was carefully selected to exclude patients with several other risk factors for atherosclerosis,<sup>9</sup> might not extend to all patients with type 1 diabetes. However, as noted previously,<sup>43</sup> at base line there were few differences between the DCCT cohort and the unselected population-based cohort with type 1 diabetes in the Wisconsin Epidemiologic Study of Diabetic Retinopathy. Therefore, the current results can probably be applied to the general population of patients with type 1 diabetes.

Finally, although cross-sectional intima-media measurements have been convincingly shown to correlate with the risk of cardiovascular disease events, data to support an association between the progression of intima-media thickness and such events are scarce.<sup>44</sup> The clinical manifestations of atherosclerosis will increase as the DCCT cohort

ages,<sup>5,45</sup> increasing the likelihood of detecting a difference in cardiovascular disease event rates between treatment groups, should one exist. Longer follow-up of this cohort will reveal whether the decrease in the progression of intima-media thickness with intensive diabetes therapy translates into a clinically meaningful reduction in cardiovascular disease events.

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Dr. Orchard reports having received honorariums from Merck, Schering-Plough, and AstraZeneca and having equity in Bristol-Myers Squibb, and Dr. Brillon honorariums from Aventis and Novo-Nordisk and equity in Aventis, Bristol-Myers Squibb, Lilly, and GlaxoSmithKline.

## APPENDIX

The following persons and institutions participated in the DCCT/EDIC Research Group: Albert Einstein College of Medicine — S. Engel, H. Martinez, H. Shamoon, H. Engel; Case Western Reserve University — W. Dahms, L. Mayer, S. Pendegras, H. Zegarra, D. Miller, L. Singerman, S. Smith-Brewer, S. Genuth (past); Cornell University Medical Center — D. Brillon, M. Lackaye, M. Heinemann, V. Reppuci, T. Lee; Henry Ford Health System — F. Whitehouse, D. Kruger, A. Galpern, J.D. Carey; International Diabetes Center — R. Bergenstal, M. Johnson, D. Kendall, M. Spencer, D. Noller, K. Morgan, D. Etzwiler (past); Joslin Diabetes Center — A. Jacobson, E. Golden, G. Sharuk, P. Arrigg, R. Baeser, O. Ganda, J. Rosenzweig, H. Wolpert, P. Economides, O. Handy, L. Rand (past); Massachusetts General Hospital — D. Nathan, S. Fritz, J. Godine, C. McKittrick, P. Lou; Mayo Foundation — F.J. Service, G. Ziegler, J. Pach, J. Lindsey; Medical University of South Carolina — J. Colwell, D. Wood, R. Mayfield, K. Hermayer, M. Szpiech, T. Lyons, J. Parker, A. Farr, S. Elsing, J. Thompson, J. Selby, M. Bracey; Northwestern University — M. Molitch, B. Schaefer, L. Jampol, D. Weinberg, A. Lyon, Z. Strugula, J. Shankle, P. Astlesford; University of California, San Diego — O. Kolterman, G. Lorenzi, M. Goldbaum; University of Iowa — W. Sivitz, M. Bayless, R. Zeither (past), T. Weingeist, E. Stone, H. Culver Boidt, K. Gehres, S. Russell; University of Maryland School of Medicine — D. Counts, A. Kowarski (past), D. Ostrowski, T. Donner, S. Steidl, B. Jones; University of Michigan — W. Herman, D. Greene (past), C. Martin, M.J. Stevens, A.K. Vine, S. Elner; University of Minnesota — J. Bantle, B. Rogness, T. Olsen, E. Steuer; University of Missouri — D. Goldstein, S. Hitt, J. Giangiacomo, D. Hainsworth; University of New Mexico — D. Schade, M. Burge, J. Canady, M. Schluter, A. Das, D. Hornbeck (past); University of Pennsylvania — S. Schwartz, P.A. Bourne, B.J. Maschak-Carey (past), L. Baker (deceased), S. Braunstein, A. Brucker; University of Pittsburgh — T. Orchard, N. Silvers, T. Songer, B. Dof, S. Olson, R.L. Bergren, L. Lobes, M. Fineman, A. Drash (past); University of South Florida — J. Malone, J. Vaccaro-Kish, C. Berger, R. Gstalder, P.R. Pavan, A. Morrison; University of Tennessee — S. Dagogo-Jack, S. Schussler, A. Kitabchi, H. Lambeth, M.B. Murphy, S. Moser, D. Meyer, A. Iannacone, M. Bryer-Ash (past); University of Texas Southwestern Medical Center — P. Raskin, S. Strowig, A. Edwards, J. Alappatt (past), C. Wilson (past), S. Park (past), Y. He; University of Toronto — B. Zinman, A. Barrie, S. MacLean, R. Devenyi, M. Mandelcorn, M. Brent; University of Washington — J. Palmer, S. Catton, J. Kinyoun, L. Van Ottingham (past), J. Ginsberg (past); University of Western Ontario — J. Dupre, J. Harth, C. Canny (past), D. Nicolle; Vanderbilt University — M. May, R. Lorenz (past), J. Lipps, L. Survant, S. Feman (past), K. Tawansy, A. Agarwal, T. Adkins; Washington University, St. Louis — N. White, J. Santiago (deceased), L. Levandoski, I. Boniuk, G. Grand, M. Thomas, D. Burgess, D. Joseph, K. Blinder, G. Shah; Yale University School of Medicine — W. Tamborlane, P. Gatcomb, K. Stoessel, K. Taylor; Clinical Coordinating Center (Case Western Reserve University) — B. Dahms, R. Trail, J. Quin; Data Coordinating Center (George Washington University, Biostatistics Center) — J. Lachin, P. Cleary, D. Kenny, J. Backlund, L. Diminick, A. Determan, K. Klump, M. Hawkins; National Institute of Diabetes and Digestive and Kidney Diseases Program Office — C. Cowie, J. Fradkin, C. Siebert (past), R. Eastman (past); Central Fundus Photograph Reading Center (University of Wisconsin) — M. Davis, L. Hubbard, P. Geithman, L. Kastorff, M. Neider, D. Badal, B. Esser, K. Miner, H. Wabers, K. Glander, J. Joyce, N. Robinson, C. Hurtenbach, C. Hannon; Central Biochemistry Laboratory (University of Minnesota) — M. Steffes, J. Bucks, B. Chavers; Central Carotid Ultrasound Unit (New England Medical Center) — D. O'Leary, L. Funk, J. Polak; Central Electrocardiographic Reading Unit (University of Minnesota) — R. Crow, C. O'Donnell (past), B. Gloeb, S. Thomas; Computed Tomography Reading Center (Harbor-UCLA Research and Education Institute) — R. Detrano, N. Wong, M. Fox, L. Kim, R. Oudiz; External Advisory Committee — G. Weir (chair), C. Clark, R. D'Agostino, M. Espeland, B. Klein, T. Manolio, L. Rand, D. Singer, M. Stern; Molecular Risk Factors Program Project (Medical University of South Carolina) — W.T. Garvey, T.J. Lyons, A. Jenkins, R. Klein, M. Lopes-Virella, G. Virella, A.A. Jaffa, D. Zheng, D. Lackland, D. McGee, R.K. Mayfield, M. Brabham; Genetic Studies Group (Hospital for Sick Children) — A. Boright, A. Paterson, S. Scherer, B. Zinman; Lipoprotein Distribution/Obesity Group (University of Washington) — J. Brunzell, J. Hokanson, S. Marcovina, J. Purnell, S. Sibley, S. Deeb, K. Edwards; Editor, EDIC Publications — D. Nathan.

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## **APPENDIX B**

Means, Standard Deviations, and Ranges for Metric Variables and Frequency Distributions for Nominal Variables as (1) reported by the EDIC DCC and (2) calculated from archived data.

## ED\_CURU6 (edicMS.Curu6 vm 414) Summary Statistics

Variable	Variable Label	Category	n	%	Stat.
Total	Total		1229	.	.
AER	AER Year 1 or 2	Mean (N)	1181	.	40.2029
		STD	.	.	185.8145
		Min	.	.	1.4400
		Max	.	.	5011.200
AER40	AER >= 40 Year 1 or 2	.	48	3.91	.
		0: No	1043	84.87	.
		1: Yes	138	11.23	.
ATT_AGE	Attained Age Year 1	Mean (N)	1229	.	35.1937
		STD	.	.	6.9399
		Min	.	.	19.0000
		Max	.	.	51.0000
ATT_DURN	Attained duration (years) Year 1	Mean (N)	1229	.	13.8114
		STD	.	.	4.8629
		Min	.	.	6.3333
		Max	.	.	26.0833
BMI	BMI Year 1	Mean (N)	1221	.	26.0669
		STD	.	.	3.8445
		Min	.	.	17.0068
		Max	.	.	49.8443
COMDF6	diff (yr6-yr1), common	Mean (N)	1219	.	0.0346
		STD	.	.	0.0999
		Min	.	.	-0.3925
		Max	.	.	1.0100
COMINT1A	Combined IMT Year 1	Mean (N)	1229	.	-0.0000
		STD	.	.	1.6478
		Min	.	.	-3.4963
		Max	.	.	9.5765
COMINT6A	Combined IMT Year 6	Mean (N)	1229	.	-0.0000
		STD	.	.	1.6542
		Min	.	.	-3.0644
		Max	.	.	14.7808
COMMON	Common IMT Year 1	Mean (N)	1229	.	0.5820
		STD	.	.	0.0859
		Min	.	.	0.3700
		Max	.	.	0.9975
COMMYR6	Common at year 6	Mean (N)	1219	.	0.6164

## ED\_CURU6 (edicMS.Curu6 vm 414) Summary Statistics

Variable	Variable Label	Category	n	%	Stat.
		STD	.	.	0.1172
		Min	.	.	0.3675
		Max	.	.	1.7800
DBP	Diastolic BP Year 1	Mean (N)	1225	.	75.0963
		STD	.	.	9.1742
		Min	.	.	40.0000
		Max	.	.	108.0000
DCCT_HBA	Average HbA1c during the DCCT	Mean (N)	1229	.	8.1442
		STD	.	.	1.3926
		Min	.	.	5.3950
		Max	.	.	13.5750
DF16A	diff (comint6a - 1a)	Mean (N)	1229	.	-0.0000
		STD	.	.	1.3291
		Min	.	.	-6.0109
		Max	.	.	7.5227
GROUP	TREATMENT GROUP	Conventional	611	49.72	.
		Intensive	618	50.28	.
HBA1C	HbA1c at Year 1	Mean (N)	1212	.	8.0568
		STD	.	.	1.3278
		Min	.	.	4.4000
		Max	.	.	15.0000
HDL	HDL Year 1 or 2	Mean (N)	1193	.	54.0109
		STD	.	.	13.9467
		Min	.	.	24.0000
		Max	.	.	121.0000
HLIP	LDL >=130 or medication Year 1 (yes=1)	.	27	2.20	.
		0: No	842	68.51	.
		1: Yes	360	29.29	.
HT	Hypertension Year 1 (yes=1)	.	18	1.46	.
		0: No	1011	82.26	.
		1: Yes	200	16.27	.
INTERN	Internal IMT Year 1	Mean (N)	1196	.	0.6478
		STD	.	.	0.2316
		Min	.	.	0.3820
		Max	.	.	2.5450
INTNYR6	Internal IMT Year 6	Mean (N)	1203	.	0.7348
		STD	.	.	0.3536

## ED\_CURU6 (edicMS.Curu6 vm 414) Summary Statistics

Variable	Variable Label	Category	n	%	Stat.
		Min	.	.	0.3567
		Max	.	.	2.9457
LA9	Ankle/arm ratio < 0.9 Year 1 (yes=1)	.	2	0.16	.
		0: No	1139	92.68	.
		1: Yes	88	7.16	.
LDL	LDL Year 1 or 2	Mean (N)	1184	.	114.4130
		STD	.	.	30.5049
		Min	.	.	26.0000
		Max	.	.	257.0000
LHRATIO	LDL/HDL ratio Year 1 or 2	Mean (N)	1184	.	2.2680
		STD	.	.	0.8799
		Min	.	.	0.4396
		Max	.	.	5.6333
LOG_AER	Natural logarithm of AER	Mean (N)	1181	.	2.5586
		STD	.	.	1.1256
		Min	.	.	0.3646
		Max	.	.	8.5194
MACH16	Ultrasonography Equipment combinations	Mean (N)	1229	.	19.2474
		STD	.	.	7.0331
		Min	.	.	11.0000
		Max	.	.	34.0000
R_INT	Reciprocal of Internal Year 1	Mean (N)	1196	.	1.6518
		STD	.	.	0.3435
		Min	.	.	0.3929
		Max	.	.	2.6178
R_INT6	reciprocal of internal year 6	Mean (N)	1203	.	1.5295
		STD	.	.	0.3972
		Min	.	.	0.3395
		Max	.	.	2.8037
SBP	Systolic BP Year 1	Mean (N)	1224	.	117.1479
		STD	.	.	12.3779
		Min	.	.	82.0000
		Max	.	.	172.0000
SEX	Sex	Female	584	47.52	.
		Male	645	52.48	.
SMOKING	Current smoking (yes=1) Year 1	.	2	0.16	.
		0: No	994	80.88	.

## ED\_CURU6 (edicMS.Curu6 vm 414) Summary Statistics

Variable	Variable Label	Category	n	%	Stat.
		1: Yes	233	18.96	.
TCHOL	Total Cholesterol Year 1 or 2	Mean (N)	1192	.	186.3582
		STD	.	.	36.1816
		Min	.	.	87.0000
		Max	.	.	399.0000
TRIG	Triglyceride Year 1 or 2	Mean (N)	1193	.	89.8541
		STD	.	.	75.8828
		Min	.	.	14.0000
		Max	.	.	1110.000
WHRATIO	Waist/hip ratio Year 1	Mean (N)	1207	.	0.8228
		STD	.	.	0.0999
		Min	.	.	0.3631
		Max	.	.	1.8618

```

log: G:\EDIC Carotid IMT\1.log
log type: text
opened on: 13 May 2006/7*, 15:31:21
*NOTE: Clock re-set to 2006 because SAS license had expired

. do "C:\DOCUME~1\CFTTHOM~1.000\LOCALS~1\Temp\STD00000000.tmp"

. describe

```

Contains data from G:\EDIC Carotid IMT\edicmscuru6.dta

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obs:          1,229
vars:         34
size:        135,190 (99.9% of memory free)

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variable name	storage type	display format	value label	variable label
common	float	%9.0g		common imt year 1
intern	float	%9.0g		internal imt year 1
r_int	float	%9.0g		reciprocal of internal year 1
sex	str1	%1s		sex
group	str12	%12s		treatment group
comdf6	float	%9.0g		diff (yr6-yr1), common
att_age	byte	%8.0g		attained age year 1
att_durn	float	%9.0g		attained duration (years) year 1
smoking	byte	%8.0g		current smoking (yes=1) year 1
sbp	int	%8.0g		systolic bp year 1
dbp	int	%8.0g		diastolic bp year 1
bmi	float	%9.0g		bmi year 1
whratio	float	%9.0g		waist/hip ratio year 1
la9	byte	%8.0g		ankle/arm ratio < 0.9 year 1 (yes=1)
tchol	int	%8.0g		total cholesterol year 1 or 2
trig	int	%8.0g		triglyceride year 1 or 2
hdl	int	%8.0g		hdl year 1 or 2
ldl	int	%8.0g		ldl year 1 or 2
lhratio	float	%9.0g		ldl/hdl ratio year 1 or 2
aer	float	%9.0g		aer year 1 or 2
aer40	byte	%8.0g		aer >= 40 year 1 or 2
hbalc	float	%9.0g		hbalc at year 1
dcct_hba	float	%9.0g		average hbalc during the dcct
commyr6	float	%9.0g		common at year 6
intnyr6	float	%9.0g		internal imt year 6
r_int6	float	%9.0g		reciprocal of internal year 6
comint1a	float	%9.0g		combined imt year 1
comint6a	float	%9.0g		combined imt year 6
df16a	float	%9.0g		diff (comint6a - 1a)
hlip	byte	%8.0g		ldl >=130 or medication year 1 (yes=1)
ht	byte	%8.0g		hypertension year 1 (yes=1)
mach16	byte	%8.0g		ultrasonography equipment combinations
log_aer	float	%9.0g		natural logarithm of aer
mask_pat	int	%8.0g		patient id number

Sorted by:



. summarize

Variable	Obs	Mean	Std. Dev.	Min	Max
common	1229	.5820098	.0858515	.37	.9975
intern	1196	.6478277	.2316232	.382	2.545
r_int	1196	1.651753	.3435208	.3929273	2.617801
sex	0				
group	0				
comdf6	1219	.0346117	.0998721	-.3925	1.01
att_age	1229	35.19365	6.939942	19	51
att_durn	1229	13.81143	4.86294	6.333333	26.08333
smoking	1227	.1898941	.3923771	0	1
sbp	1224	117.1479	12.37795	82	172
dbp	1225	75.09633	9.174178	40	108
bmi	1221	26.06692	3.84445	17.0068	49.84429
whratio	1207	.8228348	.0999408	.3630542	1.861789
la9	1227	.0717196	.2581283	0	1
tchol	1192	186.3582	36.18156	87	399
trig	1193	89.85415	75.88284	14	1110
hdl	1193	54.0109	13.94671	24	121
ldl	1184	114.413	30.50492	26	257
lhratio	1184	2.268016	.8798865	.4395604	5.633333
aer	1181	40.20295	185.8145	1.44	5011.2
aer40	1181	.1168501	.3213777	0	1
hbalc	1212	8.056766	1.327781	4.4	15
dcct_hba	1229	8.144243	1.3926	5.395	13.575
commyr6	1219	.6163871	.1172314	.3675	1.78
intnyr6	1203	.7348172	.3536264	.3566667	2.945714
r_int6	1203	1.529529	.3971663	.3394762	2.803738
comint1a	1229	-2.63e-07	1.647753	-3.496281	9.576523
comint6a	1229	-3.95e-07	1.654163	-3.06444	14.78076
df16a	1229	-1.35e-07	1.329133	-6.010858	7.522666
hlip	1202	.2995008	.45823	0	1
ht	1211	.1651528	.3714718	0	1
mach16	1229	19.24736	7.033123	11	34
log_aer	1181	2.558564	1.125555	.3646431	8.519431
mask_pat	1229	720.4068	417.553	1	1440

. tab1 aer40 group ht hlip la9 smoking

-> tabulation of aer40

aer >= 40 year 1 or 2	Freq.	Percent	Cum.
0	1,043	88.31	88.31
1	138	11.69	100.00
Total	1,181	100.00	

-> tabulation of group

treatment group	Freq.	Percent	Cum.
EXPERIMENTAL	618	50.28	50.28
STANDARD	611	49.72	100.00
Total	1,229	100.00	

-> tabulation of ht

hypertensio n year 1 (yes=1)	Freq.	Percent	Cum.
0	1,011	83.48	83.48
1	200	16.52	100.00
Total	1,211	100.00	

-> tabulation of hlip

ldl >=130 or medication year 1 (yes=1)	Freq.	Percent	Cum.
0	842	70.05	70.05
1	360	29.95	100.00
Total	1,202	100.00	

-> tabulation of la9

ankle/arm ratio < 0.9 year 1 (yes=1)	Freq.	Percent	Cum.
0	1,139	92.83	92.83
1	88	7.17	100.00
Total	1,227	100.00	

-> tabulation of smoking

current smoking (yes=1) year 1	Freq.	Percent	Cum.
0	994	81.01	81.01
1	233	18.99	100.00
Total	1,227	100.00	

## EDxCURU6 (edicMS.Curu6NRM vm 414) Summary Statistics

Variable	Variable Label	Category	n	%	Stat.
Total	Total		222	.	.
COMMYR6	Common IMT at year 6	Mean (N)	214	.	0.5773
		STD	.	.	0.0954
		Min	.	.	0.3600
		Max	.	.	1.0400
INTNYR6	Internal IMT at year 6	Mean (N)	207	.	0.6281
		STD	.	.	0.1824
		Min	.	.	0.3950
		Max	.	.	1.7200
SEX	SEX	Female	112	50.45	.
		Male	110	49.55	.

```
. use "G:\EDIC Carotid IMT\edxcuru6.dta", clear
```

```
. describe
```

```
Contains data from G:\EDIC Carotid IMT\edxcuru6.dta
```

```
obs:      222  
vars:      4  
size:     3,774 (99.9% of memory free)
```

---

variable name	storage type	display format	value label	variable label
sex	str1	%1s		sex
commyr6	float	%9.0g		common imt at year 6
intnyr6	float	%9.0g		internal imt at year 6
mask_pat	long	%12.0g		patient id number

---

```
Sorted by:
```

```
. summarize
```

---

Variable	Obs	Mean	Std. Dev.	Min	Max
sex	0				
commyr6	214	.5773403	.0953554	.36	1.04
intnyr6	207	.6281407	.1823886	.395	1.72
mask_pat	222	49888.58	27460.5	390	99677

---

```
. tab sex
```

---

sex	Freq.	Percent	Cum.
F	112	50.45	50.45
M	110	49.55	100.00
Total	222	100.00	

---

## **APPENDIX C**

Stata 8/SE Code and Output for Analyses Reported in Memo

```

log: C:\EDIC Carotid IMT\2b.log
log type: text
opened on: 23 May 2007, 17:02:32

```

```

. do "C:\DOCUME~1\CFTHOM~1.000\LOCALS~1\Temp\STD01000000.tmp"

. use "C:\EDIC Carotid IMT\edicmscuru6.dta", clear

. generate missing=.
(1229 missing values generated)

. sort group

. by group: summarize att_age smoking att_durn bmi whratio la9 sbp dbp ht
tchol hdl ldl lhratio trig missing aer aer40 dc
> ct_hba hbalc common intern if sex=="F"

```

-> group = EXPERIMENTAL

Variable	Obs	Mean	Std. Dev.	Min	Max
att_age	295	35.15593	7.141625	19	50
smoking	294	.2006803	.4011922	0	1
att_durn	295	13.89802	4.817854	6.333333	26.08333
bmi	292	26.47652	4.525977	18.81892	42.10238
whratio	285	.7592578	.0744102	.4237288	.95625
la9	294	.0884354	.2844111	0	1
sbp	292	114.1301	12.20347	90	162
dbp	293	73.50512	8.677487	48	100
ht	289	.1038062	.3055381	0	1
tchol	286	187.6958	35.65963	108	399
hdl	286	58.7972	14.3874	26	106
ldl	284	112.0035	29.37927	44	199
lhratio	284	2.029237	.7722056	.6333333	5.272727
trig	286	83.06294	75.84858	28	1110
missing	0				
aer	279	21.8271	67.33366	1.44	930.24
aer40	279	.0681004	.2523707	0	1
dcct_hba	295	7.304381	.9048686	5.498462	11.87118
hbalc	291	7.880756	1.363606	5.4	15
common	295	.565774	.0769705	.3975	.8575
intern	285	.6084818	.1646724	.41375	1.977143

-> group = STANDARD

Variable	Obs	Mean	Std. Dev.	Min	Max
att_age	289	33.97232	7.249947	19	49
smoking	289	.1903114	.3932277	0	1
att_durn	289	14.1286	5.136499	6.416667	25.66667
bmi	289	25.01792	3.451216	17.0068	39.60125
whratio	281	.760481	.0702378	.391445	1.197566
la9	289	.0865052	.2815962	0	1
sbp	289	114.2249	13.11281	82	170
dbp	289	72.2699	9.485908	40	100
ht	285	.1403509	.3479617	0	1
tchol	282	188.1383	38.07006	116	343

hdl	282	59.23759	14.00852	34	121
ldl	280	112.1	30.33925	40	204
lhratio	280	1.997175	.7238223	.4395604	4.5
trig	282	82.89362	75.93026	24	1040
missing	0				
-----					
aer	281	67.15217	330.6526	1.44	5011.2
aer40	281	.1565836	.3640561	0	1
dcct_hba	289	9.110137	1.345111	5.728919	13.575
hbalc	284	8.148239	1.432891	5.3	13.1
common	289	.5569723	.0755307	.37	.7825
-----					
intern	278	.6276088	.2506052	.382	2.37

```
. by group: summarize att_age smoking att_durn bmi whratio la9 sbp dbp ht
tchol hdl ldl lhratio trig missing aer aer40 dc
> ct_hba hbalc common intern if sex=="M"
```

```
-----
-> group = EXPERIMENTAL
```

Variable	Obs	Mean	Std. Dev.	Min	Max
att_age	323	35.77399	6.72358	19	51
smoking	323	.1950464	.3968512	0	1
att_durn	323	13.98271	4.912048	6.583333	26
bmi	321	26.72371	3.911454	19.05953	49.84429
whratio	321	.8830098	.0803522	.6499051	1.337719
-----					
la9	323	.0464396	.2107617	0	1
sbp	323	119.3065	11.11552	98	152
dbp	323	76.89164	9.099725	50	108
ht	319	.2288401	.4207461	0	1
tchol	315	187.3714	34.56175	100	335
-----					
hdl	316	49.27848	12.5922	24	97
ldl	312	119.125	29.96183	37	257
lhratio	312	2.577837	.9515922	.6607143	5.633333
trig	316	96.05063	71.51839	25	538
missing	0				
-----					
aer	311	30.02701	117.8683	1.44	1694.88
aer40	311	.0771704	.2672917	0	1
dcct_hba	323	7.226603	.8684062	5.395	10.73346
hbalc	319	7.847649	1.247079	4.4	13.6
common	323	.5973891	.0821517	.4025	.9975
-----					
intern	314	.6677754	.2204556	.3933333	2.445

```
-----
-> group = STANDARD
```

Variable	Obs	Mean	Std. Dev.	Min	Max
att_age	322	35.74224	6.560907	20	50
smoking	321	.1744548	.3800926	0	1
att_durn	322	13.27562	4.573646	6.5	25.66667
bmi	319	25.98145	3.190197	18.30577	39.31421
whratio	320	.8738495	.0934564	.3630542	1.861789
-----					
la9	321	.0685358	.2530576	0	1
sbp	320	120.3625	11.85042	90	172
dbp	320	77.29375	8.457229	40	99
ht	318	.1792453	.3841621	0	1

tchol	309	182.4628	36.39514	87	323
hdl	309	49.65049	11.47615	28	103
ldl	308	113.9643	31.79928	26	229
lhratio	308	2.420564	.8942188	.5172414	5.585366
trig	309	96.15534	79.39815	14	924
missing	0				
aer	310	42.52181	116.9985	1.44	1418.4
aer40	310	.1645161	.3713427	0	1
dcct_hba	322	8.967268	1.128859	6.284	12.319
hbalc	318	8.345912	1.215346	5.5	13.9
common	322	.6039286	.0967217	.4	.9966667
intern	319	.6809653	.2675956	.4133333	2.545

.  
.  
end of do-file

. log close  
log: C:\EDIC Carotid IMT\2b.log  
log type: text  
closed on: 23 May 2007, 17:02:53



```

log: C:\EDIC Carotid IMT\2_NEW.log
log type: text
opened on: 29 May 2007, 12:40:24

```

```

. do "C:\DOCUME~1\CFTHOM~1.000\LOCALS~1\Temp\STD01000000.tmp"

. use "C:\EDIC Carotid IMT\edicmscuru6.dta", clear

. pause off

. set more off

. generate group2=0

. replace group2=1 if group=="EXPERIMENTAL"
(618 real changes made)

. label define group2 0"STD" 1"EXP"

. label values group2 group2

. tab group group2

```

treatment group	group2		Total
	STD	EXP	
EXPERIMENTAL	0	618	618
STANDARD	611	0	611
Total	611	618	1,229

```

. sort group2

. by group2: summarize hbalc

```

```

-> group2 = STD

```

Variable	Obs	Mean	Std. Dev.	Min	Max
hbalc	602	8.252658	1.325006	5.3	13.9

```

-> group2 = EXP

```

Variable	Obs	Mean	Std. Dev.	Min	Max
hbalc	610	7.863443	1.302993	4.4	15

```

. anova hbalc group2, partial

```

Source	Partial SS	df	MS	F	Prob > F
Model	45.8990013	1	45.8990013	26.58	0.0000
group2	45.8990013	1	45.8990013	26.58	0.0000
Residual	2089.09551	1210	1.72652521		

Total | 2134.99451 1211 1.76300125

. by group2: summarize aer

-> group2 = STD

Variable	Obs	Mean	Std. Dev.	Min	Max
aer	591	54.23269	243.3242	1.44	5011.2

-> group2 = EXP

Variable	Obs	Mean	Std. Dev.	Min	Max
aer	590	26.14942	97.30754	1.44	1694.88

. anova aer group2, partial

Number of obs = 1181 R-squared = 0.0057  
Root MSE = 185.361 Adj R-squared = 0.0049

Source	Partial SS	df	MS	F	Prob > F
Model	232854.615	1	232854.615	6.78	0.0093
group2	232854.615	1	232854.615	6.78	0.0093
Residual	40509024.9	1179	34358.7997		
Total	40741879.5	1180	34527.0165		

. by group2: summarize bmi

-> group2 = STD

Variable	Obs	Mean	Std. Dev.	Min	Max
bmi	608	25.52346	3.348881	17.0068	39.60125

-> group2 = EXP

Variable	Obs	Mean	Std. Dev.	Min	Max
bmi	613	26.60596	4.213687	18.81892	49.84429

```
. anova bmi group2, partial
```

```
Number of obs = 1221      R-squared      = 0.0198  
Root MSE      = 3.80769   Adj R-squared = 0.0190
```

Source	Partial SS	df	MS	F	Prob > F
Model	357.690827	1	357.690827	24.67	0.0000
group2	357.690827	1	357.690827	24.67	0.0000
Residual	17673.6621	1219	14.4984923		
Total	18031.3529	1220	14.7797975		

```
.  
. generate sample = 1  
. label define sample 1"EDIC" 2"NORMALS"  
. label values sample sample  
. keep sex commyr6 intnyr6 group2 sample  
. save edic, replace  
file edic.dta saved
```

```
.  
. use "C:\EDIC Carotid IMT\edxcuru6.dta", clear  
. generate sample=2  
. generate group2=3  
. keep sex commyr6 intnyr6 group2 sample  
. summarize commyr6 intnyr6
```

Variable	Obs	Mean	Std. Dev.	Min	Max
commyr6	214	.5773403	.0953554	.36	1.04
intnyr6	207	.6281407	.1823886	.395	1.72

```
. pause  
. save normals, replace  
file normals.dta saved  
.   
. append using edic  
. sort sample  
. generate sex2 = 1  
. replace sex2=2 if sex=="F"  
(696 real changes made)  
. generate MFsample = (10*sex2)+sample  
. label define MFsample 11"Male Diab" 12"Male NonDiab" 21"Female Diab"  
22"Female NonDiab"
```

```

. label values MFsample MFsample
. sort MFsample
. by MFsample: summarize commyr6, detail

```

---

```

-> MFsample = Male Diab

```

```

common int at year 6

```

---

	Percentiles	Smallest		
1%	.44	.41		
5%	.4916667	.4275		
10%	.52	.4325	Obs	640
25%	.56	.4333333	Sum of Wgt.	640
50%	.62		Mean	.6398503
		Largest	Std. Dev.	.124399
75%	.6875	1.1725		
90%	.7675	1.1875	Variance	.0154751
95%	.8575	1.2725	Skewness	2.355272
99%	1.0925	1.78	Kurtosis	16.27285

---

```

-> MFsample = Male NonDiab

```

```

common int at year 6

```

---

	Percentiles	Smallest		
1%	.445	.44		
5%	.4575	.445		
10%	.495	.45	Obs	105
25%	.5325	.45	Sum of Wgt.	105
50%	.58		Mean	.6006667
		Largest	Std. Dev.	.102906
75%	.64	.7925		
90%	.75	.9025	Variance	.0105897
95%	.7725	.9075	Skewness	1.340702
99%	.9075	1.04	Kurtosis	5.849363

---

```

-> MFsample = Female Diab

```

```

common int at year 6

```

---

	Percentiles	Smallest		
1%	.415	.3675		
5%	.4525	.38		
10%	.4875	.3825	Obs	579
25%	.53	.3925	Sum of Wgt.	579
50%	.5775		Mean	.5904519
		Largest	Std. Dev.	.1028053
75%	.635	1.0325		
90%	.695	1.095	Variance	.0105689
95%	.7375	1.22	Skewness	2.434389
99%	.9475	1.513333	Kurtosis	17.91802

---

-> MFsample = Female NonDiab

common imt at year 6

---

	Percentiles	Smallest		
1%	.4	.36		
5%	.44	.4		
10%	.4525	.4	Obs	109
25%	.4975	.405	Sum of Wgt.	109
50%	.55		Mean	.55487
		Largest	Std. Dev.	.0818333
75%	.6033334	.735		
90%	.655	.765	Variance	.0066967
95%	.7075	.785	Skewness	.410602
99%	.785	.7875	Kurtosis	3.397793

. by MFsample: summarize intnyr6, detail

---

-> MFsample = Male Diab

internal imt at year 6

---

	Percentiles	Smallest		
1%	.4563636	.365		
5%	.5083333	.41		
10%	.5390909	.4216667	Obs	635
25%	.5883333	.43	Sum of Wgt.	635
50%	.6557143		Mean	.7912654
		Largest	Std. Dev.	.3924986
75%	.7728571	2.66		
90%	1.295	2.723333	Variance	.1540551
95%	1.778	2.791667	Skewness	2.606674
99%	2.457143	2.845	Kurtosis	10.11198

---

-> MFsample = Male NonDiab

internal imt at year 6

---

	Percentiles	Smallest		
1%	.4654545	.446		
5%	.4733333	.4654545		
10%	.5088889	.4672727	Obs	101
25%	.54875	.4685714	Sum of Wgt.	101
50%	.63		Mean	.6751811
		Largest	Std. Dev.	.2154651
75%	.7033333	1.3		
90%	.8445455	1.496	Variance	.0464252
95%	1.051667	1.533333	Skewness	2.695484
99%	1.533333	1.72	Kurtosis	11.54883

---

-> MFsample = Female Diab

internal imt at year 6

---

	Percentiles	Smallest		
1%	.4116667	.3566667		
5%	.4655555	.3922222		
10%	.4972727	.3945455	Obs	568
25%	.545	.395	Sum of Wgt.	568
50%	.6		Mean	.6717105
		Largest	Std. Dev.	.2920334
75%	.6795833	2.555		
90%	.84	2.604	Variance	.0852835
95%	1.27	2.851667	Skewness	4.160493
99%	1.958	2.945714	Kurtosis	24.91521

---

-> MFsample = Female NonDiab

internal imt at year 6

---

	Percentiles	Smallest		
1%	.408	.395		
5%	.4281818	.408		
10%	.455	.4172727	Obs	106
25%	.5057143	.4241667	Sum of Wgt.	106
50%	.5719643		Mean	.5833191
		Largest	Std. Dev.	.1299724
75%	.6308333	.7785714		
90%	.7266667	.82125	Variance	.0168928
95%	.75	1.178889	Skewness	2.735027
99%	1.178889	1.33	Kurtosis	15.33789

---

. graph box commyr6, over (MFsample) nooutsides

. graph export "C:\EDIC Carotid IMT\common.ps", replace  
(file C:\EDIC Carotid IMT\common.ps written in PostScript format)

. graph box intnyr6, over (MFsample) nooutsides

. graph export "C:\EDIC Carotid IMT\interal.ps", replace  
(file C:\EDIC Carotid IMT\interal.ps written in PostScript format)

. ranksum commyr6 if sex=="M" , by (sample)

Two-sample Wilcoxon rank-sum (Mann-Whitney) test

sample	obs	rank sum	expected
1	640	245983.5	238720
2	105	31901.5	39165
combined	745	277885	277885

unadjusted variance 4177600.00

adjustment for ties -450.34

adjusted variance 4177149.66

Ho: commyr6(sample==1) = commyr6(sample==2)

z = 3.554  
Prob > |z| = 0.0004

. ranksum commyr6 if sex=="F" , by (sample)

Two-sample Wilcoxon rank-sum (Mann-Whitney) test

sample	obs	rank sum	expected
1	579	206177	199465.5
2	109	30839	37550.5
combined	688	237016	237016

unadjusted variance 3623623.25

adjustment for ties -478.28

adjusted variance 3623144.97

Ho: commyr6(sample==1) = commyr6(sample==2)

z = 3.526  
Prob > |z| = 0.0004

. ranksum intnyr6 if sex=="M" , by (sample)

Two-sample Wilcoxon rank-sum (Mann-Whitney) test

sample	obs	rank sum	expected
1	635	239920.5	233997.5
2	101	31295.5	37218.5
combined	736	271216	271216

unadjusted variance 3938957.92

adjustment for ties -31.54

adjusted variance 3938926.38

Ho: intnyr6(sample==1) = intnyr6(sample==2)

z = 2.984  
Prob > |z| = 0.0028

. ranksum intnyr6 if sex=="F" , by (sample)

Two-sample Wilcoxon rank-sum (Mann-Whitney) test

sample	obs	rank sum	expected
1	568	198708	191700
2	106	28767	35775
combined	674	227475	227475

unadjusted variance 3386700.00  
adjustment for ties -39.62

adjusted variance 3386660.38

Ho: intnyr6(sample==1) = intnyr6(sample==2)

z = 3.808  
Prob > |z| = 0.0001

.

.

end of do-file

. log close

log: C:\EDIC Carotid IMT\2\_NEW.log  
log type: text  
closed on: 29 May 2007, 12:41:17



```

log: C:\EDIC Carotid IMT\3.log
log type: text
opened on: 29 May 2007, 13:45:25

```

```
. use "C:\EDIC Carotid IMT\edicmscuru6.dta", clear
```

```
. tab1 att_age sex mach16
```

```
-> tabulation of att_age
```

attained age year 1	Freq.	Percent	Cum.
19	5	0.41	0.41
20	7	0.57	0.98
21	18	1.46	2.44
22	18	1.46	3.91
23	17	1.38	5.29
24	24	1.95	7.24
25	39	3.17	10.41
26	31	2.52	12.94
27	34	2.77	15.70
28	36	2.93	18.63
29	47	3.82	22.46
30	49	3.99	26.44
31	48	3.91	30.35
32	57	4.64	34.99
33	63	5.13	40.11
34	64	5.21	45.32
35	70	5.70	51.02
36	50	4.07	55.09
37	59	4.80	59.89
38	63	5.13	65.01
39	64	5.21	70.22
40	70	5.70	75.92
41	36	2.93	78.84
42	54	4.39	83.24
43	49	3.99	87.23
44	40	3.25	90.48
45	32	2.60	93.08
46	43	3.50	96.58
47	18	1.46	98.05
48	9	0.73	98.78
49	11	0.90	99.67
50	3	0.24	99.92
51	1	0.08	100.00
Total	1,229	100.00	

```
-> tabulation of sex
```

sex	Freq.	Percent	Cum.
F	584	47.52	47.52
M	645	52.48	100.00
Total	1,229	100.00	

-> tabulation of mach16

ultrasonogr aphy equipment combination s	Freq.	Percent	Cum.
11	416	33.85	33.85
12	20	1.63	35.48
13	12	0.98	36.45
14	2	0.16	36.62
21	134	10.90	47.52
22	465	37.84	85.35
23	3	0.24	85.60
24	17	1.38	86.98
31	59	4.80	91.78
32	29	2.36	94.14
33	71	5.78	99.92
34	1	0.08	100.00
Total	1,229	100.00	

. summarize comintla

Variable	Obs	Mean	Std. Dev.	Min	Max
comintla	1229	-2.63e-07	1.647753	-3.496281	9.576523

. generate female=1

. replace female=0 if sex=="M"  
(645 real changes made)

. xi: regress commyr6 female att\_age common i.mach16 i.group  
i.mach16            \_I\_Imach16\_11-34           (naturally coded; \_Imach16\_11 omitted)  
i.group             \_I\_Igroup\_1-2             (\_Igroup\_1 for group==EXPERIMENTAL omitted)

Source	SS	df	MS	Number of obs =	1219
Model	6.37474413	15	.424982942	F( 15, 1203) =	49.33
Residual	10.3644837	1203	.008615531	Prob > F =	0.0000
				R-squared =	0.3808
				Adj R-squared =	0.3731
Total	16.7392278	1218	.013743208	Root MSE =	.09282

commyr6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.0203263	.0054858	-3.71	0.000	-.0310892	-.0095634
att_age	.0038839	.0004227	9.19	0.000	.0030546	.0047132
common	.6483727	.0359613	18.03	0.000	.5778189	.7189265
_Imach16_12	-.0019336	.0212989	-0.09	0.928	-.0437207	.0398535
_Imach16_13	.014837	.0272176	0.55	0.586	-.0385623	.0682363
_Imach16_14	-.0089898	.0658416	-0.14	0.891	-.1381669	.1201873
_Imach16_21	.0206936	.0093139	2.22	0.026	.0024203	.0389669
_Imach16_22	.0207736	.0064478	3.22	0.001	.0081234	.0334239
_Imach16_23	.012152	.0538931	0.23	0.822	-.0935828	.1178869
_Imach16_24	.0366603	.0229984	1.59	0.111	-.0084612	.0817818
_Imach16_31	.0519645	.0130843	3.97	0.000	.026294	.077635
_Imach16_32	.0556884	.0179208	3.11	0.002	.0205288	.090848
_Imach16_33	-.0077796	.0119655	-0.65	0.516	-.0312551	.015696
_Imach16_34	.0346524	.0930373	0.37	0.710	-.147881	.2171859
_Igroup_2	.0134805	.0053391	2.52	0.012	.0030055	.0239555
_cons	.0914506	.022263	4.11	0.000	.047772	.1351292

```
. xi: regress commyr6 female att_age common i.mach16 bmi
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1211
Model	6.34451904	15	.422967936	F( 15, 1195) =	49.02
Residual	10.3101864	1195	.008627771	Prob > F =	0.0000
				R-squared =	0.3809
				Adj R-squared =	0.3732
Total	16.6547054	1210	.013764219	Root MSE =	.09289

commyr6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.019825	.0055101	-3.60	0.000	-.0306355	-.0090145
att_age	.003841	.0004238	9.06	0.000	.0030096	.0046725
common	.6401744	.0364886	17.54	0.000	.5685856	.7117632
_Imach16_12	-.0022247	.0213195	-0.10	0.917	-.0440525	.0396031
_Imach16_13	.0155462	.0272383	0.57	0.568	-.037894	.0689865
_Imach16_14	-.0127826	.0659122	-0.19	0.846	-.1420992	.116534
_Imach16_21	.0220228	.0093447	2.36	0.019	.003689	.0403567
_Imach16_22	.0217817	.0064831	3.36	0.001	.0090623	.0345012
_Imach16_23	.0142662	.0539576	0.26	0.792	-.091596	.1201284
_Imach16_24	.0327316	.0230577	1.42	0.156	-.0125064	.0779696
_Imach16_31	.050627	.0130903	3.87	0.000	.0249445	.0763095
_Imach16_32	.0655446	.0182558	3.59	0.000	.0297276	.1013616
_Imach16_33	-.0077387	.0119855	-0.65	0.519	-.0312536	.0157762
_Imach16_34	.0425063	.0930661	0.46	0.648	-.1400848	.2250975
bmi	.0015564	.000709	2.20	0.028	.0001653	.0029474
_cons	.0631833	.0271649	2.33	0.020	.0098872	.1164795

```
. tab smoking
```

current smoking (yes=1) year 1	Freq.	Percent	Cum.
0	994	81.01	81.01
1	233	18.99	100.00
Total	1,227	100.00	

```
. xi: regress commyr6 female att_age common i.mach16 smoking
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1217
Model	6.476787	15	.4317858	F( 15, 1201) =	50.59
Residual	10.2497392	1201	.008534337	Prob > F =	0.0000
				R-squared =	0.3872
				Adj R-squared =	0.3796
Total	16.7265262	1216	.013755367	Root MSE =	.09238

commyr6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.0210664	.0054659	-3.85	0.000	-.0317901	-.0103428
att_age	.003843	.0004205	9.14	0.000	.003018	.0046679
common	.6441395	.0358473	17.97	0.000	.5738093	.7144697
_Imach16_12	-.0050448	.0212111	-0.24	0.812	-.0466598	.0365701
_Imach16_13	.0126322	.0271009	0.47	0.641	-.0405383	.0658026
_Imach16_14	-.0043128	.065544	-0.07	0.948	-.1329062	.1242807
_Imach16_21	.0203068	.0092737	2.19	0.029	.0021123	.0385012
_Imach16_22	.021174	.0064205	3.30	0.001	.0085774	.0337705
_Imach16_23	.006023	.0536445	0.11	0.911	-.0992244	.1112704
_Imach16_24	.0343538	.0228895	1.50	0.134	-.010554	.0792616
_Imach16_31	.0519145	.0130167	3.99	0.000	.0263765	.0774525
_Imach16_32	.0642687	.0181431	3.54	0.000	.0286731	.0998643
_Imach16_33	-.0061234	.0119106	-0.51	0.607	-.0294914	.0172446
_Imach16_34	.0456194	.0925657	0.49	0.622	-.1359891	.2272279
smoking	.024706	.0068	3.63	0.000	.0113649	.0380471
_cons	.0976639	.0219509	4.45	0.000	.0545976	.1407302

```
. xi: regress commyr6 female att_age common i.mach16 sbp
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1214
Model	6.4144546	15	.427630306	F( 15, 1198) =	49.98
Residual	10.2495959	1198	.0085555589	Prob > F =	0.0000
				R-squared =	0.3849
				Adj R-squared =	0.3772
Total	16.6640505	1213	.013737882	Root MSE =	.0925

commyr6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.0172562	.0055695	-3.10	0.002	-.0281832	-.0063292
att_age	.0037019	.0004235	8.74	0.000	.0028711	.0045327
common	.6287043	.0363888	17.28	0.000	.5573114	.7000972
_Imach16_12	-.0032339	.0212279	-0.15	0.879	-.0448818	.038414
_Imach16_13	.0126621	.0271376	0.47	0.641	-.0405804	.0659046
_Imach16_14	.0001412	.0656689	0.00	0.998	-.1286976	.1289801
_Imach16_21	.0190358	.0093021	2.05	0.041	.0007856	.037286
_Imach16_22	.0200352	.0064396	3.11	0.002	.0074011	.0326694
_Imach16_23	-.0129417	.0656959	-0.20	0.844	-.1418334	.1159501
_Imach16_24	.0339671	.0229215	1.48	0.139	-.0110036	.0789378
_Imach16_31	.0491174	.0130341	3.77	0.000	.0235452	.0746896
_Imach16_32	.0631939	.0181697	3.48	0.001	.0275459	.0988418
_Imach16_33	-.00328	.0120157	-0.27	0.785	-.0268541	.0202942
_Imach16_34	.042326	.0926748	0.46	0.648	-.139497	.2241491
sbp	.0007769	.000228	3.41	0.001	.0003295	.0012243
_cons	.0240473	.0310485	0.77	0.439	-.0368682	.0849627

. tab ht

hypertensio n year 1 (yes=1)	Freq.	Percent	Cum.
0	1,011	83.48	83.48
1	200	16.52	100.00
Total	1,211	100.00	

. xi: regress commyr6 female att\_age common i.mach16 ht  
i.mach16 \_Imach16\_11-34 (naturally coded; \_Imach16\_11 omitted)

Source	SS	df	MS	Number of obs =	1201
Model	6.43167262	15	.428778175	F( 15, 1185) =	49.83
Residual	10.1959203	1185	.008604152	Prob > F =	0.0000
Total	16.6275929	1200	.013856327	R-squared =	0.3868
				Adj R-squared =	0.3790
				Root MSE =	.09276

commyr6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.019781	.0055463	-3.57	0.000	-.0306626	-.0088994
att_age	.0037914	.0004272	8.87	0.000	.0029532	.0046297
common	.6424393	.0365143	17.59	0.000	.5707995	.7140791
_Imach16_12	-.0006027	.0218474	-0.03	0.978	-.0434666	.0422612
_Imach16_13	.0098816	.0273026	0.36	0.717	-.0436853	.0634485
_Imach16_14	-.0060716	.0658122	-0.09	0.927	-.1351931	.1230499
_Imach16_21	.0213031	.0093252	2.28	0.023	.0030072	.0395989
_Imach16_22	.0216299	.0064909	3.33	0.001	.0088949	.0343649
_Imach16_23	.0064981	.0538771	0.12	0.904	-.0992071	.1122033
_Imach16_24	.0330635	.0230092	1.44	0.151	-.0120798	.0782069
_Imach16_31	.0509765	.0133773	3.81	0.000	.0247307	.0772222
_Imach16_32	.0709608	.0185459	3.83	0.000	.0345743	.1073473
_Imach16_33	-.0083106	.012036	-0.69	0.490	-.0319248	.0153036
_Imach16_34	.0446289	.0929463	0.48	0.631	-.1377288	.2269865
ht	.0189138	.0074194	2.55	0.011	.0043572	.0334704
_cons	.1013328	.0223051	4.54	0.000	.0575709	.1450947

```
. xi: regress commyr6 female att_age common i.mach16 lhratio
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1174
Model	6.17019643	15	.411346428	F( 15, 1158) =	48.14
Residual	9.89485776	1158	.008544782	Prob > F =	0.0000
				R-squared =	0.3841
				Adj R-squared =	0.3761
Total	16.0650542	1173	.013695698	Root MSE =	.09244

commyr6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
female	-.0161527	.0057445	-2.81	0.005	-.0274235 -.0048818
att_age	.0038168	.0004306	8.86	0.000	.002972 .0046616
common	.6480933	.0366421	17.69	0.000	.5762009 .7199856
_Imach16_12	.0006624	.0223566	0.03	0.976	-.0432015 .0445263
_Imach16_13	.013126	.0271494	0.48	0.629	-.0401415 .0663934
_Imach16_14	-.002412	.0656419	-0.04	0.971	-.1312024 .1263785
_Imach16_21	.02349	.0094199	2.49	0.013	.0050081 .0419719
_Imach16_22	.0220837	.0065475	3.37	0.001	.0092375 .0349298
_Imach16_23	.0175739	.0537552	0.33	0.744	-.0878945 .1230424
_Imach16_24	.036235	.0229157	1.58	0.114	-.0087259 .0811959
_Imach16_31	.0528108	.0133414	3.96	0.000	.0266349 .0789868
_Imach16_32	.0617655	.0184755	3.34	0.001	.0255162 .0980148
_Imach16_33	-.0066781	.0120114	-0.56	0.578	-.0302447 .0168885
_Imach16_34	.043764	.0926226	0.47	0.637	-.1379629 .2254908
lhratio	.0072065	.0032408	2.22	0.026	.000848 .013565
_cons	.0817288	.0230047	3.55	0.000	.0365932 .1268645

```
. xi: regress commyr6 female att_age common i.mach16 log_aer
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1171
Model	6.38688813	14	.456206295	F( 14, 1156) =	52.20
Residual	10.1029353	1156	.008739563	Prob > F =	0.0000
				R-squared =	0.3873
				Adj R-squared =	0.3799
Total	16.4898234	1170	.014093866	Root MSE =	.09349

commyr6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
female	-.0201135	.0056419	-3.57	0.000	-.031183 -.009044
att_age	.0040542	.000438	9.26	0.000	.0031948 .0049135
common	.647918	.0369708	17.53	0.000	.5753805 .7204555
_Imach16_12	.0056561	.0226203	0.25	0.803	-.0387254 .0500375
_Imach16_13	.0141489	.0274351	0.52	0.606	-.0396792 .067977
_Imach16_14	-.0074622	.0663219	-0.11	0.910	-.1375869 .1226625
_Imach16_21	.0198999	.0095464	2.08	0.037	.0011696 .0386301
_Imach16_22	.0229753	.0066292	3.47	0.001	.0099687 .0359819
_Imach16_23	.0144552	.0542975	0.27	0.790	-.0920775 .1209879
_Imach16_24	.0342341	.0238684	1.43	0.152	-.0125961 .0810643
_Imach16_31	.0535971	.0137056	3.91	0.000	.0267064 .0804877
_Imach16_32	.0666838	.0183913	3.63	0.000	.0305997 .1027678
_Imach16_33	-.0041419	.0122266	-0.34	0.735	-.0281306 .0198468
_Imach16_34	(dropped)				
log_aer	.006838	.0024634	2.78	0.006	.0020048 .0116712
_cons	.0743348	.0233042	3.19	0.001	.0286116 .120058

```
. xi: regress commyr6 female att_age common i.mach16 dcct_hba
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1219
Model	6.41369699	15	.427579799	F( 15, 1203) =	49.82
Residual	10.3255309	1203	.008583151	Prob > F =	0.0000
				R-squared =	0.3832
				Adj R-squared =	0.3755
Total	16.7392278	1218	.013743208	Root MSE =	.09265

commyr6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.0210048	.0054789	-3.83	0.000	-.031754	-.0102556
att_age	.0040788	.0004278	9.53	0.000	.0032394	.0049182
common	.6418577	.035959	17.85	0.000	.5713084	.7124071
_Imach16_12	-.0024269	.021258	-0.11	0.909	-.0441338	.0392799
_Imach16_13	.0125992	.0271821	0.46	0.643	-.0407303	.0659288
_Imach16_14	-.00519	.0657284	-0.08	0.937	-.1341451	.1237651
_Imach16_21	.0187276	.0093196	2.01	0.045	.000443	.0370122
_Imach16_22	.0195083	.0064526	3.02	0.003	.0068487	.032168
_Imach16_23	.0097432	.0537855	0.18	0.856	-.0957807	.1152671
_Imach16_24	.0326919	.0229682	1.42	0.155	-.0123702	.077754
_Imach16_31	.0505426	.0130452	3.87	0.000	.0249487	.0761365
_Imach16_32	.0515062	.0179392	2.87	0.004	.0163106	.0867018
_Imach16_33	-.0079338	.0119425	-0.66	0.507	-.0313642	.0154966
_Imach16_34	.0477297	.0928418	0.51	0.607	-.1344201	.2298795
dcct_hba	.0064504	.0019504	3.31	0.001	.0026238	.0102771
_cons	.0438309	.0276716	1.58	0.113	-.0104591	.0981209

```
. xi: regress r_int6 female att_age r_int i.mach16 i.group
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
i.group       _Igroup_1-2        (_Igroup_1 for group==EXPERIMENTAL omitted)
```

Source	SS	df	MS	Number of obs =	1175
Model	74.7177171	15	4.98118114	F( 15, 1159) =	50.98
Residual	113.240894	1159	.097705689	Prob > F =	0.0000
				R-squared =	0.3975
				Adj R-squared =	0.3897
Total	187.958611	1174	.160101032	Root MSE =	.31258

r_int6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	.1002709	.0186743	5.37	0.000	.0636316	.1369101
att_age	-.0092844	.0014153	-6.56	0.000	-.0120612	-.0065075
r_int	.6025237	.0298407	20.19	0.000	.5439758	.6610715
_Imach16_12	.0589797	.0735469	0.80	0.423	-.0853203	.2032796
_Imach16_13	-.0103558	.0916549	-0.11	0.910	-.190184	.1694724
_Imach16_14	.2759279	.2217284	1.24	0.214	-.1591061	.7109619
_Imach16_21	-.1455233	.0323951	-4.49	0.000	-.2090828	-.0819638
_Imach16_22	-.0920186	.0218528	-4.21	0.000	-.1348942	-.0491431
_Imach16_23	.2449747	.1814774	1.35	0.177	-.1110863	.6010358
_Imach16_24	.2102689	.0776939	2.71	0.007	.0578324	.3627054
_Imach16_31	-.1600711	.0458511	-3.49	0.000	-.2500314	-.0701107
_Imach16_32	-.0839313	.0612447	-1.37	0.171	-.2040941	.0362315
_Imach16_33	.0156274	.0404192	0.39	0.699	-.0636757	.0949305
_Imach16_34	.039785	.313257	0.13	0.899	-.5748293	.6543992
_Igroup_2	-.033044	.0183098	-1.80	0.071	-.0689681	.00288
_cons	.8857747	.0813134	10.89	0.000	.7262369	1.045313

```
. xi: regress r_int6 female att_age r_int i.mach16 bmi
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1167
Model	74.7871875	15	4.9858125	F( 15, 1151) =	50.81
Residual	112.946861	1151	.098129332	Prob > F =	0.0000
				R-squared =	0.3984
				Adj R-squared =	0.3905
Total	187.734049	1166	.161006903	Root MSE =	.31326

r_int6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	.1007205	.0188021	5.36	0.000	.0638302	.1376108
att_age	-.0092705	.0014211	-6.52	0.000	-.0120588	-.0064823
r_int	.5994659	.0302076	19.84	0.000	.5401978	.658734
_Imach16_12	.0587924	.0737332	0.80	0.425	-.0858741	.2034589
_Imach16_13	-.0107315	.0918701	-0.12	0.907	-.1909832	.1695202
_Imach16_14	.2845011	.2223052	1.28	0.201	-.1516678	.72067
_Imach16_21	-.1471686	.0325398	-4.52	0.000	-.2110125	-.0833247
_Imach16_22	-.0940247	.0220249	-4.27	0.000	-.1372382	-.0508113
_Imach16_23	.2424098	.1819704	1.33	0.183	-.1146211	.5994408
_Imach16_24	.2199578	.0780493	2.82	0.005	.0668229	.3730926
_Imach16_31	-.1562949	.0459454	-3.40	0.001	-.246441	-.0661488
_Imach16_32	-.1011199	.0625137	-1.62	0.106	-.2237735	.0215337
_Imach16_33	.0164203	.0405661	0.40	0.686	-.0631715	.0960121
_Imach16_34	.0221375	.3138101	0.07	0.944	-.5935664	.6378415
bmi	-.0031668	.0024555	-1.29	0.197	-.0079845	.0016509
_cons	.9561246	.1074759	8.90	0.000	.7452539	1.166995

```
. xi: regress r_int6 female att_age r_int i.mach16 smoking
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1173
Model	75.7763871	15	5.05175914	F( 15, 1157) =	52.12
Residual	112.140407	1157	.096923429	Prob > F =	0.0000
				R-squared =	0.4032
				Adj R-squared =	0.3955
Total	187.916794	1172	.160338562	Root MSE =	.31133

r_int6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	.1021987	.0186231	5.49	0.000	.0656598	.1387376
att_age	-.0091581	.0014095	-6.50	0.000	-.0119235	-.0063927
r_int	.6017051	.029725	20.24	0.000	.5433842	.660026
_Imach16_12	.0693564	.073305	0.95	0.344	-.0744691	.213182
_Imach16_13	-.0014611	.0913321	-0.02	0.987	-.1806563	.177734
_Imach16_14	.2606507	.2208847	1.18	0.238	-.1727288	.6940302
_Imach16_21	-.1440584	.0322741	-4.46	0.000	-.2073808	-.080736
_Imach16_22	-.0928139	.0217756	-4.26	0.000	-.135538	-.0500897
_Imach16_23	.2625498	.180762	1.45	0.147	-.0921082	.6172079
_Imach16_24	.2168542	.07738	2.80	0.005	.0650333	.3686751
_Imach16_31	-.1623864	.0456621	-3.56	0.000	-.2519761	-.0727966
_Imach16_32	-.0988774	.0620664	-1.59	0.111	-.2206526	.0228978
_Imach16_33	.0109926	.0402625	0.27	0.785	-.0680031	.0899882
_Imach16_34	.0084515	.3118948	0.03	0.978	-.6034913	.6203943
smoking	-.0821664	.0231467	-3.55	0.000	-.1275805	-.0367522
_cons	.8811608	.0802173	10.98	0.000	.7237731	1.038548



```
. xi: regress r_int6 female att_age r_int i.mach16 sbp
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1170
Model	74.8125229	15	4.98750153	F( 15, 1154) =	51.26
Residual	112.271455	1154	.097288956	Prob > F =	0.0000
				R-squared =	0.3999
				Adj R-squared =	0.3921
Total	187.083978	1169	.16003762	Root MSE =	.31191

r_int6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
female	.0907798	.0190142	4.77	0.000	.0534736 .128086
att_age	-.0086726	.001423	-6.09	0.000	-.0114646 -.0058806
r_int	.5913576	.0301305	19.63	0.000	.532241 .6504742
_Imach16_12	.0613502	.0733997	0.84	0.403	-.0826617 .2053621
_Imach16_13	-.000508	.0915384	-0.01	0.996	-.1801083 .1790923
_Imach16_14	.2513968	.2214421	1.14	0.256	-.1830774 .6858711
_Imach16_21	-.1397028	.0323981	-4.31	0.000	-.2032686 -.0761369
_Imach16_22	-.0902275	.0218368	-4.13	0.000	-.1330718 -.0473832
_Imach16_23	.3180355	.2214113	1.44	0.151	-.1163783 .7524492
_Imach16_24	.2191056	.0775456	2.83	0.005	.0669595 .3712517
_Imach16_31	-.152382	.0457297	-3.33	0.001	-.2421047 -.0626594
_Imach16_32	-.0963705	.0621896	-1.55	0.122	-.2183879 .0256469
_Imach16_33	.0029737	.0406229	0.07	0.942	-.0767293 .0826768
_Imach16_34	.0192597	.3124605	0.06	0.951	-.5937945 .6323139
sbp	-.0022558	.0007787	-2.90	0.004	-.0037836 -.0007281
_cons	1.133093	.1236913	9.16	0.000	.8904075 1.375778

```
. xi: regress r_int6 female att_age r_int i.mach16 ht
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1158
Model	75.7923693	15	5.05282462	F( 15, 1142) =	52.12
Residual	110.721414	1142	.096953953	Prob > F =	0.0000
				R-squared =	0.4064
				Adj R-squared =	0.3986
Total	186.513784	1157	.161204653	Root MSE =	.31137

r_int6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
female	.0935015	.0187935	4.98	0.000	.0566279 .1303751
att_age	-.0089957	.001423	-6.32	0.000	-.0117877 -.0062038
r_int	.5816795	.0302133	19.25	0.000	.5223997 .6409593
_Imach16_12	.0698256	.0753143	0.93	0.354	-.0779444 .2175956
_Imach16_13	.0273101	.0917509	0.30	0.766	-.1527091 .2073294
_Imach16_14	.2614079	.2209168	1.18	0.237	-.1720404 .6948562
_Imach16_21	-.1443392	.0323242	-4.47	0.000	-.2077606 -.0809178
_Imach16_22	-.0914282	.0218991	-4.17	0.000	-.1343951 -.0484613
_Imach16_23	.2765306	.1808576	1.53	0.127	-.0783199 .6313811
_Imach16_24	.2333816	.0775255	3.01	0.003	.0812733 .38549
_Imach16_31	-.1608072	.04683	-3.43	0.001	-.2526898 -.0689247
_Imach16_32	-.1108131	.0632311	-1.75	0.080	-.2348753 .0132492
_Imach16_33	.0136227	.0405314	0.34	0.737	-.0659017 .0931472
_Imach16_34	.0058446	.3119502	0.02	0.985	-.6062152 .6179044
ht	-.1105436	.0257697	-4.29	0.000	-.1611048 -.0599824
_cons	.9122523	.0810632	11.25	0.000	.7532028 1.071302

```
. xi: regress r_int6 female att_age r_int i.mach16 lhratio
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1130
Model	73.44539	15	4.89635934	F( 15, 1114) =	50.67
Residual	107.655074	1114	.096638307	Prob > F =	0.0000
				R-squared =	0.4056
				Adj R-squared =	0.3975
Total	181.100464	1129	.160407851	Root MSE =	.31087

r_int6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
female	.0733276	.0195632	3.75	0.000	.0349427 .1117126
att_age	-.0085752	.0014425	-5.94	0.000	-.0114056 -.0057449
r_int	.5868884	.0303515	19.34	0.000	.5273358 .646441
_Imach16_12	.0259726	.0773616	0.34	0.737	-.1258183 .1777636
_Imach16_13	.0093707	.0913369	0.10	0.918	-.1698411 .1885825
_Imach16_14	.2327342	.2207614	1.05	0.292	-.2004208 .6658892
_Imach16_21	-.1472336	.0327325	-4.50	0.000	-.2114579 -.0830093
_Imach16_22	-.0957871	.02215	-4.32	0.000	-.1392475 -.0523267
_Imach16_23	.2033737	.180756	1.13	0.261	-.1512868 .5580342
_Imach16_24	.2124408	.0773135	2.75	0.006	.0607443 .3641373
_Imach16_31	-.1731282	.0467967	-3.70	0.000	-.2649479 -.0813085
_Imach16_32	-.0936728	.0631342	-1.48	0.138	-.217548 .0302025
_Imach16_33	.0093383	.0405241	0.23	0.818	-.0701738 .0888505
_Imach16_34	.0108553	.3114316	0.03	0.972	-.6002033 .6219139
lhratio	-.0505158	.0112918	-4.47	0.000	-.0726713 -.0283603
_cons	.9999382	.0879485	11.37	0.000	.8273748 1.172502

```
. xi: regress r_int6 female att_age r_int i.mach16 log_aer
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1128
Model	75.6338555	14	5.40241825	F( 14, 1113) =	54.74
Residual	109.85243	1113	.098699398	Prob > F =	0.0000
				R-squared =	0.4078
				Adj R-squared =	0.4003
Total	185.486286	1127	.164584105	Root MSE =	.31416

r_int6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
female	.1026751	.0191671	5.36	0.000	.0650674 .1402828
att_age	-.0101061	.0014568	-6.94	0.000	-.0129645 -.0072477
r_int	.603463	.0304629	19.81	0.000	.5436919 .6632342
_Imach16_12	.0476967	.0781594	0.61	0.542	-.1056597 .2010531
_Imach16_13	-.006982	.092215	-0.08	0.940	-.1879167 .1739528
_Imach16_14	.2705588	.2228799	1.21	0.225	-.1667534 .7078709
_Imach16_21	-.1394751	.0331948	-4.20	0.000	-.2046065 -.0743437
_Imach16_22	-.0976415	.0224009	-4.36	0.000	-.1415943 -.0536887
_Imach16_23	.2372506	.1824597	1.30	0.194	-.1207531 .5952544
_Imach16_24	.213208	.0804259	2.65	0.008	.0554046 .3710114
_Imach16_31	-.178672	.0477536	-3.74	0.000	-.2723693 -.0849747
_Imach16_32	-.1057546	.0627381	-1.69	0.092	-.2288529 .0173436
_Imach16_33	.0144467	.0412309	0.35	0.726	-.0664525 .0953458
_Imach16_34	(dropped)				
log_aer	-.0212159	.0083588	-2.54	0.011	-.0376166 -.0048152
_cons	.9503666	.0877351	10.83	0.000	.7782218 1.122511

```
. xi: regress r_int6 female att_age r_int i.mach16 dcct_hba
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1175
Model	75.2161604	15	5.01441069	F( 15, 1159) =	51.55
Residual	112.742451	1159	.097275626	Prob > F =	0.0000
				R-squared =	0.4002
				Adj R-squared =	0.3924
Total	187.958611	1174	.160101032	Root MSE =	.31189

r_int6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	.1021892	.0186394	5.48	0.000	.0656184	.13876
att_age	-.0098271	.0014286	-6.88	0.000	-.01263	-.0070242
r_int	.5986047	.0298197	20.07	0.000	.540098	.6571113
_Imach16_12	.0599973	.0733849	0.82	0.414	-.0839847	.2039793
_Imach16_13	-.0023229	.091517	-0.03	0.980	-.1818805	.1772347
_Imach16_14	.2650059	.2212735	1.20	0.231	-.1691355	.6991473
_Imach16_21	-.1397588	.0323994	-4.31	0.000	-.2033269	-.0761908
_Imach16_22	-.0882378	.0218561	-4.04	0.000	-.1311198	-.0453559
_Imach16_23	.2505283	.1810569	1.38	0.167	-.1047076	.6057642
_Imach16_24	.2217413	.0775728	2.86	0.004	.0695424	.3739402
_Imach16_31	-.1578341	.045705	-3.45	0.001	-.2475078	-.0681604
_Imach16_32	-.0724881	.061267	-1.18	0.237	-.1926948	.0477186
_Imach16_33	.0167779	.0403307	0.42	0.677	-.0623515	.0959073
_Imach16_34	.0036484	.3125036	0.01	0.991	-.6094877	.6167846
dcct_hba	-.0192702	.0066506	-2.90	0.004	-.0323188	-.0062215
_cons	1.048253	.1024059	10.24	0.000	.8473314	1.249175

```
. xi: regress comint6a female att_age comint1a i.mach16 i.group
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
i.group       _Igroup_1-2        (_Igroup_1 for group==EXPERIMENTAL omitted)
```

Source	SS	df	MS	Number of obs =	1229
Model	1708.14757	15	113.876505	F( 15, 1213) =	83.62
Residual	1651.97583	1213	1.36189269	Prob > F =	0.0000
				R-squared =	0.5084
				Adj R-squared =	0.5023
Total	3360.1234	1228	2.73625684	Root MSE =	1.167

comint6a	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.2818155	.06841	-4.12	0.000	-.4160306	-.1476004
att_age	.0358637	.0053707	6.68	0.000	.0253269	.0464006
comint1a	.6229307	.0234499	26.56	0.000	.5769238	.6689375
_Imach16_12	-.0160058	.2677939	-0.06	0.952	-.5413964	.5093849
_Imach16_13	.143558	.341931	0.42	0.675	-.5272839	.8143999
_Imach16_14	-.476899	.8277285	-0.58	0.565	-2.100837	1.147039
_Imach16_21	.4165039	.1167953	3.57	0.000	.1873608	.6456471
_Imach16_22	.4093933	.0800459	5.11	0.000	.2523496	.5664371
_Imach16_23	.0170888	.67747	0.03	0.980	-1.312054	1.346232
_Imach16_24	.1434964	.2894045	0.50	0.620	-.4242926	.7112854
_Imach16_31	.7790249	.1644053	4.74	0.000	.4564747	1.101575
_Imach16_32	.5736154	.2247631	2.55	0.011	.1326479	1.014583
_Imach16_33	-.0561512	.1503256	-0.37	0.709	-.3510783	.2387759
_Imach16_34	.2680589	1.169672	0.23	0.819	-2.026746	2.562864
_Igroup_2	.1619148	.0668767	2.42	0.016	.0307079	.2931217
_cons	-1.459367	.2017774	-7.23	0.000	-1.855238	-1.063496

```
. xi: regress comint6a female att_age comintla i.mach16 bmi
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1221
Model	1703.93719	15	113.595812	F( 15, 1205) =	83.09
Residual	1647.465	1205	1.36719087	Prob > F =	0.0000
				R-squared =	0.5084
				Adj R-squared =	0.5023
Total	3351.40219	1220	2.74705097	Root MSE =	1.1693

comint6a	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.2790667	.0688235	-4.05	0.000	-.4140939	-.1440394
att_age	.0354009	.0053892	6.57	0.000	.0248277	.0459742
comintla	.6211999	.0237769	26.13	0.000	.5745512	.6678485
_Imach16_12	-.0217364	.2683846	-0.08	0.935	-.5482895	.5048167
_Imach16_13	.1497794	.3426288	0.44	0.662	-.5224359	.8219947
_Imach16_14	-.5131688	.8296524	-0.62	0.536	-2.140893	1.114555
_Imach16_21	.4283582	.1173266	3.65	0.000	.1981711	.6585453
_Imach16_22	.4204775	.0805888	5.22	0.000	.2623674	.5785875
_Imach16_23	.0295191	.6791309	0.04	0.965	-1.302891	1.36193
_Imach16_24	.1039336	.2905713	0.36	0.721	-.4661482	.6740154
_Imach16_31	.7619215	.1647131	4.63	0.000	.4387651	1.085078
_Imach16_32	.6809209	.2292259	2.97	0.003	.2311947	1.130647
_Imach16_33	-.0560198	.1507799	-0.37	0.710	-.35184	.2398005
_Imach16_34	.3582505	1.171466	0.31	0.760	-1.940089	2.656591
bmi	.0136236	.0089045	1.53	0.126	-.0038464	.0310936
_cons	-1.721668	.3091082	-5.57	0.000	-2.328118	-1.115218

```
. xi: regress comint6a female att_age comintla i.mach16 smoking
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1227
Model	1727.89824	15	115.193216	F( 15, 1211) =	85.58
Residual	1630.0152	1211	1.34600759	Prob > F =	0.0000
				R-squared =	0.5146
				Adj R-squared =	0.5086
Total	3357.91344	1226	2.73891798	Root MSE =	1.1602

comint6a	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.2926308	.0681029	-4.30	0.000	-.4262436	-.1590179
att_age	.0354764	.0053348	6.65	0.000	.02501	.0459429
comintla	.6180018	.0233651	26.45	0.000	.5721612	.6638423
_Imach16_12	-.060545	.266397	-0.23	0.820	-.5831958	.4621058
_Imach16_13	.1078741	.3401001	0.32	0.751	-.5593768	.775125
_Imach16_14	-.4127575	.823049	-0.50	0.616	-2.027518	1.202003
_Imach16_21	.4095621	.116158	3.53	0.000	.1816689	.6374553
_Imach16_22	.4111894	.07961	5.17	0.000	.2550005	.5673783
_Imach16_23	-.0686564	.6736154	-0.10	0.919	-1.390239	1.252926
_Imach16_24	.1100034	.2877267	0.38	0.702	-.4544949	.6745016
_Imach16_31	.7784785	.1633732	4.77	0.000	.4579526	1.099004
_Imach16_32	.6685879	.2272428	2.94	0.003	.2227547	1.114421
_Imach16_33	-.0360051	.1494657	-0.24	0.810	-.3292455	.2572353
_Imach16_34	.4052135	1.162405	0.35	0.727	-1.875338	2.685765
smoking	.3467508	.085026	4.08	0.000	.1799363	.5135654
_cons	-1.424817	.1966439	-7.25	0.000	-1.810618	-1.039017

```
. xi: regress comint6a female att_age comintla i.mach16 sbp
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1224
Model	1710.3266	15	114.021773	F( 15, 1208) =	84.09
Residual	1637.95183	1208	1.35592039	Prob > F =	0.0000
				R-squared =	0.5108
				Adj R-squared =	0.5047
Total	3348.27842	1223	2.73775832	Root MSE =	1.1644

comint6a	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.2468538	.0695868	-3.55	0.000	-.3833782	-.1103294
att_age	.0340675	.0053745	6.34	0.000	.0235231	.0446118
comintla	.6100464	.0238863	25.54	0.000	.5631831	.6569097
_Imach16_12	-.0338647	.2672531	-0.13	0.899	-.5581964	.4904671
_Imach16_13	.1134562	.3414306	0.33	0.740	-.5564066	.7833191
_Imach16_14	-.3763673	.8266133	-0.46	0.649	-1.998125	1.24539
_Imach16_21	.3961213	.1168203	3.39	0.001	.1669281	.6253145
_Imach16_22	.4008179	.0800311	5.01	0.000	.2438025	.5578334
_Imach16_23	-.3156969	.8268185	-0.38	0.703	-1.937857	1.306463
_Imach16_24	.1069953	.2888517	0.37	0.711	-.4597114	.673702
_Imach16_31	.7428853	.1640323	4.53	0.000	.4210654	1.064705
_Imach16_32	.6590275	.2281141	2.89	0.004	.2114836	1.106571
_Imach16_33	-.0088159	.1511139	-0.06	0.953	-.3052907	.287659
_Imach16_34	.3579205	1.16661	0.31	0.759	-1.930885	2.646726
sbp	.0088337	.0028843	3.06	0.002	.003175	.0144925
_cons	-2.359786	.3810066	-6.19	0.000	-3.107295	-1.612278

```
. xi: regress comint6a female att_age comintla i.mach16 ht
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1211
Model	1718.76521	15	114.584347	F( 15, 1195) =	84.34
Residual	1623.55271	1195	1.35862152	Prob > F =	0.0000
				R-squared =	0.5142
				Adj R-squared =	0.5081
Total	3342.31792	1210	2.76224621	Root MSE =	1.1656

comint6a	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.2691377	.069064	-3.90	0.000	-.4046379	-.1336375
att_age	.0352848	.0054102	6.52	0.000	.0246702	.0458994
comintla	.6121199	.0238869	25.63	0.000	.5652549	.6589848
_Imach16_12	-.016614	.2745622	-0.06	0.952	-.5552917	.5220637
_Imach16_13	.0542764	.3429383	0.16	0.874	-.6185518	.7271046
_Imach16_14	-.4327996	.8269059	-0.52	0.601	-2.055149	1.189549
_Imach16_21	.4181161	.1168555	3.58	0.000	.1888513	.6473809
_Imach16_22	.4148007	.0804693	5.15	0.000	.2569239	.5726774
_Imach16_23	-.0776101	.6769697	-0.11	0.909	-1.405792	1.250571
_Imach16_24	.0805595	.289477	0.28	0.781	-.4873803	.6484992
_Imach16_31	.7667691	.1680542	4.56	0.000	.4370549	1.096483
_Imach16_32	.7389645	.2324055	3.18	0.002	.2829963	1.194933
_Imach16_33	-.0555555	.1511427	-0.37	0.713	-.3520902	.2409791
_Imach16_34	.3926732	1.167864	0.34	0.737	-1.89862	2.683966
ht	.3015655	.0939098	3.21	0.001	.117319	.485812
_cons	-1.409794	.1991068	-7.08	0.000	-1.800432	-1.019157

```
. xi: regress comint6a female att_age comintla i.mach16 lhratio
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1184
Model	1651.6582	15	110.110547	F( 15, 1168) =	82.73
Residual	1554.5054	1168	1.33091216	Prob > F =	0.0000
				R-squared =	0.5152
				Adj R-squared =	0.5089
Total	3206.1636	1183	2.71019747	Root MSE =	1.1537

comint6a	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.2023621	.0709949	-2.85	0.004	-.3416538	-.0630704
att_age	.0342729	.0054224	6.32	0.000	.0236341	.0449117
comintla	.6149021	.0237276	25.92	0.000	.5683487	.6614556
_Imach16_12	.0554611	.2790024	0.20	0.842	-.4919408	.6028629
_Imach16_13	.1015674	.3385868	0.30	0.764	-.5627388	.7658737
_Imach16_14	-.3481088	.8191449	-0.42	0.671	-1.955269	1.259051
_Imach16_21	.4470775	.1172168	3.81	0.000	.2170985	.6770565
_Imach16_22	.4279852	.0805889	5.31	0.000	.26987	.5861003
_Imach16_23	.1297148	.6706828	0.19	0.847	-1.186163	1.445592
_Imach16_24	.1388775	.2862436	0.49	0.628	-.4227316	.7004865
_Imach16_31	.8037816	.1663952	4.83	0.000	.4773147	1.130249
_Imach16_32	.64047	.2300059	2.78	0.005	.1891991	1.091741
_Imach16_33	-.0325852	.149784	-0.22	0.828	-.326461	.2612906
_Imach16_34	.3874341	1.15587	0.34	0.738	-1.880379	2.655248
lhratio	.1427372	.0404905	3.53	0.000	.063295	.2221793
_cons	-1.695554	.2207387	-7.68	0.000	-2.128643	-1.262465

```
. xi: regress comint6a female att_age comintla i.mach16 log_aer
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1181
Model	1717.8123	14	122.700878	F( 14, 1166) =	89.17
Residual	1604.52895	1166	1.37609687	Prob > F =	0.0000
				R-squared =	0.5170
				Adj R-squared =	0.5112
Total	3322.34124	1180	2.81554343	Root MSE =	1.1731

comint6a	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
female	-.2846422	.070183	-4.06	0.000	-.4223412	-.1469432
att_age	.0386176	.0055493	6.96	0.000	.0277299	.0495052
comintla	.6210588	.0239556	25.93	0.000	.574058	.6680596
_Imach16_12	.0563892	.2838482	0.20	0.843	-.5005211	.6132995
_Imach16_13	.129528	.3440059	0.38	0.707	-.5454118	.8044679
_Imach16_14	-.4581916	.8321292	-0.55	0.582	-2.09083	1.174446
_Imach16_21	.4023725	.1194731	3.37	0.001	.1679662	.6367787
_Imach16_22	.4385856	.0820335	5.35	0.000	.2776358	.5995355
_Imach16_23	.043591	.6812057	0.06	0.949	-1.292935	1.380117
_Imach16_24	.1185338	.299729	0.40	0.693	-.4695347	.7066022
_Imach16_31	.8145919	.1719497	4.74	0.000	.4772265	1.151957
_Imach16_32	.6982066	.2301575	3.03	0.002	.2466374	1.149776
_Imach16_33	-.0204787	.1533154	-0.13	0.894	-.3212836	.2803262
_Imach16_34	(dropped)					
log_aer	.0911715	.0308454	2.96	0.003	.0306528	.1516901
_cons	-1.709602	.2269039	-7.53	0.000	-2.154788	-1.264417

```
. xi: regress comint6a female att_age comint1a i.mach16 dcct_hba
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
```

Source	SS	df	MS	Number of obs =	1229
Model	1723.52485	15	114.901656	F( 15, 1213) =	85.16
Residual	1636.59855	1213	1.34921562	Prob > F =	0.0000
				R-squared =	0.5129
				Adj R-squared =	0.5069
Total	3360.1234	1228	2.73625684	Root MSE =	1.1616

comint6a	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
female	-.2918761	.0681328	-4.28	0.000	-.4255473 -.158205
att_age	.0391487	.0054229	7.22	0.000	.0285094 .0497879
comint1a	.6170217	.0234034	26.36	0.000	.571106 .6629374
_Imach16_12	-.0219819	.2665346	-0.08	0.934	-.5449018 .500938
_Imach16_13	.1022553	.3405462	0.30	0.764	-.5658695 .7703802
_Imach16_14	-.4175115	.8239991	-0.51	0.612	-2.034133 1.19911
_Imach16_21	.3853851	.1165439	3.31	0.001	.156735 .6140352
_Imach16_22	.3889286	.0798757	4.87	0.000	.2322187 .5456386
_Imach16_23	-.0129561	.6742471	-0.02	0.985	-1.335776 1.309864
_Imach16_24	.0839424	.2882418	0.29	0.771	-.4815654 .6494502
_Imach16_31	.7625185	.1634818	4.66	0.000	.44178 1.083257
_Imach16_32	.5084211	.2243369	2.27	0.024	.0682898 .9485525
_Imach16_33	-.0615441	.1496213	-0.41	0.681	-.3550894 .2320013
_Imach16_34	.4488394	1.163941	0.39	0.700	-1.834722 2.732401
dcct_hba	.1013591	.0243593	4.16	0.000	.0535681 .1491501
_cons	-2.300259	.3000063	-7.67	0.000	-2.888848 -1.711671

```
. log close
log: C:\EDIC Carotid IMT\3.log
log type: text
closed on: 29 May 2007, 13:45:26
```

```

log: C:\EDIC Carotid IMT\4.log
log type: text
opened on: 29 May 2007, 14:56:52

```

```

. use "C:\EDIC Carotid IMT\edicmscuru6.dta", clear

. generate female=1

. replace female=0 if sex=="M"
(645 real changes made)

. generate standard_age = 0

. replace standard_age = att_age if group=="STANDARD"
(611 real changes made)

. tab1 att_age sex female mach16 smoking

-> tabulation of att_age

```

attained age year 1	Freq.	Percent	Cum.
19	5	0.41	0.41
20	7	0.57	0.98
21	18	1.46	2.44
22	18	1.46	3.91
23	17	1.38	5.29
24	24	1.95	7.24
25	39	3.17	10.41
26	31	2.52	12.94
27	34	2.77	15.70
28	36	2.93	18.63
29	47	3.82	22.46
30	49	3.99	26.44
31	48	3.91	30.35
32	57	4.64	34.99
33	63	5.13	40.11
34	64	5.21	45.32
35	70	5.70	51.02
36	50	4.07	55.09
37	59	4.80	59.89
38	63	5.13	65.01
39	64	5.21	70.22
40	70	5.70	75.92
41	36	2.93	78.84
42	54	4.39	83.24
43	49	3.99	87.23
44	40	3.25	90.48
45	32	2.60	93.08
46	43	3.50	96.58
47	18	1.46	98.05
48	9	0.73	98.78
49	11	0.90	99.67
50	3	0.24	99.92
51	1	0.08	100.00
Total	1,229	100.00	

```

-> tabulation of sex

```

sex	Freq.	Percent	Cum.
F	584	47.52	47.52
M	645	52.48	100.00
Total	1,229	100.00	



-> tabulation of female

female	Freq.	Percent	Cum.
0	645	52.48	52.48
1	584	47.52	100.00
Total	1,229	100.00	

-> tabulation of mach16

ultrasonogr aphy equipment combination s	Freq.	Percent	Cum.
11	416	33.85	33.85
12	20	1.63	35.48
13	12	0.98	36.45
14	2	0.16	36.62
21	134	10.90	47.52
22	465	37.84	85.35
23	3	0.24	85.60
24	17	1.38	86.98
31	59	4.80	91.78
32	29	2.36	94.14
33	71	5.78	99.92
34	1	0.08	100.00
Total	1,229	100.00	

-> tabulation of smoking

current smoking (yes=1) year 1	Freq.	Percent	Cum.
0	994	81.01	81.01
1	233	18.99	100.00
Total	1,227	100.00	

. tab standard\_age group

standard_a ge	treatment group		Total
	EXPERIMEN	STANDARD	
0	618	0	618
19	0	2	2
20	0	4	4
21	0	12	12
22	0	11	11
23	0	12	12
24	0	11	11
25	0	19	19
26	0	12	12
27	0	16	16
28	0	18	18
29	0	23	23
30	0	24	24
31	0	29	29
32	0	26	26
33	0	32	32
34	0	37	37
35	0	35	35

36	0	25	25
37	0	27	27
38	0	31	31
39	0	36	36
40	0	33	33
41	0	21	21
42	0	17	17
43	0	22	22
44	0	19	19
45	0	19	19
46	0	23	23
47	0	5	5
48	0	2	2
49	0	7	7
50	0	1	1
-----			
Total	618	611	1,229

```
. xi: regress commyr6 att_age female common smoking sbp i.mach16 i.group
standard_age
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
i.group      _Igroup_1-2      (_Igroup_1 for group==EXPERIMENTAL omitted)
```

Source	SS	df	MS	Number of obs =	1214
Model	6.63335152	18	.368519529	F( 18, 1195) =	43.90
Residual	10.030699	1195	.00839389	Prob > F =	0.0000
-----				R-squared =	0.3981
Total	16.6640505	1213	.013737882	Adj R-squared =	0.3890
				Root MSE =	.09162

commyr6	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
att_age	.002898	.0005655	5.12	0.000	.0017886	.0040074
female	-.0173285	.0055193	-3.14	0.002	-.0281571	-.0064999
common	.6188239	.0361165	17.13	0.000	.547965	.6896827
smoking	.0264995	.0067896	3.90	0.000	.0131786	.0398205
sbp	.0007859	.0002262	3.47	0.001	.000342	.0012297
_Imach16_12	-.0027271	.021081	-0.13	0.897	-.0440869	.0386327
_Imach16_13	.0093079	.0269086	0.35	0.729	-.0434854	.0621012
_Imach16_14	-.0035408	.065193	-0.05	0.957	-.1314463	.1243647
_Imach16_21	.0182094	.0092161	1.98	0.048	.0001278	.036291
_Imach16_22	.0198324	.0063798	3.11	0.002	.0073156	.0323491
_Imach16_23	-.0139867	.0651245	-0.21	0.830	-.1417577	.1137844
_Imach16_24	.0330591	.0227124	1.46	0.146	-.0115015	.0776196
_Imach16_31	.0523112	.0129314	4.05	0.000	.0269404	.077682
_Imach16_32	.063157	.0179973	3.51	0.000	.0278471	.0984668
_Imach16_33	-.0040103	.0119274	-0.34	0.737	-.0274113	.0193907
_Imach16_34	.0407773	.0918423	0.44	0.657	-.1394127	.2209673
_Igroup_2	-.0453358	.0274286	-1.65	0.099	-.0991494	.0084779
standard_age	.0016708	.0007658	2.18	0.029	.0001682	.0031733
_cons	.0458005	.0339261	1.35	0.177	-.0207608	.1123618

```

. xi: regress comint6a att_age female comint1a smoking sbp i.mach16 i.group
standard_age
i.mach16      _Imach16_11-34      (naturally coded; _Imach16_11 omitted)
i.group      _Igroup_1-2          (_Igroup_1 for group==EXPERIMENTAL omitted)

```

Source	SS	df	MS	Number of obs =	1224
Model	1749.20792	18	97.1782177	F( 18, 1205) =	73.23
Residual	1599.0705	1205	1.32702946	Prob > F =	0.0000
				R-squared =	0.5224
				Adj R-squared =	0.5153
Total	3348.27842	1223	2.73775832	Root MSE =	1.152

comint6a	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
att_age	.0248306	.0070657	3.51	0.000	.0109681	.038693
female	-.2506305	.068871	-3.64	0.000	-.3857509	-.1155102
comint1a	.5961027	.0237805	25.07	0.000	.549447	.6427584
smoking	.3737255	.0850475	4.39	0.000	.206868	.5405831
sbp	.0092447	.0028583	3.23	0.001	.0036368	.0148525
_Imach16_12	-.0355505	.2650695	-0.13	0.893	-.5555995	.4844985
_Imach16_13	.0623412	.3381598	0.18	0.854	-.6011062	.7257886
_Imach16_14	-.4062006	.8195354	-0.50	0.620	-2.014075	1.201674
_Imach16_21	.3805554	.1156115	3.29	0.001	.1537332	.6073776
_Imach16_22	.3942891	.0791939	4.98	0.000	.2389158	.5496624
_Imach16_23	-.3276037	.8186496	-0.40	0.689	-1.933741	1.278533
_Imach16_24	.0866714	.2858837	0.30	0.762	-.4742138	.6475565
_Imach16_31	.7781128	.1624906	4.79	0.000	.4593169	1.096909
_Imach16_32	.6571976	.2256722	2.91	0.004	.2144434	1.099952
_Imach16_33	-.0144065	.149784	-0.10	0.923	-.308273	.2794599
_Imach16_34	.3404988	1.154707	0.29	0.768	-1.924961	2.605959
_Igroup_2	-.5433027	.3435357	-1.58	0.114	-1.217297	.1306918
standard_age	.0201343	.0095873	2.10	0.036	.0013246	.0389439
_cons	-2.226797	.4143702	-5.37	0.000	-3.039765	-1.41383

```

. log close
log: C:\EDIC Carotid IMT\4.log
log type: text
closed on: 29 May 2007, 14:56:58

```

# HYPERLIPIDEMIA RE-CHECK

```
log: C:\EDIC Carotid IMT-Latest\Hyperlipedemia_fix.log
log type: text
opened on: 26 Jul 2007, 05:14:59
```

```
. use "C:\EDIC Carotid IMT-Latest\edicmscuru6.dta", clear
. do "C:\DOCUME~1\CFTHOM~1.000\LOCALS~1\Temp\STD02000000.tmp"
. use "C:\EDIC Carotid IMT-Latest\edicmscuru6.dta", clear
. sort group
. by group: tab sex hlip, row
```

---

```
-> group = EXPERIMENTAL
```

```
+-----+
| Key   |
+-----+
|       |
| frequency |
| row percentage |
+-----+
```

sex	ldl >=130 or medication year 1 (yes=1)		Total
	0	1	
F	210 72.92	78 27.08	288 100.00
M	207 64.69	113 35.31	320 100.00
Total	417 68.59	191 31.41	608 100.00

---

```
-> group = STANDARD
```

```
+-----+
| Key   |
+-----+
|       |
| frequency |
| row percentage |
+-----+
```

sex	ldl >=130 or medication year 1 (yes=1)		Total
	0	1	
F	208 73.24	76 26.76	284 100.00
M	217 70.00	93 30.00	310 100.00
Total	425 71.55	169 28.45	594 100.00

```
. end of do-file
```

```
. log close
log: C:\EDIC Carotid IMT-Latest\Hyperlipedemia_fix.log
log type: text
closed on: 26 Jul 2007, 05:16:39
```