Supplementary Online Content

Elam MB, Ginsberg HN, Lovato LC, et al. Association of fenofibrate therapy with long-term cardiovascular risk in statin-treated patients with type 2 diabetes. *JAMA Cardiol*. Published online December 28, 2016. doi:10.1001/jamacardio.2016.4828

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1: Comparison of Investigator Reported Outcomes in ACCORD Versus Adjudicated Outcomes Reported by the Endpoints Committee

Outcome	Outcome Classified by:	Fenofibrate (N=2765)		Placebo (N=2753)		Treatment Effect (Fenofibrate / Placebo)		
		Number of events	Rate[¶]	Number of events	Rate	Hazard Ratio	95% Confidence Interval	P Value
Primary outcome (major fatal or nonfatal cardiovascular event)	ACCORD, Adjudication Committee *	291	2.24	310	2.41	0.92	(0.79, 1.08)	0.32
	ACCORD, Investigator reported	318	2.46	336	2.63	0.93	(0.80, 1.09)	0.38
Primary outcome or revascularization or hospitalization for congestive heart failure	ACCORD , Adjudication Committee *	641	5.35	667	5.64	0.94	(0.85, 1.05)	0.30
	ACCORD, Clinical Site	674	5.67	696	5.91	0.96	(0.86, 1.07)	0.44
Major coronary disease event (fatal coronary event, nonfatal myocardial infarction, or unstable angina)	ACCORD, Adjudication Committee*	332	2.58	353	2.79	0.92	(0.79, 1.07)	0.26
	ACCORD, Investigator reported	344	2.68	372	2.95	0.91	(0.78, 1.05)	0.20
Nonfatal myocardial infarction	ACCORD. Adjudication Committee*	173	1.32	186	1.44	0.91	(0.74, 1.12)	0.39
	ACCORD, Investigator reported	181	1.38	202	1.57	0.88	(0.72, 1.08)	0.21
Nonfatal stroke	ACCORD Adjudication Committee	47	0.35	40	0.30	1.17	(0.76, 1.78)	0.48
	ACCORD, Investigator reported	78	0.59	58	0.44	1.34	(0.96, 1.89)	0.09
Fatal or nonfatal stroke	ACCORD Adjudication Committee *	51	0.38	48	0.36	1.05	(0.71, 1.56)	0.80

	ACCORD, Investigator	82	0.62	65	0.49	1.26	(0.91, 1.74)	0.16
All cause mortality	ACCORD, Adjudication Committee	203	1.49	221	1.64	0.91	(0.75, 1.10)	0.34
	ACCORD, Investigator reported	203	1.49	221	1.64	0.91	(0.75, 1.10)	0.34
Cardiovascular mortality	ACCORD Adjudication Committee *	99	0.72	114	0.83	0.86	(0.66, 1.12)	0.26
	ACCORD, Investigator reported	93	0.68	108	0.80	0.86	(0.65, 1.13)	0.27
Fatal or nonfatal congestive heart failure	ACCORD, Adjudication Committee *	120	0.90	143	1.09	0.82	(0.65, 1.05)	0.10
	ACCORD, Investigator reported	114	0.86	146	1.11	0.77	(0.60, 0.99)	0.04
Nonfatal myocardial infarction, nonfatal stroke, or all cause mortality	ACCORD Adjudication Committee, During ACCORD	NR**	NR**	NR**	NR**	NR**	NR**	NR**
	Clinical Site, Investigator reported	417	3.23	425	3.32	0.97	(0.85, 1.11)	0.68

***As Reported in NEJM 2010;362** **¶ CVD event rate per 100 person years**

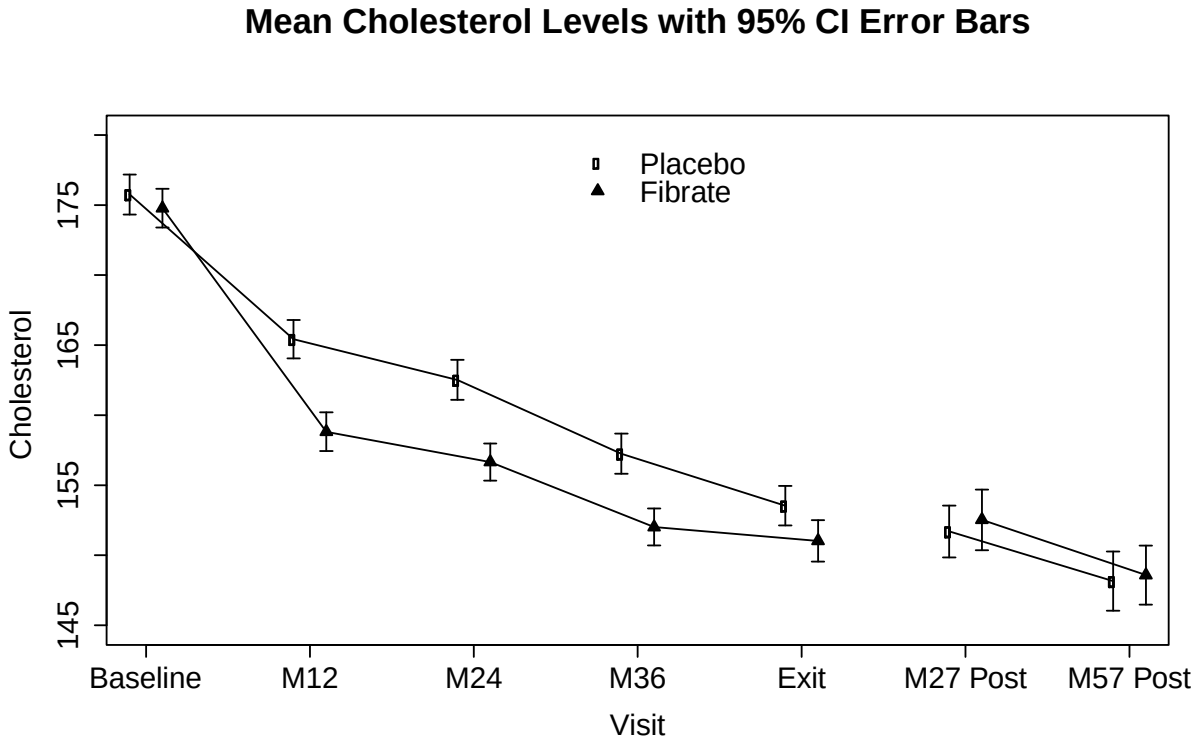
**** NR: Not reported in NEJM 2010;362 because it was not an ACCORD Protocol Outcome**

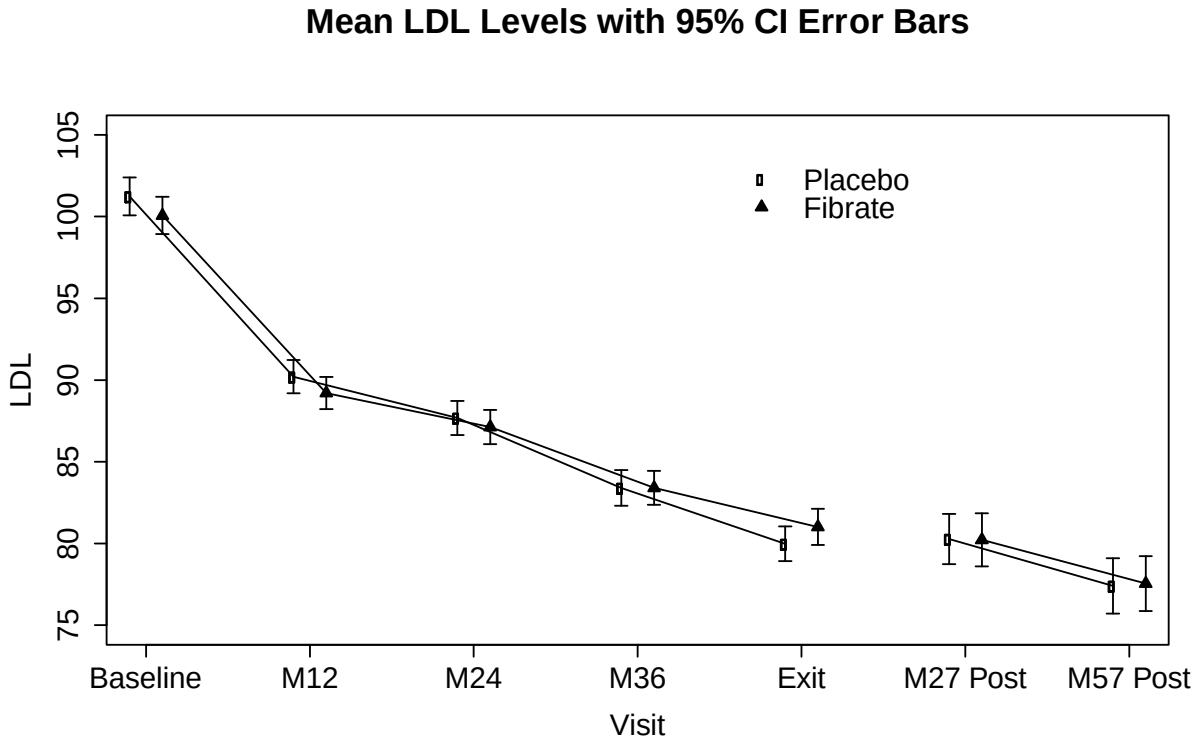
eTable 2: Comparison of CVD Outcomes by sex and dyslipidemia in ACCORD and with addition of extended follow-up in ACCORDION.

Study Period	Subgroups	CVD Events Fenofibrate Group	CVD Events Placebo Group	Hazard Ratio (95% CI)	P Value for Interaction
ACCORD*	Male	214 (11.2%)	254 (13.3%)	0.82 (0.69-0.99)	0.0106
ACCORD	Female	77 (9.1%)	56 (6.6%)	1.38 (0.98-1.95)	
ACCORDION[§]	***Male***	***374 (19.7%)***	***433 (22.8%)***	***0.84 (0.73-0.96)***	***0.0028***
ACCORDION	***Female***	***134 (15.9%)***	***106 (12.7%)***	***1.30 (1.01-1.68)***	
ACCORD	Dyslipidemia**	60 (12.4%)	79 (17.3%)	0.69 (0.49-0.97)	0.0571
ACCORD	No Dyslipidemia	229 (10.1%)	231 (10.1%)	0.99 (0.83-1.19)	
ACCORDION	***Dyslipidemia***	***99 (20.5%)***	***121 (26.7%)***	***0.73 (0.56-0.95)***	***0.0483***
ACCORDION	***No Dyslipidemia***	***407 (18.2%)***	***415 (18.3%)***	***0.99 (0.86-1.13)***	

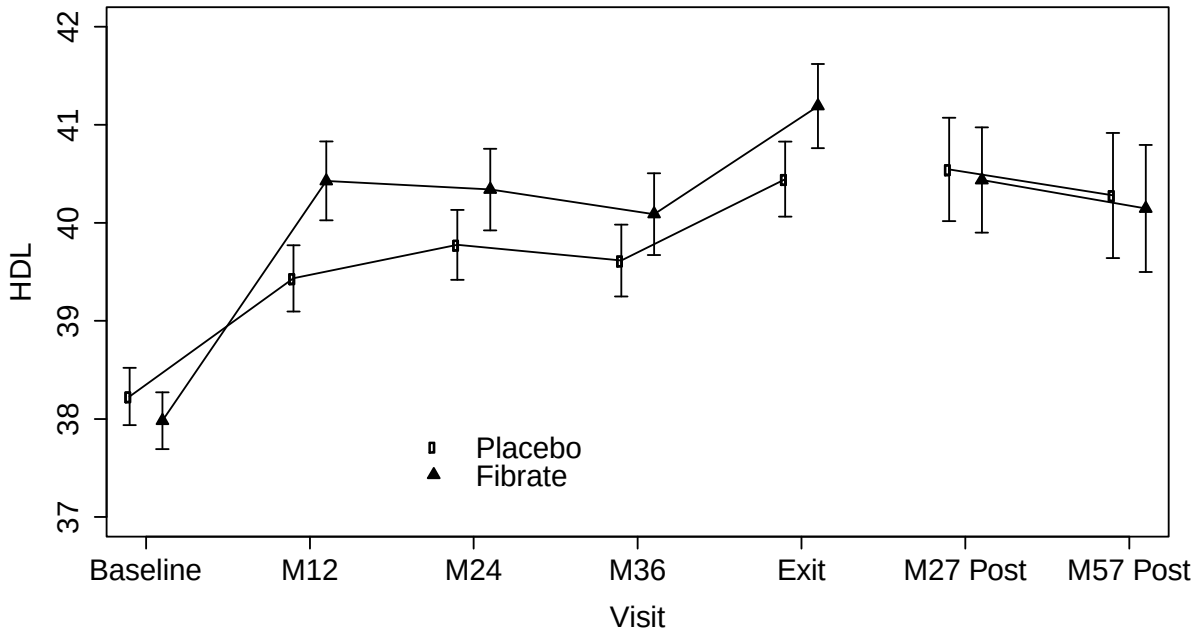
*** From Ginsberg H. et al NEJM 362:1563, 2010. ** Dyslipidemia defined as TG ≥ 204 mg/dl and HDL-C ≤ 34 mg/dl. ¶ CVD events are number of events during follow up period and percentage of participants in that subgroup who experienced a primary cardiovascular outcome (fatal and nonfatal coronary event or stroke). § ACCORDION = ACCORD events plus events during extended follow-up in ACCORDION.**

eFigure 1. Lipid Levels By ACCORD Treatment Arm from Randomization Through the End of ACCORDION

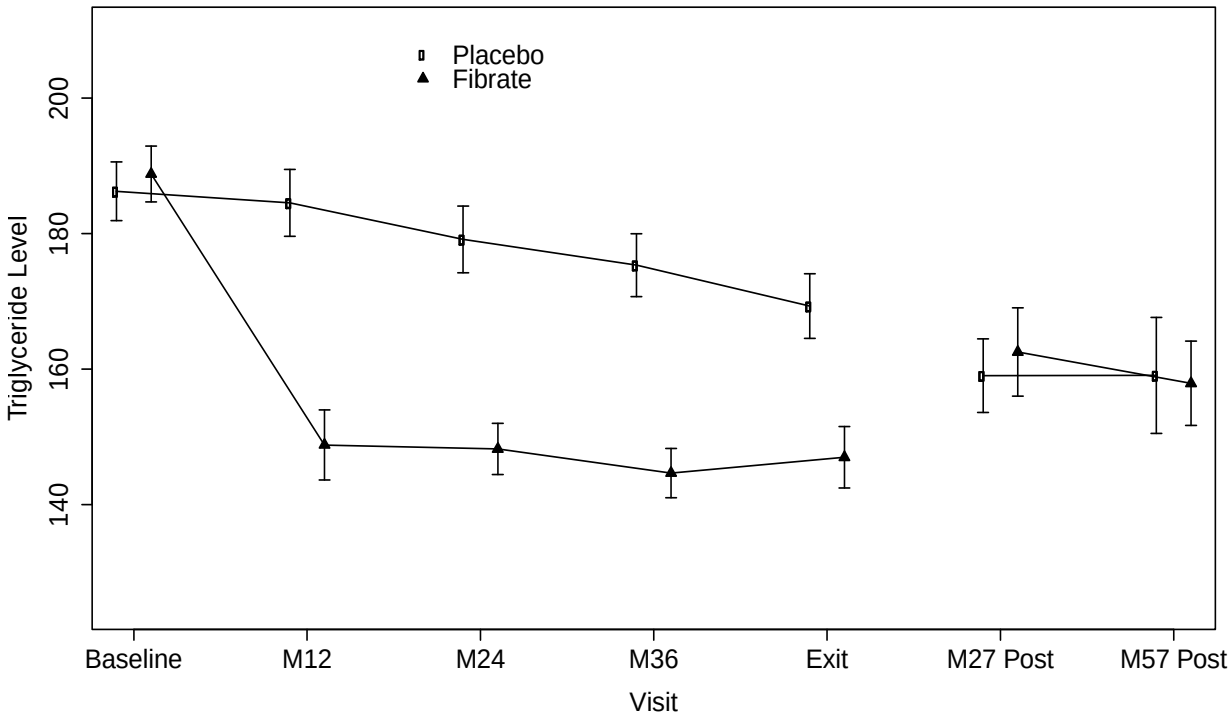




Mean HDL Levels with 95% CI Error Bars

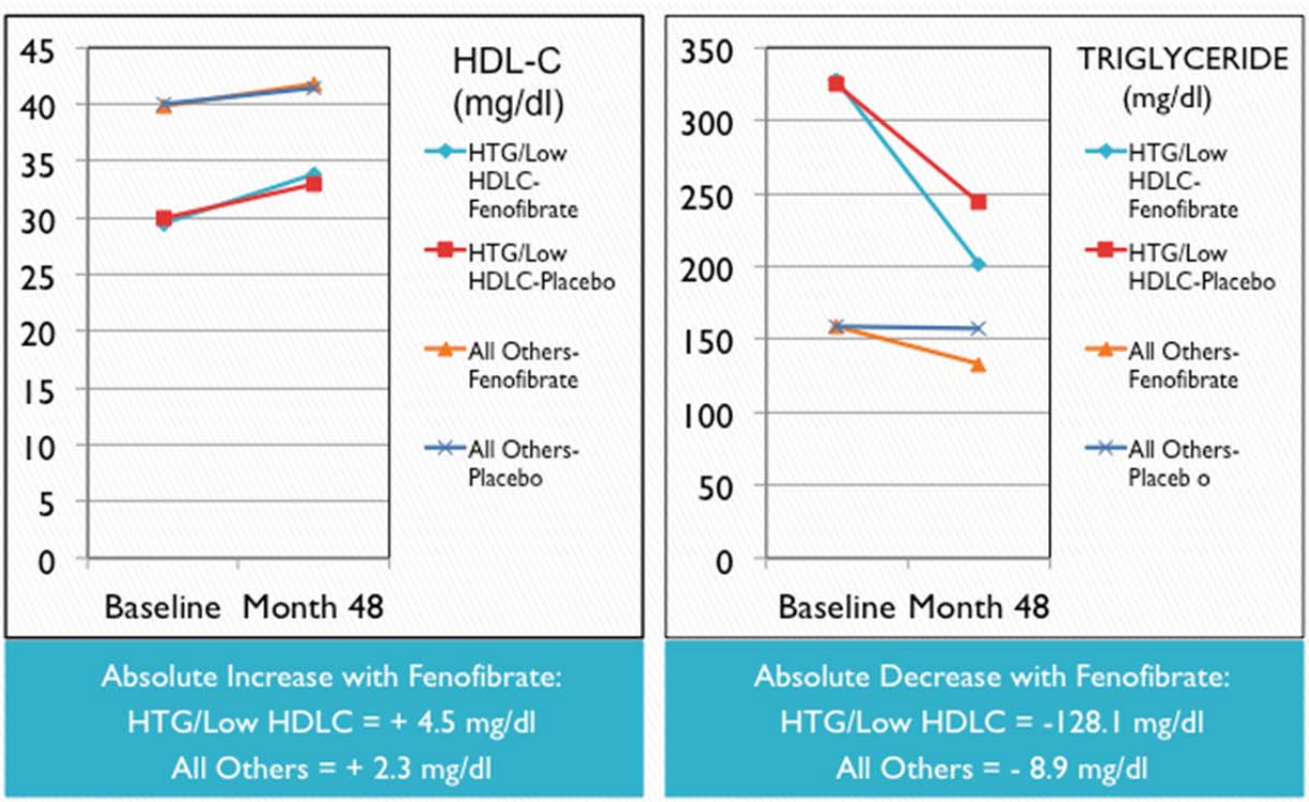


Mean Triglyceride Levels with 95% CI Error Bars



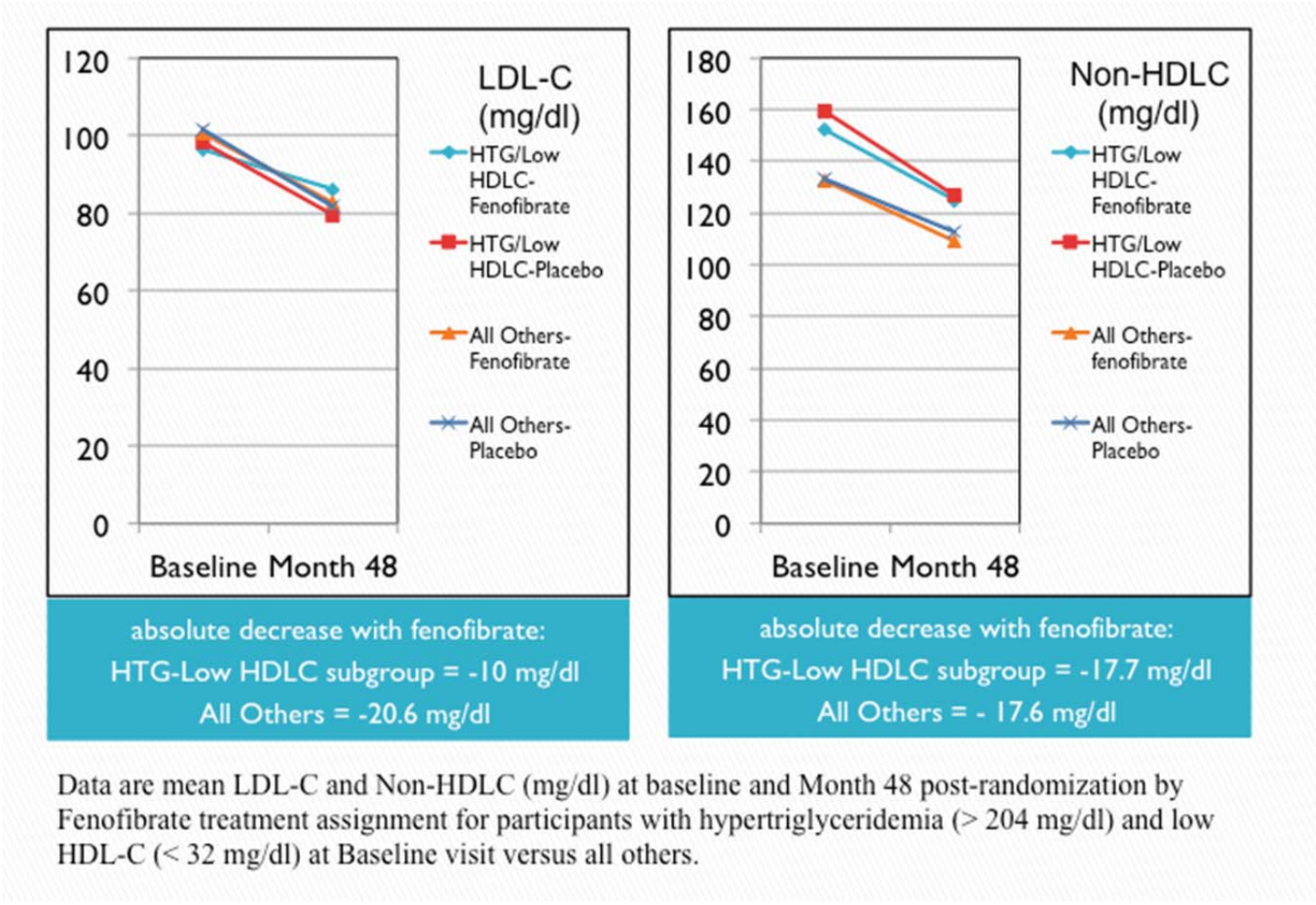
Data are plasma lipoprotein levels (total cholesterol, LDL-C, HDL-C, and total triglyceride) in mg/dl by month post-randomization for ACCORD, at the ACCORD final visit (Exit), and month post-completion of double blind treatment phase of ACCORD for ACCORDION. Following completion of ACCORD lipid therapy was directed by participant's primary care providers.

eFigure 2. Lipid Response to Fenofibrate in Hypertriglyceridemic/Low HDL-C Subgroup vs all others in ACCORD: HDL-C and Triglyceride.



Data are mean LDL-C and Non-HDLC (mg/dl) at baseline and Month 48 post-randomization by Fenofibrate treatment assignment for participants with hypertriglyceridemia (> 204 mg/dl) and low HDL-C (< 32 mg/dl) at Baseline visit versus all others.

eFigure 3. Lipid Response to Fenofibrate in Hypertriglyceridemic/Low HDL-C Subgroup vs all others in ACCORD: LDL-C and Non-HDLC.



Data are mean LDL-C and Non-HDLC (mg/dl) at baseline and Month 48 post-randomization by Fenofibrate treatment assignment for participants with hypertriglyceridemia (> 204 mg/dl) and low HDL-C (< 32 mg/dl) at Baseline visit versus all others.