

## Supplemental Material

Supplemental Table 1. Effect of intensive vs. standard anti-hyperglycemic therapy in the ACCORD-Lipid population.

<b>Outcome</b>	<b>Events Standard</b>	<b>Events Intensive</b>	<b>HR (95%CI)</b>	<b>P-value</b>	<b>Inter.P</b>
<b>HF hospitalization or Cardiovascular death</b>					
Overall population	192/2761 (7.0)	226/2757 (8.2)	1.19 (0.98-1.44)	0.075	-
Placebo	116/1370 (8.5)	112/1383 (8.1)	0.96 (0.74-1.25)		0.017
Fibrate	76/1391 (5.5)	114/1374 (8.3)	1.55 (1.16-2.07)		
<b>HF hospitalization</b>					
Overall population	133/2761 (4.8)	137/2757 (5.0)	1.04 (0.82-1.32)	0.73	-
Placebo	82/1370 (6.0)	67/1383 (4.8)	0.81 (0.59-1.12)		0.025
Fibrate	51/1391 (3.7)	70/1374 (5.1)	1.42 (0.99-2.03)		
<b>Cardiovascular death</b>					
Overall population	87/2761 (3.2)	126/2757 (4.6)	1.46 (1.11-1.92)	0.006	-
Placebo	48/1370 (3.5)	66/1383 (4.8)	1.37 (0.95-1.99)		0.62
Fibrate	39/1391 (2.8)	60/1374 (4.4)	1.58 (1.05-2.36)		
<b>Primary outcome*</b>					
Overall population	300/2761 (10.9)	301 (2757)	1.00 (0.94-1.06)	0.98	-
Placebo	159/1370 (11.6)	151/1383 (10.9)	0.99 (0.91-1.07)		0.73
Fibrate	141/1391 (10.1)	150/1374 (10.9)	1.01 (0.93-1.09)		
<b>All-cause mortality</b>					
Overall population	186/2761 (6.7)	238/2757 (8.6)	1.29 (1.07-1.57)	0.009	-
Placebo	95/1370 (6.9)	126/1383 (9.1)	1.33 (1.02-1.73)		0.78
Fibrate	91/1391 (6.5)	112/1374 (8.2)	1.26 (0.95-1.66)		

\*The primary outcome was a composite of time-to-first of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes.

Supplemental Table 2. Effect of fenofibrate on blood lipids by subgroups of glucose-lowering strategies

<b>Treatment effect</b>	<b>Beta (95%CI)</b>	<b>P-value</b>	<b>Inter.P</b>
<b>Triglycerides</b>			
Overall population	-28.4 (-31.6 to -25.1)	<0.001	
Standard anti-hyperglycemic group	-31.6 (-36.2 to -27.0)		
Intensive anti-hyperglycemic group	-25.1 (-29.7 to -20.5)		0.049
<b>Total cholesterol</b>			
Overall population	-4.9 (-6.0 to -3.8)	<0.001	
Standard anti-hyperglycemic group	-4.2 (-5.8 to -2.7)		
Intensive anti-hyperglycemic group	-5.6 (-7.2 to -4.0)		0.23
<b>VLDL cholesterol</b>			
Overall population	-5.3 (-5.9 to -4.7)	<0.001	
Standard anti-hyperglycemic group	-5.8 (-6.6 to -4.9)		
Intensive anti-hyperglycemic group	-4.8 (-5.7 to -4.0)		0.14
<b>LDL cholesterol</b>			
Overall population	-0.7 (-1.5 to 0.13)	0.098	
Standard anti-hyperglycemic group	0.5 (-0.7 to 1.7)		
Intensive anti-hyperglycemic group	-1.9 (-3.1 to -0.7)		0.005
<b>HDL cholesterol</b>			
Overall population	1.0 (0.8 to 1.3)	<0.001	
Standard anti-hyperglycemic group	1.1 (0.8 to 1.4)		
Intensive anti-hyperglycemic group	1.0 (0.7 to 1.3)		0.73

Supplemental Table 3. Prognostic association of blood lipids

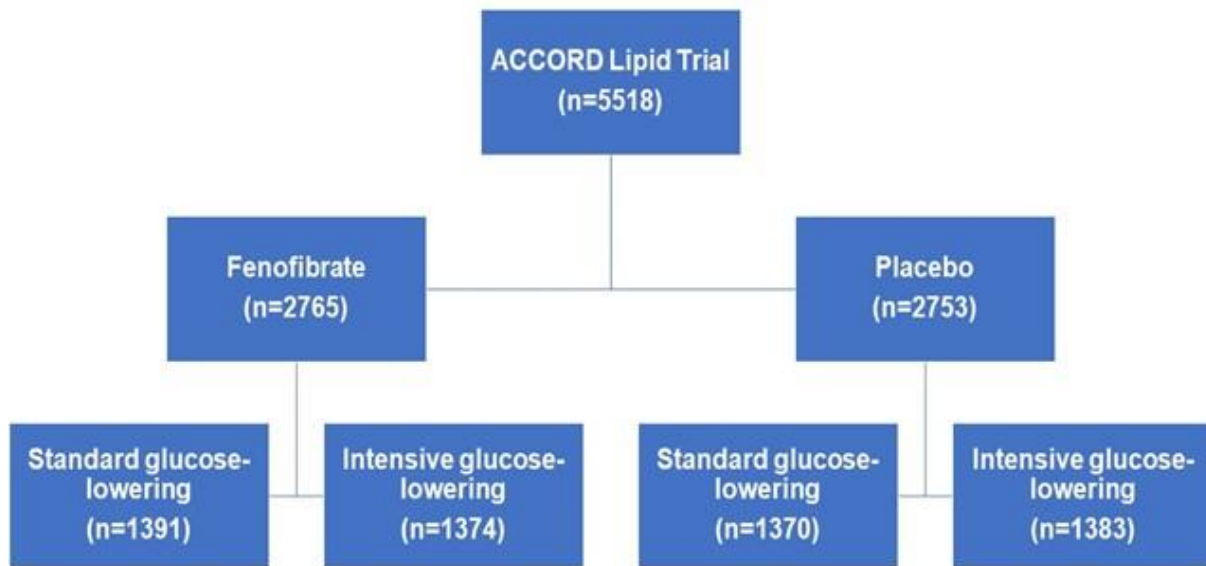
<b>Cardiovascular death or heart failure hospitalization*</b>	<b>HR (95%CI)</b>	<b>P-value</b>
Triglycerides (per doubling in concentration)	0.98 (0.86-1.11)	0.75
Total cholesterol (per doubling in concentration)	1.06 (0.76-1.46)	0.75
VLDL cholesterol (per doubling in concentration)	0.98 (0.85-1.12)	0.73
LDL cholesterol (per doubling in concentration)	1.14 (0.92-1.42)	0.23
HDL cholesterol (per doubling in concentration)	0.62 (0.45-0.86)	0.004

\*Adjusted on the TRS-HFDM score

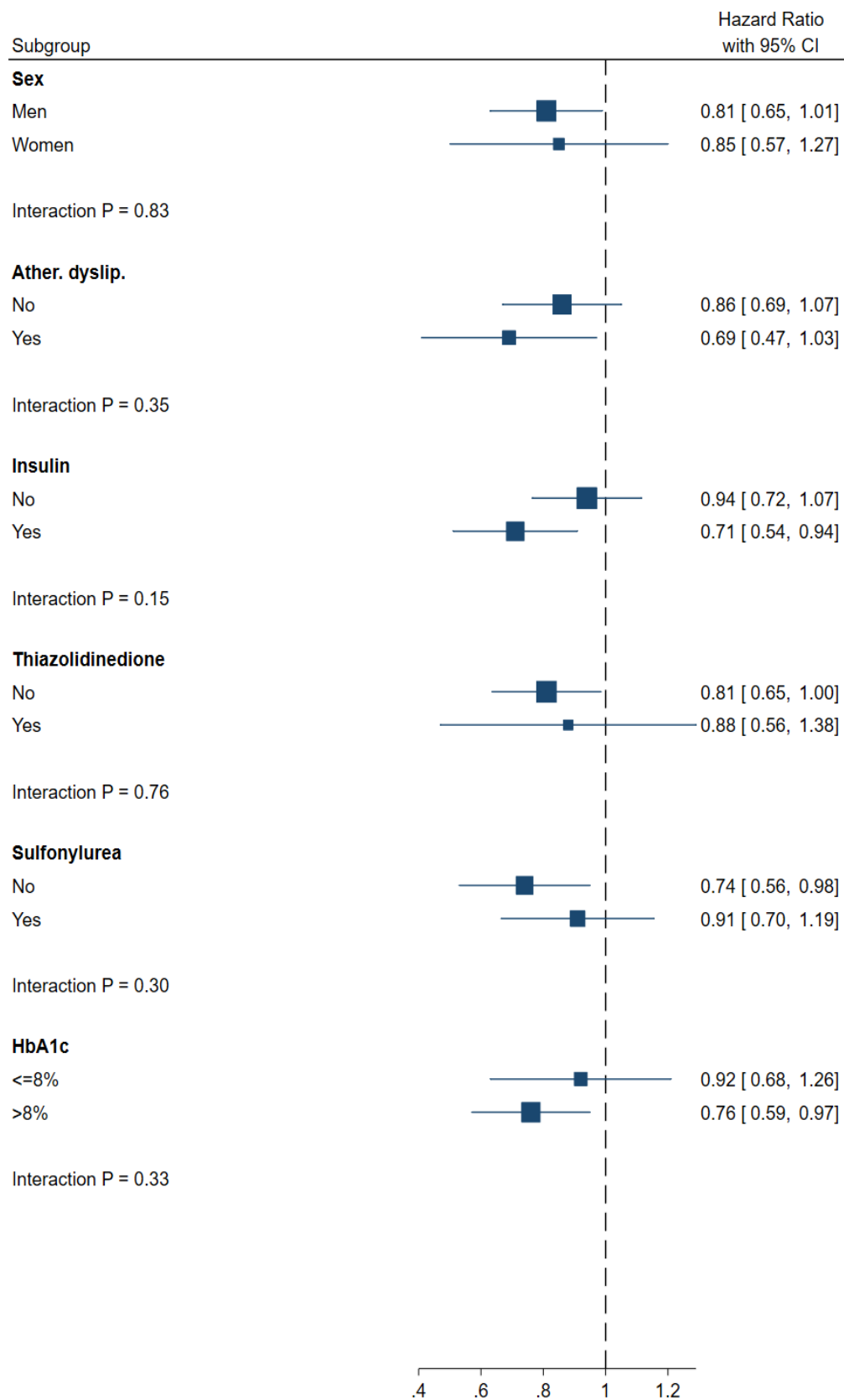
Supplemental Table 4. Adverse events by subgroups of glucose-lowering strategies

<b>Adverse Events</b>	<b>Events Placebo</b>	<b>Events Fenofibrate</b>	<b>P-value</b>	<b>Inter.P</b>
<b>Any hypoglycemia</b>				
Overall population	299/2753 (10.9)	308/2765 (11.1)	0.74	-
Standard anti-hyperglycemic group	81/1370 (5.9)	79/1391 (5.7)		0.57
Intensive anti-hyperglycemic group	218/1383 (15.8)	229/1374 (16.7)		
<b>Treatment-related hypoglycemia</b>				
Overall population	192/2753 (7.0)	209/2765 (7.6)	0.4	-
Standard anti-hyperglycemic group	49/1370 (3.6)	56/1391 (4.0)		0.86
Intensive anti-hyperglycemic group	143/1383 (10.3)	153/1374 (11.1)		
<b>Worsening kidney function</b>				
Overall population	442/2753 (16.1)	1001/2765 (36.2)	<0.001	-
Standard anti-hyperglycemic group	225/1370 (16.4)	482/1391 (34.7)		0.15
Intensive anti-hyperglycemic group	217/1383 (15.7)	519/1374 (37.8)		
<b>Non hypoglycemic AEs</b>				
Overall population	34/2753 (1.2)	48/2765 (1.7)	0.12	-
Standard anti-hyperglycemic group	19/1370 (1.4)	21/1391 (1.5)		0.26
Intensive anti-hyperglycemic group	15/1383 (1.1)	27/1374 (2.0)		

Supplemental Figure 1. Study flow-chart



## Supplemental Figure 2. Further subgroup analyses

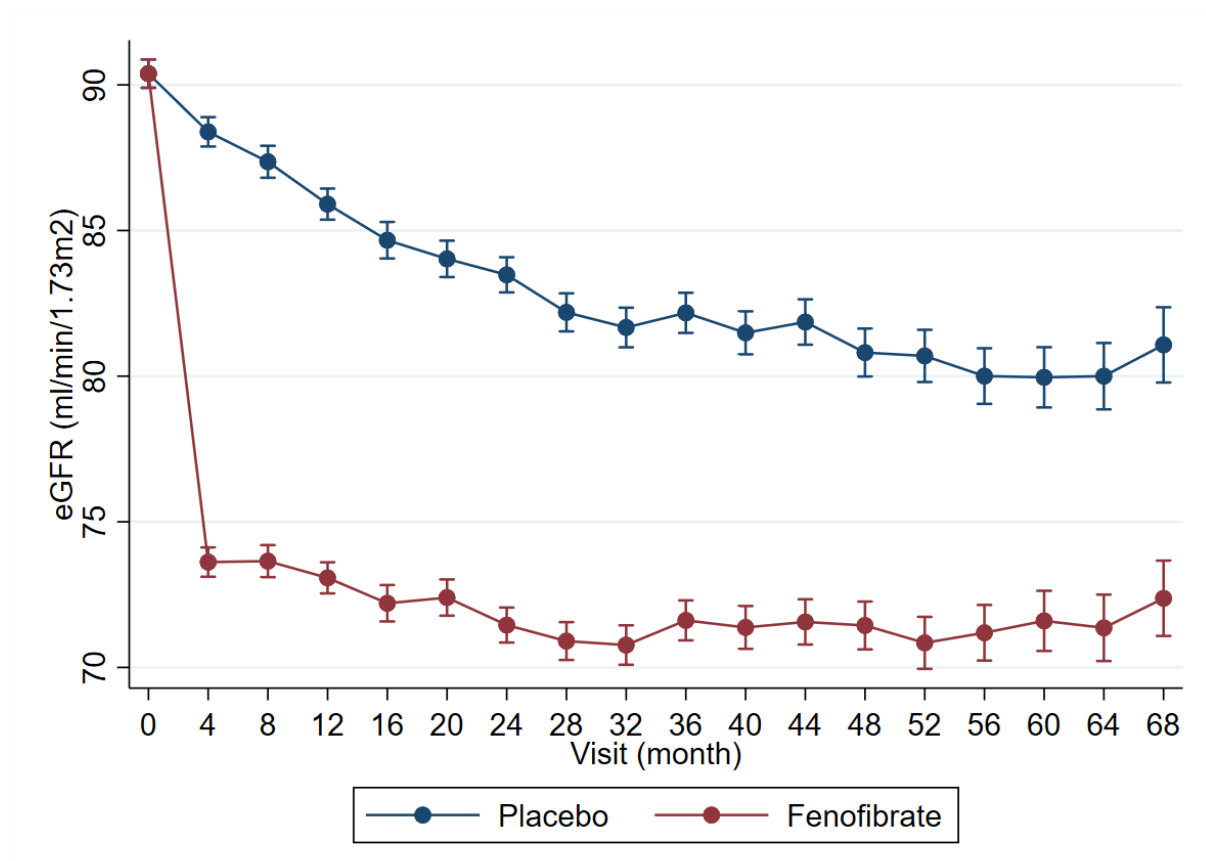


Legend: HbA1c, glycated hemoglobin.





Supplemental Figure 3. eGFR slope analysis



Caption: From baseline to month 4 fenofibrate induced an eGFR drop of -14.8 (-15.5 to -14.1) ml/min/1.73m<sup>2</sup>, after month 4 fenofibrate slowed the decline in eGFR compared with placebo: annualized eGFR slope in the placebo group = -1.7 (-2.1 to -1.3) ml/min/1.73m<sup>2</sup> vs. -0.3 (-0.8 to +0.1) ml/min/1.73m<sup>2</sup> in the fenofibrate group, corresponding to a difference in slopes of +1.4 (+0.8 to +1.9) ml/min/1.73m<sup>2</sup> per year in favor of fenofibrate.