

Fenofibrate Intervention and Event Lowering in Diabetes (FIELD)

Amputations in T2DM

- ✦ **Aims:** To explore the nature and predictors of amputations in the FIELD Trial
- ✦ **Methods:** All on study non-traumatic amputations were reviewed in a blinded fashion by two clinicians. Amputations were classified as:
 - ✦ Major: below or above the knee
 - ✦ Minor: toe and forefoot
- ✦ All analyses of the effects of treatment were by intention-to-treat

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Amputations in T2DM: Baseline Characteristics

General Characteristics	On Study Amputation n=115	Other CHD Event n=1251	Neither n=8429
Age at Visit 1 (years mean [SD])	64.7 (6.33) ****	64.4(6.58)	7.0 61.9 (6.86)
Diabetes Duration (years median)	9.0 (4-15)*****	(3-12))	29.7 5.0 (2-9)
Body-mass index (kg/m ² median)	29.5 (26.5-33.4)	.90 (26.8-33.1)	29.8 (26.6-33.6)
Waist-hip ratio [IQR]	(.91-1.0)****	144.1 (15.76)	0.93 (0.88-0.98)
Blood Pressure (mmHg mean [SD])	144.3 (15.10)****	82.6 (8.94)	139.9 (15.21)
Systolic	81.7 (8.41)*	152 (12.2%)	81.9 (8.47)
Diastolic	23 (20.0%)****	944 (75.5%)	747 (8.9%)
Current Smoker	93 (80.9%)****		5101 (60.5%)
Male			

P-value from 3-way comparison *p<0.05, ** p<0.01, ***p<0.001 ****p< 0.0001

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Clinical History of	On Study Amputation n=115	Other CHD Event n=1251	Neither n = 8429
Amputation	3 (2.6%) ****	n/a	512 (0.2%)
Cardiovascular Disease	67 (58.3%)****	(40.9%)	383 (1552 (18.4%))
MI/Angina/CABG/PTCA	34 (29.6%)****	(30.6%)	80 (988 (11.7%))
Stroke	12 (10.4%)****	(6.4%)	167 (255 (3.0%))
PVD	43 (37.4%)****	(13.3%)	380 (502 (18.7%))
Microvascular Disease	65 (56.5%)****	(30.4)	1580 (8.94)
Retinopathy	34 (29.6%)****	162 (12.9)	618 (7.3%) 1081
Neuropathy	57 (49.6%)****	257 (20.5%)	(12.8%) 229
Nephropathy	8 (7.0%)*	42 (3.4%)	(2.7%)

P-value from 3-way comparison *p<0.05, ** p<0.01, ***p<0.001 ****p< 0.0001

MI = myocardial infarction; CABG = coronary bypass grafting,
PTCA = percutaneous transluminal coronary angioplasty

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Laboratory Data	On Study Amputation n=115	Other CHD Event n=1251	Neither = 8429	n
Total cholesterol (mean [SD])	189 (24.7)*	195 (26)	193 (27)	117
LDL-C	HDL- 115 (26)** 40.4	120 (24.3) 40	(25.1) 42.6	
C	TG (10.2)****	(9.1) 165	(10.0) 156	
HbA1c	161 (118-210)	(126-221)	(121-210) 6.8	
Creatinine	Homocysteine 7.5	7.1	(6.1-7.8)	
(µM median [QR])	(6.8-8.7)****	(6.4-8.1)	.86 (.17) 9.4	
	96 (.20)**** 11.2	93 (.19)	(7.9-11.3)	
	(9.2-13.8)****	10.1 (8.5-12.5)		
Dyslipidemia	46 (40.0%)*	162 (12.9)	3127 (37.1%)	
Microalbuminuria	46 (10.0%)*	257 (20.5%)	1697 (20.1%)	
Macroalbuminuria	20 (17.0%)*	42 (3.4%)	287 (3.4%)	

P-value from 3-way comparison *p<0.05, ** p<0.01, ***p<0.001

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Amputations in T2DM: Baseline Characteristics

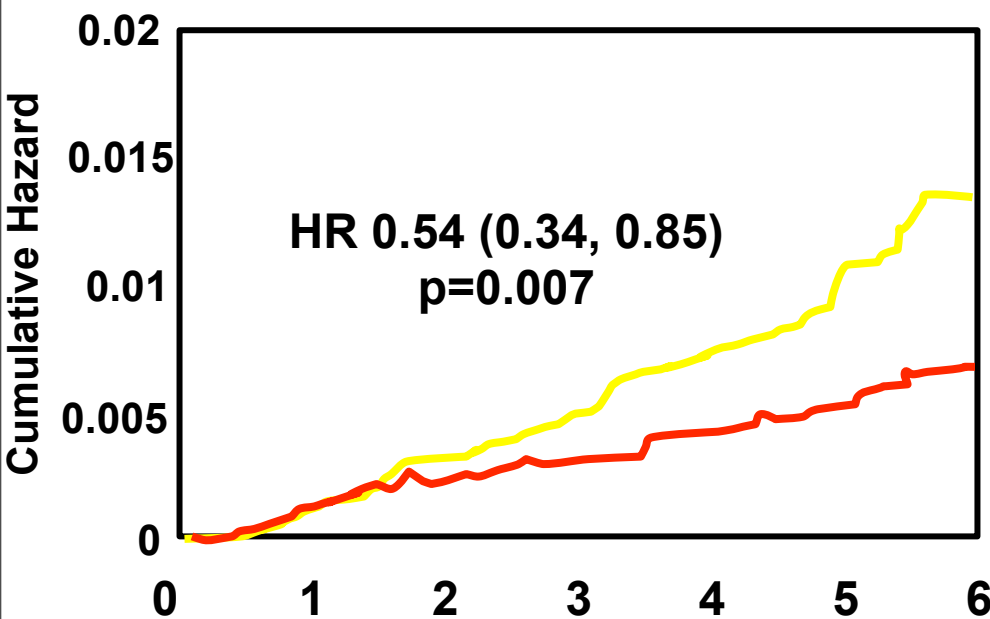
Baseline glucose-lowering	On Study Amputation n=115	Other CHD Event n=1251	Neither n = 8429
Diet alone	8 (7.0)****	234 (18.7%)	2386 (28.1%)
Metformin alone	10 (8.7)***	181 (14.5%)	1530 (18.2%)
Metformin + sulfonylurea	(34.8)****	363 (28.9%)	1916 (22.8%)
Metformin and/or Sulfonylurea + other agent	(4.3%)*	27 (2.2%)	138 (1.6%)
Other oral agent alone	18 (15.7%)****	106 (8.5%)	483 (5.7%)
Insulin alone	22 (19.1%)****	2 (0.2%)	17 (0.2%)
Insulin + oral agent		131 (10.5%)	588 (7.0%)

P-value from 3-way comparison *p<0.05, ** p<0.01, ***p<0.001 ****p< 0.0001

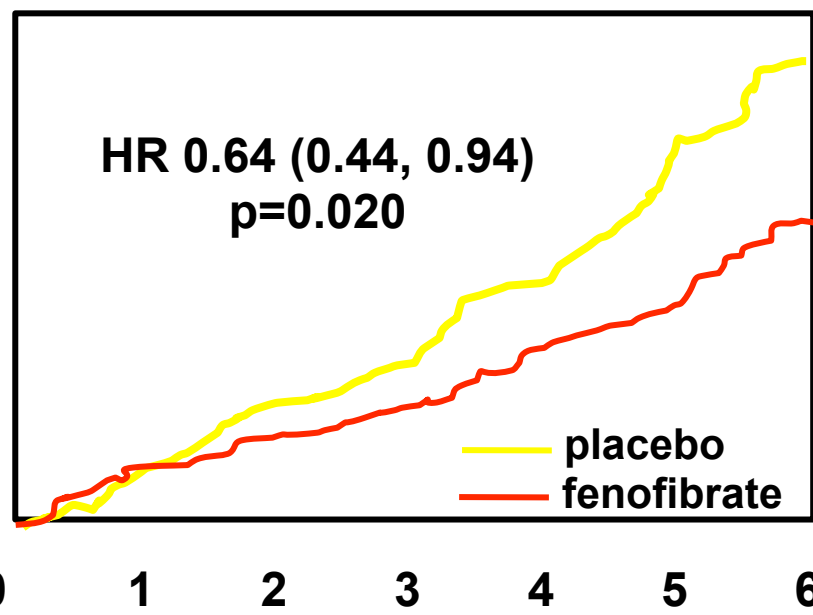
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Non-traumatic Amputations

Minor Amputations

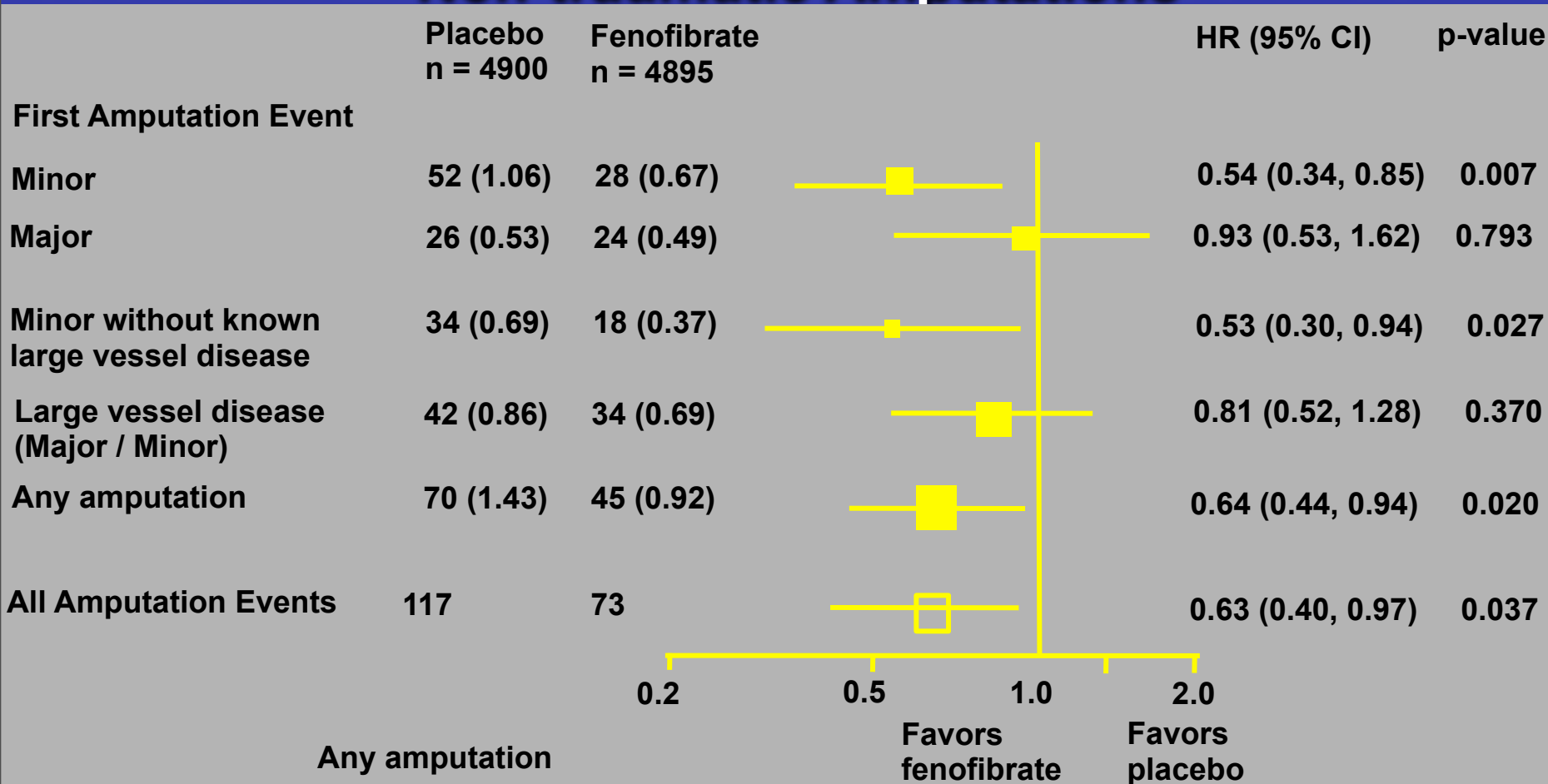


All Amputations



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Non-traumatic Amputations



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Risk Factors for Non-traumatic Amputations

Predictor	Risk	P-value
Peripheral Vascular Disease	3.34	<0.001
Neuropathy	3.00	
Smoking	2.527	0.0001
HbA 1c (1% increase)	1.247	0.0005
Macroalbuminuria	1.875	0.0005
Age (5 year increase)	1.286	0.0006
Male gender	2.182	0.0010
Retinopathy	2.007	0.0017
Microalbuminuria	1.875	0.0032
Fenofibrate	0.64	0.0212
Previous nontraumatic amputation	3.88	0.0258

Proportional Hazard Model for time to first amputation

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Risk Factors for Minor Non-traumatic Amputations

Predictor	Risk	P-value
Retinopathy	4.705	<0.001
Vascular Disease	2.574	0.0002
Peripheral Vascular Disease	2.574	0.0002
Male gender	2.574	0.0002
Previous nontraumatic amputation	2.490	0.0020
Diabetes duration (additional 5 years)	5.997	0.0039
Macroalbuminuria	1.248	
HbA1c (per 1% increase)	2.470	0.0044
Fenofibrate	1.223	0.0097
Diabetic Retinopathy	0.539	0.0097
	1.907	0.0147

Proportional Hazard Model for time to first amputation

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Amputations in T2DM CONCLUSIONS

Minor amputations with/without known large vessel disease occur in a population with higher levels of established microvascular complications of diabetes.

The effect of fenofibrate on amputations was particularly striking in this group, supporting the important clinical benefits of fenofibrate treatment on microvascular disease in type 2 diabetes mellitus