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Table S1 Baseline Characteristics of those VFQ Responders and Non-Responders by Eligibility to be sent the VFQ

		the VFQ (n=11,301)	Ineligible to be sen		
Pagalina Charactariatia	Responders	Non-responders	the VFQ		
Baseline Characteristic	(n=8846)*	(n=2455)	(n=4179)		
Age at randomisation (years)					
Mean (SD)	62.5±8.3	62.8±9.0	65.2±10.7		
<60 ` ´	3339 (37.7%)	901 (36.7%)	1350 (32.3%)		
60<70	3860 (43.6%)	1024 (41.7%)	1363 (32.6%)		
70	1647 (18.6%)	530 (21.6%)	1466 (35.1%)		
	,	,	,		
ex					
fale	5529 (62.5%)	1550 (63.1%)	2605 (62.3%)		
emale	3317 (37.5%)	905 (36.9%)	1574 (37.7%)		
ype of diabetes					
ype 1	559 (6.3%)	138 (5.6%)	214 (5.1%)		
ype 2	8287 (93.7%)	2317 (94.4%)	3965 (94.9%)		
uration of diabetes (years)	7/2 42\	7 (4 42)	7 (4 40)		
ledian (IQR)	7(3-12)	7 (4-13)	7 (4-13)		
0<5 years	2918 (33.0%)	751 (30.6%)	1222 (29.2%)		
5<10 years	2544 (28.8%)	690 (28.1%)	1100 (26.3%)		
10<20 years	1952 (22.1%)	552 (22.5%)	1033 (24.7%)		
20 years	1020 (11.5%)	313 (12.7%)	529 (12.7%)		
nknown	412 (4.7%)	149 (6.1%)	295 (7.1%)		
iabetes management					
iet only	1508 (17.0%)	396 (16.1%)	625 (15.0%)		
ral hypoglycaemic agent(s) only	5166 (58.4%)	1416 (57.7%)	2438 (58.3%)		
sulin +/- oral hypoglycaemic agent(s)	2172 (24.6%)	643 (26.2%)	1116 (26.7%)		
	,				
articipant-reported diabetic retinopathy es	1620 (10.40/)	537 (34.00/)	959 (20 59/)		
es O	1628 (18.4%)	537 (21.9%)	858 (20.5%)		
o nknown	7151 (80.8%) 67 (0.8%)	1895 (77.2%) 23 (0.9%)	3267 (78.2%) 54 (1.3%)		
TINTOWIT	01 (0.070)	23 (0.970)	J4 (1.3%)		
articipant-reported treatment for					
ypertension					
es	5386 (60.9%)	1534 (62.5%)	2613 (62.5%)		
0	3405 (38.5%)	904 (36.8%)	1526 (36.5%)		
nknown	55 (0.6%)	17 (0.7%)	40 (1.0%)		
vestalla bland mus					
systolic blood pressure mmHg)					
	135.8±14.9	136.3±15.2	136 9±15 0		
lean (SD)			136.8±15.9		
130	2023 (22.9%)	522 (21.3%)	849 (20.3%)		
130<140	1822 (20.6%)	491 (20.0%)	778 (18.6%)		
140 Inknown	2626 (29.7%)	720 (29.3%)	1209 (28.9%)		
HINIUWII	2375 (26.8%)	722 (29.4%)	1343 (32.1%)		
iastolic blood pressure					
nmHg)					
lean (SD)	77.4±9.2	77.0±9.6	76.4±9.9		
75	2371 (26.8%)	650 (26.5%)	1202 (28.8%)		
75 <85	2788 (31.5%)	753 (30.7%)	1078 (25.8%)		
35	1311 (14.8%)	326 (13.3%)	554 (13.3%)		
nknown	2376 (26.9%)	726 (29.6%)	1345 (32.2%)		
adv mass index					
ody mass index cg/m²)					
lean (SD)	30.6±6.1	30.9±6.3	30.9±6.5		
25					
25 25, <30	1313 (14.8%) 3230 (36.5%)	` ,	627 (15.0%)		
· ·	3230 (36.5%)	` '	1398 (33.5%)		
30<35	2429 (27.5%) 1610 (18.3%)	688 (28.0%)	1123 (26.9%)		
35 Inknown	1619 (18.3%)	472 (19.2%)	870 (20.8%)		
IIWUIWII	255 (2.9%)	85 (3.5%)	161 (3.9%)		
igarette smoking					
urrent	555 (6.3%)	224 (9.1%)	500 (12.0%)		
ormer	3947 (44.6%)	1133 (46.2%)	1971 (47.2%)		
lever	4243 (48.0%)	1067 (43.5%)	1667 (39.9%)		
Nevei	TZTO (TO.070)	1001 (10.070)			

Aspirin use before screening Thiazide or related diuretic Calcium channel blocker Statin Total cholesterol (mmol/L) Mean (SD) ≥4 < 5	FQ (59.3%) (35.2%) (20.4%) (25.8%) (72.3%)
Non-study medication ACE-inhibitor or ARB 5115 (57.8%) 1461 (59.5%) 2479 (35.8%) Aspirin use before screening 3157 (35.7%) 879 (35.8%) 1472 (35.8%) Thiazide or related diuretic 1639 (18.5%) 465 (18.9%) 853 (24.6%) Calcium channel blocker 2088 (23.6%) 605 (24.6%) 1080 (24.6%) Statin 6769 (76.5%) 1862 (75.8%) 3022 (75.8%) Total cholesterol (mmol/L) Mean (SD) 4.1±0.9 4.1±0.9 4.1±0.9 4 2681 (30.3%) 704 (28.7%) 1169 (24.2%) ≥4 <5 2246 (25.4%) 595 (24.2%) 954 (24.2%) ≥5 817 (9.2%) 226 (9.2%) 427 (25.2%) Not available 3102 (35.1%) 930 (37.9%) 1629 (25.4%) HDL cholesterol (mmol/L) Mean (SD) 1.3±0.4 1.3±0.4 1.2±0 (25.4%) <1 1222 (13.8%) 343 (14.0%) 605 (24.6%) ≥1<.5 3202 (36.2%) 870 (35.4%) 1451 (25.6%) ≥1 1310 (14.8%) 307 (12.5%) 490 (25.4%)	(59.3%) (35.2%) (20.4%) (25.8%) (72.3%) 0.9 (28.0%) (22.8%) (10.2%)
ACE-inhibitor or ARB Aspirin use before screening Thiazide or related diuretic Calcium channel blocker Statin Total cholesterol (mmol/L) Mean (SD) ≥5 Not available HDL cholesterol (mmol/L) Mean (SD) +DL cholesterol (mmol/L) Mean (SD) +DL cholesterol (mmol/L) Mean (SD) +1±0.9 -24 (25.4%) -25 -3102 (35.1%) +3102 (35.1%) 1461 (59.5%) 879 (35.8%) 1472 -465 (18.9%) 853 -605 (24.6%) 1080 -605 (24.6%) 1	(35.2%) (20.4%) (25.8%) (72.3%) (72.3%) (28.0%) (22.8%) (10.2%)
ACE-inhibitor or ARB Aspirin use before screening Thiazide or related diuretic Calcium channel blocker Statin Total cholesterol (mmol/L) Mean (SD) ≥5 Not available HDL cholesterol (mmol/L) Mean (SD) +DL cholesterol (mmol/L) Mean (SD) +DL cholesterol (mmol/L) Mean (SD) +1±0.9 -24 (25.4%) -25 -3102 (35.1%) +3102 (35.1%) 1461 (59.5%) 879 (35.8%) 1472 -465 (18.9%) 853 -605 (24.6%) 1080 -605 (24.6%) 1	(35.2%) (20.4%) (25.8%) (72.3%) (72.3%) (28.0%) (22.8%) (10.2%)
Aspirin use before screening 3157 (35.7%) 879 (35.8%) 1472 Thiazide or related diuretic 1639 (18.5%) 465 (18.9%) 853 Calcium channel blocker 2088 (23.6%) 605 (24.6%) 1080 Statin 6769 (76.5%) 1862 (75.8%) 3022 Total cholesterol (mmol/L) Mean (SD) 4.1±0.9 4.1±0.9 4.2±0 <4	(20.4%) (25.8%) (72.3%) 0.9 (28.0%) (22.8%) (10.2%)
Calcium channel blocker 2088 (23.6%) 605 (24.6%) 1080 Statin 6769 (76.5%) 1862 (75.8%) 3022 Total cholesterol (mmol/L) Mean (SD) 4.1±0.9 4.1±0.9 4.2±0 ≥4 <5	(25.8%) (72.3%) 0.9 (28.0%) (22.8%) (10.2%)
Statin 6769 (76.5%) 1862 (75.8%) 3022 Total cholesterol (mmol/L) Mean (SD) 4.1±0.9 4.1±0.9 4.2±0 <4	(72.3%) 0.9 (28.0%) (22.8%) (10.2%)
Total cholesterol (mmol/L) Mean (SD) 4.1±0.9 4.1±0.9 4.2±0 <4).9 (28.0%) (22.8%) (10.2%)
(mmol/L) 4.1±0.9 4.1±0.9 4.2±0.9 <4	(28.0%) (22.8%) (10.2%)
Mean (SD) 4.1±0.9 4.1±0.9 4.2±0 <4	(28.0%) (22.8%) (10.2%)
<4	(28.0%) (22.8%) (10.2%)
≥5 817 (9.2%) 226 (9.2%) 427 Not available 3102 (35.1%) 930 (37.9%) 1629 HDL cholesterol (mmol/L) Mean (SD) 1.3±0.4 1.3±0.4 1.2±0 <1 1222 (13.8%) 343 (14.0%) 605 12<1.5 3202 (36.2%) 870 (35.4%) 1451 121.5 1310 (14.8%) 307 (12.5%) 490	(10.2%)
Not available 3102 (35.1%) 930 (37.9%) 1629 HDL cholesterol (mmol/L) (mmol/L) 1.3±0.4 1.3±0.4 1.2±0 ✓1 1222 (13.8%) 343 (14.0%) 605 605 ≥1<<1.5	` '
HDL cholesterol (mmol/L) 1.3±0.4 1.3±0.4 1.2±0 Mean (SD) 1.222 (13.8%) 343 (14.0%) 605 ≥1<1.5	(39 0%)
(mmol/L) 1.3±0.4 1.3±0.4 1.3±0.4 1.2±0 <1	(30.070)
Mean (SD) 1.3±0.4 1.3±0.4 1.2±0 <1	
<1	١.4
≥1<1.5 3202 (36.2%) 870 (35.4%) 1451 151.5 1310 (14.8%) 307 (12.5%) 490 151.5 1310 (14.8%)	(14.5%)
≥1.5 1310 (14.8%) 307 (12.5%) 490	(34.7%)
\	(11.7%)
3112 (33.270) 933 (30.170) 1033	(39.1%)
Non-HDL cholesterol	
(mmol/L)	
Mean (SD) 2.9±0.8 2.9±0.8 3.0±0).9
, ,	(19.0%)
≥2.5 < 3.5 2558 (28.9%) 716 (29.2%) 1119	(26.8%)
	(14.2%)
Not available 3112 (35.2%) 935 (38.1%) 1633	(39.1%)
Glycosylated haemoglobin - HbA1c	
IFCC (mmol/mol) mean (SD) 54.0±12.2 55.6±13.5 56.1±1	4.0
DCCT (%) mean (SD) 7.1±1.1 7.2±1.2 7.3±1	
	(19.6%)
	(28.1%)
	(13.2%) (39.0%)
	(,
CKD-EPI estimated GFR (ml/min/1.73m²)	
Mean (SD) 87.8±19.8 84.8±20.4 79.5±2	23.1
	(22.7%)
	(25.3%)
	(13.0%)
Not available 3105 (35.1%) 931 (37.9%) 1629	(39.0%)
Urinary albumin:creatinine ratio† (mg/mmol)	
Median (IQR) 0.50 (0.00-1.14) 0.59 (0.16-1.40) 0.71 (0.27	7-1.88)
<3 5120 (57.9%) 1313 (53.5%) 2093	(50.1%)
≥3 613 (6.9%) 197 (8.0%) 438 (6.9%) 438 (6.9%) 613 (6.9%) 613 (6.9%)	(10.5%)
Not available 3113 (35.2%) 945 (38.5%) 1648	(39.4%)
Townsend Deprivation Index 3101 (35.1%) 764 (31.1%) 1239	(20 7 0/.)
, , , , , , , , , , , , , , , , , , , ,	(29.7%) (36.0%)
	(14.4%)
, , , , , , , , , , , , , , , , , , , ,	(10.7%)
	(6.4%)
≥6 118 (1.3%) 37 (1.5%) 106	(2.5%)
Unknown 20 (0.2%) 4 (0.2%) 14	(0.9%)
Ethnic origin	
	(96.3%)
	(0.9%)
	` '
Other/unknown 121 (1.4%) 41 (1.7%) 59	(0.9%) (1.4%) (1.4%)

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blockers; DCCT = Diabetes Control and Complications Trial; FAs = Fatty acids; GFR = Glomerular Filtration Rate; HDL=High-density lipoprotein; IFCC =International Federation of Clinical Chemistry; IQR = Interquartile range; SD = Standard Deviation

*Out of 8846 VFQ respondents, 7 answered a bespoke first page of questions that sought incident eye diagnoses but did not complete the NEI-VFQ-25, and 8839 completed both parts of the form. Separate analyses of the baseline characteristics for the 8839 NEI-VFQ-25 respondents have not been performed because it is unlikely that excluding those 7 participants would make meaningful differences to the average results.

†There was an analysis rule in ASCEND which stated that those with a below detectable threshold albumin component of their urinary albumin:creatinine ratio, would be recorded as zero. This applied to just over 25% of participants with no baseline eye screening records.

Categories that were "unknown" or "not available" were excluded from balance diagnostic testing. Percentages may not total 100 because of rounding.

Table S2 Duration of Follow-Up- All Randomized ASCEND Participants

	Aspirin Rand	omization	Omega-3 FAs Ra	andomization	
	Active	Placebo	Active	Placebo	Overall
	(n=7740)	(n=7740)	(n=7740)	(n=7740)	(n=15,480)
Mean(SD) length of follow-up (years)	7.4 (1.8)	7.4 (1.8)	7.4 (1.8)	7.4 (1.8)	7.4 (1.8)
Median (IQR) length of follow-up (years)	7.3 (6.4-8.5)	7.3 (6.4-8.5)	7.3 (6.4-8.5)	7.3 (6.4-8.5)	7.3 (6.4-8.5)

FAs=Fatty Acids; IQR=Interquartile range; SD=Standard deviation.

Table S3 Person-Years of Follow-up, Overall and by Follow-Up Method – All Randomized ASCEND Participants

		Aspirin Ra	ndomization		0	mega-3 FAs	Randomization	า		
	Active (n=7740)			Placebo		Active		Placebo		all
Follow-up method	(n=//	40)	(n=7740)		(n=7740)		(n=7740)		(n=15,480)	
	40.007.0	(70 50()	40.050.7	(75.00()	40 440 0	(70.40()	10.001.1	(70.00()	00 000 7	(70.40()
Participant	43,627.0	(76.5%)	43,053.7	(75.6%)	43,416.6	(76.1%)	43,264.1	(76.0%)	86,680.7	(76.1%)
General practitioner	8018.3	(14.1%)	8423.6	(14.8%)	8274.2	(14.5%)	8167.7	(14.3%)	16,441.9	(14.4%)
Record linkage	1742.2	(3.1%)	1674.1	(2.9%)	1685.9	(3.0%)	1730.4	(3.0%)	3416.3	(3.0%)
Died with complete follow-up	3309.2	(5.8%)	3410.3	(6.0%)	3286.2	(5.8%)	3433.3	(6.0%)	6719.5	(5.9%)
Incomplete follow-up information	303.7	(0.5%)	383.4	(0.7%)	358.7	(0.6%)	328.4	(0.6%)	687.1	(0.6%)
Total	57,000	0.4	56,94	56,945.0		57,021.5		56,923.9		45.4

FAs=Fatty Acids. All figures represent person-years of follow-up. Percentages may not total 100 because of rounding.

Table S4 Completeness of Follow-Up – All Randomized ASCEND Participants

		Aspirin Ra	ndomization			Omega-3 FAs F	Randomizatio	on		
Fig. 1 fallows on a tatus	Active n=7740			cebo	_	tive		cebo		erall
Final follow-up status			n=/	n=7740		n=7740		n=7740		n=15,480
Complete follow-up information	7671	(99.1%)	7670	(99.1%)	7672	(99.1%)	7669	(99.1%)	15,341	(99.1%)
Final FU completed by participant or carer	5763	(74.5%)	5682	(73.4%)	5730	(74.0%)	5715	(73.8%)	11,445	(73.9%)
Final FU completed by GP	999	(12.9%)	1045	(13.5%)	1032	(13.3%)	1012	(13.1%)	2044	(13.2%)
Final FU completed by registry linkage	224	(2.9%)	218	(2.8%)	221	(2.9%)	221	(2.9%)	442	(2.9%)
Died (FU for morbidity complete)	685	(8.9%)	725	(9.4%)	689	(8.9%)	721	(9.3%)	1410	(9.1%)
Incomplete follow-up information	69	(0.9%)	70	(0.9%)	68	(0.9%)	71	(0.9%)	139	(0.9%)
Consent withdrawn	35	(0.5%)	30	(0.4%)	26	(0.3%)	39	(0.5%)	65	(0.4%)
Moved abroad	17	(0.2%)	14	(0.2%)	19	(0.2%)	12	(0.2%)	31	(0.2%)
Died (FU for morbidity not complete)	9	(0.1%)	13	(0.2%)	11	(0.1%)	11	(0.1%)	22	(0.1%)
No final FU information	8	(0.1%)	13	(0.2%)	12	(0.2%)	9	(0.1%)	21	(0.1%)

FAs=Fatty Acids; FU=Follow up; GP=General practitioner. Percentages represent the proportion each follow-up method contributed to the total number of person-years of follow-up. Percentages may not total 100 because of rounding.

Table S5 Reported Definite or Probable Adherence with Study Treatment Stratified by Years Post-Randomization – All Randomized ASCEND Participants

	Asp	oirin Randomiza	ition	Omega-3 FAs Randomization					
	Active (%) PI		Overall (%)	Active (%)	Placebo (%)	Overall (%)			
Years post-									
randomization									
<3	82.0%	81.7%	81.9%	86.1%	85.7%	85.9%			
≥3<5	66.0%	64.9%	65.5%	74.1%	73.6%	73.9%			
≥5<7	56.2%	55.1%	55.6%	66.9%	66.2%	66.6%			
≥7	46.2%	45.6%	46.0%	58.9%	58.1%	58.5%			
All	68.0%	67.3%	67.7%	75.6%	75.1%	75.4%			

FAs=Fatty Acids.

Criteria used to define definite or probable adherence:

- Definitely adherent = participant reported taking treatment every or most days during the follow-up period.
- Probably adherent = participant was previously adherent, is still receiving medication and has not reported stopping treatment within the last seven months.

Table S6 Use of Anti-platelet or Anti-coagulant Therapy in the Aspirin Randomization during Follow-Up – All Randomized ASCEND Participants

		Aspi	rin Randomization				
		Active (n=7740)		Placebo (n=7740)			
Years post-randomization <3	Study aspirin	Study aspirin or non-study anti- platelet	Study aspirin or non-study anti-platelet agent or anti- coagulant	Non-study anti- platelet	Non-study anti-platelet agent or anti- coagulant		
Years post-randomization							
•	82.0%	85.3%	85.8%	4.1%	4.6%		
≥3<5	66.0%	73.4%	74.9%	8.8%	10.5%		
≥5<7	56.2%	65.9%	68.3%	11.0%	13.9%		
≥7	46.2%	59.1%	61.9%	12.9%	16.3%		
All	68.0%	74.9%	76.4%	7.9%	9.6%		

Table S7 Study Average Reported Definite or Probable Adherence in each Treatment Arm, Overall and by Baseline Characteristics – All Randomized ASCEND Participants

		rin Randomiz			3 FAs Rando	
D 11 O1 11 11	Active	Placebo	Overall	Active	Placebo	Overall
Baseline Characteristic	(n =7740)	(n=7740)	(n=15,480)	(n=7740)	(n=7740)	(n=15,480)
Age at randomization						
(years)	CO 20/	CO 50/	CO 00/	74.00/	74.70/	74.00/
<60 >60 <70	69.3%	68.5%	68.9%	74.9%	74.7%	74.8% 77.4%
≥60<70	69.3%	68.9%	69.1%	77.3%	77.4%	
≥70	63.5%	62.3%	62.9%	73.6%	71.7%	72.6%
Sex						
Male	69.8%	68.9%	69.3%	77.8%	77.2%	77.5%
Female	65.2%	64.7%	64.9%	77.8% 72.0%	71.6%	77.3 <i>%</i> 71.8%
remale	03.276	04.7 /0	04.970	12.070	71.070	11.070
Type of diabetes*						
Type 1	68.7%	69.9%	69.3%	77.3%	74.5%	75.9%
Type 2	68.0%	67.1%	67.6%	75.5%	75.1%	75.3%
.7,6-2	00.070		0.1010			
Duration of diabetes						
(years)						
≥0<5 years	69.7%	68.6%	69.2%	76.4%	76.5%	76.4%
≥5<10 years	68.2%	66.6%	67.4%	75.8%	74.3%	75.1%
≥10<20 years	67.2%	67.7%	67.5%	75.6%	75.3%	75.4%
≥20 years	66.9%	68.1%	67.5%	76.7%	74.9%	75.8%
Unknown	63.4%	60.2%	61.8%	68.0%	70.6%	69.3%
2	- /-	- ·-	- / -	/ -		
Diabetes management						
Diet only	67.1%	65.6%	66.3%	75.9%	73.2%	74.5%
Oral hypoglycaemic agent(s) only	68.4%	67.7%	68.0%	75.6%	75.9%	75.8%
Insulin +/- oral hypoglycaemic agent(s)	67.9%	67.5%	67.7%	75.6%	74.4%	75.0%
,, e,						
Participant-reported diabetic						
retinopathy						
Yes	66.4%	65.9%	66.2%	75.6%	74.9%	75.3%
No	68.5%	67.7%	68.1%	75.6%	75.1%	75.4%
Participant-reported treatment for						
hypertension						
Yes	67.6%	67.2%	67.4%	76.2%	74.8%	75.5%
No	68.8%	67.5%	68.2%	74.7%	75.5%	75.1%
Systolic blood pressure						
(mmHg) †						
<130	69.8%	70.1%	69.9%	76.9%	76.9%	76.9%
≥130<140	69.9%	69.1%	69.6%	78.1%	76.8%	77.5%
≥140	68.5%	68.3%	68.4%	77.2%	77.4%	77.3%
Unknown	64.9%	62.9%	63.9%	71.4%	70.2%	70.8%
-						
Diastolic blood pressure						
(mmHg) †	70.007	00.007	00.407	00.007	07 701	07.007
<75	79.9%	80.3%	80.1%	88.2%	87.7%	87.9%
≥75 <85	70.6%	69.9%	70.3%	78.1%	78.0%	78.1%
≥85 Llakasura	68.4%	69.4%	68.9%	76.6%	77.8%	77.2%
Unknown	65.0%	62.9%	63.9%	71.4%	70.2%	70.8%
Pody mass index						
Body mass index						
(kg/m²) ‡ <25	68.6%	69.2%	68.9%	77.1%	76.0%	76.6%
≥25, <30 ≥30<35	68.6% 68.2%	68.3% 66.5%	68.5% 67.3%	76.2% 74.9%	76.5% 74.9%	76.3% 74.9%
≥35 Unknown	66.9% 58.8%	65.7% 63.8%	66.3% 61.4%	74.9% 69.5%	72.9% 60.0%	73.9% 64.8%
UTIKTIOWN	58.8%	03.0%	61.4%	09.0%	00.0%	04.0%
Cigarette smoking						
Cigarette smoking Current	60.7%	61 30/	60.9%	67.3%	67.9%	67.6%
Former	60.7%	61.3% 67.3%	60.9% 67.4%		67.9% 75.3%	67.6% 75.8%
Never	67.4%	67.3% 68.5%	67.4% 69.2%	76,2% 76.5%	75.3% 76.1%	75.8% 76.3%
Unknown	70.6%	68.5% 64.1%	69.2% 67.3%	76.5% 74.2%	76.1% 79.9%	76.3% 77.1%
UNKNOWN	10.0%	04.1%	01.3%	14.270	19.9%	11.170
Non-study medication						
ACE-inhibitor or ARB	67.4%	67.6%	67.5%	76.5%	74.8%	75.7%
Aspirin use before screening	70.8%	69.5%	70.1%	76.5% 79.3%	74.6% 78.1%	73.7% 78.7%
Thiazide or related diuretic	68.9%	67.7%	68.3%	79.3% 76.3%	74.9%	76.7% 75.7%

	Aspi	rin Randomiz	ation	Omega-	3 FAs Rando	mization
	Active	Placebo	Overall	Active	Placebo	Overall
Baseline Characteristic	(n =7740)	(n=7740)	(n=15,480)	(n=7740)	(n=7740)	(n=15,480)
Calcium channel blocker	67.5%	67.1%	67.3%	76.8%	76.5%	76.7%
Statin	69.7%	68.2%	68.9%	76.9%	76.6%	76.7%
Total cholesterol (mmol/L)						
<4	71.1%	69.4%	70.3%	78.6%	78.4%	78.5%
≥4 <5	69.2%	68.3%	68.8%	77.1%	76.9%	76.9%
≥5	64.1%	65.2%	64.7%	72.3%	71.1%	72.2%
Not available	65.9%	65.4%	65.7%	73.1%	71.9%	72.5%
HDL cholesterol (mmol/L)						
<1	80.7%	80.6%	80.7%	89.5%	87.9%	88.7%
≥1<1.5	68.7%	68.1%	68.4%	78.9%	76.9%	77.9%
≥1.5	69.6%	70.1%	69.8%	77.7%	76.8%	77.2%
Not available	65.9%	65.5%	65.7%	73.1%	72.0%	72.6%
Non-HDL cholesterol (mmol/L)						
Non ribe diolesterol (milowe)						
<2.5	70.8%	70.2%	70.5%	78.9%	78.3%	78.6%
≥2.5 <3.5	70.3%	68.1%	69.2%	77.0%	77.8%	77.4%
≥3.5	64.6%	65.5%	65.1%	74.1%	72.3%	73.2%
Not available	65.9%	65.5%	65.7%	73.1%	72.0%	72.6%
Glycosylated haemoglobin - HbA1c						
(IFCC mmol/mol (DCCT %))	60.20/	67.40/	60 40/	70.40/	76 40/	77 40/
<48 (6.5) ≥48 (6.5), <64 (8.0)	69.3% 69.9%	67.4% 69.7%	68.4% 69.8%	78.1% 77.1%	76.1% 78.3%	77.1% 77.7%
≥48 (0.5), <64 (8.0) ≥64 (8.0)	67.9%	66.6%	67.3%	77.1% 75.1%	76.3% 74.8%	74.9%
Not available	65.9%	65.5%	65.7%	73.1%	71.9%	72.5%
. 101 47443	00.070	00.070	00 /0	. 61.1,6		. 2.0 / 0
CKD-EPI estimated GFR						
(ml/min/1.73m2) §						
≥90	62.1%	61.5%	61.8%	71.8%	70.7%	71.2%
≥60<90	67.8%	67.4%	67.6%	76.9%	76.2%	76.6%
<60 Not available	72.4%	70.9%	71.6%	78.4%	79.0%	78.7%
Not available	65.7%	65.5%	65.7%	73.1%	71.9%	72.5%
Urinary albumin:creatinine ratio						
(mg/mmol)						
(g ,)	69.9%	68.8%	69.4%	77.3%	77.3%	77.3%
≥3	64.6%	65.2%	64.9%	75.6%	75.11%	75.4%
Not available	65.8%	65.4%	65.6%	73.1%	71.7%	72.4%
Townsend Deprivation Index						
<-3	68.8%	67.7%	68.2%	77.7%	75.8%	76.7%
≥-3<0	68.9%	68.2%	68.5%	76.1%	75.7%	75.9%
≥0<2 ≥2<4	68.6% 64.3%	68.2%	68.4%	74.5% 70.5%	75.9% 72.5%	75.1% 71.5%
≥2<4 ≥4<6	64.3%	63.1% 63.1%	63.7% 63.7%	70.5% 71.7%	72.5% 70.9%	71.5% 71.3%
≥4<0	59.9%	63.5%	61.9%	69.7%	66.9%	68.4%
Unknown	60.5%	82.5%	70.8%	70.9%	72.6%	71.7%
		,-				
Ethnic origin						
White	68.1%	67.4%	67.8%	75.8%	75.2%	75.5%
Indian/Pakistani/Bangladeshi	71.9%	65.6%	68.8%	73.5%	78.3%	75.9%
African/Caribbean	55.0%	57.8%	56.4%	57.9%	68.0%	62.9%
Other/unknown	67.4%	67.6%	67.5%	73.2%	72.9%	73.1%

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blockers; DCCT = Diabetes Control and Complications Trial; FA = Fatty acids; GFR = Glomerular Filtration Rate; HDL=High-density lipoprotein; IFCC =International Federation of Clinical Chemistry; IQR = Interquartile range; SD = Standard Deviation

Criteria used to define definite or probable adherence:

Definitely adherent = participant reported taking treatment every- or most days during the follow-up period.

^{*}The presence of type 2 diabetes was based on a broad clinical definition involving the participant's age at the diagnosis of diabetes, the use of insulin within one year after diagnosis, and the body-mass index.

[†] From blood and urine consent forms, generally before randomization.

[‡] The body-mass index (the weight in kilograms divided by the square of the height in metres) was based on values for height and weight the participants reported on their randomization questionnaires.

[§] Calculated from blood cystatin c concentration using the CKD-EPI formula (Inker LA, Schmid CH, Tighiouart H, et al. Estimating Glomerular Filtration Rate from Serum Creatinine and Cystatin C. New England Journal of Medicine 2012; 367(1): 20-9)

Probably adheren treatment within th	nt = participant was ne last seven months	previously s.	adherent,	is still	receiving	medication	and ha	as not	reported	stopp

Table S8 Reasons for Stopping Treatment – All Randomized ASCEND Participants

			Aspirin Rar	ndomization)			On	nega-3 FAs F	Randomiza	tion		
		tive		ebo		erall	Active		Plac			rall	
Reasons for Stopping Treatment	(n=7	740)	(n =7	7740)	(n=15	(n=15,480)		(n=7740)		(n=7740)		(n=15,480)	
Participant wishes	1372	(35.8%)	1424	(36.4%)	2796	(36.1%)	1755	(61.0%)	1778	(60.5%)	3533	(60.7%)	
Minor bleeding/bruising	115	(3.0%)	72	(1.8%)	187	(2.4%)	8	(0.3%)	4	(0.1%)	12	(0.2%)	
Major Bleeding	42	(1.1%)	24	(0.6%)	66	(0.9%)	8	(0.3%)	7	(0.2%)	15	(0.3%)	
Aspirin or anti-platelet therapy prescribed by a doctor (clear indication)	630	(16.5%)	748	(19.1%)	1378	(17.8%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	
Aspirin or anti-platelet therapy prescribed by a doctor (no clear indication)	257	(6.7%)	241	(6.2%)	498	(6.4%)	0	(0.0%)	0	(0.0%)	0	(0.0%)	
Other contraindicated drugs started	249	(6.5%)	267	(6.8%)	516	(6.7%)	15	(0.5%)	12	(0.4%)	27	(0.5%)	
Upper GI symptoms/diagnoses/procedures	195	(5.1%)	205	(5.2%)	400	(5.2%)	88	(3.1%)	81	(2.8%)	169	(2.9%)	
Lower GI symptoms/diagnoses/procedures	74	(1.9%)	50	(1.3%)	124	(1.6%)	55	(1.9%)	84	(2.9%)	139	(2.4%)	
Respiratory or cardiovascular	16	(0.4%)	23	(0.6%)	39	(0.5%)	11	(0.4%)	18	(0.6%)	29	(0.5%)	
symptoms/diagnoses/procedures		, ,		` ,		, ,		` ,		,		, ,	
GU symptoms/diagnoses/procedures	13	(0.3%)	13	(0.3%)	26	(0.3%)	11	(0.4%)	14	(0.5%)	25	(0.4%)	
Skin symptoms/diagnoses/procedures	17	(0.4%)	14	(0.4%)	31	(0.4%)	14	(0.5%)	9	(0.3%)	23	(0.4%)	
Other symptoms/diagnoses/procedures	312	(8.2%)	341	(8.7%)	653	(8.4%)	305	(10.6%)	333	(11.3%)	638	(11.0%)	
Administrative reasons (e.g. moved abroad)	237	(6.2%)	257	(6.6%)	494	(6.4%)	279	(9.7%)	266	(9.1%)	545	(9.4%)	
Other miscellaneous	32	(0.8%)	22	(0.6%)	54	(0.7%)	34	(1.2%)	33	(1.1%)	67	(1.2%)	
Does not have diabetes	23	(0.6%)	29	(0.7%)	52	(0.7%)	23	(0.8%)	21	(0.7%)	44	(0.8%)	
Medical advice other	192	(5.0%)	150	(3.8%)	342	(4.4%)	177	(6.1%)	188	(6.4%)	365	(6.3%)	
Difficulties swallowing tablets	14	(0.4%)	14	(0.4%)	28	(0.4%)	73	(2.5%)	72	(2.5%)	145	(2.5%)	
Difficulties getting tablets out of blister pack	38	(1.0%)	21	(0.5%)	59	(0.8%)	23	(0.8%)	18	(0.6%)	41	(0.7%)	
Total stopped for any reason	3828	(49.5%)	3915	(50.6%)	7743	(50.0%)	2879	(37.2%)	2938	(38.0%)	5817	(37.6%)	

FAs=Fatty Acids; GI=Gastrointestinal; GU=Genitourinary. Reasons were ascertained from free text on questionnaires or following a telephone call to the participant or their managing doctor. The predominant reason was recorded with adverse events taking priority over patient wishes or administrative reasons. Percentages represent the proportion of the total number of participants who stopped treatment for each reason in each column, except for the total row, which represents the proportion of the total population who stopped for any reason. Percentages may not total 100 because of rounding.

Table S9 Heterogeneity of Baseline Characteristics between VFQ Responders and Non-Responders of among those who were Eligible to be sent the VFQ (n=11,301)

		be sent the VFQ	
Pagalina Charactaristis	Responders (8846)*	Non-responders	D Values !
Baseline Characteristic		(n=2455)	P Values†
Age at randomization (years)			
Mean (SD)	62.5±8.3	62.8±9.0	P=0.11
<60	3339 (37.7%)	901 (36.7%)	1 -0
≥60<70	3860 (43.6%)	1024 (41.7%)	
≥00<70 ≥70	1647 (18.6%)	` ,	P<0.001
270	1647 (18.6%)	530 (21.6%)	P<0.001
Sex			
Male	5529 (62.5%)	1550 (63.1%)	
Female	3317 (37.5%)	905 (36.9%)	P = 0.58
	` ,	,	
Type of diabetes	550 (0.00()	400 (5.00()	
Type 1	559 (6.3%)	138 (5.6%)	D 0.00
Гуре 2	8287 (93.7%)	2317 (94.4%)	P = 0.22
Ouration of diabetes (years)			
Median (IQR)	7(3-12)	7 (4-13)	P=0.02
≥0<5 years	2918 (33.0%)	751 (30.6%)	
≥5<10 years	2544 (28.8%)	690 (28.1%)	
≥10<20 years	1952 (22.1%)	552 (22.5%)	
≥20 years	1020 (11.5%)	313 (12.7%)	P<0.001
Jnknown	412 (4.7%)	149 (6.1%)	. 30.001
	(,0)	(===,0)	
Diabetes management			
Diet only	1508 (17.0%)	396 (16.1%)	
Oral hypoglycaemic agent(s) only	5166 (58.4%)	1416 (57.7%)	
nsulin+/- oral hypoglycaemic agents	2172 (24.6%)	643 (26.2%)	P = 0.20
Participant raparted dishetis ratin spath.			
Participant-reported diabetic retinopathy /es	1628 (18.4%)	537 (21.9%)	
ves No	7151 (80.8%)	1895 (77.2%)	P<0.001
Jnknown	67 (0.8%)	23 (0.9%)	1 <0.001
STRATOWN	(0.070)	20 (0.070)	
Participant-reported treatment for hypertension			
Yes	5386 (60.9%)	1534 (62.5%)	
No	3405 (38.5%)	904 (36.8%)	P = 0.14
Jnknown	55 (0.6%)	17 (0.7%)	
0			
Systolic blood pressure (mmHg)			
	105.0.11.0	420.2.45.2	D 0.04
Mean (SD)	135.8±14.9	136.3±15.2	P = 0.21
<130	2023 (22.9%)	522 (21.3%)	
≥130<140 >140	1822 (20.6%)	491 (20.0%)	P = 0.82
≥140 Jnknown	2626 (29.7%) 2375 (26.8%)	720 (29.3%) 722 (29.4%)	P = 0.82
ווייטוואווכ	2375 (26.8%)	722 (29.4%)	
Diastolic blood pressure			
mmHg)			
Mean (SD)	77.4±9.2	77.0±9.6	P=0.11
<75	2371 (26.8%)	650 (26.5%)	
≥75 <85	2788 (31.5%)	753 (30.7%)	
285	1311 (14.8%)	326 (13.3%)	P=0.41
Jnknown	2376 (26.9%)	726 (29.6%)	
Body mass index			
body mass index (kg/m²)			
Mean (SD)	30.6±6.1	30.9±6.3	P = 0.13
325	1313 (14.8%)	309 (12.6%)	. = 0.10
25, <30	3230 (36.5%)	901 (36.7%)	
:30<35	2429 (27.5%)	688 (28.0%)	
:35	1619 (18.3%)	472 (19.2%)	P = 0.05
Jnknown	255 (2.9%)	85 (3.5%)	1 = 0.03
	200 (2.070)	(0.070)	
Digarette smoking			
	FEE (C 20/)	224 (9.1%)	1
Current	555 (6.3%)		
	3947 (44.6%)	1133 (46.2%)	
Current			P<0.001

	Fligible to b	e sent the VFQ	
	Responders (8846)*	Non-responders	
Baseline Characteristic	,	(n=2455)	P Values†
Non-study medication			
ACE inhibitor or ARB	5115 (57.8%)	1461 (59.5%)	P = 0.05
Aspirin use before screening	3157 (35.7%)	879 (35.8%)	P = 0.93
Thiazide or related diuretic	1639 (18.5%)	465 (18.9%)	P = 0.66
Calcium channel blocker	2088 (23.6%)	605 (24.6%)	P = 0.30
Statin	6769 (76.5%)	1862 (75.8%)	P = 0.50
Total cholesterol			
(mmol/L)			
Mean (SD)	4.1±0.9	4.1±0.9	P = 0.97
<4	2681 (30.3%)	704 (28.7%)	
≥4 <5	2246 (25.4%)	595 (24.2%)	
≥5	817 (9.2%)	226 (9.2%)	P = 0.83
Not available	3102 (35.1%)	930 (37.9%)	
HDL cholesterol			
(mmol/L)			
Mean (SD)	1.3±0.4	1.3±0.4	P=0.02
<1	1222 (13.8%)	343 (14.0%)	. 5.52
≥1<1.5	3202 (36.2%)	870 (35.4%)	
≥1.5	1310 (14.8%)	307 (12.5%)	P=0.07
Not available	3112 (35.2%)	935 (38.1%)	
		,	
Non-HDL cholesterol			
(mmol/L)		0.0.00	D 0.00
Mean (SD)	2.9±0.8	2.9±0.8	P=0.30
<2.5	2053 (23.2%)	505 (20.6%)	
≥2.5 <3.5 ≥3.5	2558 (28.9%)	716 (29.2%)	D 044
Not available	1123 (12.7%)	299 (12.2%) 935 (38.1%)	P = 0.14
Not available	3112 (35.2%)	933 (30.1%)	
Glycosylated haemoglobin - HbA1c			
IFCC (mmol/mol) mean (SD)	54.0±12.2	55.6±13.5	P<0.001
DCCT (%) mean (SD)	7.1±1.1	7.2±1.2	P<0.001
<48 (6.5)	1957 (22.1%)	496 (20.2%)	
≥48 (6.5), <64 (8.0)	2792 (31.6%)	697 (28.4%)	
≥64 (8.0)	990 (11.2%)	332 (13.5%)	P<0.001
Not available	3107 (35.1%)	930 (37.9%)	
CKD-EPI estimated GFR			
(ml/min/1.73m²)			
Mean (SD)	87.8±19.8	84.8±20.4	P<0.001
≥90	2902 (32.8%)	671 (27.3%)	
≥60<90	2299 (26.0%)	659 (26.8%)	
<60	540 (6.1%)	194 (7.9%)	P<0.001
Not available	3105 (35.1%)	931 (37.9%)	
Urinary albumin:creatinine ratio			
(mg/mmol) ‡			
Median (IQR)	0.50 (0.00-1.14)	0.59 (0.16-1.40)	P<0.001
<3	5120 (57.9%)	1313 (53.5%)	
≥3	613 (6.9%)	197 (8.0%)	P=0.01
Not available	3113 (35.2%)	945 (38.5%)	
Townsend Deprivation Index			
<-3	3101 (35.1%)	764 (31.1%)	
≥-3<0	3588 (40.6%)	930 (37.9%)	
≥0<2	1071 (12.1%)	364 (14.8%)	1
≥2<4	625 (7.1%)	244 (9.9%)	1
≥4<6	323 (3.7%)	112 (4.6%)	
≥6	118 (1.3%)	37 (1.5%)	P<0.001
Unknown	20 (0.2%)	4 (0.2%)	
Ethnic origin			
White	8564 (96.8%)	2346 (95.6%)	
Indian/Pakistani/Bangladeshi	107 (1.2%)	39 (1.6%)	1
African/Caribbean	54 (0.6%)	29 (1.2%)	
Other/unknown	121 (1.4%)	41 (1.7%)	P<0.001
OCCT = Diabetes Control and Complications	\ /	\ /	

DCCT = Diabetes Control and Complications Trial; FAs = Fatty acids; GFR = Glomerular Filtration Rate; HDL=High-density lipoprotein; IFCC =International Federation of Clinical Chemistry; IQR = Interquartile range; SD = Standard Deviation Figures presented are counts with percentages unless otherwise stated.

*Out of 8846 VFQ respondents, 7 answered a bespoke first page of questions that sought incident eye diagnoses but did not complete the NEI-VFQ-25, and 8839 completed both parts of the form. Separate analyses of the baseline characteristics for the 8839 NEI-VFQ-25 respondents have not been performed because it is unlikely that excluding those 7 participants would make meaningful differences to the average results.

†Formal testing for differences in baseline characteristics between those included in and excluded from the analysis cohort used the Chi-squared test for heterogeneity for categorical variables and grouped continuous variables (including age, duration of diabetes, systolic blood pressure, diastolic blood pressure, body mass index, total cholesterol, HDL-cholesterol, non-HDL cholesterol, HbA1c, eGFR and urinary albumin:creatinine ratio), the Mantel-Haenszel Chi-square test for trend for ordinal variables (i.e. Townsend Deprivation Index), and the t-test or Wilcoxon-Mann-Whitney U test for continuous variables with a normal (summarised by mean±SD) or non-normal (summarised by median and interquartile range) distribution respectively. Categories that were "unknown" or "not available" were excluded.

Percentages may not total 100 because of rounding

Table S10 Duration Follow-up in the Visual Function Questionnaire Respondents

	Aspirin Rand	lomization	Omega-3 FAs Ra	ndomization	
	Active	Placebo	Active	Placebo	Overall
	(n=4447)	(n=4399)	(n=4417)	(n=4429)	(n=8846)
Mean(SD) length of follow-up (years)	7.5 (1.4)	7.5 (1.4)	7.5 (1.4)	7.5 (1.4)	7.5 (1.4)
Median (IQR) length of follow-up (years)	7.3 (6.4-8.3)	7.3 (6.4-8.3)	7.3 (6.4-8.7)	7.3 (6.4-8.2)	7.3 (6.4-8.3)
Mean (SD) time from randomization to	8.6 (1.4)	8.6 (1.4)	8.6 (1.4)	8.6 (1.4)	8.6 (1.4)
completing the VFQ (years) Median (IQR) time from randomization	8.3 (7.5-9.5)	8.4 (7.5-9.6)	8.4 (7.5-9.6)	8.3 (7.5-9.5)	8.4 (7.5-9.5)
to completing the VFQ (years)	,	, ,	,	,	` '

FAs=Fatty Acids; IQR=Interquartile range; SD=Standard deviation; VFQ= Visual Function Questionnaire

Table S11 Reported Definite or Probable Adherence with Study Treatment Stratified by Years Post-Randomization – Visual Function Questionnaire Respondents

	Asp	irin Randomiza	ition	Omega	a-3 FAs Randomiza	ation
	Active (%)	Placebo (%)	Overall (%)	Active (%)	Placebo (%)	Overall (%)
Years post-						
randomization						
<3	89.3%	90.3%	89.5%	93.8%	93.2%	93.5%
≥3<5	78.2%	78.3%	78.2%	87.8%	86.9%	87.4%
≥5<7	70.5%	70.6%	70.5%	83.8%	82.6%	83.2%
≥7	62.9%	64.0%	63.5%	79.6%	78.4%	79.0%
All	79.3%	79.3%	79.3%	88.4%	87.5%	87.9%

FAs=Fatty Acids.

Criteria used to define definite or probable adherence:

- Definitely adherent = participant reported taking treatment every or most days during the follow-up period.
- Probably adherent = participant was previously adherent, is still receiving medication and has not reported stopping treatment within the last seven months.

Table S12 Use of Anti-platelet or Anti-coagulant Therapy in the Aspirin Arm during Follow-Up – Visual Function Questionnaire Respondents

		Aspi	rin Randomization		
		Active (n=4447)		Placel	oo (n=4399)
	Study aspirin	Study aspirin or non-study anti- platelet	Study aspirin or non-study anti-platelet agent or anti- coagulant	Non-study anti- platelet	Non-study anti-platelet agent or anti- coagulant
Years post-randomization					
<3	89.5%	92.1%	92.5%	3.3%	3.8%
≥3<5	78.2%	84.6%	86.2%	7.3%	8.9%
≥5<7	70.5%	79.4%	81.9%	9.8%	12.9%
≥7	63.5%	75.9%	78.7%	12.6%	16.4%
All	79.3%	85.5%	86.9%	6.9%	8.6%

Table S13 Study Average Reported Definite or Probable Adherence in each Treatment Arm, Overall and by Baseline Characteristics – Visual Function Questionnaire Respondents

		rin Randomiz			-3 FAs Rando	
B 11 01 1 1 1	Active	Placebo	Overall	Active	Placebo	Overall
Baseline Characteristic	(n =4447)	(n=4399)	(n=8846)	(n=4417)	(n=4429)	(n=8846)
Age at randomization						
(years) <60	82.7%	82.3%	82.5%	89.1%	88.8%	88.9%
<00 ≥60<70	77.9%	79.3%	78.6%	88.2%	87.4%	87.8%
≥70	74.9%	73.6%	74.3%	87.1%	84.9%	86.0%
=10	7 4.5 70	70.070	7 7.0 /0	37.170	04.070	00.070
Sex						
Male	80.3%	80.8%	80.5%	89.8%	89.4%	89.6%
Female	77.6%	77.2%	77.4%	86.1%	84.3%	85.2%
Type of diabetes*						
Type 1	82.4%	81.3%	81.9%	89.7%	88.3%	89.1%
Type 2	79.0%	79.3%	79.2%	88.3%	87.4%	87.9%
Duration of diabetes (years)						
≥0<5 years	80.9%	80.5%	80.7%	89.4%	88.4%	88.9%
≥5<10 years	77.6%	78.8%	78.2%	87.7%	85.7%	86.7%
≥10<20 years	79.5%	79.4%	79.4%	88.6%	88.8%	88.7%
≥20 years	79.7%	79.2%	79.5%	88.3%	87.8%	88.0%
Unknown	76.3%	76.3%	76.3%	85.2%	85.5%	85.3%
Diabetes management				22.20/		
Diet only	76.6%	78.3%	77.5%	88.8%	84.4%	86.5%
Oral hypoglycaemic agent(s) only	79.9%	79.3%	79.6%	88.2%	88.3%	88.3%
Insulin +/- oral hypoglycaemic agent(s)	79.4%	80.6%	79.9%	88.5%	87.8%	88.2%
Participant-reported diabetic retinopathy						
Yes	77.5%	79.1%	78.3%	88.5%	87.9%	88.2%
No	79.6%	79.6%	79.6%	88.4%	87.4%	87.9%
Participant-reported treatment for hypertension Yes No	78.2% 80.8%	79.1% 79.9%	78.6% 80.3%	88.3% 88.5%	87.3% 87.8%	87.8% 88.2%
Systolic blood pressure						
(mmHg) † <130	79.4%	80.8%	80.1%	88.5%	88.0%	88.2%
<130<140 ≥130<140	81.9%	79.0%	80.1%	89.7%	88.4%	89.1%
≥140	78.0%	79.2%	78.6%	88.5%	88.2%	88.3%
Unknown	78.6%	78.9%	78.8%	87.2%	85.6%	86.4%
						- · ·
Diastolic blood pressure (mmHg) †	70.00	70.467	70.467	07.50	07.407	07.55
<75 >75 <85	78.2%	78.1% 80.4%	78.1% 80.6%	87.5%	87.1%	87.3%
≥75 <85 ≥85	80.8% 79.4%	80.4% 80.7%	80.6% 80.1%	89.7% 89.3%	88.5% 89.7%	89.1% 89.5%
≥oo Unknown	79.4% 78.6%	78.9%	78.7%	87.3%	85.6%	86.4%
	7 3.0 /0	10.070	10.170	07.070	00.070	JJ. 7/0
Body mass index						
(kg/m²) ‡	00.50/	04.50/	00.007	00.007	00.007	00.007
<25	80.5%	81.5%	80.9%	89.6%	88.0%	88.8%
≥25, <30	78.4%	79.9%	79.1%	88.3%	87.7%	88.0%
≥30<35 >35	79.9% 79.1%	79.3% 77.4%	79.6% 78.3%	88.1%	88.4% 85.0%	88.2% 87.1%
≥35 Unknown	79.1% 76.5%	77.4% 80.4%	78.3% 78.6%	88.2% 86.1%	85.9% 73.6%	87.1% 80.5%
Unknown	70.5%	80.4%	78.6%	00.176	13.0%	00.5%
Cigarette smoking						
Current	77.4%	78.2%	77.8%	85.3%	86.7%	86.1%
Former	78.5%	79.5%	78.9%	88.4%	88.2%	88.3%
Never	80.1%	79.8%	79.9%	88.8%	86.9%	87.9%
Unknown	83.4%	70.9%	76.9%	89.6%	87.9%	88.8%
	I			I		

	Aspi	rin Randomiz	ation	Omega-	3 FAs Rando	mization
	Active	Placebo	Overall	Active	Placebo	Overall
Baseline Characteristic	(n =4447)	(n=4399)	(n=8846)	(n=4417)	(n=4429)	(n=8846)
Non-study medication						
ACE-inhibitor or ARB	78.3%	79.7%	79.0%	88.7%	87.7%	88.2%
Aspirin use before screening	80.0%	80.2%	80.1%	90.1%	88.9%	89.6%
Thiazide or related diuretic	78.6%	79.3%	78.9%	88.2%	86.9%	87.5%
Calcium channel blocker	77.7%	77.7%	77.7%	89.2%	87.9%	88.5%
Statin	80.3%	79.9%	80.1%	88.8%	88.2%	88.5%
Total cholesterol (mmol/L)						
<4	80.5%	78.9%	79.7%	88.6%	89.3%	88.9%
≥4 <5	79.6%	79.9%	79.8%	89.9%	87.5%	88.7%
≥5	77.0%	76.7%	76.9%	86.9%	85.3%	86.1%
Not available	78.5%	80.3%	79.4%	87.5%	86.5%	87.0%
HDL cholesterol (mmol/L)						
<1	80.8%	78.7%	79.8%	90.5%	89.8%	90.2%
≥1<1.5	78.8%	78.6%	78.8%	88.7%	87.4%	88.0%
≥1.5	80.5%	80.2%	80.4%	87.9%	87.9%	87.9%
Not available	78.5%	80.3%	79.4%	87.4%	86.6%	86.9%
Non-HDL cholesterol (mmol/L)						
2.5	00.50/	00.00/	00.00/	00.00/	00.00/	00.40/
<2.5 ≥2.5 <3.5	80.5%	80.2%	80.3%	89.3%	88.8%	89.1%
≥2.5 < 5.5	80.2% 77.1%	78.7% 77.6%	79.5% 77.3%	88.9% 88.2%	88.4% 85.6%	88.6% 86.9%
Not available	78.5%	80.3%	77.3 <i>%</i> 79.4%	87.4%	86.6%	86.9%
Not available	70.576	00.570	7 3.4 70	07.470	00.070	00.970
Glycosylated haemoglobin - HbA1c						
(IFCC mmol/mol (DCCT %))						
<48 (6.5)	78.5%	78.5%	78.5%	89.5%	87.2%	88.3%
≥48 (6.5), <64 (8.0)	79.9%	79.4%	79.6%	88.4%	88.7%	88.5%
≥64 (8.0)	81.6%	79.1%	80.3%	88.9%	87.9%	88.5%
Not available	78.5%	80.2%	79.3%	87.5%	86.5%	87.0%
CKD EDI antimata d CED						
CKD-EPI estimated GFR (ml/min/1.73m2) §						
(111/1111/1117/31112) § ≥90	73.1%	71.8%	72.5%	84.3%	83.6%	83.9%
≥60<90	77.4%	77.8%	77.6%	88.4%	87.1%	87.8%
<60	82.5%	81.2%	81.9%	90.0%	89.5%	89.7%
Not available	78.5%	80.3%	79.4%	87.5%	86.5%	87.0%
Urinary albumin:creatinine ratio						
(mg/mmol)						
<3	80.1%	79.6%	79.8%	88.7%	88.3%	88.5%
≥3 Nat available	76.7%	74.2%	75.4%	89.7%	85.9%	87.9%
Not available	78.4%	80.3%	79.4%	87.5%	86.5%	87.0%
Townsend Deprivation Index						
<-3	78.8%	78.8%	78.8%	88.8%	87.7%	88.2%
≥-3<0	78.4%	79.4%	78.9%	87.8%	86.8%	87.3%
≥0<2	81.4%	80.8%	81.1%	88.7%	88.5%	88.6%
≥2<4	81.3%	79.3%	80.3%	87.1%	88.0%	87.6%
≥4<6	82.9%	80.09%	81.9%	92.1%	89.7%	90.9%
≥6	80.3%	78.8%	79.5%	87.6%	86.7%	87.2%
Unknown	74.2%	94.2%	86.1%	99.2%	86.9%	91.9%
Ethnic origin						
Ethnic origin White	79.2%	79.5%	79.3%	88.5%	87.4%	87.9%
Indian/Pakistani/Bangladeshi	79.2% 81.2%	79.5% 78.6%	79.3% 79.9%	83.2%	87.4% 88.8%	86.0%
African/Caribbean	70.2%	80.1%	75.2%	88.3%	91.7%	90.3%
Other/unknown	88.5%	77.0%	82.6%	86.2%	91.4%	88.2%
Other, driving	33.070		02.070	00.270	J 1.470	00.270
			DOOT F			

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blockers; DCCT = Diabetes Control and Complications Trial; FA = Fatty acids; GFR = Glomerular Filtration Rate; HDL=High-density lipoprotein; IFCC =International Federation of Clinical Chemistry; IQR = Interquartile range; SD = Standard Deviation

^{*}The presence of type 2 diabetes was based on a broad clinical definition involving the participant's age at the diagnosis of diabetes, the use of insulin within one year after diagnosis, and the body-mass index.

[†] From blood and urine consent forms, generally before randomization.

[‡] The body-mass index (the weight in kilograms divided by the square of the height in metres) was based on values for height and weight the participants reported on their randomization questionnaires.

§ Calculated from blood cystatin c concentration using the CKD-EPI formula (Inker LA, Schmid CH, Tighiouart H, et al. Estimating Glomerular Filtration Rate from Serum Creatinine and Cystatin C. New England Journal of Medicine 2012; 367(1): 20-9)

Criteria used to define definite or probable adherence:

- Definitely adherent = participant reported taking treatment every or most days during the follow-up period.
- Probably adherent = participant was previously adherent, is still receiving medication and has not reported stopping treatment within the last seven months.

Table S14 Reasons for Stopping Treatment – Visual Function Questionnaire Respondents

			Aspirin Rar	ndomization				Ome	ega-3 FAs	Randomizati	ion	
	Ac	tive	Pla	cebo	Ov	erall	Ac	tive	PI	acebo	0	verall
Reasons for stopping treatment	(n=4	447)	(n =	4399)	(n=8	8846)	(n =	4417)	(n	=4429)	(n=	:8846)
Participant wishes	406	(27.6%)	429	(29.6%)	835	(28.6%)	486	(65.4%)	550	(67.0%)	1036	(66.2%)
Minor bleeding/bruising	59	(4.0%)	46	(3.2%)	105	(3.6%)	4	(0.5%)	3	(0.4%)	7	(0.4%)
Major Bleeding	22	(1.5%)	7	(0.5%)	29	(1.0%)	3	(0.4%)	2	(0.2%)	5	(0.3%)
Aspirin or anti-platelet therapy prescribed by a	347	(23.6%)	381	(26.3%)	728	(24.9%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
doctor (clear indication)		,		,		,		,		,		` ,
Aspirin or anti-platelet therapy prescribed by a	138	(9.4%)	126	(8.7%)	264	(9.0%)	0	(0.0%)	0	(0.0%)	0	(0.0%)
doctor (no clear indication		,		, ,		` ,		,		,		` ,
Other contraindicated drugs started	140	(9.5%)	152	(10.5%)	292	(10.0%)	7	(0.9%)	10	(1.2%)	17	(1.1%)
Upper GI symptoms/diagnoses/procedures	107	(7.3%)	101	(7.0%)	208	(7.1%)	42	(5.7%)	23	(2.8%)	65	(4.2%)
Lower GI symptoms/diagnoses/procedures	37	(2.5%)	26	(1.8%)	63	(2.2%)	27	(3.6%)	40	(4.9%)	67	(4.3%)
Respiratory or cardiovascular	2	(0.1%)	9	(0.6%)	11	(0.4%)	2	(0.3%)	1	(0.1%)	3	(0.2%)
symptoms/diagnoses/procedures		, ,		, ,		, ,		, ,		, ,		, ,
GU symptoms/diagnoses/procedures	5	(0.3%)	6	(0.4%)	11	(0.4%)	4	(0.5%)	6	(0.7%)	10	(0.6%)
Skin symptoms/diagnoses/procedures	8	(0.5%)	6	(0.4%)	14	(0.5%)	4	(0.5%)	3	(0.4%)	7	(0.4%)
Other symptoms/diagnoses/procedures	83	(5.6%)	73	(5.0%)	156	(5.3%)	49	(6.6%)	61	(7.4%)	110	(7.0%)
Administrative reasons (e.g. moved abroad)	3	(0.2%)	4	(0.3%)	7	(0.2%)	2	(0.3%)	5	(0.6%)	7	(0.4%)
Other miscellaneous	4	(0.3%)	7	(0.5%)	11	(0.4%)	6	(0.8%)	6	(0.7%)	12	(0.8%)
Does not have diabetes	13	(0.9%)	17	(1.2%)	30	(1.0%)	8	(1.1%)	14	(1.7%)	22	(1.4%)
Medical advice other	75	(5.1%)	42	(2.9%)	117	(4.0%)	58	(7.8%)	56	(6.8%)	114	(7.3%)
Difficulties swallowing tablets	6	(0.4%)	6	(0.4%)	12	(0.4%)	30	(4.0%)	35	(4.3%)	65	(4.2%)
Difficulties getting tablets out of blister pack	17	(1.2%)	9	(0.6%)	26	(0.9%)	11	(1.5%)	6	(0.7%)	17	(1.1%)
Total stopped for any reason	1472	(33.1%)	1447	(32.9%)	2919	(33.0%)	743	(16.8%)	821	(18.5%)	1564	(17.7%)

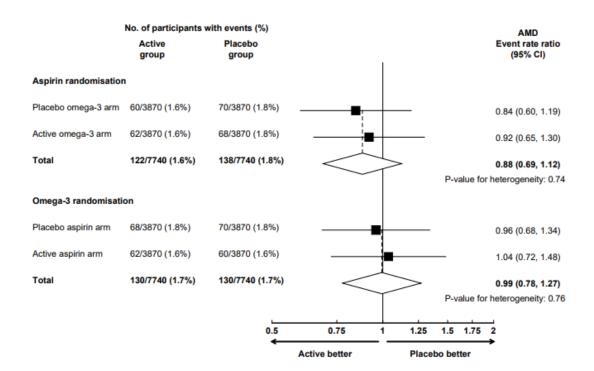
FAs=Fatty Acids; GI=Gastrointestinal; GU=Genitourinary; Reasons were ascertained from free text on questionnaires or following a telephone call to the participant or their managing doctor. The predominant reason was recorded with adverse events taking priority over patient wishes or administrative reasons. Percentages represent the proportion of the total number of participants who stopped treatment for each reason in each column, except for the total row, which represents the proportion of the total population who stopped for any reason. Percentages may not total 100 because of rounding.

Table S15 Source of Age-Related Macular Degeneration Events

	٧	FQ form returned	k		
Confirmed or unrefuted AMD events reported on ASCEND follow-up questionnaires	AMD reported on VFQ	AMD not reported on VFQ	Total	No VFQ	Total
Yes	33	13	46	34	80
No	180	8620	8800	6600	15400
Total	213	13	8846	6634	15480

AMD= Age-Related Macular Degeneration; VFQ=Visual Function Questionnaire

Table S16 Effects of Aspirin and Omega-3 Fatty Acids on Age-Related Macular Degeneration Events Stratified by the Other Treatment in the Factorial Design



ASCEND Follow-Up Questionnaire

	CEND: Follow-	-up Questionna	ire		Need neip con	npleting this fo	THE REAL PROPERTY.	l Events		118 0000 585	7020
STRUCTIONS FOR COMI ase complete the question		ck ink		4.1	Since completing your l	200.00	Service Service			d ANY of the fo	llowing?
ase place a cross in the a					(If Yes, please give the		and tow				
you make a mistake, fill th		he correct box, e.g. Yes	No X)	a)	Heart attack		Yes	No.			
write clearly in the appro	priate boxes, e.g. 2 0	/04/2004			Name and town of hospital				Day	Month.	Year
	1. Contact and	d GP Details		_	attended:		Yes	No			
			please telephone 0800	b)	Admission to hospital any chest pains	with angina or			Say	Month /	Year
vering letter on the front	t of this questionnaire.		ence number from the		Name and town of hospital attended:						
r details: Frederick Jones	Alternative contact Mrs Jane Jones	Dr Roger	Smith	-	Stroke		Yes	No			
he Street	The House Bigtown	The Surg Toytown	gery	cj					Cwy	Month /	Year
hire 1PY	Toyshire WW3 2MM	Toyshire WW2 8X	x		Name and town of hospital attended:						
e Tel.: 01456 789 101 me Tel.: 01456 987654	Tel.: 01234 765432			d)	Ministroke		Yes	No			
10. 10. 01430 307034	* VANC-455600				(sometimes called TIA) Name and town of hospital				Day	Month	Year
	2. ASCEND	The second secon		_	attended:		Yes	No			
Please indicate now reg		ite Tablets Red Capsu	during the last 6 months:	e)	Coronary artery bypa: (CABG or "cabbage")	ss operation			/	Marth /	Year
Every day	(asp	oirin/placebo) (one or other nat	Please cross		Name and town of hospital attended:					100 Table	-0-11
Most days		i i	ONE box only in each column				Yes	No			TT
Only occasion	nally		iii caaii caaiiiii	1)	Coronary angioplasty ("balloon", "stent" inser	tion or PTCA)			Day	Month /	Year
Never					Name and town of hospital attended:						
are you willing to contin	nue taking the white (as	pirin/placebo) ASCEND	tablets?	g)	Other arterial surgery	or angioplasty	Yes	No			888
Yes No				-	(e.g. leg bypass) Name and town of hospital		_		Day	Wanth	Year
If No, please tell us wi				-	attended:		Yes	No			
and a little and	nue taking the red (one o	or other natural oil) ASCE	END capsules?	h)	Cancer (e.g. skin, breas	st, lung, bowel etc)		No			
Yes No					Type of cancer:				Ouy	MUNIT	1100
If No, please tell us w	3. Other Currer	at Madiantian			Name and town of hospital attended:						
On you currently take a		larly (i.e. more than one	day per week\?	_		2005-2010-2010-2010-2010-2	Yes	No			
	nocoumarol (Nicoumalone,		7 11-17	i)	Bleeding for which yo (e.g. serious nose bleed, b Do not include bleeding as a r	u saw a doctor leeding in the eye)			Day	Moreth	Year
or Phenindione	er-the-counter (e.g. Anadin	-	cross ONE		Site in body of bleeding:	esult of an accident.					
Imazin, PostMI). Do not in	nclude your ASCEND stud	ly tablets.	No box only for each		Were you admitted to hospit	-12	Yes	No			
Clopidogrel (Plavix)		Yes L	No question			air.					
Dipyridamole (Persantin,	Persantin Retard or Asasa										
	2		No	Follow	Name and town of hospital attended: up Quest [V2_190504]		3			Reference 123-45	67
5. Othe	pleting this form? Per Serious Illnesses	Please call Freefone or Hospital Admiss	Reference 123-4567	Follow-	attended:	AS	C			Reference 123-45	67
Need help comp 5. Othe If since completing your leadmission to hospital (e.g.	pleting this form? Per Serious Illnesses ast questionnaire on 1 Feb p. pneumonia, day surgery	Please call Freefone or Hospital Admiss	National Statements 123-4567 0800 585323 ions any other serious illness or e) please give details of the	Follow-	attended:	AS A Study of Car	C			ASCEND	(1
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ASCEND-Eye Visual Function Questionnaire

ALDER DESCRIPTIONS TO LUCIOUS PROPERTY	PI PI	D: A129-4567		(2)780/A425-04	04G	ASCEND-EYE: Visual Function Questionnaire
PART 3 – RESPONSES TO VISION PROBLE? The next questions are about how things you do	may be	affected b	y your vis	ion. For e	ach one,	INSTRUCTIONS FOR COMPLETION: Please complete the questionnaire in BLOCK CAPITALS using him or black ink.
please cross the box to indicate whether for you a little, or none of the time.	the state	ement is tr	rue for you	all, mos	t, some.	Please complete the questionnaire in BLOCK CAPITALS using blue or black ink. Please place a cross in the appropriate box, e.g. Yes X No
(please cross ONE box only for EACH question)	All of the time	Most of the time	Some of the time	A little of the time	None of the time	(If you make a mistake, fill the entire box and mark the correct box, e.g. Yes No X)
3.17 Do you accomplish less than you would like because of your vision?						OR write clearly in the appropriate boxes, e.g. 2 6 0 1 2 0 1 7
3.18 Are you limited in how long you can work or do other activities because of your vision?						Please complete all the questions as if you were wearing your classes or contact lenses (if any).
3.19 How much does pain or discomfort in or around						Please answer <u>every</u> question (unless you are asked to skip questions because they don't apply to you).
your eyes, for example, burning, itching or aching, keep you from doing what you'd like to						Participant Name and Address
be doing?					-	Mr Thomas WHITE Form ID: A425-945 24 Raspberry Road, Gardentown Participant Study Ret: A123-456
For each of the following statements, please cro statement is <u>definitely true</u> , <u>mostly true</u> , <u>mostly</u>						Gardenshire, GA3 5TR
(please cross ONE box only for EACH question)	Definitely true	Mostly true	Not sure	Mostly false	Definitely false	2. Eye Events
3.20 I stay home most of the time because of my eyesight.						2.1 Have you had ANY of the following?
3.21 I feel trustrated a lot of the time because of my eyesight.						(If Yes, please give the date you were first diagnosed and the name and fown of the hospital you first attended). Yes No
3.22 I have much less control over what I do.						a) Cataract
because of my eyesight. 3.23 Because of my eyesight, I have to rely too						Name and town of hospital attacked:
much on what other people tell me. 3.24 I need a lot of help from others because of my						b) Age-related macular degeneration
eyesight.						Name and fown of hospital
3.25 I worry about doing things that will embarrass myself or others, because of my eyesight.						attended:
4. Person	al Detai	ls	-			c) Glaucoma
						Name and lown of hospital attended:
I.1 Please reconfirm your date of birth:	/	1 9		V.F		Yes No
Thank you for completing the questionnaire. Please SIGN and DATE the form below using blue	or black	leb	1	1	+	d) Retinal vein thrombosis
	or DIBON	III.				Name and town at hospital attacked:
Signature		Γ		1/2	0	e) Other eye problems
a PRINTED name:	Too	day's date:	-/-	Mostle /	Year	
Please check that you have answered every question, Return the completed questionnaire in the Freepost er	and signe	ed and date	d the form. stamps nee	ided) to:		Name and sown of booptal attended:
Freepost RLUJ-TKES-SURB, ASCEND, Richard Do Headington, Oxford, OX3 7LF					Campus,	Date:
If you have any questions about the study, please cont	act the coo	ordinating or	entre in Oxfo	ord on		
FREEFONE: 0800 585323 (preferably during office ho Thank you for your pa				γ)	_	Pt ID: A123-4667 K2:790:A425-9454G 8th September 2017 +
MODEL EVE VISUAL PLANTAGE COMMUNICATION (C. S.						ACCIDENT THAT THE GARDON (\$1,000)
Need help completing this form? 3. National Eye-institute Visual	_			- Contract	3	Prio Arza-der Romandas-essa Bin Supunee 2017 3.10 Because of your eyesight, how much difficulty do you have noticing objects off to the side whit you are walking along?
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