

# Comparison of baseline characteristics and outcome rates of 15,480 ASCEND trial participants with a matched population of 92,612 people with diabetes and no prior cardiovascular disease

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## Introduction

### The ASCEND (A Study of Cardiovascular Events in Diabetes) trial<sup>1</sup>

- Assessed aspirin and, separately, omega-3 fatty acids in people with diabetes and no prior cardiovascular disease.
- Recruited 15,480 participants in the UK using centrally mailed invitations.
- Used mail-based assessment of eligibility, informed consent, and treatment supply, with telephone support.

### This streamlined design

- Enabled reliable randomised evidence to be generated cost-efficiently, but
- May have recruited a healthy, low risk population.

We used primary care data from the **Clinical Practice Research Datalink (CPRD)** to compare characteristics and outcomes rates in the trial participants with those who could have joined the trial.

## Results

**Table 1: Baseline characteristics for ASCEND participants and the reference CPRD cohort**

	ASCEND (n=15,480)	CPRD (n=92,612)
Female, n (%)	5796 (37.4)	34,776 (37.6)
Age, years (mean (SD))	63.3 (9.2)	63.3 (9.2)
Ethnicity, n (%)		
White	14,935 (96.5)	58,247 (62.9)
South Asian	184 (1.2)	5400 (5.8)
Black African/Caribbean	140 (0.9)	2766 (3.0)
Other	174 (1.1)	1593 (1.7)
Unknown	47 (0.3)	24,606 (26.6)
On aspirin at start of follow-up, n(%)	7740 (50)	23,531 <sup>1</sup> (25.4)
Charlson Comorbidity Index > 0, n(%) <sup>2</sup>	1624 (10.5)	9740 (10.9)
Hospital Frailty Index > 0, n(%) <sup>3</sup>	1770 (11.5)	9678 (10.8)
Deciles of Index of Multiple Deprivation (median (IQR))	6 (4-9)	5 (3-8)

<sup>1</sup> Based on keyword search for "aspirin" in the year prior to selection  
<sup>2,3</sup> For the frailty and comorbidity indices, the percentage is among those with non-missing values (N=15,434 in ASCEND and 89,836 in CPRD).

## Methods

### ASCEND trial participants

- Individuals with diabetes, aged at least 40 years, recruited between 2005 and 2011
- No prior cardiovascular disease, gastrointestinal bleed or peptic ulcer in the previous 6 months, active liver disease, other life-threatening medical problem or anti-coagulant therapy use

**Outcomes** from linked mortality data, Hospital Episode Statistics, and, for ASCEND participants, equivalent data in Scotland and Wales.

### Reference population identified from CPRD (i.e. primary care data from participating practices in England)

- ICD-10, OPCS 4 and READ codes used to reproduce the trial eligibility criteria (as much as possible)
- Age and sex-matched reference cohort selected within each year 2006 to 2011, weighted so distribution by year matched that in ASCEND

## Results

**Table 2: Outcome rates of events in ASCEND participants and the matched CPRD reference cohort**

	ASCEND (n=15,436) <sup>1</sup>			CPRD (n=92,612)		
	Number of events	Rate	(95% CI)	Number of events	Rate	(95% CI)
Serious vascular events	1127	99	(93-105)	8407	127	(124-129)
Serious vascular events excluding TIA	1026	90	(85-96)	7806	118	(115-120)
Any arterial revascularisation	736	65	(60-69)	4723	71	(69-73)
Major bleed	599	53	(48-57)	4254	64	(62-66)

Serious vascular event = Primary outcome (cardiovascular death, stroke, transient ischaemic attack (TIA), myocardial infarction, excluding intracranial haemorrhage)<sup>1</sup> Limited to participants in England, Wales and Scotland. Rates are per 10 000 person years

- ASCEND participants were less deprived and more likely to be of white ethnicity (Table 1)
- Few individuals had significant comorbidities or evidence of frailty in either cohort (Table 1)
- Serious vascular event rates were higher in the CPRD cohort (Table 2)
- Arterial revascularisation and major bleed rates were similar in the two cohorts (Table 2)

### References

- The ASCEND Study Collaborative Group. Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus. *N Engl J Med* 2018;379:1529-1539
- Gilbert T, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. *Lancet*. 2018;391(10132):1775-1782
- Quan H, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. *Med Care*. 2005;43(11):1130-9

## Discussion

- Prevalence of comorbidities and frailty was low in both the ASCEND and the age and sex matched reference CPRD cohort.
- The ASCEND trial, using mail-based recruitment, did not select a population at substantially lower risk than the reference population, but trial participants were less deprived and more likely to be of white ethnicity.
- Healthcare datasets, such as CPRD, provide a method of comparing outcome rates in trials with those in the target population.

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