

Arrhythmia outcome definitions

and comparisons between self-reported and hospital episode data

Additional data for death and hospitalisations were obtained from NHS Digital, the NHS Wales Informatics Service, and the Information Services Division of NHS Scotland. Data on hospitalisations were available for a mean of 14 years before randomization and throughout the study treatment period.

ICD-10 (International Classification of Diseases, 10th revision) diagnoses and OPCS-4 (OPCS Classification of Interventions and Procedures version 4) codes recorded during any admissions to an NHS hospital from the Hospital Episodes Statistics (HES) dataset and ICD-10 codes recorded on the death record were used to define atrial fibrillation (AF, which included atrial flutter) and non-fatal ventricular arrhythmia (VA) which included resuscitated cardiac arrest but excluded events occurring on the day of death (Table 1). VAs were restricted to non-fatal events because we could not reliably ascertain all such arrhythmias contributing to death, and it was not possible to determine which cardiac arrests without resuscitation had involved an arrhythmia; all AFs recorded were non-fatal. (Information was not available from primary care records, so any diagnoses of an arrhythmia by a participant's general practitioner without admission to hospital would only be captured if the participant reported it.)

The presence of any relevant diagnoses or procedures in HES records prior to the date of randomization was used to define prior history of AF (which was not recorded at baseline). The HES records can provide evidence of incident acute arrhythmias (ventricular arrhythmias) but only evidence of the presence of chronic arrhythmias (AFs) because admission records typically include several diagnoses and it is not

possible to determine reliably which diagnosis was the cause of the admission. The arrhythmic outcomes defined were therefore: AF onset among participants without known AF at randomization; and the first recorded incidence of non-fatal VA. Onset of AF was defined as the first occurrence of one of the relevant codes (Table 1) in post-randomization HES or death records (in any diagnostic position) or a reported hospitalisation or serious event of AF in the trial among participants without prior history of AF. A relevant code (Table 1) in any diagnostic position within a post-randomization HES episode or a hospitalisation or serious event reported in the trial with survival to the next day was regarded as evidence of non-fatal ventricular arrhythmia.

Numbers of arrhythmias in electronic records versus reported in trial

Prior AF was recorded in 106 participants. Among the remaining 15 374 participants new onset of AF was identified in 1121 participants in HES, compared to 287 by self-report, including 231 reported in both, giving a total of 1177 from either source (Table 2, Figure 1). A VA was identified in 132 participants in HES, in only 12 in the trial data including 9 with a report in both sources yielding 135 in total.

Frequency of hospitalisation

The frequency of hospitalisation for a diagnosis other than an arrhythmia (providing the opportunity for incidental diagnosis of AF) was similar in the two treatment groups: 71% of participants in each treatment arm had a hospital episode prior to randomization for a non-arrhythmia diagnosis and the median (inter-quartile range) of the number of episodes was 1 (0-3) in each arm; three-quarters of participants (75.9% allocated omega-3 FA vs. 75.5% allocated placebo), had at least one such

hospitalisation post-randomization and the number of episodes of hospitalisation (median 2, inter-quartile range 1-5) and time to first hospitalisation were similar in the two treatment groups (rate ratio 1.005, 95% CI, 0.97,1.04).

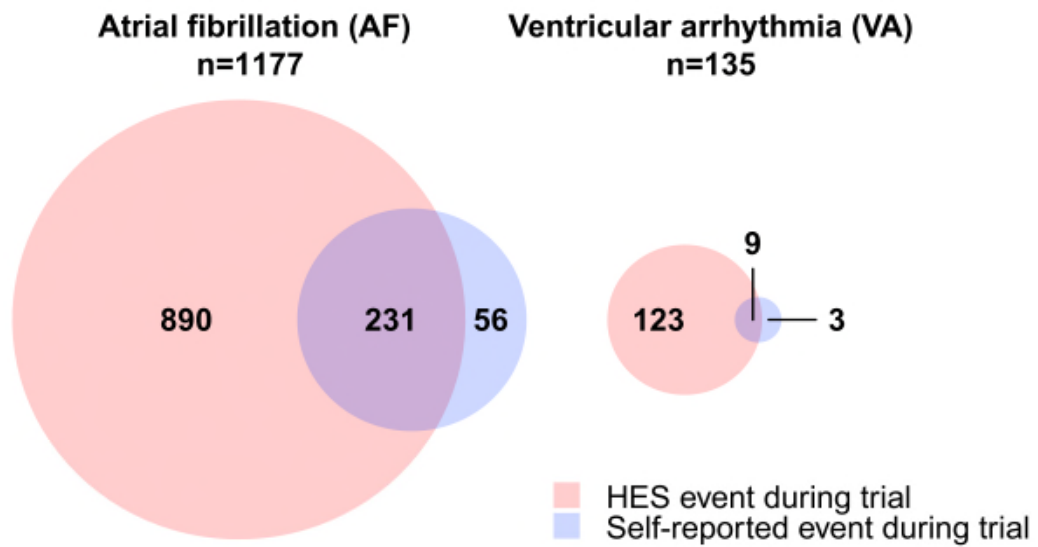
Table 1. International Classification of Disease (ICD-10) and OPCS Classification of Interventions and Procedures (OPCS-4) codes used for arrhythmia definitions

Code type	Code	Description
Non-fatal ventricular arrhythmia		
ICD10	I46.0	Cardiac arrest with successful resuscitation
	I46.9	Cardiac arrest, unspecified
	I47.0	Re-entry ventricular arrhythmia
	I47.2	Ventricular tachycardia
	I49.0	Ventricular fibrillation and flutter
OPCS4	K57.6	Percutaneous transluminal ablation of ventricular wall NEC
	K64.1	Percutaneous radiofrequency ablation of epicardium
	X50.3	Advanced cardiac pulmonary resuscitation
	X50.4	External ventricular defibrillation
	X50.8	Other specified external resuscitation
	X50.9	Unspecified external resuscitation
Atrial fibrillation		
ICD10	I48	Atrial fibrillation or flutter
	I48.0	Paroxysmal atrial fibrillation
	I48.1	Persistent atrial fibrillation
	I48.2	Chronic atrial fibrillation
	I48.3	Typical atrial flutter
	I48.4	Atypical atrial flutter
	I48.9	Unspecified
OPCS4	K22.3	Exclusion of left atrial appendage NEC
	K57.1	Percutaneous transluminal ablation of atrioventricular node
	K62.1	Percutaneous transluminal ablation of pulmonary vein to left atrium conducting system
	K62.2	Percutaneous transluminal ablation of atrial wall for atrial flutter
	K62.3	Percutaneous transluminal ablation of conducting system of heart atrial flutter NEC
	K62.4	Percutaneous transluminal internal cardioversion NEC
	X50.1	Direct current cardioversion
	X50.2	External cardioversion NEC

Table 2. Numbers of participants with post-randomization arrhythmia events from self-report and Hospital Episode Statistics data

Arrhythmia category	Self-reported event among all individuals			Self-reported event in individuals with no pre-randomization events of this type		
	Yes	No	Total	Yes	No	Total
Atrial fibrillation (AF)						
No HES linkage	8	388	396	8	388	396
AF event from HES record in any position	244	938	1182	231	890	1121
No AF event from HES record post randomization	49	13853	13902	48	13809	13857
Total	301	15179	15480	287	15087	15374
Non-fatal ventricular arrhythmia (VA)						
No HES linkage	1	395	396	1	395	396
VA event from HES record in any position	9	123	132	9	123	132
No VA event from HES record post randomization	2	14950	14952	2	14943	14945
Total	12	15468	15480	12	15461	15473

HES=hospital episode statistics. The number of participants with onset of AF is the 1121 with an onset of AF in HES (ie those with an event in HES during the trial but no pre-randomization AF), plus the 287 with a self-reported onset of AF in trial, minus the 231 with both HES and self-report. The number with non-fatal VA is the 132 HES events among all participants, plus the 12 self-reported events in trial, minus the 9 events with both HES and self-report, giving 135 in total.



Number of participants with events

Among participants with no report of pre-randomization AF:

AF reported in trial	287	Non-fatal VA reported in trial	12
AF in HES	1121	Non-fatal VA in HES	132
Any onset of AF	1177	Any non-fatal VA	135

Figure 1. Numbers of participants with post randomization arrhythmia events from self-report and Hospital Episode Statistics data. Venn diagrams showing the overlap between events recorded in the Hospital Episode Statistics (red circles) and the ASCEND trial events (blue circles) for onset of AF and non-fatal VA. Eight of the AF events and one of the VA events recorded in the trial but not in HES were in participants without HES linkage.