Supplementary Online Content

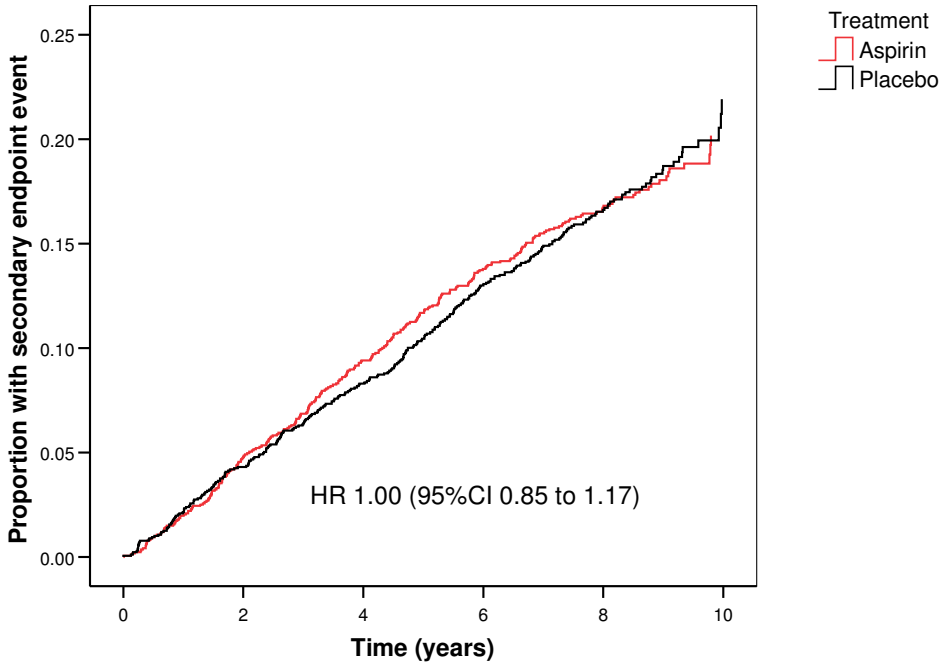
Fowkes FGR, Price JF, Stewart MCW, et al; Aspirin for Asymptomatic Aherosclerosis Trialists. Aspirin for prevention of cardiovascular events in a general population screened for low ankle brachial index: a randomized controlled trial. *JAMA*. 2010:303(9):841-848.

eFigure. Patients With Secondary End Point Events

eSupplementary Material. Primary and Secondary Outcome Events

This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure. Patients With Secondary End Point Events



Numbers at risk for secondary all vascular endpoint event:

Years:	0	2	4	6	8	10
Aspirin	1675	1579	1486	1383	886	114
Placebo	1675	1594	1501	1390	870	107

eSupplementary Material. Primary and Secondary Outcome Events

NON-FATAL CORONARY EVENTS

1. Definite MI

For a Definite Non-Fatal MI, subject must meet one of five sets of criteria:-

(see pages 15-16 for definitions of ECG changes on Minnesota coding, cardiac pain and abnormal enzymes)

1.1 An evolving diagnostic ECG on Minnesota coding

1.2 Prolonged cardiac pain and either

(i) a diagnostic ECG with changes indicative of either acute or chronic ischaemia on Minnesota coding, or

(ii) if no ECG available, a doctor's report of an ECG diagnostic of an acute MI

1.3 Prolonged cardiac pain and abnormal enzymes

1.4 Abnormal enzymes and either

(i) ECG with changes indicative of either acute or chronic ischaemia on Minnesota coding, or

(ii) if no ECG available, a doctor's report of an ECG diagnostic of either acute or chronic ischaemia

1.5 Prolonged cardiac pain and a doctor's report of early ECG changes suggestive of an acute MI and administration of thrombolytic therapy.

2. Probable MI

For a Probable Non-Fatal MI, subject must meet one of six sets of criteria:-

(see pages 15-16 for definitions)

2.1 Prolonged cardiac pain and equivocal ECG

2.2 Prolonged cardiac pain and equivocal enzymes

2.3 ECG with changes indicative of either acute or chronic ischaemia and equivocal enzymes

2.4 Abnormal enzymes and equivocal ECG

2.5 Equivocal enzymes and equivocal ECG

2.6 Cardiologist diagnosis of Acute Coronary Syndrome

3. Primary Cardiac Arrest with Successful Resuscitation

No evidence of MI (as defined above) and no obvious non-atherosclerotic cause of cardiac arrest.

FATAL CORONARY EVENTS

4. Definite Fatal MI

For a Definite Fatal MI, subject must meet one of two sets of criteria:-

4.1 Post Mortem: acute MI

and

No known non-atherosclerotic or noncardiac atherosclerotic process that was probably lethal according to death certificate, post-mortem or hospital records.

4.2. Criteria for definite MI within 4 weeks of death (see page 1)

and

No known non-atherosclerotic or noncardiac atherosclerotic process that was probably lethal according to death certificate, post-mortem or hospital records.

5. Definite Death due to Ischaemic Heart Disease

For a Definite Death due to IHD, subject must meet one of three sets of criteria:-

5.1 Death certificate codes with consistent underlying or immediate cause (s) (ICD-9: 410,411,412,414 or ICD-10: I21, I22, I23, I24, I25)

and

Previous history of probable MI according to hospital records (no defined time period) (see page 2)

and

No known non-atherosclerotic or noncardiac atherosclerotic process that was probably lethal according to death certificate, post-mortem or hospital records.

5.2 Death certificate codes with consistent underlying or immediate cause (s) (ICD-9: 410,411,412,414 or ICD-10: I21, I22, I23, I24, I25)

and

Post-mortem evidence of severe coronary atherosclerosis or old MI without acute MI

and

No known non-atherosclerotic or noncardiac atherosclerotic process that was probably lethal according to death certificate, post-mortem or hospital records.

5.3 Death certificate codes with consistent underlying or immediate cause (s) (ICD-9: 410,411,412,414 or ICD-10: I21, I22, I23, I24, I25)

and

Rapid death: occurring greater than 1 hour and less than or equal to 24 hours after the onset of severe cardiac symptoms or after subject was last seen without symptoms

and

No known non-atherosclerotic or noncardiac atherosclerotic process that was probably lethal according to death certificate, post-mortem or hospital records.

6. Probable Death due to Ischaemic Heart Disease

For a Probable Death due to IHD, subject must meet the following criteria:-

Death Certificate Codes with consistent underlying or immediate cause (s)
(ICD-9: 410,411,412,414 or ICD-10: I21, I22, I23, I24, I25)

and

No known non-atherosclerotic or noncardiac atherosclerotic process that was probably lethal according to death certificate, post-mortem or hospital records.

7. Sudden Death due to Ischaemic Heart Disease

For a Sudden Death due to IHD, subject must meet the following criteria:-

Death occurring within 1 hour after the onset of severe cardiac symptoms (prolonged cardiac pain, shortness of breath, fainting), or within 1 hour of having been seen symptom free.

and

No documentation of a definite acute MI within 4 weeks prior to death.

and

No known non-atherosclerotic or noncardiac atherosclerotic process that was probably lethal according to death certificate, post-mortem or hospital records.

NON-FATAL STROKE

8. Definite Stroke

For a Definite Stroke, subject must meet one of two sets of criteria:-

8.1 History of rapid onset (maximal deficit within 48 hours)

and

Confirmation by CT scan of cerebral (cerebellar or brain stem) infarction or haemorrhage.
(If there are clinical symptoms of a stroke and the CT scan is clear and done in less than 3 days after first symptoms, the stroke can be classified as an infarction)

and

No other disease process or event such as brain tumour, subdural haematoma, subarachnoid haemorrhage, metabolic disorder, or peripheral lesion that could cause localising neurologic deficit or coma according to hospital records.

Please use the following codes to specify the type of stroke for section 8.1:-

8.1.1 Definite non-fatal stroke due to infarction
8.1.2 Definite non-fatal stroke due to haemorrhage

8.2 History of rapid onset (maximal deficit within 48 hours)

and

Clinical confirmation of signs of focal (or global) disturbance of cerebral function within 6 weeks of onset lasting > 24 hours

and

No other disease process or event such as brain tumour, subdural haematoma, subarachnoid haemorrhage, metabolic disorder, or peripheral lesion that could cause localising neurologic deficit or coma according to hospital records.

If a CT scan is clear and is carried out 3 days or more after the first symptoms, the stroke should be classified as ‘not known infarct or haemorrhage’

9. Probable Stroke

For a Probable Stroke, subject must meet the following criteria:-

Discharge diagnosis with primary or secondary codes:-
(ICD-9: 431,432,434,436,437; ICD-10: I61,I62, I63, I64)

and

No clinical or laboratory evidence of any other disease process or event causing focal brain deficit or coma other than cerebral infarction or haemorrhage according to hospital records.

FATAL STROKE

For a Definite Stroke, subject must meet one of two sets of criteria:-

10. Definite stroke

10.1 Post Mortem: cerebral infarction or haemorrhage

and

No other disease process or event such as brain tumour, subdural haematoma, subarachnoid haemorrhage, metabolic disorder, or peripheral lesion that could cause localising neurologic deficit or coma according to hospital records.

Please use the following codes to specify the type of stroke for section 10.1:-

10.1.1 Definite fatal stroke due to cerebral infarction
10.1.2 Definite fatal stroke due to cerebral haemorrhage

10.2 Criteria of definite stroke within 6 weeks of death (see page 6 for criteria)

and

No other disease process or event such as brain tumour, subdural haematoma, subarachnoid haemorrhage, metabolic disorder, or peripheral lesion that could cause localising neurologic deficit or coma according to hospital records.

Please use the following codes to specify the type of stroke for section 10.2:-

10.2.1 Definite fatal stroke due to cerebral infarction
10.2.2 Definite fatal stroke due to cerebral haemorrhage
10.2.3 Definite fatal stroke – unknown cause

11. Probable stroke

For a Probable Stroke, subject must meet the following criteria:-

Death certificate code of underlying or immediate cause:-
(ICD-9: 431-437; ICD-10: I61,I62, I63, I64)

and

No evidence at post mortem examination of the brain (if performed), of any disease process other than cerebral infarction or haemorrhage that could cause localising neurologic signs.

Revascularisation

For the following primary events (numbers 14-17 and 21) the criteria will be a statement by a doctor or written evidence from hospital or GP notes.

14. Coronary angioplasty +/- stenting

15. Peripheral angioplasty +/- stenting

16. Coronary artery bypass grafting

17. Peripheral arterial bypass / surgery

21. Carotid Intervention:
Please use the following codes to specify the type of carotid intervention for section 21

21.1 Carotid surgery
21.2 Carotid stenting
21.3 Carotid angioplasty without stenting

SECONDARY OUTCOME EVENTS

12. Angina

Definition:-
Pain or discomfort in the centre of the chest or (L) anterior chest and (L) arm when walking up hill or hurrying requiring the person to stop or slow down for 10 minutes or less whereupon the pain is relieved.

To meet criteria for diagnosis of angina, subject must meet one of 3 sets of criteria :

12.1 Diagnosis of angina recorded by a doctor

12.2 In the absence of a doctor's recorded diagnosis of angina, chest pain typical of angina and on regular medication for angina

12.3 Either of 12.1 or 12.2 plus a positive exercise tolerance test.

13. Intermittent Claudication

Definition:-
Pain in the calf of either leg which does not begin when standing still or sitting, but occurs when walking uphill, hurrying, or at an ordinary pace on the level. The pain does not disappear while walking but is relieved in 10 minutes or less if the person slows down or stops.

Criteria for diagnosis:-

- Diagnosis of intermittent claudication recorded by a doctor (either GP or hospital if no previous diagnosis of PVD, or a new hospital diagnosis if recruit had a previous diagnosis by GP)

18. Possible Transient Ischaemic Attack
Criteria : Diagnosis of possible TIA recorded by a doctor.

19. Death – other causes
Criteria: Cause of death according to death certificate (or, in absence of death certificate, other verified information), for any cause of death which is NOT

(i) a fatal MI, fatal stroke or death due to IHD
(primary outcomes, codes 4-7,10-11)

(ii) death due to another cardiovascular cause [code 20]

(iii) death due to an adverse event [codes 50 - 52]

This will normally be the underlying COD (which is underlined) on the death certificate extract received from NHSCR except where this is an 'invalid' COD, or the OEC has reason to doubt its accuracy (in which case, information from hospital notes and / or the GP will be taken into account).

20. Cardiovascular death - other
Death due to a cardiovascular cause, other than MI, stroke or IHD, according to death certificate +/- information from hospital notes

20.1 Aortic aneurysm
20.2 Malignant hypertension
20.3 Pulmonary embolism
20.4 Other

MAJOR ADVERSE EVENTS

FATAL

50. GI Haemorrhage

Criteria: COD on death certificate, verified by OEC, consistent with haemorrhage from any site within GI tract.

K25.0, K25.2, K25.4, K25.6	(GI ulcer + haemorrhage)
K26.0, K26.2, K26.4, K26.6	(Duodenal ulcer + haemorrhage)
K27.0, K27.2, K27.4, K27.6	(Peptic ulcer + haemorrhage)
K28.0, K28.2, K28.4, K28.6	(Gastrojejnunal ulcer + haemorrhage)
K29.0	(Acute haemorrhagic gastritis)
K92.0, K92.1 K92.2	(GI haemorrhage unspecified)

51. GI Ulcer

Criteria: COD on death certificate, verified by OEC, consistent with death due to GI ulcer (other than due to haemorrhage eg. perforation).

K25.1, K25.3, K25.5, K25.7, K25.9	(GI ulcer without haemorrhage)
K26.1, K26.3, K26.5, K26.7, K26.9	(Duodenal ulcer w/out haemorrhage)
K27.1, K27.3, K27.5, K27.7, K27.9	(Peptic ulcer without haemorrhage)
K28.1, K28.3, K28.5, K28.7, K28.9	(Gastrojejnunal ulcer w/out haemorrhage)

52. SAH/SDH

Criteria: SAH or SDH given as COD on death certificate, verified by OEC.

52.1 SAH ICD10 code - I60

52.2 SDH ICD10 code - I62

NON – FATAL

53. GI Haemorrhage

Criteria: Diagnosis of haemorrhage from GI tract recorded by a doctor AND requiring hospitalisation to control bleeding.

K25.0, K25.2, K25.4, K25.6	(GI ulcer + haemorrhage)
K26.0, K26.2, K26.4, K26.6	(Duodenal ulcer + haemorrhage)
K27.0, K27.2, K27.4, K27.6	(Peptic ulcer + haemorrhage)
K28.0, K28.2, K28.4, K28.6	(Gastrojejunal ulcer + haemorrhage)
K29.0	(Acute haemorrhagic gastritis)
K92.0, K92.1 K92.2	(GI haemorrhage unspecified)

54. GI Ulcer

Criteria: Doctor diagnosis of GI ulcer without haemorrhage based on hospital investigations.

K25.1, K25.3, K25.5, K25.7, K25.9 (GI ulcer without haemorrhage)
K26.1, K26.3, K26.5, K26.7, K26.9 (Duodenal ulcer w/out haemorrhage)
K27.1, K27.3, K27.5, K27.7, K27.9 (Peptic ulcer without haemorrhage)
K28.1, K28.3, K28.5, K28.7, K28.9 (Gastrojejunal ulcer w/out haemorrhage)

55. SAH / SDH

Criteria: Diagnosis of SAH or SDH recorded by a doctor
55.1 SAH ICD10 code - I60
55.2 SDH ICD10 code - I62

56. Retinal Haemorrhage

Criteria: Ophthalmologist diagnosis.
ICD10 code - H35

57. Major bleed from other site (non GI & extra - cranial)

Criteria: Extra – cranial haemorrhage from site other than GI tract, requiring hospitalisation (eg. haematuria, epistaxis etc) to control bleeding.

58. Severe anaemia

Criteria: Doctor diagnosis of anaemia (due to blood loss and NOT due to vitamin deficiency) PLUS prolonged treatment.
ICD10 code - D50.0, D50.9, D62

CORONARY EVENT DEFINITIONS

1. Prolonged cardiac pain:-

Pain anywhere in the anterior chest, left arm, or jaw (which may also involve back, shoulder, right arm, abdomen) and lasting at least 20 minutes or doctor's description of pain consistent with an MI.

2. Abnormal enzymes:-

2 cardiac enzymes greater than twice the upper limits of normal or
CK-MB and/or Tropinon T above normal limits
If only CK measured, must be greater than twice the upper limits of normal

3. Equivocal enzymes:-

At least one cardiac enzymes raised, but less than twice normal limits.

4. Evolving Diagnostic ECG:-

An evolving pattern of changes [appearance or disappearance within lead groups: anterior (V1-V5); lateral (I, aVL, V6); inferior (II, III or aVF)] establishes the infarct as acute. Two or more ECG recordings during the hospitalisation are needed for this classification.

Criteria (Minnesota Code):-

a) No Q code on one ECG record followed by a record with a diagnostic Q code (Minn. Code 1.1.1-1.2.5, 1.2.7) or

b) An equivocal Q code (Minn. Code 1.2.8 or any 1.3 code) and no major ST segment depression in one ECG record followed by a record with a diagnostic Q code PLUS a major ST segment depression (Minn. Code 4.1 or 4.2) or

c) An equivocal Q code and no ST segment elevation in one ECG record followed by a record with a diagnostic Q code PLUS an ST segment elevation (Minn. Code 9.2) or

d) An equivocal Q code and no major T wave inversion in one ECG record followed by a record with a diagnostic Q code PLUS a major T wave inversion (Minn. Code 5.1 or 5.2) or

e) No Q code and neither Minn. code 4.1 nor 4.2 followed by a record with an equivocal Q code plus a 4.1 or a 4.2 or

f) No Q code and no Minn. code 9.2 followed by a record with an equivocal Q-code plus a 9.2 or

g) No Q code and neither Minn. Code 5.1 nor 5.2 followed by a record with an equivocal Q code plus a 5.1 or a 5.2.

5. Diagnostic ECG:-
Minnesota Codes 1.1.1-1.2.5., 1.2.7, or 9.2 + 5.1 or 5.2 (see Appendix for Minn. Code definitions)

6. Equivocal ECG
Minnesota Codes 1.2.8.-1.3.6., 4.1-4.3, 5.1-5.3, or 9.2 (see Appendix for Minn. Code definitions)