

Antiplatelet agents and anticoagulants for hypertension

NICE has developed the Cochrane Quality and Productivity (QP) topics to help the NHS identify practices which could be significantly reduced or stopped completely, releasing cash and/or resources without negatively affecting the quality of NHS care. Each topic has been derived from a Cochrane systematic review that has concluded that the evidence shows that the practice is harmful or ineffective and should not be used, or that there is insufficient evidence to support widespread use of the practice

Summary

NICE summary of review conclusions

Aspirin cannot be recommended for the primary prevention of cardiovascular events in patients with hypertension because the benefit does not outweigh the harm. The size of the benefit is much greater for secondary prevention, so aspirin is recommended for this indication. Warfarin, glycoprotein IIb/IIIa inhibitors, ticlopidine, and clopidogrel are not recommended for primary prevention of cardiovascular events in patients with hypertension. Further trials are needed to investigate the benefits and harms of antithrombotic therapy in people with high blood pressure.

Stopping or reducing the use of antiplatelets or anticoagulants for the primary prevention of occlusive vascular disease in patients with hypertension is likely to lead to improved patient safety and productivity savings through reduced prescribing costs and adverse events.

The 'Implications for practice' section of the Cochrane review stated:

'For primary prevention in patients with elevated blood pressure antiplatelet therapy with acetylsalicylic acid (aspirin) cannot be recommended since the magnitude of the benefit, reduced myocardial infarctions, is similar to the magnitude of harm, increased major haemorrhagic events.

For secondary prevention in patients with elevated blood pressure, antiplatelet therapy with aspirin is recommended, as the magnitude of the absolute benefit, reduced major vascular events is much greater than in primary prevention and appears to be greater than for secondary prevention in patients with normal blood pressure.

Antithrombotic therapy with warfarin alone or in combination with aspirin in patients with elevated blood pressure is not recommended because of lack of effectiveness in reducing cardiovascular events as well as a trend towards increased haemorrhagic events. Glycoprotein IIb/IIIa inhibitors as well as ticlopidine and clopidogrel have not been sufficiently evaluated in order to recommend their use in patients with elevated blood pressure.'

Details of Cochrane review

Cochrane review title

Antiplatelet agents and anticoagulants for hypertension

Citation

[Lip GYH, Felmeden DC. Antiplatelet agents and anticoagulants for hypertension. Cochrane](#)

Cochrane Quality and Productivity topics

[Database of Systematic Reviews 2004, Issue 3. Art. No.: CD003186. DOI: 10.1002/14651858.CD003186.pub2](#)

When the review content was assessed as up to date

24/05/2004

QIPP category

Right care

Relevant codes

OPCS

ICD10

HRG

Not relevant –
relates to
prescribing

Not relevant –
relates to
prescribing

Not relevant – relates
to prescribing

Programme budget

Problems of circulation

Evidence

Relevance to the NHS

The primary analysis in the Cochrane review was based on 4 double-blind, randomised controlled trials (RCTs) in patients with hypertension.

Patients with at least a mild increase in blood pressure or isolated systolic or diastolic increases in blood pressure were included. Generally a systolic blood pressure of > 160mmHg and/ or a diastolic blood pressure > 100mmHg was considered to be elevated.

Patients with atrial fibrillation, congestive heart failure, pre-eclampsia, eclampsia or pulmonary hypertension were excluded. The presence or absence of elevated blood pressure related target organ damage at baseline was analysed separately if possible. For example participants who have had a stroke and have elevated blood pressure represent secondary prevention as compared to studies in individuals who have elevated blood pressure but no prior vascular disease (primary prevention).

Trials where treatment duration with antiplatelet agents or oral anticoagulants was at least 3 months were included.

Primary outcome measures included all cause mortality and cardiovascular mortality (stroke, myocardial infarction, sudden death, thromboembolic events). Secondary outcome measures included all non-fatal cardiovascular events (stroke, myocardial infarction, thromboembolic events such as acute coronary syndrome, acute limb ischaemia, pulmonary embolism, deep vein thrombosis) as a composite endpoint and all major bleeding events (fatal, non-fatal) as a composite endpoint. A major bleed was defined as haemorrhagic stroke or major blood loss. Tertiary outcome measures included all cardiovascular events (sudden death, fatal and non-fatal stroke, myocardial infarction, thromboembolic events, coronary revascularisation) as a composite endpoint.

Two of the trials compared aspirin with placebo; one compared aspirin alone, warfarin alone and aspirin plus warfarin; the fourth compared aspirin with clopidogrel. One looked at primary prevention, one high risk patients and two secondary prevention.

One study had a duplicate publication with two different definitions for elevated blood pressure being used: patients with systolic blood pressure >145mmHg or patients treated

Cochrane Quality and Productivity topics

with antihypertensive drugs at entry or during the trial. This trial (5499 participants) looked at primary prevention in male patients with high risk of cardiovascular disease. It compared aspirin versus placebo, warfarin versus placebo and aspirin plus warfarin versus placebo.

Only one randomised placebo-controlled trial was designed to investigate the effects of aspirin on cardiovascular events and haemorrhagic complications in treated hypertensive patients. This trial was a primary prevention trial in patients with elevated blood pressure (diastolic blood pressure between 100-115 mmHg).

A large meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients conducted by the Antithrombotic Trialists' Collaboration was excluded from analysis due to inability to obtain data on the hypertensive subgroup analysed in this paper. The majority of trials included in this analysis were secondary prevention trials.

Aspirin did not reduce stroke or 'all cardiovascular events' compared to placebo in primary prevention patients with elevated blood pressure and no prior cardiovascular disease. Based on one large trial, aspirin taken for five years reduced myocardial infarction (NNT 200 for 5 years), increased major haemorrhage (NNT 154) and did not reduce all cause mortality or cardiovascular mortality.

There was no significant difference between aspirin and clopidogrel for the composite endpoint of stroke, myocardial infarction or vascular death in one trial. In two small trials warfarin alone or in combination with aspirin did not reduce stroke or coronary events.

The Antithrombotic Trialists' Collaboration's (ATC) previous meta-analysis established the benefit of antiplatelet therapy for secondary prevention in patients with or without elevated blood pressure. The data also suggested that the absolute benefit of antiplatelet therapy for secondary prevention is greater in patients with elevated blood pressure than in patients with normal blood pressure.

Considering the results of this systematic review and the ATC meta-analysis the following conclusions can be drawn:

- The antiplatelet drug, aspirin, taken daily by patients treated for elevated blood pressure reduces the incidence of heart attacks to a small degree, but it increases the incidence of major bleeding events to a similar degree. Aspirin is therefore not recommended in patients with elevated blood pressure who have not had a prior stroke or heart attack. It is not recommended as primary prevention.
- In patients with elevated blood pressure who have had a stroke or heart attack, daily low-dose aspirin is recommended, because the magnitude of the absolute benefit is many times greater than the risk of harm from bleeding events. It is recommended as secondary prevention.
- Antithrombotic therapy with warfarin alone, or in combination with aspirin is not recommended in patients with elevated blood pressure because no benefit has been demonstrated.

Trials of the newer drugs such as glycoprotein IIb/IIIa inhibitors, ticlopidine and clopidogrel are needed in patients with elevated blood pressure.

Relevant NICE guidance

[Clopidogrel and modified-release dipyridamole for the prevention of occlusive vascular events \(review of NICE technology appraisal 90\) – NICE technology appraisal guidance 210](#)

(Published: December 2010; expected review date July 2013)

Cochrane Quality and Productivity topics

1.1 Clopidogrel is recommended as an option to prevent occlusive vascular events:

- for people who have had an ischaemic stroke or who have peripheral arterial disease or multivascular disease **or**
- for people who have had a myocardial infarction only if aspirin is contraindicated or not tolerated.

1.2 Modified-release dipyridamole in combination with aspirin is recommended as an option to prevent occlusive vascular events:

- for people who have had a transient ischaemic attack **or**
- for people who have had an ischaemic stroke only if clopidogrel is contraindicated or not tolerated.

1.3 Modified-release dipyridamole alone is recommended as an option to prevent occlusive vascular events:

- for people who have had an ischaemic stroke only if aspirin and clopidogrel are contraindicated or not tolerated **or**
- for people who have had a transient ischaemic attack only if aspirin is contraindicated or not tolerated.

[Hypertension: management of hypertension in adults in primary care – NICE clinical guideline 34](#)

(Published: June 2006; expected review date: August 2011)

1.4.1 Drug therapy to treat hypertension reduces the risk of cardiovascular disease and death. Offer drug therapy to:

- patients with persistent high blood pressure of 160/100 mmHg or more
- patients at raised cardiovascular risk (10-year risk of cardiovascular disease of 20% or more, or existing cardiovascular disease or target organ damage) with persistent blood pressure of more than 140/90 mmHg.

Other information

[Aspirin in the primary and secondary prevention of vascular disease: collaborative meta-analysis of individual participant data from randomised trials](#) The Lancet, Volume 373, Issue 9678, Pages 1849 - 1860, 30 May 2009

This analysis concludes that in primary prevention of cardiovascular disease, aspirin is of uncertain net value as the reduction in occlusive events needs to be weighed against any increase in major bleeds.

Potential productivity savings

Estimate of current NHS use

Relevant guidance on hypertension (for example NICE clinical guideline 34) does not comment on the use of antiplatelet agents as a primary therapy to prevent thrombosis-related complications of elevated blood pressure in patients with hypertension.

The BNF states that long-term use of aspirin, in a dose of 75mg daily is of benefit for all patients with established cardiovascular disease; unduly high blood pressure must be controlled before aspirin is given. Use of aspirin in primary prevention, in those with or without diabetes is of unproven benefit.

Exact estimate of NHS usage of aspirin for the primary prevention of cardiovascular events in

Cochrane Quality and Productivity topics

patients with hypertension cannot be quantified.

Level of productivity savings anticipated

The cost of aspirin per patient is 82p for 28 days and £10.69 per year.

Stopping the use of aspirin for the primary prevention of cardiovascular events in patients with hypertension would save the NHS £10.69 per person annually. Further savings may be generated from the reduction in associated side effects of aspirin use. Exact savings cannot be quantified. Drug costs are from the NHS electronic drug tariff accessed 10/01/11.

Type of saving

Any savings generated are likely to be cash releasing efficiency savings

Any costs required to achieve the savings

There is not likely to be a cost barrier to implementation

Other information

Any savings are likely to effect community prescribing.

Potential impact on quality of NHS care

Impact on clinical quality

Clinical quality will be improved through reduced use of interventions with known side effects

Impact on patient safety

There may be improvements in patients' safety through the reduction of adverse events such as haemorrhage associated with aspirin use

Impact on patient and carer experience

No significant impact on patient and carer experience anticipated

Likely ease of implementation

Time taken to implement

Can be achieved in the medium term: 3 months to 1 year

Healthcare sectors affected

Affects several teams or departments accross several organisations

Stakeholder support

Likely to receive good buy-in from most key influencers although some individuals may be slow to change
