Aspirin in Primary Prevention (CVD risk ≥ 20%)

Historically aspirin has been widely used for both people with established cardiovascular disease (secondary prevention) and of healthy people with a 10 year CVD risk of 20% or more (primary prevention).

Recent studies have shown that whilst aspirin is beneficial in preventing heart attacks and strokes with secondary prevention patients, its benefits do not clearly outweigh the risks of bleeding in healthy people. As a result of which many GP’s and nurses have asked for further clarification on the matter. The prescribing board commissioned the disease management team to produce a report that would help clinicians decide what would be best for their patients.

When prescribing aspirin to healthy individuals we have no clear evidence that the benefits of long-term aspirin exceed the risks. However, there remains a possibility that for primary prevention some individuals may have a risk/benefit profile for aspirin which is favourable.

Summary & Key Points

- Aspirin is associated with a risk of serious bleed.
- Aspirin is not licensed for primary prevention in the UK.
- Do not routinely start aspirin 75mg for primary prevention of cardiovascular disease (including diabetics)
- Review patients currently on aspirin individually, involving them in the decision to continue or stop, click on the following link to access a NPC patient decision aid on this topic (details on page 2).

Until more evidence is available recent data supports treating patients on an individual basis.

- Reduce all modifiable risk factors before considering aspirin
- The greater number of risk factors that can be reduced means that there is less likelihood of benefit from aspirin and increases possible harm.
- If non or few modifiable risk factors can be reduced aspirin, may be considered

When might aspirin provide benefit

- Unsuccessful healthy lifestyle interventions – e.g. exercise, salt intake, alcohol, diet
- Smoker (unsuccessful cessation or otherwise)
- Unable to tolerate statins
- BP below 150/90 mmHg with or without treatment
- BMI higher than normal (BMI within ideal range 18.5-24.9) note for adults of south Asian origin, a BMI of 23 or above can indicate increased risk of health problems
- Increasing Age
- Family history of IHD

When might aspirin not produce additional benefit or may cause harm

- Previous history of GI bleeds/GI ulcers
- Improved lifestyle
- Taking medicines that can increase possibility of GI bleeds, i.e. NSAID’s, anticoagulants, corticosteroids, SSRI’s,
- Ex smoker or non-smoker
- Taking a statin
- BP > 150/90 mmHg
- BMI within normal range *
- BMI within ideal range
- Increasing Age (increase risk of G/I bleed)**
- No FH of IHD

**Harms**

Harms from aspirin include the risks of serious upper GI bleeding and hemorrhagic stroke. An individual’s risk for GI bleeding from aspirin increases with age:

- Concomitant use of NSAIDs with aspirin increases the risk of serious GI complications by a factor of 3-4.
- Prior GI ulcer, GI bleeding, or GI pain also increases risk by a factor of 2-3.
- Aspirin increases the risk of hemorrhagic stroke in men by a factor of 1.7 but does not appear to increase this risk in women. This risk does not increase with age.

<table>
<thead>
<tr>
<th>Age</th>
<th>Risk of serious upper GI complications over 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
</tr>
<tr>
<td>&lt;60</td>
<td>8 / 1,000</td>
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<tr>
<td>60-69</td>
<td>24 / 1,000</td>
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</tbody>
</table>
Reducing harm where aspirin is still prescribed

**Gastrointestinal (GI)**
Consider gastro protection in patients with increased GI risks:
- Age 65yrs
- History of gastric bleed
- Concomitant use of medications which also affect the GI e.g. anticoagulants, NSAIDs, corticosteroids, SSRIs
- Excessive alcohol use
- Heavy smoking

**Blood Pressure (BP)**
Ensure BP <150/90mmHg (<145/90mmHg diabetics)

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**Secondary Prevention**
Patients should take aspirin unless contra-indicated

**Patient decision aid: aspirin for primary prevention of cardiovascular disease**

Decision aids are intended to prepare patients to participate with their health care professionals in making deliberated, personalised choices about health care options. They supplement counselling by providing information on options. The aim is that patients are better able to judge the value of the benefits versus the harms.

This decision aid is intended to assist health professionals in consultations with patients who do not have established cardiovascular disease and in whom treatment with aspirin is being considered to reduce the risk of CV events (primary prevention). For further information see link below, [http://www.npci.org.uk/therapeutics/cardio/antiplatelets/resources/antiplatelets_pda.pdf](http://www.npci.org.uk/therapeutics/cardio/antiplatelets/resources/antiplatelets_pda.pdf)

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**Evidence for change**

Previous recommendations for aspirin in primary prevention were based on trials completed when statins were not widely available or included secondary prevention patients.

Currently, primary prevention with statins and other interventions may significantly reduce CVD risk.

The additional absolute benefit of adding aspirin may be too small to warrant the increased risk of bleeding for many patients.

More recent trials found that, in the primary prevention of CV disease, the balance of benefits and risks with aspirin is unclear. While there appeared to be a small absolute reduction (around 0.06%) in some CV outcomes (e.g. non-fatal MI), there was also an increased absolute risk of major bleeds (around 0.03%).

(NNT approx 2000, NNH approx 3300)

In a subgroup analysis of primary prevention patients with diabetes in this meta-analysis, aspirin did not significantly reduce the risk of serious vascular events (RR 0.88; 95%CI 0.67 to 1.15).

**POPADAD trial** - conducted in diabetics – outcome - aspirin was ineffective for the primary prevention of cardiovascular events.

<table>
<thead>
<tr>
<th>Patients taking aspirin</th>
<th>Patients not on aspirin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatal and non-fatal MIs, strokes and amputations (P=0.86).</td>
<td>18.2%</td>
</tr>
<tr>
<td>Deaths from CHD or stroke (P=0.36).</td>
<td>43 (6.7%)</td>
</tr>
</tbody>
</table>

**Sex specific meta-analysis of the 6 primary prevention trials mean treatment of 6.4yrs**

<table>
<thead>
<tr>
<th></th>
<th>Per 1000 men</th>
<th>Per 1000 women</th>
</tr>
</thead>
<tbody>
<tr>
<td>absolute benefit of CVD events</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Additional major bleeds</td>
<td>3</td>
<td>2.5</td>
</tr>
</tbody>
</table>

Further clinical trials are taking place in patients with diabetes and using aspirin if you would like to know how you could get involved click on the links [Research Ready & Ascend study](http://www.npci.org.uk/therapeutics/cardio/antiplatelets/resources/antiplatelets_pda.pdf) or contact Dr Manny Samra on [manny.samra@wolvespct.nhs.uk](mailto:manny.samra@wolvespct.nhs.uk)

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**References**

7. The prevention of progression of arterial disease and diabetes (POPADAD) trial: factorial randomised placebo controlled trial of aspirin and antioxidants in patients with diabetes and asymptomatic peripheral arterial disease. *BMJ* 2008;337:a1840