Antiplatelets patient decision aid: aspirin for primary prevention of cardiovascular disease

What this decision aid is for

This decision aid is intended to assist health professionals in consultations with patients who do not have established cardiovascular (CV) disease (e.g. angina, myocardial infarction [MI], stroke) and in whom treatment with aspirin is being considered to reduce the risk of CV events (primary prevention). Leaflets for patients explaining CV disease can be found on the Clinical Knowledge Summaries website http://cks.library.nhs.uk/home.

The balance of risks and benefits

Evidence has been accumulating suggesting that the balance of benefits and risks of aspirin in patients who do not have existing CV disease may not be as favourable as previously thought. The MHRA has advised that, if aspirin is used for primary prevention, the balance of benefits and risks should be considered for each individual, particularly the presence of risk factors for vascular disease, for example diabetes, and the risk of gastro-intestinal (GI) bleeding. The MHRA also reminded healthcare professionals that aspirin is not licensed for the primary prevention of CV disease.1

The ATT meta-analysis found that, for primary prevention, the absolute benefits and absolute risks of aspirin were often similar. Although there was a small absolute reduction in serious vascular events of around 0.06%, mainly due to a reduction in non-fatal MI, the absolute risk of major bleeds increased by around 0.03%, and rates of all cause mortality, death due to coronary heart disease, and stroke, did not differ significantly between the aspirin and control groups.2 It is possible that the ATT meta-analysis may overestimate the benefits of aspirin. Certainly other studies have found no benefit from aspirin for primary prevention of CV events3,4,5,6 and use in low risk patients remains controversial. More information can be found in the technical note at the end of this patient decision aid (PDA).

The presence of personal risk factors may change the risk:benefit profile, so it is important to take these into account. In addition, priority should be given to evidence-based interventions where appropriate, for example management of lipid levels and hypertension, along with lifestyle measures, such as smoking cessation.

The Cates plots on the following pages express the risks and benefits of aspirin for primary prevention of CV events in graphical form, based on data from the ATT meta-analysis, including modeling conducted by the authors.2 The diagrams on the next pages relate to different levels of risk: use the diagram most appropriate to the patient’s estimated risk. Baseline risk of having CV disease can usually be estimated using a suitable tool, as recommended by NICE.
Benefits from taking aspirin for primary prevention in people at 5% CV disease risk over 10 years

Imagine 1,000 people without a history of CV disease, but at 5% risk of CV disease over the next 10 years. If they don’t take aspirin, about 50 of them would be expected to have a CV event in that time. So about 950 of them would not have a CV event.

However, if those same 1,000 people each take aspirin for 10 years:

1. About six people will be ‘saved’ from dying or having a non-fatal MI or stroke by taking aspirin (the **yellow** faces)
2. About 950 people will not die or have a non-fatal MI or stroke – but would not have done even if they had not taken aspirin (the **green** faces)
3. About 44 people will still die or have a non-fatal MI or stroke (the **red** faces), even though they take aspirin.

But remember:

- It is impossible to know for sure what will happen to each individual person
- All 1,000 people will have to take aspirin for 10 years.
Harms from taking aspirin for primary prevention in people at around 5% risk of a CV event over 10 years

From the ATT meta-analysis, people at around 5% CV risk over 10 years had a risk of a major bleed of around 0.4% over 10 years.

Imagine 1,000 people at 0.4% risk of a major bleed over 10 years. If they don’t take aspirin, about four would have a major GI or other extracranial bleed in that time, so 996 would not.

However, if those same 1,000 people each take aspirin for 10 years:

1. About two extra people will have a major bleed because they take aspirin (the green faces with a red cross)
2. About 994 people will still not have a major bleed, just as if they had not taken aspirin (the green faces)
3. About four people will still have a major bleed (the red faces), just as he or she would if they had not taken aspirin.

But remember:

- It is impossible to know for sure what will happen to each individual person.
Benefits from taking aspirin for primary prevention in people at 10% CVD risk over 10 years

Imagine 1,000 people without a history of CV disease, but at 10% risk of CV disease over the next 10 years. If they don’t take aspirin, about 100 of them would be expected to have a CV event in that time. So about 900 of them would not have a CV event.

However, if those same 1,000 people each take aspirin for 10 years:

1. About 12 people will be ‘saved’ from dying or having a non-fatal MI or stroke by taking aspirin (the yellow faces)
2. About 900 people will not die or have a non-fatal MI or stroke – but would not have done even if they had not taken aspirin (the green faces)
3. About 88 people will still die or have a non-fatal MI or stroke (the red faces), even though they take aspirin.

But remember:

- It is impossible to know for sure what will happen to each individual person
- All 1,000 people will have to take aspirin for 10 years.
Harms from taking aspirin for primary prevention in people at around 10% risk of a CV event over 10 years

From the ATT meta-analysis, people at around 10% CV risk over 10 year, had a risk of a major bleed of around 1.1% over 10 years.

Imagine 1,000 people at 1.1% risk of a major bleed over 10 years. If they don’t take aspirin, about 11 would have a major GI or other extracranial bleed in that time, so 989 would not.

However, if those same 1,000 people each take aspirin for 10 years:

1. About six extra people will have a major bleed because they take aspirin (the green faces with a red cross)
2. About 983 people will still not have a major bleed, just as if they had not taken aspirin (the green faces)
3. About 11 people will still have a major bleed (the red faces), just as he or she would if they had not taken aspirin.

But remember:

- It is impossible to know for sure what will happen to each individual person.
Benefits from taking aspirin for primary prevention in people at 20% CVD risk over 10 years

Imagine 1,000 people without a history of CV disease, but at 20% risk of CV disease over the next 10 years. If they don’t take aspirin, about 200 of them would be expected to have a CV event in that time. So about 800 of them would not have a CV event.

However, if those same 1,000 people each take aspirin for 10 years:

1. About 24 people will be ‘saved’ from dying or having a non-fatal MI or stroke by taking aspirin (the yellow faces)
2. About 800 people will not die or have a non-fatal MI or stroke – but would not have done even if they had not taken aspirin (the green faces)
3. About 176 people will still die or have a non-fatal MI or stroke (the red faces), even though they take aspirin.

But remember:
- It is impossible to know for sure what will happen to each individual person
- All 1,000 people will have to take aspirin for 10 years.
Harms from taking aspirin for primary prevention in people at around 20% risk of a CV event over 10 years

From the ATT meta-analysis, people at around 20% CV risk over 10 years, had a risk of a major bleed of around 1.8% over 10 years.

Imagine 1,000 people at 1.8% risk of a major bleed over 10 years. If they don’t take aspirin, about 18 would have a major GI or other extracranial bleed in that time, so 982 would not.

However, if those same 1,000 people each take aspirin for 10 years:

1. About 10 extra people will have a major bleed because they take aspirin (the green faces with a red cross)
2. About 972 people will still not have a major bleed, just as if they had not taken aspirin (the green faces)
3. About 18 people will still have a major bleed (the red faces), just as he or she would if they had not taken aspirin.

But remember:

- It is impossible to know for sure what will happen to each individual person.
Technical note

Evidence has been accumulating which suggests that the balance of benefits and risks of aspirin in patients who do not have existing CV disease may not be as favourable as previously thought. For many patients the small absolute reduction in CV events is likely to be cancelled out by an increase in the number of major GI and other extracranial bleeds. However, for high-risk patients, although the absolute benefits of treatment are still only modest, data suggests that they may outweigh the harms. In October 2009, the MHRA advised that balance of benefits and risks should be considered on an individual basis, particularly the presence of risk factors for vascular disease, for example diabetes, and the risk of GI bleeding.\(^1\)

Data used for this PDA

The ATT meta-analysis included six primary prevention trials with 95,000 participants. The overall results showed that aspirin reduced the relative risk (RR) of any serious vascular event (non-fatal MI, stroke or vascular death) by 12% (0.51% aspirin vs. 0.57% control per year; RR 0.88, 95% confidence interval [CI] 0.82 to 0.94, \(P=0.0001\), number needed to treat [NNT] 1667) mainly due to a 23% relative risk reduction in non-fatal MI (0.18% aspirin vs. 0.23% control per year; RR 0.77, 95%CI 0.67 to 0.89, \(P<0.0001\), NNT 2000). Over 1,600 patients would need to be treated with aspirin over one year to prevent one extra serious vascular event, compared with control. There was no statistically significant difference between the aspirin and control groups for any stroke or any vascular death.\(^2\)

Aspirin increased the risk of major GI and other extracranial bleeds (0.10% aspirin vs. 0.07% control per year; RR 1.54, 95%CI 1.30 to 1.82, \(P<0.0001\), number needed to harm 3333). In other words, over 3,300 people would need to be treated with aspirin, rather than control, over a year, for one extra person to suffer a major bleed.\(^2\)

The authors concluded that in primary prevention, the balance of benefits and risks with aspirin is unclear as the reduction in occlusive events needs to be weighed against any increase in major bleeds.\(^2\)

The overall relative risk reduction of 12% for serious vascular event which was obtained in the ATT meta-analysis was applied to patients with baseline CV disease risks of 5%, 10% and 20% over 10 years to produce the figures in this patient decision aid (PDA). The relative risk increase of 54% for major bleeds was used for harms.\(^2\)

In the ATT meta-analysis, subgroup analyses were performed according to participants’ predicted 5-year risk of coronary heart disease (CHD) (< 2.5%, 2.5–5%, 5–10% and >10%).\(^2\) Note that CHD risk is similar to, but not the same as, the CV risk disease estimated by risk calculators recommended by NICE. The estimated 10-year risk of CV disease of the subgroups is about <6.7%, 6.7–13.3%, 13.3–26.7% and >26.7%. Since risk prediction based on estimation tools is not an exact science; there is uncertainty with regard to the precise magnitude of the relative risk reduction; and the decision aid is intended as a guide only, we have used the control event rates from Figure 7 in the Supplementary web appendix to estimate the harms with aspirin in patients at around 5%, 10% and 20% risk of a CV event over 10 years. In these three risk groups of patients, the baseline risk of non-fatal GI or other major extracranial bleeds was 0.4%, 1.1% and 1.8% over ten years.

Other evidence

The Aspirin for Asymptomatic Atherosclerosis trial found that, in patients without clinically evident CV disease but with a low ankle brachial index (a risk factor for CV events), aspirin did not significantly reduce fatal or non-fatal coronary events, stroke or revascularization compared with placebo, or significantly increase the incidence of major bleeds, over a mean follow up of 8 years.\(^3\)

A recent meta-analysis found that aspirin did not statistically significantly reduce the risk of major CV events, CV mortality or all-cause mortality, or significantly increase the risk of bleeding, in people with diabetes and no pre-existing CV disease.\(^4\) The POPADAD trial, which was one of the studies included in the meta-analysis, was conducted specifically in patients with diabetes and found aspirin was ineffective for the primary prevention of CV events. Over a median follow up of 6.7 years, fatal and non-fatal MIs, strokes and amputations occurred in 18.2% of patients taking aspirin, compared with 18.3% of those taking no aspirin. There was no significant difference in the number of deaths from coronary heart disease or stroke, or significant increase in major bleeding.\(^5\) However, there remains a possibility that aspirin may show a small benefit for primary prevention in people with diabetes in larger, longer-term studies. Until more evidence is available, these data support treating people with diabetes with aspirin on an individual basis, as recommended by the MHRA.\(^1\) NICE has recently updated their webpage on type 2 diabetes with the MHRA advice.

A Cochrane Review considered the use of aspirin for primary prevention of CV events in patients with hypertension and concluded that aspirin cannot be recommended because the benefits do not outweigh the harms. Based on one large trial (the HOT study), 200 people with high blood pressure would need to be treated with aspirin for 5 years to prevent one additional MI. However, only 154 would need to be treated with aspirin over the same timescale for one extra person to suffer a major bleed compared with control.\(^5\)

Source of images

The images have been produced using Dr Chris Cates’s software VisualRx 3.0. More information can be obtained from the website www.nntonline.net.
References


