

Education and debate

For and against

Aspirin for everyone older than 50?

Current population screening for vascular disease is neither efficient nor effective. Peter Elwood and colleagues believe we should have a public information strategy highlighting the benefits (and risks) of aspirin for older people, but Colin Baigent argues that the evidence of benefit is not yet strong enough

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FOR

It is 30 years since the first randomised trial was published showing a link between aspirin and myocardial infarction.¹ We believe that the evidence now supports more widespread use of aspirin prophylaxis, and there needs to be a strategy to inform the public and enable older people to make their own decision. The evidence focuses on a crucial question—namely, at what age does the balance between benefit and risk justify low dose aspirin prophylaxis? Of further relevance is a possible reduction of cancer and dementia by aspirin.

Recommendations for aspirin prophylaxis

Although several groups have recommended aspirin prophylaxis based on age alone, including a recommendation of daily aspirin for everyone over 50,²⁻³ cardioprotection is usually given only to people at vascular risk. Many formulas are available to assess risk, and one of these⁴ is the basis of the recommendation that prophylactic aspirin be considered if the five year risk of a vascular event is 3% or more.⁵

Application of the Framingham risk formula⁴ to the Caerphilly cohort,⁶ a representative population sample of men aged 45-59 years, shows that half the men had a risk above 3% by the age of 45. This is

apparent both from the application of risk assessment formulas (table 1) and from the actual occurrence of vascular events (table 2). Comparable data for women are available from the Heart Beat Wales survey,⁷ and estimates based on these show a 3% five year risk is reached by half the women by age 50 (table 1).

Risk of undesirable effects

Aspirin is inappropriate for people with known contraindications. At low dose, however, undesirable effects are unusual and seldom serious,⁸ and probably 90-95% of the population could take low dose aspirin without problems. The advice that people without symptoms should consult a doctor before starting aspirin prophylaxis is unreasonable and places the doctor in an impossible position. Without symptoms or a history suggestive of a contraindication, undesirable effects cannot be predicted. Each person, not a doctor, should evaluate the risks and benefits. A heart attack or stroke has serious physical and psychological effects as well as effects on the family, work colleagues, and friends. Most older people know this from experience and many will dread a vascular event. They are likely to accept a small increased risk of bleed or other side effect in exchange for a reduced risk of a heart attack or stroke.

Table 1 Estimates of age at which 50% and 80% of population reach a 3% risk of a vascular event within the next five years and 1% risk in one year

	Age (years)		
	Never smoked	Current smokers	All
Men*			
3% risk in 5 years:			
50%	46	38	42
80%	55	44	49
1% risk in 1 year:			
50%	60	50	54
80%	68	56	62
Women†			
50% at 3% risk in 5 years	53	47	50
50% at 1% risk in 1 year	≥65	55	62

*Results obtained by applying Framingham risk assessment formula³ to 2258 men in Caerphilly cohort⁷ using baseline values of total cholesterol, high density lipoprotein cholesterol, and systolic blood pressure. Men who had had a stroke (17) or a myocardial infarction (246) before the study period were excluded.

†Results in women were obtained by the application of the Framingham formula to grouped data for 550 women in the Heart Beat Wales survey.⁷ Evidence on previous vascular events was not available.

Table 2 Risk of a vascular event in Caerphilly cohort based on numbers of events observed and numbers predicted with Framingham risk formula⁵

Age group (year)	No of men at baseline*	No of vascular events in 5 years†	Five year risk of a vascular event (95% CI)	
			Observed (%)	Predicted (%)
45-49	756	20	2.6 (1.7 to 4.1)	4.9 (3.4 to 6.5)
50-54	725	36	5.0 (3.6 to 6.8)	6.7 (5.0 to 8.7)
55-59	768	54	7.0 (5.5 to 9.1)	8.9 (6.7 to 10.9)

* Men who had had a stroke (17) or a myocardial infarction (246) before the study were excluded.

† Ischaemic heart disease events plus ischaemic strokes.

Other benefits

Evidence is growing that regular aspirin may reduce cancer and dementia as well as vascular events. A low incidence of cancer has been reported in habitual aspirin users.⁹ In addition, studies have shown apoptosis in cancer cells cultured with salicylate,¹⁰ a reduction in cancer in people with a genetic mutation that mimics an aspirin effect,¹¹ and secretion of salicylate by plants to achieve programmed cell death.¹² Randomised controlled trials have detected a reduction in the growth of colon adenomas with aspirin,¹³ but no adequate randomised controlled trial of cancer prophylaxis by aspirin has been reported.

By reducing the incidence of cerebrovascular events, aspirin is already of value in reducing dementia. Evidence also suggests that aspirin and other non-steroidal anti-inflammatory drugs could reduce Alzheimer's disease.¹⁴

These further benefits of aspirin are not proved in randomised trials. However, if they occur they would be a bonus to the vascular protective effects and could affect some people's decision whether to take aspirin.

Why we need treatment for everyone

Within the United Kingdom, population screening to identify and treat those at high risk does not seem to be successful in controlling vascular disease. Many people at high risk remain undetected, and a survey of 1300 patients known to be at high risk within a representative sample of practices across Wales in 2003 found that only about half (53%) were taking aspirin.

Health promotion initiatives seem to achieve little behavioural change in the general community,¹⁵ and without additional social support, health education seems effective only in higher social classes. Although not an alternative to health promotion, nor a substitute for the appropriate treatment of high blood pressure, raised blood lipids concentrations, etc, the possibility that a simple, daily, inexpensive low dose pill would achieve a reduction in vascular disease events, and might achieve reductions in cancer and dementia, without the need for screening, deserves serious consideration.

Although we judge that aspirin should be taken from around 50 years, we recommend wide discussions on the threshold that include the general public, and we insist that the general public should be well informed and the final decision should lie with each person. Such discussions would not only fulfil the recommendations in the recent white paper that "people should make their own choices ... but these choices should be informed by good information and advice about the choices available ... to help people make and carry out the right decisions for their own health."¹⁶

They would also help meet expectations expressed by members of the public questioned in a recent King's Fund survey.¹⁷ Eighty six per cent of respondents said that information should be provided to the general public, and half said that the NHS should provide information, advice and support "To enable everyone to prevent illness and lead healthier lives." In fact, what we recommend would help put the public back into public health.—Peter Elwood, Gareth Morgan, Ginevra Brown, Janet Pickering

Contributors and sources: PE directed the Caerphilly Cohort Study, has been responsible for studies of aspirin in Wales, led the research leading to this article, and is lead author and guarantor. GM took part in discussions during the research leading to this article and helped write it. GB did some of the statistical analyses that guided the thinking behind this article. JP was involved in the studies on aspirin, worked with GB on the statistical analyses, and had a minor part in writing the article.

Competing interests: None declared.

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AGAINST An age threshold approach to aspirin prophylaxis in people without known vascular disease has two important problems. The balance of benefits and risks of aspirin in people aged 70 or over has not been clearly defined in randomised trials, and the benefits do not clearly exceed the risks in younger people without vascular disease. Consequently, it would be unwise to adopt such a policy, whatever age threshold is chosen, until we are sure that older patients will derive net benefit from it.

What studies show

Among high risk patients with known occlusive arterial disease and a greater than 3% annual risk of a vascular event (defined as non-fatal myocardial infarction, non-fatal stroke, or vascular death), the benefits of aspirin substantially outweigh the risks of bleeding. A recent meta-analysis of randomised trials of antiplatelet drugs versus control showed that for every 1000 such patients treated for a year, aspirin would be expected to prevent about 10-20 vascular events and cause one or two major gastrointestinal bleeds.¹ In a wide range of high risk patients, aspirin reduces the risk of a vascular event by around one quarter, with reductions of one third in non-fatal myocardial infarction, one quarter in non-fatal stroke, and one sixth in vascular death. In a patient with occlusive arterial disease, therefore, the expected benefit can be quantified as about a quarter of that person's baseline risk of a vascular event. For anyone with a definite history of arterial disease, the expected benefits far exceed the hazards, and so all should be considered for aspirin (or, if appropriate, another antiplatelet drug) unless there is a clear contraindication.¹

Unfortunately, predicting the benefits and hazards of aspirin in someone without known arterial disease is far less straightforward. To date, six primary prevention trials comparing aspirin versus control have reported their findings.²⁻⁷ A meta-analysis of the first five of these trials indicates that aspirin reduces myocardial infarction by about one third, but (in contrast to patients with known vascular disease) has little or no effect on stroke or death from vascular causes.⁸ More recently, data from the women's health study suggested that aspirin may protect against stroke in healthy women, but myocardial infarction was not significantly reduced.⁷ Although the 95% confidence intervals for the effect on myocardial infarction in this study were wide, and compatible with a modest benefit, these findings add to uncertainty about the net effects of aspirin in women.

Aside from this uncertainty, we can perhaps be moderately confident of preventing myocardial infarction in people without vascular disease, but it would be prudent to assume that aspirin would not necessarily reduce the risk of stroke or vascular death. (Nor indeed, is there reliable evidence from randomised trials that aspirin can prevent cancer or dementia, so these potential benefits should not be assumed.)

Risk of vascular events and bleeding

Estimating the current annual risks of myocardial infarction in the UK is complicated by the fall in event rates over the past two decades, when most cohort

studies were conducted. Consequently, the rates calculated from the Caerphilly study may have overestimated current UK annual risks of a vascular event. However, based on Elwood and colleagues' calculations from Caerphilly data,⁹ and assuming that a myocardial infarction is the first vascular event in around half of individuals, the annual risk of myocardial infarction for the age group 55-59 is 7 per 1000 population (from their table 2: 7.0% over 5 years, divided by 5, multiplied by one half). If aspirin reduces this risk by one third, then the absolute benefit (which may be an overestimate), is around two first myocardial infarctions avoided per 1000 population each year.

How does this compare with the expected risks of aspirin? The first thing to note is that the absolute excess risk of haemorrhagic stroke attributable to aspirin is small (around 0.1/1000 a year). However, the risks of major gastrointestinal bleeding (that is, bleeds that are fatal or require transfusion) also need considering. To assess these risks for unselected individuals we have to turn to observational studies because people with risk factors for bleeding have been excluded from the primary prevention trials. A review of observational studies suggests that the background risk of major gastrointestinal complications rises steeply from 1-2/1000 a year at age 60 to around 7/1000 above age 80,¹⁰ and since aspirin roughly doubles the risk of gastrointestinal bleeding, the attributable excess risks at each age are likewise 1-2/1000 a year at age 60, rising to 7/1000 a year at age 80. Among unselected people younger than 60, therefore, the expected benefit on myocardial infarction (2/1000/year avoided) does not clearly exceed the expected risk of a major gastrointestinal bleed (1-2/1000/year).

Given this lack of a clear benefit at age 60, we might consider raising the age threshold to 65 or 70. But, whereas the benefits of aspirin on myocardial infarction are reasonably well defined in middle age, little is known of its effects in older people. In particular, primary prevention trials have included relatively small numbers of people over 70, for whom the potential benefit may be largest. Given that the observational studies strongly suggest that the risks of bleeding might increase substantially in older people (as does fatality



ERIC O'CONNELL/PHOTONICA

Who would benefit from daily aspirin?

from a bleed), we need decisive evidence of benefit in this age group before exposing large numbers of healthy people to potential harm. In my view, therefore, we should not contemplate an age threshold approach to primary prevention with aspirin until we have much better evidence of its benefits in older people. We therefore need further randomised trials comparing low dose aspirin with placebo, such as the aspirin in reducing events in the elderly (ASPREE) study,¹¹ which aims to randomise 15 000 people aged 70 or over to aspirin 100 mg daily versus placebo. A recommendation that aspirin be used for primary prevention of vascular disease in unselected people over a certain age could result in net harm, and we must have very good evidence to the contrary before instituting such a policy.—Colin Baigent

Contributors and sources: CB coordinates the Antithrombotic Trialists' Collaboration, which is currently reviewing the evidence from the primary prevention trials of aspirin versus placebo.

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GMC and the future of revalidation

Obstacles to maintaining licensure in the United States

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Although relicensing of doctors is well established in the US, systems to evaluate competence rigorously are still some way off

Public pressure for accountability of doctors is increasing in the United States as it is in the United Kingdom. The release of several high profile reports in the 1990s regarding systems based errors and patient safety prompted US medical licensing and regulatory agencies to review their role in assuring the ability of healthcare practitioners to practise safely, not just at the point of initial licensure but over the course of their careers. Before effective systems to assess doctors' continuing competence can be implemented, however, medical licensing authorities need to establish what should be measured and how, and to consider the potential repercussions on medical regulation as a whole.

US licensing procedures

Medical licensure in the United States is granted by state licensing boards comprising doctors, other health care providers, and public representatives. The licensing board is charged by statute to ensure that only qualified, competent, and ethical doctors are licensed to practise medicine in that state. The medical boards also have a judicial role to protect citizens from being harmed by doctors who do not meet these qualifications or who violate standards of practice. To obtain a medical licence, a doctor must have completed a



Is he fit for the job?

medical degree from a recognised or accredited medical school, postgraduate training in the United States, and a national, standardised medical licensing examination that includes assessment of clinical skills. Some states have additional requirements, such as passing a jurisprudence or medical ethics examination or a personal interview.

This is the sixth in a series of articles examining regulation of doctors

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