Evidence from a wide range of sources suggests that individuals taking aspirin and related non-steroidal anti-inflammatory drugs have reduced risk of large bowel cancer. Work in animals supports cancer reduction with aspirin, but no long-term randomised clinical trials exist in human beings, and randomisation would be ethically unacceptable because vascular protection would have to be denied to a proportion of the participants. However, opportunistic trials of aspirin, designed to test vascular protection, provide some evidence of a reduction in cancer, but only after at least 10 years. We summarise evidence for the potential benefit of aspirin and natural salicylates in cancer prevention. Possible mechanisms of action and directions for further work are discussed, and implications for clinical practice are considered.

Introduction

When aspirin was first marketed, unsubstantiated claims were made that the drug could benefit a wide range of conditions, including cancer, without harm to the heart. Presently, the benefit of aspirin for ischaemic heart disease is supported by meta-analyses of many randomised trials, whereas its effect on the reduction of cancer incidence is suggestive and under intense investigation.

The suggestion that aspirin could be of benefit against cancer initially arose from the observation that tumour metastases are reduced in rats with thrombocytopenia.1–3 Subsequently, prostaglandin concentration proved to be raised in rat colorectal tumour tissue,4 which strengthened the expectation that benefit was mediated through inhibition of cyclo-oxygenase (COX). A case-control study of 700 patients with colorectal cancer was first to show a possible effect on human cancer.4 An inverse association between the incidence of various cancers and the use of aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs) has since been supported by many epidemiological findings,7–9 work in animals, and the study of natural salicylates in plants. Several cellular mechanisms that could plausibly mediate this benefit have been identified and less than 1 mmol concentrations of aspirin salts can induce apoptosis in human tumour-cell lines.10

Because of the diversity of the evidence base on aspirin and cancer, this Review is the outcome of a collaboration between individuals in various disciplines, each with specialist knowledge in their area. Each author has presented evidence and the framework for the paper is a hierarchy of this evidence. Because of the range of sources of evidence, we believe that the form of a systematic review would be restrictive and inappropriate.

Evidence from randomised trials

The most conclusive evidence for an association between aspirin and cancer would be shown by randomised controlled trials. However, the risks of vascular events and cancer increase with age, and denial of vascular benefits to participants in the control group of new cancer-reduction trials would probably be judged unethical. Nevertheless, we have gathered evidence from previous studies, which involved the random allocation of aspirin or other NSAIDs for purposes other than cancer reduction.

Randomised trials and cancer

Three studies were designed to examine the effect of aspirin on vascular disease.11–14 In the US Physicians’ Health Study,13 22 071 men were randomised to 325 mg aspirin or placebo every other day. After a 5-year follow-up, the relative risk (RR) of developing colorectal cancer in men given aspirin compared with placebo was 1·15 (95% CI 0·80–1·65). In a UK study of 5000 male doctors,12 two-thirds were randomised to 500 mg aspirin daily for 6 years. Cancer deaths were 18% lower in the aspirin-treated group, but there was no effect on non-fatal cancer incidence.15 In the US Women’s Health Study,12 16 400 000 women were randomised to 100 mg aspirin or placebo every other day and followed up for 10 years. The women given aspirin showed no reduction in total cancer, breast cancer, or colon cancer incidence. Lung cancer deaths were, however, reduced in the aspirin groups of these three trials, by 22%, 36%, and 18%, respectively.15

Aspirin effects on cancer were not the primary endpoint in these trials. Two of the trials were limited by the frequency of aspirin use13,15 and all three trials had a short follow-up, which might have masked benefits. Observational studies in women suggest that at least a decade of aspirin use might be needed for protection to become
apparent,10–18 which is consistent with re-examination of data from the UK study of male doctors12 and the UK Transient Ischaemic Attack Aspirin Trial.19 An overall reduction was detected in colorectal cancer (hazard ratio 0.74 [95% CI 0.56–0.97]), but there was a pronounced trend of reduction over time, which was significant only after 10 years’ prophylaxis (0.60 [0.42–0.87]). Additionally, in the two UK trials,12,20 aspirin was given at 300 mg and 1500 mg daily, respectively, whereas in the two US trials,11,13 the aspirin doses were 325 mg and 100 mg, respectively, on alternate days.

**Randomised trials in colon polyps**

Adenomatous polyps are a precursor in the putative pathway of colon cancer development. Treatment of 635 patients, who previously had colorectal cancer, with 325 mg aspirin daily, reduced the incidence of recurrent adenomas (RR 0.65 [95% CI 0.46–0.91]) and delayed the development of a new polyp.21 In a randomised study of the prevention of polyps by aspirin in 1121 patients,22 the relative risk of a poly after 1 year, compared with placebo, was 0.81 (0.69–0.96) in the patients treated with 81 mg aspirin daily, and 0.96 (0.81–1.13) in those treated with 325 mg aspirin. The relative risk of histologically advanced polyps was 0.58 (0.37–0.90) and 0.83 (0.55–1.23), respectively. The researchers postulated that the greater benefit on advanced polyps suggested that the effect of aspirin might increase in the later stages of the adenoma-carcinoma transformation.

**Mendelian randomisation studies**

These randomised trials are based on the assumption that population distribution of genetic variants is independent of behavioural, dietary, and environmental factors. Confounding by such factors, which can distort associations in observational studies, is therefore avoided and comparisons between patients with and without a particular mutation are similar to that from a trial with randomised intervention.23 A polymorphism that changes a nucleotide in COX-2 (an isof orm of prosta-
glandin H2 synthase) leads to effects that mimic some of the effects of aspirin—a case-control analysis of African-American people showed an odds ratio for colorectal adenomas of 0.56 (95% CI 0.25–1.27) in 161 carriers relative to 219 controls.24 In another study the odds ratio for colorectal cancer in 138 carriers was 0.67 (0.28–1.56) relative to 238 controls.25 However, study of a larger population sample is needed to substantiate these interpretations.

**Randomised trials in animals**

Studies of chemically induced cancer in animals have shown a high degree of protection by aspirin and other NSAIDs, both in cell cultures26 and in live animals.27–29 In a review of work in animals, the International Agency for Research on Cancer judged that a causal relationship had been established.27 Thun and co-workers30 reviewed more than 40 animal studies and drew three conclusions: tumour suppression is greatest if prophylaxis is started before, or coincident with, exposure to a carcinogen; both selective and non-selective NSAIDs inhibit tumour development; and prophylaxis should continue without interruption.

**Evidence from observational studies**

Several groups have examined participants taking aspirin for reasons other than the reduction of cancer risk. The studies varied in strategy, population examined, type of cancer, and the aetiological and pathological processes of the cancer. Evidence of benefit in such diverse studies could be suggestive of a true effect on carcinogenesis. However, this consistency could also be affected by unknown lifestyle, dietary, or other factors.

**Colorectal studies**

Rectal and colonic polyps are the precursor to most colorectal cancer, and patients with familial adenomatous polyposis have a very high risk of cancer.31 Published work on aspirin and NSAID use in this context is extensive. In several observational studies, the reduction in polyp number and growth was attributable to aspirin treatment, and the effects ceased once aspirin or NSAID was no longer given. Overviews of observational studies have suggested relative risks attributable to aspirin of 0.71 (95% CI 0.65–0.76), 0.71 (0.67–0.75),32 and 0.77 (0.61–0.96).33 A review of six case-control and three cohort studies of 5-aminosalicylates resulted in an odds ratio of 0.51 (95% CI 0.38–0.69).34 In another overview, non-aspirin NSAID treatment was associated with a relative risk of 0.63 (95% CI 0.57–0.70).35 Regular reports from the US Nurses’ Study36 of 79,439 women showed a substantial reduction in cancer deaths for current aspirin users (0.88 [0.81–0.96]), which became significant after 10 years’ use, and increased by 20 years’ use.37 Examination of 146,113 participants in the Cancer Prevention Study II38 also showed a significant reduction in overall cancer (but only in men: 0.84 [0.76–0.93] in men and 0.86 [0.73–1.03] in women), colon cancer, and prostate cancer, and a non-significant reduction in breast cancer for those who had taken “adult-strength” aspirin for at least 5 years. However, no reduction was shown in participants who had taken 14 or more tablets per week (1.14 [0.98–1.32]).

**Studies of other cancers**

Aspirin use has also been associated with reduced incidence of other cancers, including those of the oesophagus, stomach, breast, lung, bladder, ovary, prostate, mouth, and skin, and some of which have pathological changes very different from those of colonic cancers. Benefits of aspirin to other cancer sites are less consistent than in the colorectal studies—according to Khuder and Mutgi,39 there is considerable heterogeneity. Assessment of 34 case-control and 13 cohort studies
showed that the relative risk of oesophagus, stomach, and breast cancer were 0·51 (0·38–0·69), 0·73 (0·63–0·84), and 0·77 (0·69–0·86), respectively, in those taking aspirin,9 and in meta-analysis of eight case-control and six cohort studies the relative risk of breast cancer was 0·82 (0·75–0·89).10 From 20 observational studies, NSAIDs seem to offer some protection against breast cancer and might be of benefit to women with cancer.11 Several factors increase the robustness of findings from observational studies: (1) cancer reduction is similar for both men and women; (2) stopping prophylaxis is followed by a rapid loss of protection; (3) several NSAIDs seem to have an effect similar to aspirin; and (4) analgesics other than NSAIDs do not reduce cancer incidence.12

**Dose and duration of prophylaxis**

Since the dose of aspirin differs substantially across studies, we cannot draw firm conclusions about the best dose for reduction of cancer incidence. Two studies suggest that 81 mg aspirin daily is the optimum dose,13,14 whereas data from the Women's Health Initiative,7 showed a protective effect only with doses of more than 100 mg daily, but a subsequent study based on subgroups within this same cohort failed to find evidence of benefit.14

Several researchers have reported increased benefit with larger doses,15,16 and one study showed that at least 300 mg daily is necessary for substantial reduction in adenomas.17 Two further reports detected a significant reduction in cancer incidence, but one used between 300 and 1200 mg daily18 and the other used only one to 14 tablets of “standard strength” per week.19

Several reviews of cancer prophylaxis with aspirin have identified the importance of duration and continuity of use.20 For most cancers, the time from carcinogenesis to clinically detected disease is at least 10 years. As we have noted, in the Nurses’ Health Study, reduction of disease was significant only after 10 years of aspirin use,21 and the relative risk was 0·56 (0·36–0·90) after 20 years.22 This result was supported by a nested case-controlled study within the same cohort, which showed a relative risk after 10 years of 0·75 (0·61–0·92).23

**Evidence from plants**

A range of salicylates is found in plants and the actions of salicylic acid have been well characterised by plant physiologists. Because aspirin is rapidly metabolised to salicylic acid in human serum, research in plants could provide a model for the effects of aspirin in man. In fact, Pierpoint24 has speculated that the medicinal properties of salicylates in man are a logical result of their role in plants.

In most species, salicylic acid concentration in unstressed plants, in fresh weight, is around 0·05 μg/g. Plants challenged by pathogens show a rise to about 4–8 μg/g at the site of infection and whole plant concentration of about 1 μg/g. Concentration is further raised during heating and cooling, and present agricultural practices that environmentally cosset plants tend to grow produce with lower concentrations of salicylates than do organic practices.25 Many herbs and spices are especially rich in salicylates,26,27 which could be of relevance to international differences in cancer incidence.

In plants, the hypersensitive response to pathogens has striking similarities to mammalian apoptosis:28 longlasting increase in cytoplasmic calcium, an oxidative burst, and nitric oxide production29 leads to activation of cysteine proteases—although not caspases, which do not seem to exist in plants—and causes cytoplasmic shrinkage and DNA degradation. The pathogen is deprived of nutrients and entrapped in a region undergoing rapid cellular collapse. During the hypersensitive response salicylic acid potentiates the oxidative burst, which determines the speed of cell death.30 One of the most important oxygen species for this process is a nicotinamide adenine dinucleotide phosphate (NADPH) oxidase superoxide-generating complex, which has high sequence homology to the equivalent component—cytochrome b558—in mammalian neutrophils.31 Modulation of NADPH oxidase by salicylic acid is a probable mechanism for increased oxidative stress and accelerated cell death,32 but this mechanism needs further characterisation in man. Salicylate has been usefully used to potentiate NADPH oxidase-mediated reactive oxygen generation in some cancer cells to promote apoptosis.33 However, salicylate can also generate reactive oxygen species, in both plants and animals, by disrupting mitochondrial function34–36 or inhibiting antioxidant enzyme activities.37

Several studies have shown an inverse relation between cancer risk and plant consumption. For example, in a study of 6000 people, the fifth with the highest fruit and vegetable intake had a hazard ratio for cancer deaths of 0·65 (95% CI 0·45–0·93) compared with the fifth with the lowest intake.7 Neither the mechanism nor the components of fruit and vegetables that protect against cancer are known, but natural salicylates are widely distributed in fruits, vegetables, herbs, and spices,38,39 and might explain the reduction in cancer risk. A preventive role for plant salicylates necessitates that they are absorbed in substantial quantities and the concentration in western diets is probably too low to affect disease risk.30 Serum and urinary concentrations of salicylates in vegetarians are, however, greater than those in omnivores, and overlap with those in individuals taking low-dose aspirin.34–36

**Possible mechanisms of salicylates**

Evidence from a wide range of sources is consistent with an association between the intake of dietary or pharmaceutical salicylates and a reduction in the risk of cancer. Thus we can consider mechanisms that might account for such an association because the identification of biologically plausible mechanisms should enhance the probability that a causal association will be identified.
The processes by which normal cells are transformed into cancer cells is highly complex and despite substantial research, the way in which salicylates might affect carcinogenesis is still not certain. However, a common characteristic in the early stages of cancer development is that cells no longer respond to signals to prevent proliferation and differentiation, but autonomously generate signals to promote growth. The involvement of aspirin in moderation of these processes will probably be of relevance.

Inhibition of cyclo-oxygenase

One obvious molecular target for aspirin is COX-2 since this enzyme is strongly and rapidly induced in response to mediators of inflammation, growth factors, cytokines, and endotoxins, and is involved in cell proliferation and tumour promotion. This mechanism is supported by the fact that aspirin can decrease the production of potentially neoplastic prostaglandins which arise from COX-2-mediated catalysis of arachidonic acid. The carcinogenic contribution of prostaglandins has generated much interest; their deleterious effects include promotion of cell survival, stimulation of cell proliferation, and promotion of angiogenesis. These effects can also enhance cancer spread and thus underscore the chemopreventive potential of aspirin.

Aspirin (81 mg or more) suppresses prostaglandin concentration in colon mucosal biopsy samples. Aspirin also inhibits COX-1, which is constitutively expressed on the endoplasmic reticulum membrane of all cells and is associated with normal cellular functions—eg, platelet aggregation, vascular homoeostasis, renal blood flow, and glomerular function. The therapeutic effect of aspirin in myocardial infarction is postulated to be attributable to the inhibition of COX-1 in platelets, by the attachment of the aspirin acetyl group to serine 530, located within the enzyme active site. As a result, access of arachidonic acid to the active site is hindered and inhibition of thromboxane synthesis causes inhibition of platelet aggregation. By contrast, inhibition of COX-2 by aspirin might not be caused by the acetylation of its active site. Aspirin is about 160 times more specific to COX-1 than COX-2, despite the similar structure of both forms of cyclo-oxygenase. Furthermore, the active site of COX-2 is larger than that of COX-1 and so it can accept arachidonic acid even when acetylated.

The main metabolite of aspirin, salicylic acid, could suppress COX-2 expression during transcription because at therapeutic concentrations (10–3–10–4 mol/L), it suppresses COX-2 messenger RNA (mRNA) and protein synthesis in human endothelial cells and fibroblasts. Moreover, in mice with salicylate-rich diets, COX-2 mRNA expression is suppressed in peritoneal macrophages. The fact that salicylic acid can decrease the production of prostaglandins is supported by its use as a natural anti-inflammatory agent long before aspirin was synthesised, and might suggest that dietary salicylates (which are not acetylated) can also prevent cancer.

Cellular apoptosis

Mounting evidence suggests that the acquired ability of cells to resist apoptosis is a hallmark of most, and perhaps all, types of cancer, and pro-apoptotic effects of aspirin could be mediated through inhibition of COX-2. However, the chemopreventive effect of aspirin and NSAIDs cannot be explained by the inhibition of prostaglandin synthesis alone, since several NSAIDs have antiproliferative effects in cells without COX activity. High aspirin doses induce apoptosis through COX-independent mechanisms, by regulating several different targets—a proapoptotic gene PAWR, and an antiapoptotic gene BCL2L1. Additionally, NSAIDs including aspirin also induce apoptosis by the activation of caspases, the activation of p38 MAP kinase, release of mitochondrial cytochrome c, and activation of the ceramide pathway. These effects might not be universal to all cell types, however, and the range of doses of aspirin needed in such COX-independent pathways could be higher than for the inhibition of COX-2.

Aspirin-mediated inhibition of activation of NFκB—a transcription factor that activates genes involved in inflammatory responses and apoptosis—could also be an important chemopreventive mechanism in some cancers. The NFκB response to aspirin has clear differences dependent on the tissue origin of the cell, and these differences parallel the epidemiological evidence relating to the effects of aspirin on incidence of colorectal, breast, and gynaecological cancers. The effect of aspirin on NFκB signalling and apoptosis does not seem to be related to COX-2 expression, providing further evidence that both COX-2-independent and dependent mechanisms have a role in the anti-tumour effects of aspirin and other NSAIDs.

Another mechanism that might contribute to the potential chemopreventive effects of aspirin is the upregulation of tumour suppressor genes such as TP53, CDKN1A, and BAX, and the downregulation of antiapoptotic genes such as BCL2. Indeed, research in progress has shown that submmol concentrations of a range of aspirin salts, at doses that might occur in natural exposure to low amounts of dietary salicylate, can induce and enhance apoptosis in several human tumour cell lines.

DNA mismatch repair

Aspirin might also affect the DNA mismatch-repair system, which is designed to protect against the accumulation of mutations and the development of neoplasia during DNA replication at cell division. An element in the DNA polymerase complex proof-reads the DNA, and a mismatch-repair process attempts to restore the integrity of the DNA if mutations occur. If this process fails a DNA mutation might persist. Additionally, many tumours, especially those in the colon and rectum, acquire somatic mutations or epigenetic silencing of
repair sequences, or both, which can inhibit the DNA-repair process.

Individuals with inherited mutations at one of four mismatch genes exhibit microsatellite instability, accounting for perhaps 5–10% of colonic tumours.90–92 One study has shown that exposure of cultured cells to aspirin reduces the microsatellite instability in mismatch-repair-deficient colon cancer cells.93 In another, aspirin treatment resulted in an increase in mismatch-repair proteins and subsequent apoptosis in a mismatch-repair-proficient cell line, or growth inhibition in the mismatch-repair-deficient line.94 Neither of these cell lines expresses COX-2, further emphasising the COX-2-independent mechanism of aspirin.

Other possible mechanisms
Several other mechanisms possibly contribute to the chemopreventive and therapeutic effects of aspirin and other NSAIDs. For example, salicylic acid might inhibit tumour cell proliferation by inhibiting mitochondrial calcium uptake, which is a necessary ubiquitous influx pathway for cell proliferation.95 Salicylic acid might also have a role in decreasing DNA damage since its inclusion in the diet of rats, which were injected with an alkylating agent, decreased markers of oxidant stress and upregulated glutathione peroxidase 2, a key antioxidant enzyme in the colon.96 Furthermore, aspirin inhibits phenolsulphotransferase, a carcinogen activator,97 and might have prostaglandin-independent effects on angiogenesis.98 The extent to which such effects are important in cancer prevention needs to be established.

Existing and future studies
Thun and coworkers29 have identified more than 20 randomised trials in progress, all of which are investigating the effects of aspirin or other NSAIDs on the growth or regression of polyps, colon or rectal epithelial growths, or prostaglandin production in colon mucosa. None of these investigators propose to explore cancer incidence.

Placebo-controlled trials that have cancer as the primary endpoint are unlikely to be acceptable in healthy elderly people. However, randomised trials in patients at high risk of cancer might be acceptable, and at least one placebo-controlled trial in patients with Barrett’s oesophagus is in progress.99 Placebo-controlled trials might also seek to recruit younger patients in remission from cancer or those with an oncogene. Evidence from such trials would be highly informative, though it might not be appropriate to extrapolate the results from such selected patients to the general population.

Further conventional observational cohort studies and studies of cellular mechanisms will be useful, although evidence from these sources cannot be conclusive with respect to cancer prevention. However, large-scale observational studies of the effect of functional polymorphisms that relate to or mimic the effect of aspirin can provide important evidence, especially if they are linked to environmental exposures. In view of the ethical restrictions to the conduct of aspirin-related randomised controlled trials, large gene-environment interaction studies will probably be very valuable. Furthermore, the correlation between cancer incidence and salicylate concentration in stored blood or urine, obtained from participants in existing large, long-term cohort studies could be examined.48

The future will largely rely on pharmacological advances, including improvement of the selectivity of NSAIDs, reduction of undesirable gastrointestinal effects of NSAIDs, and the possible combination of several drugs that are individually effective.97 Aspirin has an unsatisfactory side-effect profile, but, regrettably, little research has been done to produce a more tolerated form of aspirin.72

The role of *Helicobacter pylori* in bleeding also needs to be defined. Such infection increases the risk of bleeding attributable to aspirin by perhaps four-fold96 and both eradication of the infection and adjuvant proton-pump inhibitor therapy, seems to substantially reduce the incidence of gastric bleeding.101,102

Relevance to clinical and public health practice

**Epidemiology of cancer**
Every year in the UK, almost 250 000 cancers are diagnosed and 140 000 deaths occur, which is equivalent to a quarter of all UK deaths. During the past 25 years, cancer mortality has fallen by about 5% in men, and risen by about 20% in women. Most cancers are age-related, and both the risk and the overall mortality rate increases
by about 50% every 10–15 years of age.202 By the age of 70 years, around 25% of men and 20% of women in the UK will have been diagnosed with some form of cancer.

Colon cancer, with 22,000 cases per year in the UK, is the second leading cause of cancer. People with familial adenomatous polyposis have a very high lifetime risk of cancer, believed to be more than 95%, and first-degree relatives are at increased risk from about 20 years of age.203 Whereas only a tiny proportion of all cancers occur in those with familial polyposis, colon polyps are frequent in healthy individuals, with post-mortem examinations identifying polyps in about a third of those aged 50 years, rising to about half of those aged 70 years.204

Aspirin prophylaxis

Regular aspirin is recommended for people at known increased risk of cancer, although risk has not been defined in this context. Marcus205 says “we, as physicians, must advise our patients now” and advocates that patients who might be at increased risk are advised to take prophylactic aspirin. From present epidemiological and clinical evidence, Elder and colleagues206 believe that there is little doubt that aspirin and related compounds have considerable potential as chemopreventive agents for colorectal cancer. Jacobs and Thun,207 commenting on the absence of benefit in the Women’s Health Study,208 judge that the totality of the evidence from laboratory studies, observational epidemiology, and randomised trials of colorectal polyp recurrence support the hypothesis that moderate or high doses of aspirin might reduce the risk of colorectal cancer, and possibly the risk of other cancers as well. Harris and co-workers209 report the evidence of NSAID benefit to be compelling, and Flossman and Rothwell210 describe the evidence on aspirin and colon cancer as “an epidemiological success story”.

By contrast, several researchers believe that in view of the adverse effects of NSAIDs, and uncertainties about dose and duration of use, to recommend their use as standard medical practice for cancer prevention would be premature.211,212,213 The average lifetime risk of colorectal cancer for the population is only 5% or 6%, and therefore the balance of risk and benefit of aspirin precludes its use.29 These researchers, however, add a most important caveat—NSAIDs should not be promoted for cancer prevention unless the benefits extend to other health endpoints. Aspirin certainly benefits conditions other than cancer—namely, vascular diseases—which is relevant to assessments of the overall risk-benefit balance of the drug if it were to be used in cancer prophylaxis. Aspirin, even at the low doses appropriate for vascular use, roughly doubles the incidence of gastric bleeding, and one or two people in every thousand are likely to have a bleed every year.214 The risk, however, rises with age and in people older than 80 years, it might be as high as seven per 1000 people every year.215,216 Evidence for a relation between cerebral bleeding and aspirin is less certain, but in a meta-analysis of data from 13 randomised trials (mean age of participants between 60 and 70 years) the relative risk of a cerebral bleed from aspirin was estimated to be between about 1·4 and 2·2, with an absolute incidence of bleeding attributable to the drug of 1·2 per 1000 persons per year (95% CI 0·5–2·0).217 Finally, in any assessment of the possible benefit of aspirin for cancer prophylaxis, or for protection from vascular disease, patients’ value of the possible outcomes should be given appropriate consideration.218

Conclusions

Dietary or pharmaceutical salicylates might reduce the risk of cancer—there is evidence that aspirin affects mechanisms relevant to carcinogenesis—but the value of aspirin in cancer prophylaxis is limited by the constraints on randomised placebo-controlled clinical trials. More evidence from every possible source is therefore needed before the role of aspirin in clinical practice can be more clearly defined.

Aspirin is prone to undesirable side-effects, in particular bleeding, and development of a safer form of aspirin, or a drug combination, should be urgently undertaken to improve the risk-benefit balance. In this context, the relevance of infection with H pylori should be further investigated. The risk–benefit balance of aspirin for cancer prophylaxis should also be assessed in conjunction with its well established benefits in vascular disease.

Contributors

PCE searched for relevant articles for the Review. PCE, AMG, and GM contributed to writing of the report. GGD contributed expert knowledge about fruit and vegetable consumption, and mechanisms such as COX inhibition and apoptosis. LAJM contributed expert information about salicylate function in pants, and wrote this section of the Review.

Conflict of interest statement

PCE reports receiving lecture fees from Bayer; GGD reports receiving research grants from the Scottish Executive Rural Affairs Department (SEERAD), the Scottish Enterprise, the Cranberry Research Institute, the European Union Framework programme, and the UK Food Standard Agency; we declare that we have no conflict of interest.

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References


