Taking aspirin together with cancer treatment results in reductions in death from cancer and all-cause mortality, both by around one fifth. The meta-analysis, published in ecancermedicalscience, (online 2 July), demonstrates benefits for aspirin across a range of cancers and shows fatal bleeding adverse effects to be rare.

"We judge that the body of evidence now available on the efficacy and safety of aspirin justifies its use as an adjunct treatment in a wide range of cancers," write the authors, led by Peter Elwood, from Cardiff University, Wales.

Substantial epidemiological evidence has indicated that regular use of aspirin is associated with both reduced risk of developing cancer, and of dying from cancer. It is well-known that aspirin affects multiple intracellular pathways, influencing physiological processes (such as apoptosis and angiogenesis) important in the growth and development of malignancies. Results from several randomised trials are currently awaited that should provide clear evidence of benefit in colon, breast and prostate cancer. However, since the biological effects of aspirin are likely to be relevant to metastatic spread of cancer in general, Elwood and colleagues decided to test the hypothesis that taking aspirin was associated with increased survival in a range of different cancers.

Overall the investigators have conducted three consecutive systematic literature searches in 2016, 2018 and finally in 2020 (including studies published up to March 2020), with the final analysis including a total of 118 published observational studies involving 18 different cancers. Of the papers, 81 included information on aspirin and cancer deaths and 63 on aspirin and all-cause mortality. The team also considered risks from aspirin and requested information about gastrointestinal bleeding from an author on each of the selected papers.

Results show that aspirin taking was associated with a reduction of about one fifth in a range of 18 cancers (HR: 0.79) across 70 observational studies, and the effect of aspirin on all-cause mortality was (HR: 0.80) across 56 observational studies. Additional results found:

- For colon cancer mortality analysis of 24 studies showed HR favouring aspirin of 0.72,
- For breast cancer mortality analysis of 13 studies showed an HR favouring aspirin of 0.84,
- For prostate cancer mortality, analysis of 15 studies showed an HR favouring aspirin of 0.89.

While the frequency of bleeding increased in patients taking aspirin, fatal bleeding was rare with no author reporting a significant excess in fatal bleeds associated with aspirin or cerebral bleeding in the patients they had followed.

"A reasonable interpretation of these results is – that at any time after a diagnosis of a wide range of different cancers, about 20% more patients who take aspirin are likely to be alive, compared with patients not taking aspirin," conclude the authors of the meta-analysis.

The authors stress that aspirin is not a possible alternative to any other treatment. "Although in poorer countries aspirin could be one of very few, or perhaps the only acceptable treatment on the grounds of cost and availability," they write.

Commenting on the study Mangesh Thorat, from the Centre for Cancer Prevention, at the Wolfson Institute of Preventive Medicine, Queen Mary University of London, UK, says, "This review pooled data from numerous observational studies, which are hypothesis generating. It is randomised trials that provide definitive evidence to consider changes to clinical practice. The results of this review provide impetus for cancer patients to consider participation in these trials and for the scientific community to consider developing trials in cancers that are not already being investigated."

Until results from major trials become available, he says, cancer patients should not be rushing to

take aspirin. "But (they) should certainly discuss trial participation with their treating clinicians."

Investigators are also exploring the cancer preventive effects of combining aspirin with metformin, a first-line antidiabetic agent associated with reduced cancer incidence and mortality in diabetic patients. In the ongoing <u>ASAMET</u> trial, led by Andrea DeCensi (Ospedali Galliera, Genoa), 160 patients who have undergone surgery for stage I-III colorectal cancer are being randomly assigned in a 2X2 design to aspirin, metformin, their combination or placebo.