

Lynch syndrome: should I take aspirin to reduce my chance of getting bowel cancer?

Patient decision aid: user guide and data sources

Background

Recommendation 1.1.1 of the [NICE guideline on colorectal cancer](#) states:

1.1.1 Consider daily aspirin, to be taken for more than 2 years, to prevent colorectal cancer in people with Lynch syndrome.

The choice for someone with Lynch syndrome about whether or not to take aspirin to reduce their risk of bowel cancer involves weighing up the likely benefits against the possible harms and inconvenience of taking daily aspirin. This is in the context of an evolving evidence base, where answers to some key questions are currently uncertain, such as the optimal dose and duration of aspirin and the risk of adverse effects from prolonged high-dose use. It is therefore a highly preference-sensitive choice, and the NICE patient decision aid may help with shared decision-making by the person and their healthcare team.

At the time of publication (August 2020), aspirin does not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, obtaining and documenting informed consent. See the [General Medical Council's Prescribing guidance: prescribing unlicensed medicines](#) for further information.

Summary of the evidence

The decision aid is based on [NICE evidence review A1](#) of the [NICE guideline on colorectal cancer](#). The icon arrays show the possible benefits from at least 2 years of taking aspirin, and are based on the CAPP2 study because this had the most suitable data.

The CAPP2 study included 861 people who had Lynch syndrome, who were randomised to receive either 600 mg aspirin or placebo for 2 years, with an option to continue for a further 2 years (the mean duration of aspirin use was 25 months, range 0.8–61 months).

At the time of guideline publication, only 5-year follow-up data from the CAPP2 study had been published ([Burn et al 2011](#)). No statistically significant benefit from aspirin was seen in the intention to treat (ITT) population after a mean 4.6 years of follow up, though a statistically significant benefit was seen in the per-protocol analysis of people who took aspirin or placebo for at least 2 years.

Data from a mean 10 years of follow up became available after guideline publication ([Burn et al 2020](#)). Information from this study was used in the decision aid because this longer duration of follow up provides improved information for decision-making.

A statistically significant benefit from aspirin was seen in both the ITT and the per-protocol analysis with the longer follow-up period. The decision aid shows the results from the 10-year per-protocol analysis because this reflects the duration of treatment recommended in the guideline. Additionally, the statistically significant benefit in the ITT population at 10 years is most likely to be driven by the benefit within the sub-population who took aspirin for at least 2 years.

After a mean 10-year follow up, the hazard ratio (HR) for first colorectal cancer was 0.65 (95% confidence interval [CI] 0.43 to 0.97) in the ITT population and 0.56 (95% CI 0.34 to 0.91) in the per-protocol analysis. Incidence rate ratios (IRRs) were 0.58 (95% CI 0.39 to 0.87) and 0.50 (95% CI 0.31 to 0.82) respectively.

The event rate in the ITT population of people randomised to placebo (control event rate) over 10 years was $58/434 = 13.36\%$ (rounded to 13 per 100 for the decision aid). Applying the HR from the per-protocol analysis to this gives an event rate in the aspirin group of 7.48%, 95% CI 4.54% to 12.16% (rounded to 7 per 100 for the decision aid). Applying the IRR to the ITT control event rate gives a similar figure. There are methodological limitations to using HR instead of relative risk, but the

[project development group](#) agreed that, given the limitations of the evidence, the difficulty of conveying confidence intervals graphically and the primary purpose of the icon array (giving an indication of the magnitude of the likely effects of aspirin), using the point estimate HR was appropriate.

The CAPP2 study found no statistically significant difference in the risk of adverse events between aspirin and placebo groups. These data were only collected during the intervention period (mean 29 months) and not during the follow-up. There were also no age-stratified data available to assess the risk in older participants. Information on potential adverse effects in the decision aid is taken from the [summary of product characteristics \(SPC\) for aspirin 300 mg tablets](#) (Accord UK Ltd). Information on safety in pregnancy and breastfeeding is taken from the [National Teratology Information Service](#) and [NHS Specialist Pharmacy Services](#) monographs.

Developing and updating the decision aids

This patient decision aid was developed by NICE and a project group drawn from the guideline committee including health professionals and lay members, according to the [NICE process guide](#). Stakeholders who responded to the guideline consultation commented on a draft of the patient decision aid.

NICE decision aids are based on NICE recommendations. If the recommendations are updated, the decision aid will also be updated.

References

Burn J, Gerdes A-M, Macrae F et al. (2011) [Long-term effect of aspirin on cancer risk in carriers of hereditary colorectal cancer: an analysis from the CAPP2 randomised controlled trial](#). Lancet 378: 2081–7.

Burn J, Sheth H, Elliott F et al. (2020) [Cancer prevention with aspirin in hereditary colorectal cancer \(Lynch syndrome\), 10-year follow-up and registry-based 20-year data in the CAPP2 study: a double-blind, randomised, placebo-controlled trial](#). Lancet 395: 1855-63.