



2020 exceptional surveillance of colorectal cancer (NICE guideline NG151)

Surveillance report

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Surveillance decision

We will not update the [NICE guideline on colorectal cancer](#).

Reason for the exceptional review

[Recommendation 1.1.1](#) states to consider daily aspirin, to be taken for more than 2 years, to prevent colorectal cancer in people with Lynch syndrome. This recommendation was partially informed by the [CAPP2 study \(2011\)](#) which had a 4.7 years mean follow-up. In June 2020 the [10-year follow-up of the CAPP2 study](#) was published. The aim of this surveillance review is to determine if recommendation 1.1.1 needs to be updated following the 10-year follow-up.

Methods

The exceptional surveillance process consisted of:

- Considering the [10-year follow-up of the CAPP2 study](#) that triggered the exceptional review.
- Feedback from topic experts.
- Considering the evidence used to develop recommendation 1.1.1.
- Examining related NICE quality standards.
- Assessing the new evidence and expert feedback against current recommendations to determine whether or not to update the guideline.

We decided that full updated literature searches were not needed because the information we had from the [10-year follow-up of the CAPP2 study](#) was sufficient to establish whether an update to the guideline was needed.

For further details about the process and the possible update decisions that are available, see [ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual](#).

Information considered in this exceptional surveillance review

In June 2020 the [10-year follow-up of the CAPP2 study](#) was published which provides data with a mean 10-year follow-up that compares the risk of developing colorectal cancer in patients receiving aspirin compared with placebo in participants with Lynch syndrome. This is a follow-up to the [CAPP2 study \(2011\)](#) that was used during guideline development and provided a mean 4.7 years follow-up.

CAPP2 study design

CAPP2 is a double blind, two-by-two factorial randomised controlled trial (n=937 people over 25 years of age with proven Lynch syndrome mutation or clinical diagnosis of Lynch syndrome). Participants were randomised to 600 mg aspirin per day (n=427) or placebo (n=434); 76 were not randomised and opted for resistant starch or placebo (n=76). The primary outcome was number, size, and histological stage of colorectal carcinomas found after a minimum of 2 years' intervention with aspirin, presented as hazard ratios (HR) and 95% confidence intervals (CIs). Secondary clinical outcomes were the size and number of adenomas and of other Lynch syndrome-related cancers. Analyses were conducted according to intention to treat (ITT) and per protocol (participants receiving at least 2 years of aspirin or placebo).

CAPP2 results – 10-year follow-up

At 10-year follow-up there was a statistically significantly reduced risk of developing colorectal cancer in the ITT population (HR 0.65, 95% CI 0.43 to 0.97, p=0.035) and per protocol population (HR 0.56, 95% CI 0.34 to 0.91, p=0.019) with aspirin compared with placebo. The authors found that the effect was most apparent and greatest in people who took aspirin for at least 2 years with good adherence, but some benefit was seen even when people who had not taken aspirin for all that time were included.

There was no significant difference in the risk of developing non-colorectal Lynch syndrome associated cancers or non-Lynch syndrome cancers with aspirin versus placebo. Adverse events were reported as similar between groups, but full details were not presented. However, it should be noted that adverse events were only collected during the intervention phase and the number of adverse events reported was small.

The authors found that the effects on the incidence of colorectal cancer began to be seen after 5 years of follow-up and concluded that the 10-year results continue to demonstrate that aspirin reduces the risks of colorectal cancer in patients with Lynch syndrome.

The authors noted that the limitations of the study included:

- uncertainty if certain subgroups have different effect sizes and risks due to underpowering,
- the inclusion of a relatively younger cohort and caution that side effects may be higher in older populations,
- uncertainty as to the best dose of aspirin, which the [CAPP3 study](#) aims to address in 2024.

Topic expert feedback

Five topic experts were contacted who had clinical expertise in colorectal cancer, including Lynch syndrome. Three experts replied and agreed with the proposal to not update the guideline. One expert considered there could be a benefit in including the data from the CAPP2 10-year follow-up study into the guideline as the results demonstrate an important decrease in the risk of developing colorectal cancer which is sustained. One expert did not reply.

Information considered when developing the guideline

Evidence from the [CAPP2 study \(2011\)](#) (n=937), showed that taking 600 mg of aspirin daily for a mean of 4.7 years follow-up reduces the risk of colorectal cancer in people with Lynch syndrome, although this was only statistically significant in the per protocol analysis (HR 0.41, 95% CI 0.19 to 0.86), not in the ITT group (HR 0.63, 95% CI 0.35 to 1.13). There was no difference in adverse events. One observational study ([Ouakrim et al. 2015](#)) of aspirin twice a week for 1 month or longer versus never having aspirin (n=1,858) also found that aspirin reduced the risk of colorectal cancer in people with Lynch syndrome.

The potential harm from long-term aspirin use is thought to include an increased risk of bleeding. CAPP2 found no difference in bleeding events but data was only collected on adverse events for 2 years and not during follow-up. There was also no stratification by

age. Therefore, the committee deemed that the long-term safety of aspirin was uncertain.

However, on balance the committee agreed that taking aspirin long term was appropriate in most, but not all, cases (for example in people with history of peptic ulcers). Evidence from the [10-year follow-up of the CAPP2 study](#) was expected to clarify uncertainties regarding the longer-term benefits.

Equalities

No equalities issues were identified during the surveillance process.

Quality standards

NICE's [quality standard on colorectal cancer](#) does not contain a statement on aspirin for Lynch syndrome and is not impacted by the decision to not update the guideline.

Overall decision

We will not update the NICE guideline on colorectal cancer. The [10-year follow-up of the CAPP2 study](#) provides additional support for recommendation 1.1.1 that the benefits of aspirin in preventing colorectal cancer outweigh the risks of side effects for most people with Lynch syndrome. It does not provide any further certainty on subgroups who may be at increased risk of side effects of aspirin, such as people with a history of peptic ulcers or elderly patients. The evidence also does not provide any information on the dose of aspirin that will optimally balance the benefits with the risks of gastrointestinal bleeding, but the [CAPP3 study](#) is expected to provide this clarity in 2024 and we will monitor its publication status. The majority of topic experts agreed with the proposal to not update the guideline at this time.

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