

**Abstract Title:** Prevention of Cancer

**Author Name:** Prof. Sir John Burn, Professor of Clinical Genetics

**Author Institute:** Translational & Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK

**Abstract:** The global health burden of cancer is rising steadily with ageing populations, changing lifestyles and therapy costs. The war on tobacco is winning but impact of obesity is increasing. HPV vaccination, colorectal polypectomy and mastectomy/oophorectomy for hereditary breast/ovarian cancer are examples of interventional success. We have focused on exploring chemoprevention. By targeting people at high genetic risk it has been possible to establish effective interventions using a factorial randomised double-blind controlled trial; CAPP2 recruited 1007 people with Lynch syndrome from 43 centres in 16 countries between 1999 and 2005 to receive 600mg aspirin versus placebo and 30 grams of resistant starch (Novelose) versus corn starch for 2-4 years. After planned 10 year follow-up, supplemented for a second decade with national registry data, both interventions proved significant.

600mg aspirin had significantly fewer colorectal cancers on Intention-to-Treat. Per Protocol Analysis, focused on those who completed 2 years treatment, revealed 50% colorectal cancer reduction and a non-significant 50% reduction in endometrial cancers. These findings validate the multiple other evidence that aspirin reduces colorectal cancer. CaPP3 involves three doses of aspirin in 1879 LS carriers across five countries. Five year intervention ends for last recruits in 2024. This will establish whether lower doses of aspirin are effective. If so, it would support the theory that suppression of platelet activation is a major element of the protective effect of aspirin.

Unexpectedly, resistant starch had no effect on the Lynch syndrome colorectal cancers possibly reflecting the potential for mismatch repair deficient cancers to progress direct from aberrant crypts. For the secondary endpoint of "other Lynch syndrome cancers", there were 63% fewer; upper GI cancers were most reduced, possibly reflecting microbiome change leading to a long-term reduction in secondary bile acids.

Both approaches are relevant to the wider global population given their availability and low cost.

*Burn et al Lancet 2020. Mathers et al Cancer Prevention Research 2022.*

**Area of expertise:** Clinical Genetics, cancer genomics cancer prevention