The Medical Journal of Australia • MJA
MEDIA RELEASE

LYNCH SYNDROME AND COLORECTAL CANCER RISK: TESTING COST-EFFECTIVENESS

EMBARGOED UNTIL 12:01am Monday 28 October 2019

LYNCH syndrome, a mutation of four genes involved in DNA repair, is associated with increased risk of developing a range of cancers, particularly colorectal cancer (CRC).

In the most comprehensive analysis for Australia to date, published online by the *Medical Journal of Australia* today, an international team of researchers led by Professor Karen Canfell from the Cancer Council NSW, evaluated the health impact and cost-effectiveness of systematic testing of people with incident CRC for Lynch syndrome, with the aim of providing evidence that could inform a national Lynch syndrome testing policy.

“Our specific aims were to determine the most cost-effective Lynch syndrome testing strategy for people with incident CRC; and to estimate the health and economic impacts of limiting testing to specific CRC diagnosis age ranges and of different colonoscopic surveillance intervals for confirmed Lynch syndrome carriers,” wrote Canfell and colleagues.

The researchers modelled the cost of testing all patients diagnosed with CRC during 2017, with detailed modelling of outcomes for patients identified as Lynch syndrome carriers (probands) and their at-risk relatives throughout their lifetimes (censored at 100 years). In Stage 1 they examined eight testing strategies -- no testing (strategy 1); universal mismatch repair deficiency (dMMR) tumour testing (immunohistochemistry or microsatellite instability testing) with or without somatic *BRAF* V600E or *MLH1* promoter methylation testing, followed by germline gene panel testing for confirmation of Lynch syndrome (strategies 2–7); and universal germline gene panel testing (strategy 8). In Stage 2 they investigated the impact of key parameters in an exploratory analysis of both the most cost-effective strategy in Stage 1 and the universal germline gene panel testing strategy. In Stage 3 they investigated the effects of key parameters on the cost-effectiveness of the most cost-effective testing strategy identified in Stage 1 and the universal gene panel testing strategy.

In Stage 1, the most cost-effective strategy was immunohistochemistry and reflex *BRAF* V600E testing followed by gene panel testing to confirm Lynch syndrome (strategy 3). “It would require an additional 30 995 colonoscopies over the lifetimes of 2420 Lynch syndrome carriers and would avert 189 CRC deaths (164 extra colonoscopies to avert one CRC death).” The discounted costs for immunohistochemistry with *BRAF* V600E testing are $10 645 per Lynch syndrome proband identified and $7044 including both proband and identified Lynch syndrome-positive relatives.

In Stage 2, the most cost-effective strategy was MMR immunohistochemistry and reflex *BRAF* V600E testing, with 2-yearly colonoscopic surveillance of confirmed Lynch syndrome carriers. “An additional 4778–15 860 colonoscopies would be required over the lifetimes of 2420 LS carriers, and 46–181 CRC deaths would be averted (88–103 extra colonoscopies per averted CRC death),” the researchers wrote.

In the Stage 3, the parameter with the greatest influence on cost-effectiveness was the assumed impact of colonoscopic surveillance on CRC incidence; that is, colonoscopic surveillance down-stages diagnosed cancers but does not reduce the incidence.

“We found that all universal dMMR tumour testing strategies for people with incident CRC, without age limit and with annual colonoscopic surveillance of confirmed Lynch syndrome carriers, were similarly cost-effective (compared with no testing) at an indicative willingness-to-pay threshold of $30 000–$50 000/life years saved; the most cost-effective strategy was immunohistochemistry with reflex *BRAF* V600E testing.

“Universal dMMR tumour testing strategies could reduce the number of CRC deaths by 184–189 while increasing the number of colonoscopies by 30 597–31 084 over the lifetimes of 1000 people with CRC and Lynch syndrome and 1420 relatives confirmed to be Lynch syndrome carriers (164–166 additional colonoscopies per death averted),” Canfell and colleagues wrote.

“Universal gene panel testing is not yet cost-effective, but should be re-evaluated should its costs drop, as is expected,” they concluded.

Please remember to credit *The MJA*.

The *Medical Journal of Australia* is a publication of the Australian Medical Association.

CONTACTS: Mark Evans
Public Relations Officer
Cancer Council NSW
Ph: (02) 9334 1477 or 0434 995 936
Email: Mark.Evans@nswcc.org.au