Genetic and lifestyle calculator reveals which younger adults are most at risk of colorectal cancer

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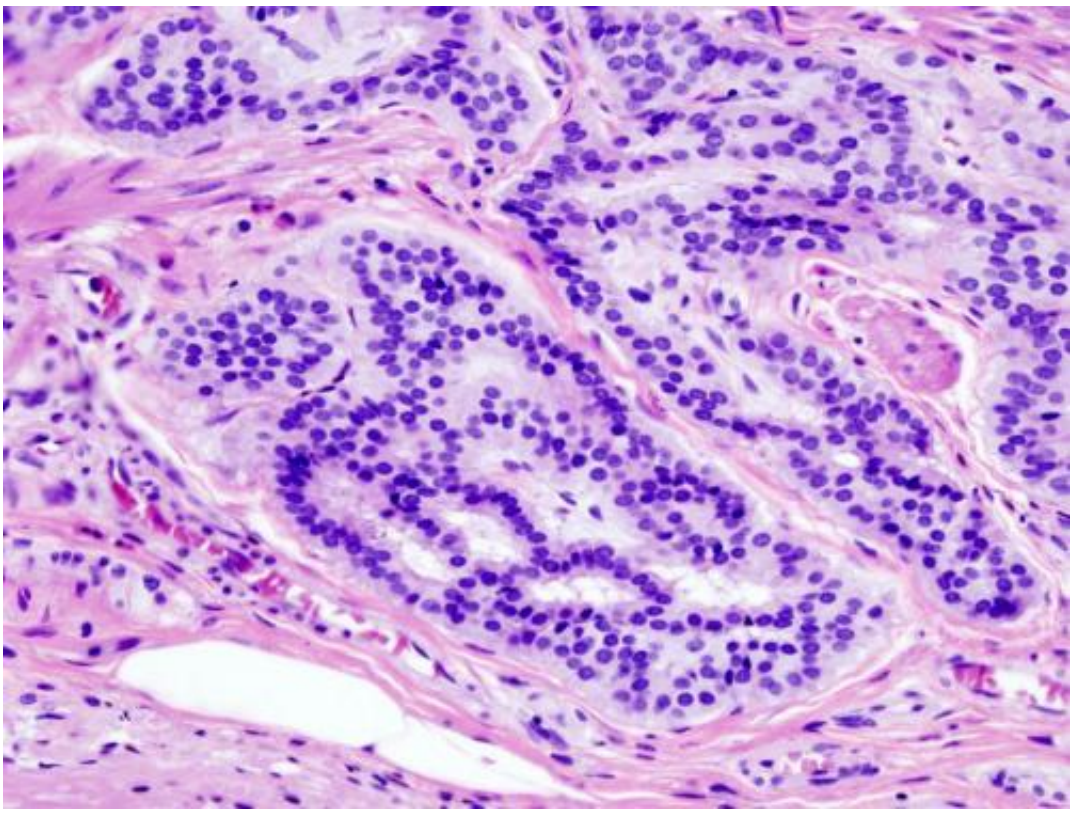

Cancer—Histopathologic image of colonic carcinoid. Credit: Wikipedia/CC BY-SA 3.0

A new risk score can identify men and women under age 50 most likely to develop a cancer of the colon or rectum, an international study shows.

The score, a number between 0 and 1, is made from a calculation of people's risk of developing cancers in either digestive tract organ based on 141 genetic variants (changes in the DNA code) more common in people with the disease. This so-called polygenic risk score is then added to a parallel risk calculation based on 16 lifestyle factors known to increase people's chances of bowel cancers, including smoking, age, and how much dietary fiber and red meat are being consumed.

Rates of colon and rectal cancers have been on the rise among younger adults in the United States, as well as many other nations. In the U.S. alone, rates have increased every year from 2011 to 2016 by 2% among people younger than 50.

Led by researchers at NYU Langone Health and its Laura and Isaac Perlmutter Cancer Center, the new study showed that those with the highest, or top third, combined polygenetic and environmental risk scores were four times more likely to develop colorectal cancers than men and women who scored in the bottom third.

"Our study results help address the rising rates of colorectal cancer among younger adults in the United States and other developed countries, and show that it is feasible to identify those most at risk of the disease," says study co-senior investigator Richard Hayes, Ph.D., DDS, MPH.

Published in the *Journal of the National Cancer Institute* online Jan. 13, the study involved a comparison of 3,486 adults under age 50 who developed bowel cancer between 1990 and 2010 with 3,890 similar young men and women without the disease. All were participants in research studies monitoring people for cancer in North America, Europe, Israel, and Australia.

Hayes, a professor in the Departments of Population Health and

Environmental Medcine at NYU Grossman School of Medicine, cautions that his team's tool is not yet ready for clinical use. Before it can be widely adopted, he says further testing is needed in larger trials to refine the model, describe how it can best be used by physicians, and demonstrate that, when used, the scoring system can in fact prevent illness and death.

Hayes says it remains unclear why the number of colorectal cancers is increasing in younger adults. By contrast, case numbers among older adults have decreased considerably due to advances in screening and increased removal of suspect growths before they advance to cancer.

Still, he notes, colorectal cancer kills more than 53,000 people every year in the United States. And it is for this reason that the American Cancer Society and federal guidelines now recommend the start of routine screening at age 45.

"Our ultimate goal is to have a predictive test for all people to gauge when they, based on their own genetic and personal health factors, need to start routine screening for colorectal cancer," says Hayes. Physicians, ideally, need a tool that can be used long before early warning signs appear, such as abdominal pain, low blood counts, and rectal bleeding.

The latest investigation analyzed data collected from 13 cancer studies in the United States, Canada, the United Kingdom, Germany, Spain, Israel, and Australia.

Currently, more than 150,000 Americans are diagnosed annually with cancers of the colon and rectum.

More information: Risk Stratification for Early-Onset Colorectal Cancer Using a Combination of Genetic and Environmental Risk Scores: An International Multi-Center Study, *Journal of the National Cancer*

Institute (2022). DOI: 10.1093/jnci/djac003