

Risk of a Second Cancer in Colorectal Cancer Survivors

August 19, 2013

SJ Lowry

A history of colorectal cancer (CRC) is associated with a greater risk of being diagnosed with a subsequent primary cancer, distinct from any risk of metastasis. CRC survivors are up to 40% more likely to be diagnosed with either a second CRC (not a metastasis), or a primary cancer arising in another site (such as in digestive, reproductive, or urinary tract organs). Studies have also suggested that the risk of a second primary cancer varies somewhat depending on the site of the initial cancer within the colorectum. Specifically, CRC in the proximal colon is associated with a higher risk of a second primary CRC than a first CRC in the distal colon or rectum.

Dr. Amanda Phipps in Public Health Sciences, along with colleagues from Massachusetts General Hospital and the Harvard School of Public Health, hypothesized that the risk of a second cancer, as well as the site of this second cancer, might vary depending on the location of the first CRC. They used Surveillance Epidemiology and End Results (SEER) cancer registries to estimate the risk of a second primary cancer, by cancer site, in CRC survivors, compared to the risk of cancer in the general population. CRC cases were between the ages of 40-79 years at their initial CRC diagnosis between 1992-2009.

Phipps *et al.* observed that, overall, persons who had had a primary CRC were 15% more likely to later be diagnosed with a second primary cancer, whether CRC or another type (95% confidence interval (CI) 1.13-1.16), as compared to the general population. Those whose initial CRC was located between the transverse and descending colon were approximately 30% more likely to develop a second primary cancer of any kind, and twice to three times as likely to develop a second primary CRC. They also found a 10-40% higher risk of a second primary cancer in the lung, bladder, kidney, and stomach; but a 9% lower risk of prostate cancer (95% CI 0.88-0.95).

The risk of a subsequent cancer of the small intestine was more than 4-fold higher in CRC cases overall compared to the general population (95% CI 3.70-4.77). An initial CRC in the proximal colon was associated with a 40-80% higher risk of a subsequent endometrial cancer.

Phipps *et al.* discuss several possible explanations for the elevated risk of non-CRCs, including a genetic predisposition to cancer, misclassification of metastases in the SEER database (though measures are taken to minimize these), and the contribution of shared risk factors, such as smoking,

which increase the risk of both CRC and other cancers. Another possibility is that tissues of shared embryonic origin with the colorectum, i.e. those tissues which also arise from endoderm-derived epithelia, are more similar in their susceptibility to carcinogens and other environmental factors. This hypothesis is supported by Dr. Phipps' findings, and could explain why they observed no elevated risk of lymphoma or leukemia in CRC survivors.

This study may provide clues into the variability across CRC cases; notes Dr. Phipps, "These findings reinforce a growing understanding that colorectal cancer isn't just one disease." She also notes the need for additional research: "Tumor subsite appears to be important for a person's risk of subsequent cancer, but we have much left to learn as to what other factors might influence cancer risk in colorectal cancer survivors."

[Phipps AI, Chan AT, Ogino S.](#) 2013. Anatomic subsite of primary colorectal cancer and subsequent risk and distribution of second cancers. *Cancer*. doi: 10.1002/cncr.28076. [Epub ahead of print]

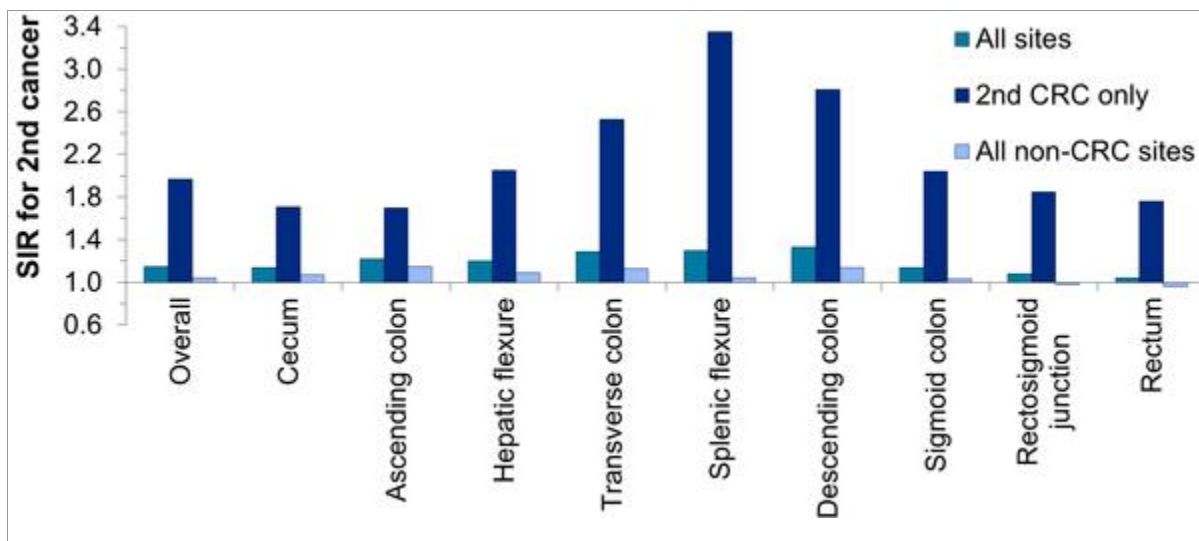


Image provided by Dr. Amanda Phipps

Original colorectal cancer (CRC) diagnosis, by site, is shown along the x-axis. Standardized incidence ratios (SIRs) for second primary cancer by anatomic site of index CRC (from the Surveillance, Epidemiology, and End Results [SEER] 13 registries, 1992-2009), shown along the y-axis.