

Study quantifies risk for gastric, breast cancer for germline CDH1 P/LP variants

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The cumulative risk for advanced gastric cancer varies from 6.5 to 10.3% for carriers of germline CDH1 pathogenic/likely pathogenic (P/LP) variants, according to a study [published](#) online June 14 in the *Journal of the American Medical Association* to coincide with presentation at the International Gastric Cancer Linkage Consortium,

held from June 13 to 15 in Porto, Portugal.

Carrie E. Ryan, M.D., from the National Institutes of Health in Bethesda, Maryland, and colleagues describe gastric and breast cancer risk estimates for individuals with CDH1 variants in a multicenter retrospective cohort and modeling study. Data were included from 213 families from North America with a germline CDH1 P/LP variant; 883 of the 7,323 individuals had a CDH1 P/LP variant.

The researchers found that the prevalence of gastric cancer was 13.9% among those with a CDH1 P/LP variant, and the prevalence of breast cancer was 26.3% among female carriers. The estimated hazard ratio for advanced gastric cancer was 33.5 and 3.5 at ages 30 and 70 years, respectively. In male and female carriers, the lifetime cumulative risk for advanced gastric cancer was 10.3 and 6.5%, respectively.

A [carrier](#) with three affected first-degree relatives had a penetrance of about 38% in gastric cancer risk estimates based on [family history](#). The hazard ratio for breast cancer among female carriers was 5.7 and 3.9 at ages 30 and 70 years, respectively; the lifetime cumulative risk for [breast cancer](#) was 36.8% among female carriers.

"These findings inform current management of individuals with germline CDH1 variants," the authors write.

Two authors disclosed ties to the biopharmaceutical industry.

More information: Carrie E. Ryan et al, Germline CDH1 Variants and Lifetime Cancer Risk, *JAMA* (2024). [DOI: 10.1001/jama.2024.10852](#)

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