

Clinician Management Resource for *CDH1* (Hereditary diffuse gastric cancer)

This overview of clinical management guidelines is based on this patient's positive test result for a *CDH1* gene mutation. Please consult the referenced guideline for complete details and further information.

Clinical correlation with the patient's past medical history, treatments, surgeries and family history may lead to changes in clinical management decisions; therefore, other management recommendations may be considered. Genetic testing results and medical society guidelines help inform medical management decisions but do not constitute formal recommendations. Discussions of medical management decisions and individualized treatment plans should be made in consultation between each patient and his or her healthcare provider, and may change over time.

SCREENING/SURGICAL CONSIDERATIONS	AGE TO START	FREQUENCY
Gastric Cancer^{1,2*}		
Prophylactic gastrectomy is recommended. <ul style="list-style-type: none"> Baseline endoscopy prior to prophylactic total gastrectomy Intraoperative frozen sections should be performed to verify proximal margin contains esophageal squamous mucosa and distal margin contains duodenal mucosa, to ensure complete removal of gastric tissue. A D2 lymph node dissection is not necessary for prophylactic total gastrectomy. Not recommended under 18 years of age, but may be considered for certain patients (i.e. family history of gastric cancer diagnosed under age 25) 	Between 18-40 years old	N/A
Patients who elect not to undergo prophylactic gastrectomy should be offered upper endoscopy with multiple random biopsies	Individualized	Every 6-12 months
Female Breast Cancer²		
Breast Screening <ul style="list-style-type: none"> Mammography Consider breast MRI with contrast 	30 years old, or 5-10 years before the earliest known breast cancer in the family	Annually
Discuss option of risk reducing mastectomy	Individualized	N/A

* Due to limited data, the management of gastric cancer risk in individuals with pathogenic/likely pathogenic variants in *CDH1* in the absence of a family history of gastric cancer is not straightforward. However, studies have shown that some apparently unaffected individuals in breast cancer-only families had early stage diffuse gastric cancer at the time of prophylactic gastrectomy (Jacobs MF, et al. *Gastroenterology* 2019; 157:87-96). Annual endoscopic surveillance should be offered to these individuals, and prophylactic gastrectomy can be considered (Blair V et al. *Lancet Oncol.* 2020 Aug;21(8):e386-e397).

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Gastric Cancer version 2.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed February 14, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.
2. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. V1.2023. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed February 14, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

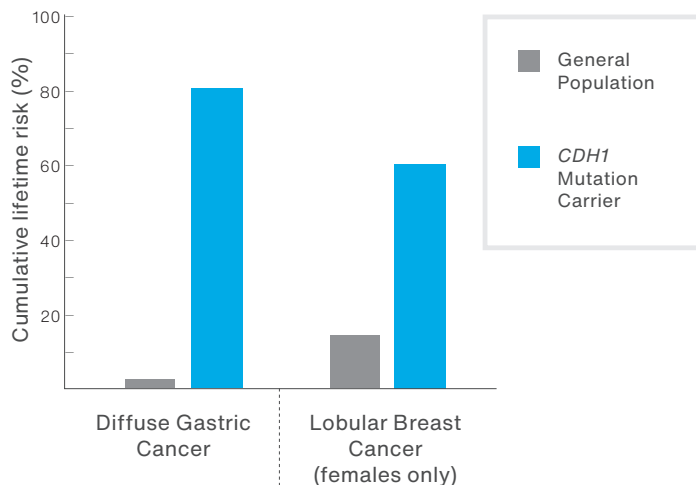
Understanding Your Positive *CDH1* Genetic Test Result

INFORMATION FOR PATIENTS WITH A **PATHOGENIC MUTATION OR VARIANT, LIKELY PATHOGENIC**

5 Things To Know

1	<i>CDH1</i> mutation	Your testing shows that you have a pathogenic mutation or a variant that is likely pathogenic in the <i>CDH1</i> gene.
2	<i>CDH1</i> -related diffuse gastric and lobular breast cancer (DGLBC)	People with <i>CDH1</i> mutations have <i>CDH1</i> -related diffuse gastric and lobular breast cancer (DGLBC)
3	Cancer risks	You have an increased chance to develop a particular type of gastric cancer (diffuse) and a particular type of female breast cancer (lobular).
4	What you can do	Risk management decisions are very personal. There are options to detect cancer early or lower the risk to develop cancer. It is important to discuss these options with your doctor and decide on a plan that works for you.
5	Family	Family members may also be at risk—they can be tested for the <i>CDH1</i> mutation that was identified in you. It is recommended that you share this information with your family members so they can learn more and discuss with their healthcare providers.

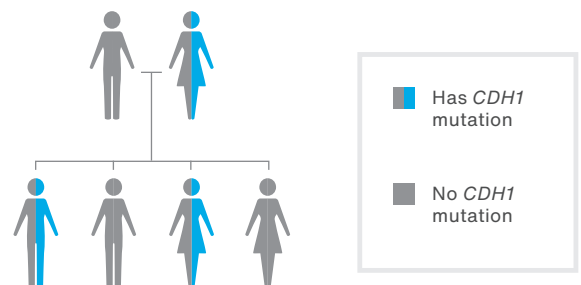
CDH1 Cancer Risks (%)*



*Cancer risks will differ based on individual and family history.

CDH1 Mutations in the Family

There is a 50/50 random chance to pass on a *CDH1* mutation to your sons and daughters. The image below shows that both men and women can carry and pass on these mutations.



Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your *CDH1* result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or interpreted as medical advice.

Reach Out	RESOURCES	Ambry's Hereditary Cancer Site for Families patients.ambrygen.com/cancer No Stomach for Cancer nostomachforcancer.org Genetic Information Nondiscrimination Act (GINA) ginahelp.org National Society of Genetic Counselors nsgc.org Canadian Society of Genetic Counsellors cagc-accg.ca
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