

CDH1

The *CDH1* gene is a tumor suppressor gene. Tumor suppressor genes slow down cell division, repair DNA mistakes, or tell cells when to die. When they don't work properly, cells can grow out of control, which can lead to cancer. The primary role of *CDH1* is to send signals between epithelial cells, or the cells that cover the surfaces and cavities of the body. This signaling allows epithelial cells to interact and stick together to prevent cancer cells from spreading and invading tissues.

Like most genes, each person has two copies of the *CDH1* gene: one inherited from each parent. A mutation in a single *CDH1* gene inherited from either parent is known to cause hereditary diffuse gastric cancer (HDGC). *CDH1* mutations are associated with increased risk of breast cancer (particularly a type called lobular breast cancer) and stomach cancer (particularly a rare type called diffuse gastric cancer) over a lifetime.

How common are mutations in the *CDH1* gene?

Mutations in the *CDH1* gene are rare—but they are estimated to account for about 1% of all stomach cancers.¹

How mutations in this gene impact risk

Women

If a woman has a mutation in the *CDH1* gene, her chances of developing breast cancer (particularly a type called lobular breast cancer) and stomach cancer (particularly a rare type called diffuse gastric cancer) are greater than that of the average US woman. This does not mean that she has a diagnosis of cancer or that she will definitely develop cancer in her lifetime.

Cancer by age 80	Average US woman ²	With <i>CDH1</i> mutation
Breast	10%	39-42% ^{3,4}
Stomach	<1%	56-83% ^{3,4}

Elevated: Risk is increased, but further research may clarify the exact risk figure.

¹ Brooks-Wilson AR, Kaurah P, Suriano G, et al. Germline E-cadherin mutations in hereditary diffuse gastric cancer: assessment of 42 new families and review of genetic screening criteria. *J Med Genet.* 2004;41(7):508-17.

² Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute. 2010-2012. DevCan software (<http://surveillance.cancer.gov/devcan>) V 6.7.0, Accessed June 2015.

³ Hansford S, Kaurah P, Li-chang H, et al. Hereditary Diffuse Gastric Cancer Syndrome: CDH1 Mutations and Beyond. *JAMA Oncol.* 2015;1(1):23-32.

⁴ Pharoah PD, Guilford P, Caldas C. Incidence of gastric cancer and breast cancer in CDH1 (E-cadherin) mutation carriers from hereditary diffuse gastric cancer families. *Gastroenterology.* 2001;121(6):1348-53.

Men

If a man has a mutation in the *CDH1* gene, his chance of developing stomach cancer, (particularly a rare type called diffuse gastric cancer), is greater than that of the average US man. This does not mean that he has a diagnosis of cancer or that he will definitely develop cancer in his lifetime.

Cancer by age 80	Average US man	With <i>CDH1</i> mutation
Stomach	<1%	Elevated ^{3,4}

Elevated: Risk is increased, but further research may clarify the exact risk figure.

Screening guidelines

Below is a summary of screening guidelines from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) established by experts at the National Comprehensive Cancer Network (NCCN).⁵ They are for individuals who have a mutation in the *CDH1* gene. If you have a mutation in this gene, your healthcare provider may use these NCCN Guidelines® to help create a customized screening plan for you.

Women

Breast cancer⁶

- **Starting at age 30:** Your provider may discuss mammogram and breast MRI with contrast every year.
- Your provider may discuss the option of having a risk-reducing bilateral mastectomy (the surgical removal of both breasts) based on family history.

Gastric cancer⁷

- **Between ages 18-40, or earlier based on family history of gastric cancer:** NCCN recommends a risk-reducing gastrectomy (the surgical removal of the stomach). Prior to gastrectomy, NCCN recommends an initial endoscopy (examination of digestive tract) with multiple biopsies.

⁵ Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast and Ovarian V.1.2017 and Gastric Cancer V.3.2016. © National Comprehensive Cancer Network, Inc 2016. All rights reserved. Accessed September 20, 2016. To view the most recent and complete version of the guideline, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

⁶ National Comprehensive Cancer Network. Genetic/Familial High-Risk Assessment: Breast and Ovarian. *NCCN Guidelines Version 1.2017*. Available at www.nccn.org. Published September 2016.

⁷ National Comprehensive Cancer Network. Gastric Cancer. *NCCN Guidelines Version 3.2016*. Available at www.nccn.org. Published August 2016.

- For those who choose not to undergo risk-reducing gastrectomy: upper endoscopy with multiple biopsies every 6-12 months.

Men

Gastric cancer⁷

- **Between ages 18-40, or earlier based on family history of gastric cancer:** NCCN recommends a risk-reducing gastrectomy (the surgical removal of the stomach). Prior to gastrectomy, NCCN recommends an initial endoscopy (examination of digestive tract) with multiple biopsies.
- For those who choose not to undergo risk-reducing gastrectomy: upper endoscopy with multiple biopsies every 6-12 months.

Useful resources

FORCE

Providing support, education, research, and resources for survivors and people at increased risk of cancer due to an inherited mutation or family history of cancer.

www.facingourrisk.org

No Stomach For Cancer

Supporting research and uniting the caring power of people worldwide affected by stomach cancer and Hereditary Diffuse Gastric Cancer.

www.nostomachforcancer.org

Susan G. Komen

Dedicated to reducing deaths from breast cancer by funding breast cancer research, ensuring access to care through community programs worldwide and supporting public health policies that help people facing breast cancer.

www.komen.org/

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