**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.

<table>
<thead>
<tr>
<th>Cancer by age 80</th>
<th>Average US woman²</th>
<th>With CDH1 mutation³,⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>10%</td>
<td>39-42%³,⁴</td>
</tr>
<tr>
<td>Stomach</td>
<td>&lt;1%</td>
<td>56-83%³,⁴</td>
</tr>
</tbody>
</table>

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

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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.

<table>
<thead>
<tr>
<th>Cancer by age 80</th>
<th>Average US man</th>
<th>With CDH1 mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>&lt;1%</td>
<td>Elevated&lt;sup&gt;3,4&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

*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).<sup>5</sup> 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 cancer<sup>6</sup>
- **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 cancer<sup>7</sup>
- **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.

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<sup>5</sup> 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.


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

Men
Gastric cancer

● 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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