EPCAM

The EPCAM gene is associated with an increased risk of cancer because it is located next to the MSH2 gene. MSH2 works together with other genes, including MSH6 and MSH3, to scan the DNA for mistakes and signal for other genes, including MLH1 and PMS2, to make repairs. Certain large deletions at the far end of the EPCAM gene can overlap with the MSH2 gene, which inactivates MSH2.

Like most genes, each person has two copies of the EPCAM gene: one inherited from each parent. A mutation in a single EPCAM gene inherited from one parent that impairs the function of the MSH2 gene causes Lynch syndrome, which is known to increase risks of colorectal, uterine, ovarian, and other cancers over a lifetime.

How common are mutations in the EPCAM gene?
Mutations that cause Lynch syndrome are rare—found in approximately 1 in 370 individuals. Lynch syndrome accounts for approximately 3% of all colorectal cancers.

How mutations in this gene impact risk
Women
If a woman has a mutation in the EPCAM gene, her chances of developing ovarian, colorectal, uterine, brain, hepatobiliary tract, pancreatic, sebaceous neoplasms, small bowel, stomach, and urinary tract 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 70</th>
<th>Average US woman</th>
<th>With EPCAM mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>1.6%</td>
<td>37-48%.4,5,6</td>
</tr>
<tr>
<td>Uterine</td>
<td>1.7%</td>
<td>21-30%.4,5,6</td>
</tr>
<tr>
<td>Ovarian</td>
<td>&lt;1%</td>
<td>8-10%.4,5</td>
</tr>
</tbody>
</table>

### EPCAM

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Average US Man</th>
<th>With EPCAM Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Brain</strong></td>
<td>&lt;1%</td>
<td>3-6%&lt;sup&gt;5,7&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Hepatobiliary tract</strong></td>
<td>&lt;1%</td>
<td>Elevated&lt;sup&gt;5&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Pancreatic</strong></td>
<td>&lt;1%</td>
<td>3.7%&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Sebaceous neoplasms</strong></td>
<td>&lt;0.1%</td>
<td>Elevated&lt;sup&gt;9&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Small bowel</strong></td>
<td>&lt;1%</td>
<td>1-3%&lt;sup&gt;5,7&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Stomach</strong></td>
<td>&lt;1%</td>
<td>5-8%&lt;sup&gt;5,7&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Urinary tract</strong></td>
<td>&lt;1%</td>
<td>4-10%&lt;sup&gt;5,7&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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

### Men

If a man has a mutation in the *EPCAM* gene, his chances of colorectal, brain, hepatobiliary tract, pancreatic, sebaceous neoplasms, small bowel, stomach, and urinary tract cancer are 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 70</th>
<th>Average US man&lt;sup&gt;3&lt;/sup&gt;</th>
<th>With EPCAM mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>2%</td>
<td>48%&lt;sup&gt;4,6&lt;/sup&gt;</td>
</tr>
<tr>
<td>Brain</td>
<td>&lt;1%</td>
<td>3-6%&lt;sup&gt;5,7&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hepatobiliary tract</td>
<td>&lt;1%</td>
<td>Elevated&lt;sup&gt;5&lt;/sup&gt;</td>
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<td>Pancreatic</td>
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</tr>
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<td>Sebaceous neoplasms</td>
<td>&lt;0.01%</td>
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</tr>
<tr>
<td>Small bowel</td>
<td>&lt;1%</td>
<td>1-6%&lt;sup&gt;5,7&lt;/sup&gt;</td>
</tr>
<tr>
<td>Stomach</td>
<td>&lt;1%</td>
<td>5-8%&lt;sup&gt;5,7&lt;/sup&gt;</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>2.2%</td>
<td>3-8%&lt;sup&gt;4,5&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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

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Additional information

Mutations in five different genes can lead to Lynch syndrome.

Having a mutation in EPCAM, MLH1, MSH2, MSH6, or PMS2 can cause Lynch syndrome. Lynch syndrome used to be referred to as Hereditary Non-Polyposis Colorectal Cancer, or HNPCC. It is an inherited condition that increases the risk of colorectal and other cancers. The associated cancer types and risk levels vary, depending on the gene in which the mutation is found.

The relationship between EPCAM and MSH2.

Cancer risks for individuals with mutation in the EPCAM gene are estimated to be the same as for those with a mutation in the MSH2 gene. This is because the type of mutations in EPCAM that cause Lynch syndrome (called large deletions and duplications including the 3’ end of the gene) silence or inactivate the MSH2 gene.

Not all EPCAM mutations are linked to increased cancer risk.

For EPCAM, only large deletions and duplications including 3’ end of the gene are analyzed, because other positions are not known to impact cancer risk.

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). They are specific to individuals who have a mutation in the EPCAM 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

Uterine and ovarian cancer

- When you are finished having children: Your healthcare provider may discuss a risk-reducing hysterectomy (the surgical removal of the uterus) and salpingo-oophorectomy (the surgical removal of the ovaries and fallopian tubes) with you to lower the risk of developing uterine and ovarian cancer.

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10 Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Colorectal. V.2.2016. © National Comprehensive Cancer Network, Inc 2016. All rights reserved. Accessed October 26, 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.

● Your healthcare provider may discuss the benefits and limitations of a transvaginal ultrasound along with endometrial biopsies (sampling) every year.
● You should be aware of any uterine cancer symptoms, such as uterine bleeding that is not typical.
● While there may be circumstances where ovarian cancer screening with transvaginal ultrasound and a blood test for a protein called CA-125 are helpful, these techniques have not been shown to be effective in detecting early ovarian cancer.

Colorectal cancer\(^\text{11}\)
● Starting at age 20-25 or 2-5 years prior to the earliest colorectal cancer diagnosis in your family if the first diagnosis was before age 25: Colonoscopy every 1-2 years.
● Your provider may discuss the use of medications such as aspirin that might reduce the risk of developing colorectal cancer.

Brain cancer\(^\text{11}\)
● Starting at age 25-30: Physical and neurological examination by your provider every year.

Hepatobiliary tract cancer\(^\text{11}\)
● Currently, there are no hepatobiliary tract cancer screening guidelines from the NCCN specific to \textit{EPCAM} mutation carriers. Your provider may discuss screening or referral to a specialist.

Pancreatic cancer\(^\text{12}\)
● Currently, there are no pancreatic cancer screening guidelines from the NCCN specific to \textit{EPCAM} mutation carriers. Your provider may discuss screening or referral to a specialist.

Sebaceous neoplasms\(^\text{11}\)
● Currently, there are no sebaceous neoplasm screening guidelines from the NCCN specific to \textit{EPCAM} mutation carriers. Your provider may discuss screening or referral to a specialist.

Stomach and small bowel cancer\(^\text{11}\)
● Starting at age 30-35: Your healthcare provider may discuss an upper endoscopy every 3-5 years, depending on your risk factors such as family history or ancestry.
● Your provider may discuss testing and treatment for a bacteria called H. pylori.

Urinary tract cancer\(^\text{11}\)
● Starting at age 30-35: Your healthcare provider may discuss a urinalysis every year.

Men

Colorectal cancer\textsuperscript{11}
- Starting at age 20-25 or 2-5 years prior to the earliest colorectal cancer diagnosis in your family if the first diagnosis was before age 25: Colonoscopy every 1-2 years.
- Your provider may discuss the use of medications such as aspirin that might reduce the risk of developing colorectal cancer.

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Useful resources

Hereditary Colon Cancer Foundation
A nonprofit organization serving the hereditary colorectal cancer community.
www.hcctakesguts.org

Lynch Syndrome International
Primary mission is to provide support for individuals afflicted with Lynch syndrome.
www.lynchcancers.com

Kintalk
An educational and family communication site for individuals and their families with hereditary cancer conditions
www.kintalk.org

Last updated May 15, 2017