CHEK2

The *CHEK2* 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 *CHEK2* is to pause cell division in order to make the critical decision of whether to repair damaged DNA or instruct the cell to die by a process known as apoptosis. The death of cells with significant DNA damage helps to prevent these cells from replicating out of control and forming a tumor.

Like most genes, each person has two copies of the *CHEK2* gene: one inherited from each parent. A mutation in a single *CHEK2* gene inherited from either parent is known to increase risk of certain cancers over a lifetime, including breast, colorectal, prostate, and possibly others.

Lifetime breast cancer risk estimates for women with *CHEK2* mutations range from 20% for those with no relatives with breast cancer to 44% for those with strong family history (defined as more than one close relative affected with breast cancer).[1,2] Further research is needed to understand the interactions of *CHEK2* and family history on lifetime breast cancer risk.

If an individual inherits two *CHEK2* mutations (one from each parent), they may have a significantly increased risk for cancer, particularly female breast cancer as an adult.[3]

How common are mutations in the *CHEK2* gene?

Mutations in the *CHEK2* gene are rare—one mutation is found in approximately 3-7 out of 1,000 (0.3-0.7%) people of Dutch descent.[4,5] Studies to establish how common *CHEK2* mutations are in other populations are ongoing.

How mutations in this gene impact risk

Women

If a woman has a mutation in the *CHEK2* gene, her chances of developing breast and colorectal 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.

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[1] Cybulski C, Wokołorczyk D, Jakubowska A, et al. Risk of breast cancer in women with a CHEK2 mutation with and without a family history of breast cancer. *J Clin Oncol.* 2011 Oct 1;29(28):3747-52.
[2] Weischer M, Bojesen SE, Ellervik C, Tybjaerg-Hansen A, Nordestgaard BG. CHEK2*1100delC genotyping for clinical assessment of breast cancer risk: meta-analyses of 26,000 patient cases and 27,000 controls. *J Clin Oncol.* 2008 Feb 1;26(4):542-8.
[3] Adank MA, Jonker MA, Kluijt I, et al. CHEK2*1100delC Homozygosity is Associated With a High Breast Cancer Risk in Women. *J Med Genet.* 2011;48(12):860-863.
[4] Offit K, Pierce H, Kirchhoff T, et al. Frequency of CHEK2*1100delC in New York breast cancer cases and controls. BMC Med Genet. 2003;4:1.
[5] Neuhausen S, Dunning A, Steele L, et al. Role of CHEK2*1100delC in unselected series of non-BRCA1/2 male breast cancers. Int J Cancer. 2004;108(3):477-8.

Cancer by age 70	Average US woman[6]	With *CHEK2* mutation
Breast	7.1%	20-44%[1,2]
Colorectal	1.6%	Elevated (2-5%)[7]

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

Men

If a man has a mutation in the *CHEK2* gene, his chances of developing prostate and colorectal cancers 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.

Cancer by age 70	Average US man[6]	With *CHEK2* mutation
Colorectal	2.0%	Elevated (3-6%)[7]
Prostate	7.2%	Elevated[8]

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

Additional information

CHEK2 studies have focused on one specific mutation.

The majority of studies related to *CHEK2* are for individuals with one specific mutation called 1100delC. This mutation is more commonly reported in those of Dutch ancestry.

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).[9] They are for individuals with a mutation in the *CHEK2* gene. If you have a

[6] 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.
[7] Xiang HP, Geng XP, Ge WW, Li H. Meta-analysis of CHEK2 1100delC variant and colorectal cancer susceptibility. *Eur J Cancer.* November 2011; 47(17):2546-51.
[8] Cybulski C, Wokołorczyk D, Huzarski T, Byrski T, Gronwald J, Górski B, et al. A large germline deletion in the Chek2 kinase gene is associated with an increased risk of prostate cancer. *J Med Genet.* 2006 Nov;43(11):863-6.
[9] 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 Genetic/Familial High Risk Assessment: Colorectal V.2.2016. © National Comprehensive Cancer Network, Inc 2016. All rights reserved. Accessed November 1, 2016. To view the most recent and complete

mutation in this gene, your healthcare provider may use these NCCN Guidelines® to help create a customized screening plan for you.

Women

Breast cancer[10]

- Starting at age 40: Your provider may discuss mammogram and breast MRI with contrast every year.

Colorectal cancer[11]

- **Beginning at age 40 or 10 years younger than the earliest diagnosis of colorectal cancer in a parent, sibling, or child (whichever is earlier):** Colonoscopy every 5 years.
- These recommendations may change if you have polyps, colorectal cancer, inflammatory bowel disease (IBD), or family history of colorectal cancer.

Men

Colorectal cancer[11]

- **Beginning at age 40 or 10 years younger than the earliest diagnosis of colorectal cancer in a parent, sibling, or child (whichever is earlier):** Colonoscopy every 5 years.
- These recommendations may change if you have polyps, colorectal cancer, inflammatory bowel disease (IBD), or family history of colorectal cancer.

Prostate cancer

- Currently, there are no prostate cancer screening guidelines from the National Comprehensive Cancer Network (NCCN) specific to *CHEK2* mutation carriers. Your provider may discuss earlier or more frequent screening or referral to a specialist.

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

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.

[10] 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.

[11] National Comprehensive Cancer Network. Genetic/Familial High Risk: Colorectal Cancer. *NCCN Guidelines Version 2.2016.* Available at www.nccn.org. Published September 2016.

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