RED FLAGS FOR HEREDITARY CANCER*

Hereditary Breast & Ovarian Cancer (HBOC) Syndrome

An individual with, or a family history^ of, any of the following:

- Ovarian cancer
- Breast cancer diagnosed before age 50
- Two primary breast cancers
- Male breast cancer
- Triple negative breast cancer
- Ashkenazi Jewish with an HBOC-associated cancer[†‡]
- Three or more HBOC-associated cancers at any age[†‡]
- A previously identified HBOC syndrome mutation in the family

^Close blood relatives includes first-, second-, or third-degree in the maternal or paternal lineage
[†]In the same individual or on the same side of the family
[‡]HBOC-associated cancers include breast (including DCIS), ovarian, pancreatic, and aggressive prostate cancer (Gleason score of ≥7)

Lynch Syndrome

An individual with any of the following:

- Colorectal or endometrial cancer before age 50
- Two or more Lynch syndrome cancers[§] at any age
- A Lynch syndrome cancer[§] with one or more relative(s) with a Lynch syndrome cancer[¶]

An individual with any of the following family histories:

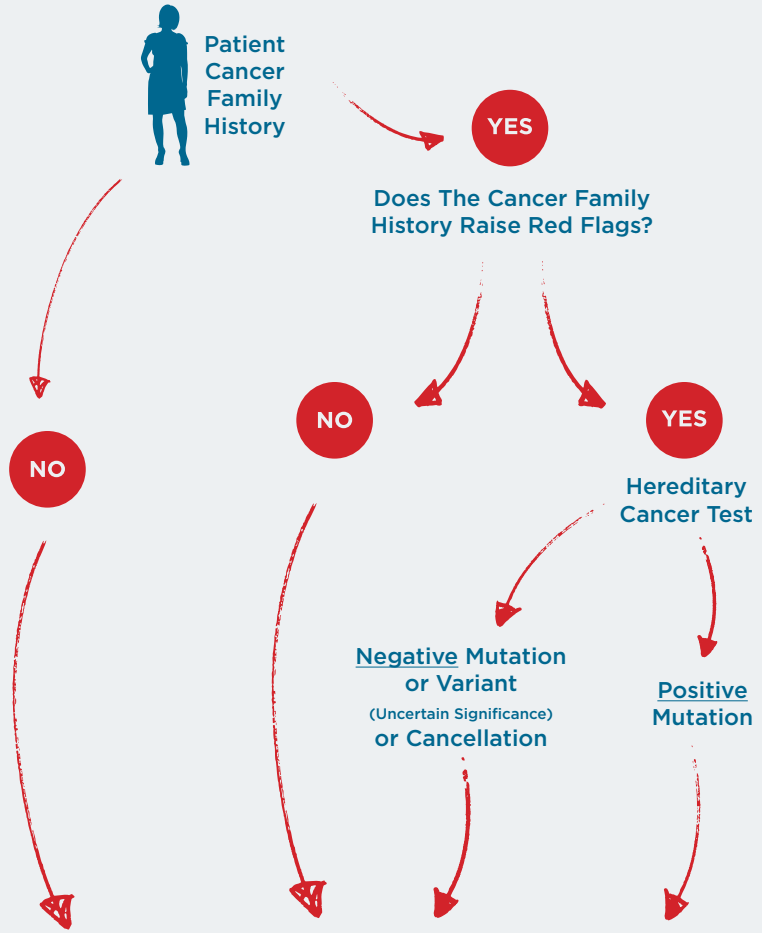
- A first- or second-degree relative with colorectal or endometrial cancer before age 50
- Two or more relatives with a Lynch syndrome cancer[§], one before age 50[¶]
- Three or more relatives with a Lynch syndrome cancer[§] at any age[¶]
- A previously identified Lynch syndrome or MAP syndrome mutation in the family

[§]Lynch syndrome-associated cancers include colorectal, endometrial, gastric, ovarian, ureter/renal pelvis, biliary tract, small bowel, pancreas, brain, sebaceous adenomas
[¶]Cancer history should be on the same side of the family

* Assessment criteria based on medical society guidelines. For these individual medical society guidelines go to www.MyriadPro.com/guidelines.

1. Saslow, et al. CA Cancer J Clin. 2007 Mar-Apr;57(2)75-89. **2.** NCCN Clinical Practice Guidelines in Oncology: http://www.nccn.org.

Managing Patients at Risk for Cancer



GENERAL POPULATION	FAMILIAL ⟵ RISK ⟶	HEREDITARY RISK

A GUIDE TO MANAGING YOUR PATIENT'S RISK

from NCCN Guidelines

RISK CATEGORIES	BREAST CANCER MEDICAL MANAGEMENT RECOMMENDATIONS	OVARIAN CANCER MEDICAL MANAGEMENT RECOMMENDATIONS	COLON CANCER MEDICAL MANAGEMENT RECOMMENDATIONS	ENDOMETRIAL CANCER MEDICAL MANAGEMENT RECOMMENDATIONS
GENERAL POPULATION - No family history of cancer and/or - Negative for a known deleterious mutation in the family	**Under 40 years:** - Breast awareness, clinical breast exam every 1-3 years **40 years and over:** - Clinical breast exam once a year - Mammogram once a year	- No published guidelines	**Begin one of the following at age 50:** - Colonoscopy (preferred if available) every 10 years if negative, or - Flexible sigmoidoscopy every 5 years if negative, or - Stool based screening: Guaiac or IHC based testing annually +/- flexible sigmoidoscopy every 5 years	- No published guidelines
FAMILIAL RISK[1,2] - Family history of cancer and/or - Negative, or Variant, on Genetic Testing or Untested	*Medical management options should be individualized based on family history* - Breast awareness - Clinical breast exam, every 6-12 months, starting at age 30 - Annual mammogram, starting at age 30 or individualized based on the earliest age of onset in the family - Consider annual breast MRI, starting at age 30 - Consider risk reduction strategies (see NCCN Guidelines for Breast Cancer Risk Reduction[2])	- No published guidelines	*Medical management options should be individualized based on family history* - If colon cancer occurred in a first degree relative before the age of 50 or if two first degree relatives were diagnosed with colon cancer at any age, begin colonoscopy at age 40 or 10 years prior to the youngest diagnosis in the family, whichever comes first with a frequency of every 3-5 years pending findings on colonoscopy - If colon cancer occurred in a single first degree relative at or after age 50, begin colonoscopy at age 50 or 10 years prior to the youngest diagnosis in the family, whichever comes first with a frequency of every 5 years - Some combinations of affected first-, second-, and third-degree relatives increase risk sufficiently to alter screening guidelines For full colon cancer screening recommendations, refer to professional society guidelines	- No published guidelines
HEREDITARY RISK[2] - Positive for a deleterious mutation	**Increased Surveillance:** - Breast awareness and education starting at age 18 - Clinical breast exam every 6-12 months starting at age 25 - Annual mammograms and MRI starting at age 25 (or individualized based on earliest age of onset in family) **Risk Reducing Drug Therapy:** - Consider chemoprevention options such as tamoxifen or raloxifene **Risk Reducing Surgery:** - Discuss prophylactic mastectomy which can significantly reduce the risk of breast cancer	**Increased Surveillance:** - For women who have not yet undergone risk reducing salpingo-oophorectomy consider concurrent transvaginal ultrasound (preferably day 1-10 of menstrual cycle) and CA-125 (preferably after day 5 of menstrual cycle) every 6 months starting at age 30 or 5-10 years prior to the youngest ovarian cancer diagnosis in the family. - Data does not support routine ovarian screening for Lynch syndrome; CA-125 and pelvic ultrasound may be considered at the clinician's discretion **Risk Reducing Surgery:** - Risk reducing salpingo-oophorectomy recommended ideally between age 35 and 40 and upon completion of childbearing, or individualized based on youngest ovarian cancer diagnosis	**Increased Surveillance:** - Colonoscopy every 1-2 years beginning at age 20-25 (or 2-5 years prior to the earliest colorectal cancer if it is diagnosed under age 25) **Risk Reducing Surgery:** - Discuss option of prophylactic colectomy with unaffected patients who are unwilling or unable to undergo regular screening colonoscopies For surveillance recommendations for *MSH6* and *PMS2* carriers, refer to professional society guidelines	**Increased Surveillance:** - Notify patients that dysfunctional uterine bleeding warrants evaluation. - There is no clear evidence to support endometrial screening for Lynch syndrome; however, annual office endometrial sampling is an option and CA-125 and pelvic ultrasound may be considered at the clinician's discretion **Risk Reducing Surgery:** - Prophylactic hysterectomy and bilateral salpingo-oophorectomy is a risk-reducing option that should be considered by women who have completed childbearing For surveillance recommendations for *MSH6* and *PMS2* carriers, refer to professional society guidelines