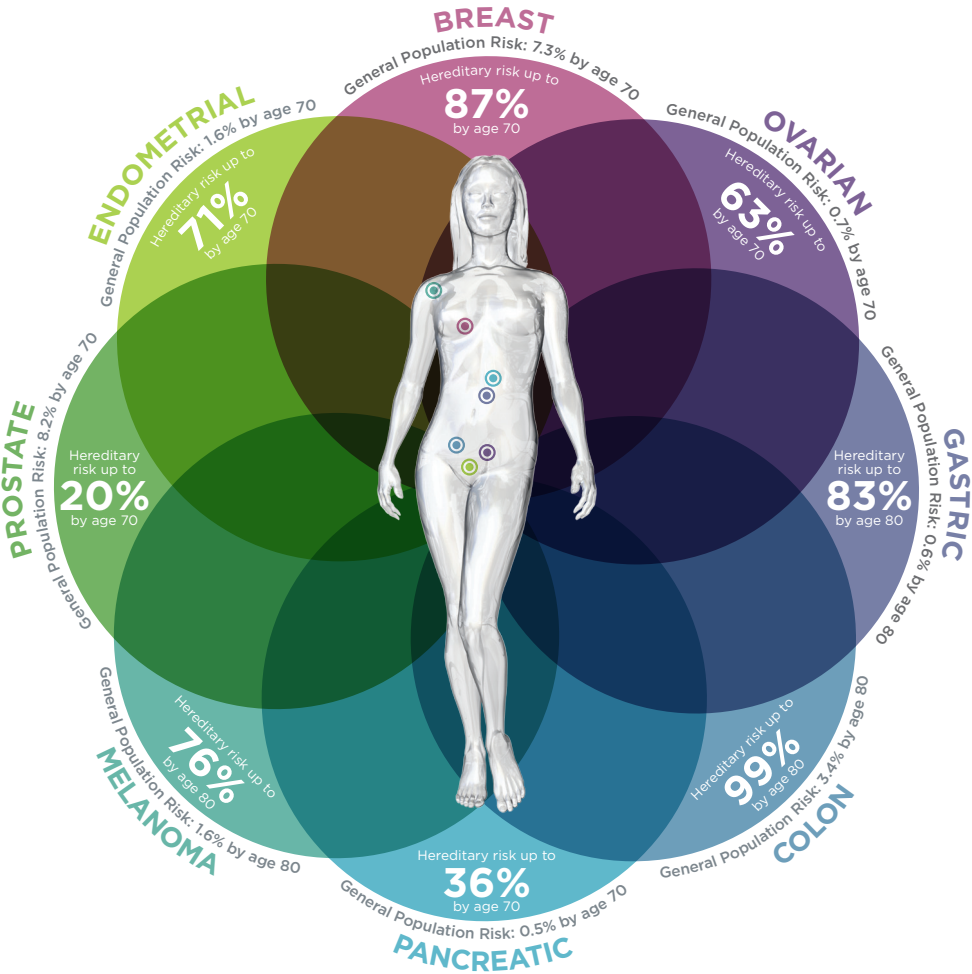
KNOW YOUR PATIENTS. KNOW THEIR RISK.



A Guide to Managing Your Patients' Cancer Risks

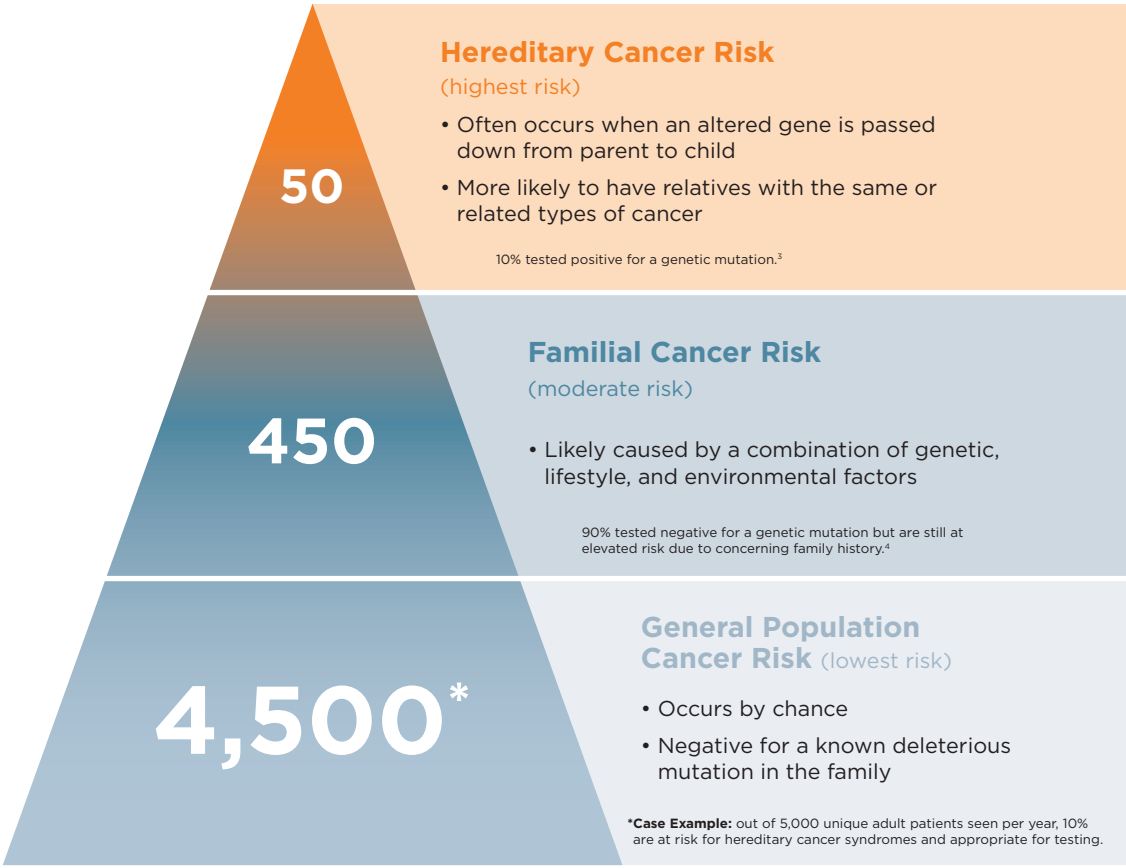
myriad®
WHEN DECISIONS MATTER

THEIR CANCER FAMILY HISTORY...

Medical society guidelines recommend collecting and evaluating family history as a screening tool for hereditary cancer risk. Family history information should be reviewed and updated on a regular basis.[1,2]

...CAN DRAMATICALLY IMPACT THE MEDICAL MANAGEMENT DECISIONS YOU MAKE TODAY

Every patient has some risk of developing cancer. Taking a personal and family cancer history is essential to assessing a patient's risk and stratifying them into the appropriate cancer risk category.



1. Family History as a Risk Assessment Tool, Committee Opinion No. 478. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117-747-50, reaffirmed 2015. **2.** Lu KH, Wood ME, Daniels M, Burke C, Ford J, Kauff ND, et al. American Society of Clinical Oncology Expert Statement: collection and use of a cancer family history for oncology providers. American Society of Clinical Oncology. J Clin Oncol 2014;32:833–40. **3.** Rosenthal E. et al. Outcomes of Clinical Testing for 76,000 Patients Utilizing a Panel of 25 Genes Associated with Increased Risk for Breast, Ovarian, Colorectal, Endometrial, Gastric, Pancreatic, Melanoma, Cancers. Abstract #1515 presented at ASCO, June 2015. **4.** Alico L. et al. Implementation of Hereditary Cancer Risk Assessment in an Independent Breast Imaging Center. Poster presented at NCBC, March 2015.

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HEREDITARY CANCER RISK ASSESSMENT IS SIMILAR TO OTHER ROUTINE PROTOCOLS

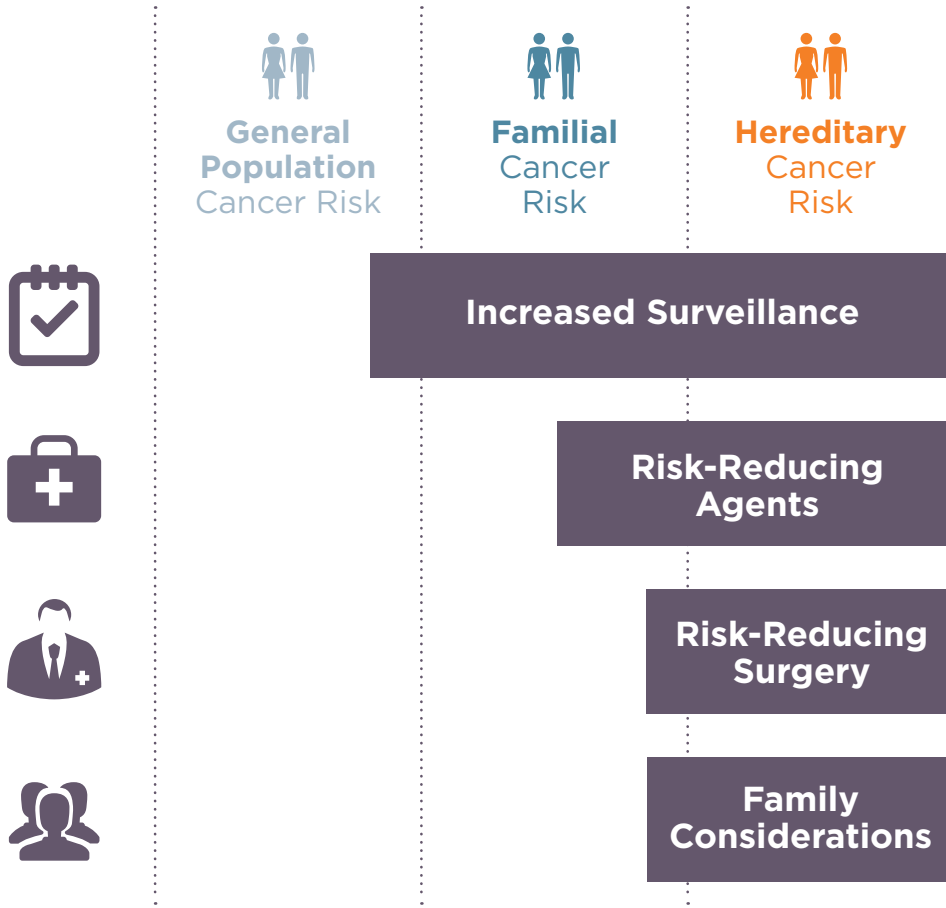
	Clinical Breast Exam	Pap Test	Cancer Family History
1 **SCREEN** (Rate of Abnormal)	7%[1]	6%[6,7]	10%[9]
2 **EVALUATE**	Palpable Mass / Screening Imaging Studies	High Risk HPV+ Cytology Higher than Low-Grade Squamous Lesion (LSIL) Biopsy proven High-Grade Squamous Lesion (HSIL)	Significance of Cancer Family History
3 **DIAGNOSE†**	Diagnostic Imaging Studies Breast Aspiration and/or Biopsy[2]	Colposcopy / Biopsy	Hereditary Cancer Testing
4 **Result Rate** (% of Abnormal Screens)	**CANCER DIAGNOSIS:**	**CANCER DIAGNOSIS:**	**HEREDITARY CANCER DIAGNOSIS:**
Positive	**~10%**[3,4,5]	**<1%**[8]	Hereditary Risk **~10%**[10]
Negative	**~90%**	**>99%**	Familial Risk **~90%**
MANAGE	Develop a plan for appropriate medical management		

1. Bobo,JK et al., Findings From 752 081 Clinical Breast Examinations Reported to a National Screening Program From 1995 Through 1998. J Natl Cancer Inst 2000; 92 (12): 971-976. **2.** Haas J, et al, Evaluation and Outcomes of Women with a Breast Lump and a Normal Mammogram Result. Journal of General Internal Medicine. (2005) 20;8:692-696. **3.** Klein S, Evaluation of Palpable Breast Masses. Am Fam Physician. (2005) 71(9):1731-1738. **4.** Salzman B, et al, Common Breast Problems. Am Fam Physician. (2012) 86(4):343-349. **5.** Barton MB, et al, Breast Symptoms Among Women Enrolled in a Health Maintenance Organization: Frequency, Evaluation, and Outcome. Ann Intern Med. (1999) 130(8):651-7. **6.** Weinmann S, Williams AE, Kamineni A, et al. Cervical Cancer Screening and Follow-Up in 4 Geographically Diverse US Health Care Systems, 1998 Through 2007. Cancer. 2015;121(17):2976-2983. **7.** Gilbert TJ, Sugarman JR, Cobb N. Abnormal Papanicolaou smears and colposcopic follow-up among American Indian and Alaska Native women in the Pacific northwest J Am Board Fam Pract. 1995 May-Jun;8(3):183-8. https://www.ncbi.nlm.nih.gov/pubmed?term=((abnormal%20papanicolaou%20smears%5BTitle%2FAbstract%5D%20AND%20colposcopic%20follow-up%5BTitle%2FAbstract%5D))%20AND%20gilbert%5BAuthor%5D. **8.** Screening for Cervical Cancer. Practice Bulletin No. 131. American College of Obstetricians and Gynecologists. Obstet Gynecol (2012) 120(5):1222-38, reaffirmed 2015. **9.** Hughes K, et al. Rate of Abnormal is defined by cancer family history meeting red flags. The Breast Journal. (2003) 9(1):19-25. **10.** Rosenthal, E. et al. Outcomes of Clinical Testing for 76,000 Patients Utilizing a Panel of 25 Genes Associated with Increased Risk for Breast, Ovarian, Colorectal, Endometrial, Gastric Pancreatic, Melanoma and Prostate Cancers. Abstract #1515 presented at ASCO June 1, 2015. https://myriad-web.s3.amazonaws.com/ASCO2015_myRisk%20Series_Presented_Rosenthal_01JUNE2015.pdf.

†Diagnose all appropriate patients

MEDICAL MANAGEMENT CONSIDERATIONS

A patient's cancer risk category will determine the medical management and screening recommendations you make. According to societal guidelines, patients at increased risk typically require more intervention.



The cancer risk estimates on the following pages will vary based on specific gene mutation and/or cancer family history characteristics. Hereditary cancer risk percentages and management consideration examples are typically based on the gene mutation associated with the greatest cancer risk. Familial and hereditary risk management guidelines are examples based on specific options provided by National Comprehensive Cancer Network (NCCN) and other professional medical societies. Specific patient recommendations will vary based on gene mutation, cancer family history and other risk factors. The ages to initiate different interventions for cancer risk reduction may be adjusted 5-10 years earlier than those listed based on the earliest age of diagnosis of that cancer in a patient's family.

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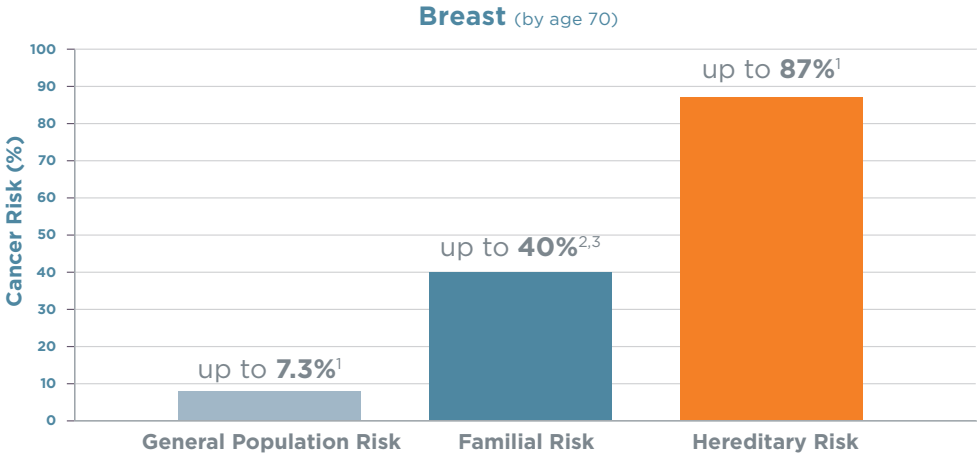
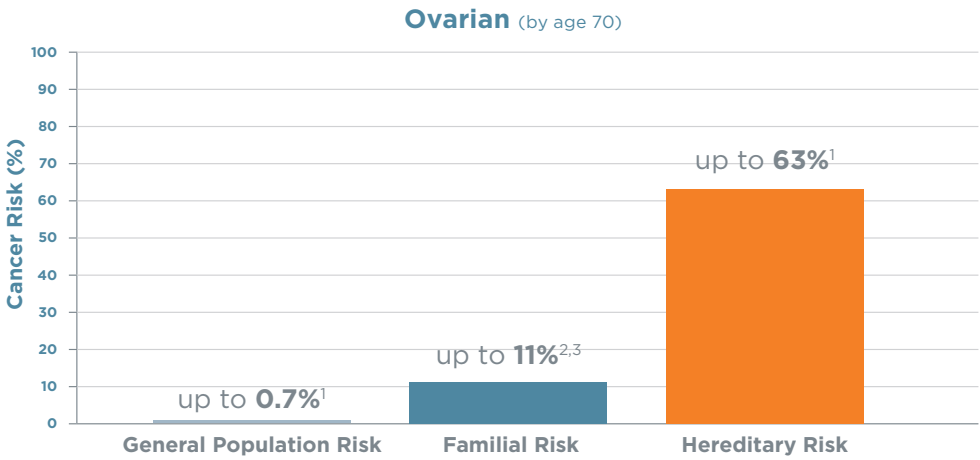
MANAGING **BREAST CANCER** RISK FOR AN UNAFFECTED PATIENT BASED ON FAMILY HISTORY AND HEREDITARY CANCER STATUS



Breast | Management Considerations	
General Population Risk[1,4]	**FEMALE:** • Education about breast awareness and clinical breast exams every 1-3 years beginning at age 25 • Annual clinical breast exams and screening mammography beginning at age 40 **MALE** (cancer risk <0.1%[1] by age 70)**:** No current screening guidelines exist
Familial Risk*[4]	**FEMALE:** • Consider annual screening mammogram + clinical breast exam every 6-12 months to begin 10 years prior to youngest family member but not less than age 30 • Consider annual breast MRI to begin 10 years prior to youngest family member but not less than age 25 • Consider additional risk reduction strategies, such as chemoprevention **MALE** (cancer risk up to 1%[5] by age 70)**:** No current screening guidelines exist
Hereditary Risk[1,4,6]	**FEMALE:** • Breast awareness education beginning at age 18 • Clinical breast exams every 6-12 months beginning at age 25 • Annual breast MRI beginning at age 25 • Annual mammography beginning at age 30 • Consider options for breast cancer risk-reducing agents (i.e., tamoxifen) • Consider risk-reducing mastectomy • Consider investigational screening studies within clinical trials **MALE** (cancer risk up to 6.8%[1] by age 70)**:** • Breast self-exam training and education starting at age 35 • Clinical breast exam, every 12 months, starting at age 35

1. For the most up-to-date general population, gene-associated cancer risks, management criteria, and other syndrome-related cancers not listed here refer to the Gene Tables located at https://www.MyriadPro.com/myRisk. Risks are for patients who have never had cancer. Patients with hereditary risk may have increased risk for other syndrome related cancers. **2.** Metcalfe KA, et al. Br J Cancer. 2009 Jan 27;100(2):421-5.Epub 2008 Dec 16. **3.** Sutcliffe, et al. Int J Cancer. 2000 Jul 1;(87)1:110-7 *These familial management options are only considerations when a female's lifetime risk of breast cancer is assessed to be 20% or greater using Claus, BOADICEA, BRCAPro or T-C. The ages to initiate different interventions for cancer risk reduction may be adjusted 5-10 years earlier than those listed based on the earliest age of diagnosis of that cancer in a patient's family. **4.** NCCN Clinical Practice Guidelines in Oncology: Breast Cancer Screening and Diagnosis. V1. 2016. **5.** Brinton LA, Richesson DA, Gierach GL, et al. Prospective evaluation of risk factors for male breast cancer. J Natl Cancer Inst. 2008 Oct 15;100(20):1477-81. **6.** Hereditary Breast and Ovarian Cancer Syndrome, Practice Bulletin No. 103. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;113:957–66, reaffirmed 2016.

MANAGING **OVARIAN CANCER** RISK FOR AN UNAFFECTED PATIENT BASED ON FAMILY HISTORY AND HEREDITARY CANCER STATUS



Ovarian | Management Considerations	
General Population Risk[1]	• No current screening guidelines exist
Familial Risk	• No current screening guidelines exist
Hereditary Risk[1,4,5]	• Consider options for ovarian cancer risk-reducing agents (i.e., oral contraceptives) • Consider transvaginal ultrasound and CA-125 measurement • Consider investigational screening studies within clinical trials at age 30-35 or individualized • Bilateral salpingo-oophorectomy at age 35 to 40, upon completion of childbearing, or 40 to 45 for women who have already maximized their breast cancer risk prevention

1. For the most up-to-date general population, gene-associated cancer risks, management criteria, and other syndrome-related cancers not listed here refer to the Gene Tables located at https://www.MyriadPro.com/myRisk/. Risks are for patients who have never had cancer. Patients with hereditary risk may have increased risk for other syndrome related cancers. **2.** Pharoah Paul PD and Pnder BA. Best Practice & Research Clinical Obstetrics and Gynaecology. Vol 16. No.4. 449-68. 2002. **3.** Sutcliffe, et al. Int J Cancer. 2000 Jul 1;(87)1:110-7. **4.** NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Breast and Ovarian Guidelines. V2. 2017 **5.** Hereditary Breast and Ovarian Cancer Syndrome, Practice Bulletin No. 103. American College of Obstetricians and Gynecologists. Obstet Gynecol 2009;113:957–66, reaffirmed 2016.

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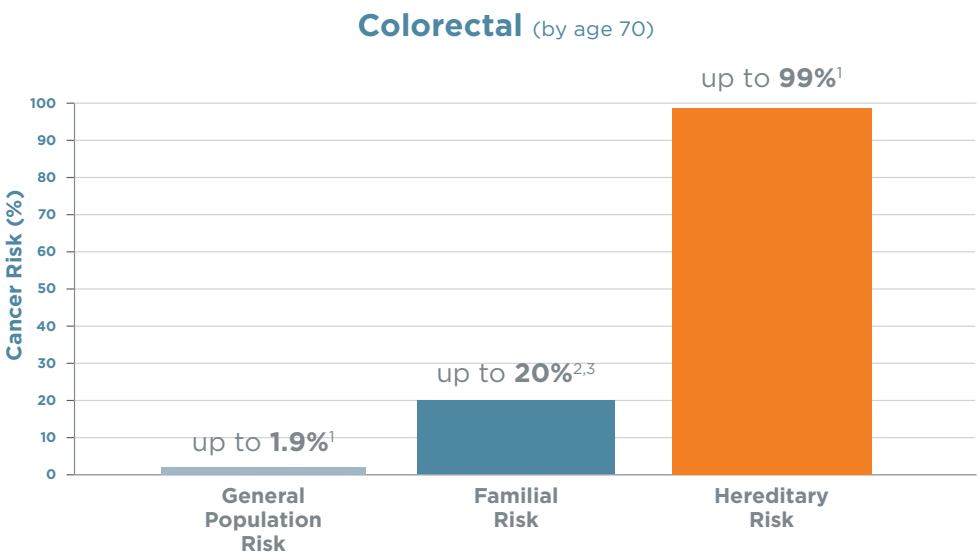
MANAGING **COLORECTAL CANCER** RISK FOR AN UNAFFECTED PATIENT BASED ON FAMILY HISTORY AND HEREDITARY CANCER STATUS



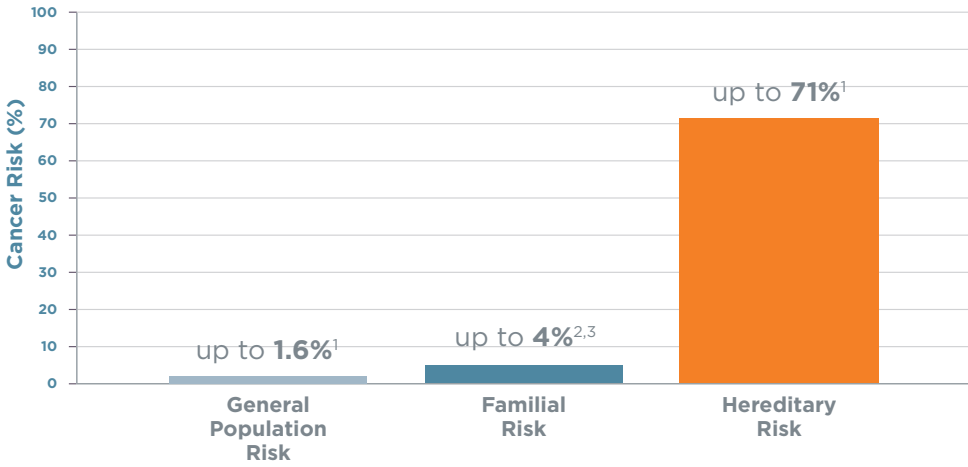
Colorectal | Management Considerations

General Population Risk[1]	• Screening beginning at age 50 by colonoscopy or a combination of other modalities such as stool testing and flexible sigmoidoscopy
Familial Risk[4]	• Colonoscopy screening beginning as early as age 40 or 10 years before the earliest diagnosis of colorectal cancer, repeating every 5-10 years or based on colonoscopy findings
Hereditary Risk[1,5,6]	• Annual colonoscopy beginning as early as age 10-15 • Consider chemoprevention with NSAIDs • Consider colectomy based on polyp burden and other clinical features

1. For the most up-to-date general population, gene-associated cancer risks, management criteria, and other syndrome-related cancers not listed here refer to the Gene Tables located at https://www.MyriadPro.com/myRisk/. Risks are for patients who have never had cancer. Patients with hereditary risk may have increased risk for other syndrome related cancers. **2.** Taylor DP et al., Gastroenterology. 2010;138;2044-58 **3.** Grady WM, et al. Gastroenterology. 2003;124; 1574-94 **4.** NCCN Clinical Practice Guidelines in Oncology: Colorectal Cancer Screening. v2.2016. **5.** Lynch Syndrome , Practice Bulletin No. 147. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;124:1042–54. **6.** NCCN Clinical Practice Guidelines in Oncology: Genetic/Familial High-Risk Assessment: Colorectal Cancer V2. 2016

MANAGING **ENDOMETRIAL CANCER** RISK FOR AN UNAFFECTED PATIENT BASED ON FAMILY HISTORY AND HEREDITARY CANCER STATUS

Endometrial (by age 70)



Endometrial | Management Considerations

General Population Risk[1]	• No current screening guidelines exist
Familial Risk	• No current screening guidelines exist
Hereditary Risk[1,4]	• Educate patient about endometrial cancer symptoms • Consider annual pelvic examination, endometrial sampling and transvaginal ultrasound at age 30-35 • Consider hysterectomy after completion of childbearing

1. For the most up-to-date general population, gene-associated cancer risks, management criteria, and other syndrome-related cancers not listed here refer to the Gene Tables located at https://www.MyriadPro.com/myRisk/. Risks are for patients who have never had cancer. Patients with hereditary risk may have increased risk for other syndrome related cancers. **2.** Hemminki K., et al. European Journal of Cancer. 2004;40:90-95 **3.** Hemminki K., et al. European Journal of Cancer. 2005;41:2155-2159. **4.** Lynch Syndrome , Practice Bulletin No. 147. American College of Obstetricians and Gynecologists. Obstet Gynecol 2014;124:1042–54.

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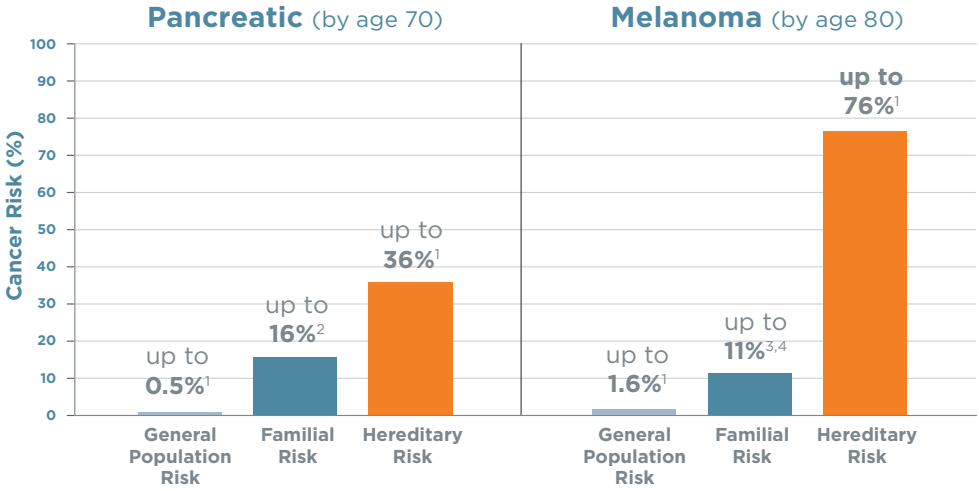
MANAGING **PANCREATIC & MELANOMA CANCER** RISK FOR AN UNAFFECTED PATIENT BASED ON FAMILY HISTORY AND HEREDITARY CANCER STATUS

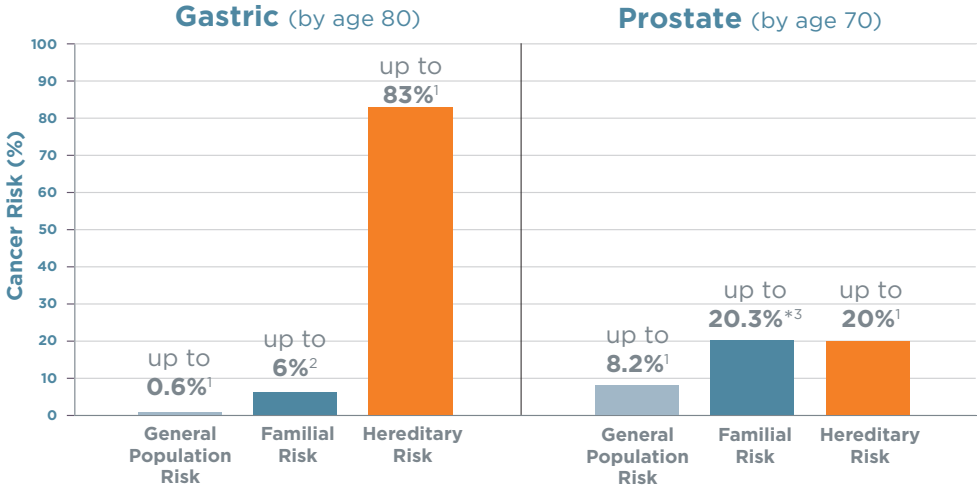


Pancreatic | Management Considerations	
General Population[1]	• No current screening guidelines exist
Familial Risk[5]	• Consider available options for screening with Magnetic Resonance Cholangiopancreatography (MRCP) or Endoscopic Ultrasound (EUS) within a clinical trial
Hereditary Risk[1]	• Screening with MRCP or EUS individualized or every 1-2 years as early as age 30-35

Melanoma | Management Considerations	
General Population[1]	• Education about the importance of skin protection, such as sun avoidance, protective clothing and sunscreen • Education about the characteristics of moles worrisome for melanoma
Familial Risk[6,7]	• Education about the importance of skin protection, such as sun avoidance, protective clothing and sunscreen • Education about the characteristics of moles worrisome for melanoma
Hereditary Risk[1]	• Strong emphasis on education about the importance of skin protection, such as sun avoidance, protective clothing and sunscreen beginning in infancy • Clinical skin examinations by an appropriately trained provider every 6-12 months beginning at age 10 • Monthly whole-body skin exams conducted by the patient and/or family beginning at age 10 • Consider whole-body photography and close-up photography of atypical nevi for ongoing comparison

1. For the most up-to-date general population, gene-associated cancer risks, management criteria, and other syndrome-related cancers not listed here refer to the Gene Tables located at https://www.MyriadPro.com/myRisk/. Risks are for patients who have never had cancer. Patients with hereditary risk may have increased risk for other syndrome related cancers. **2.** Klein AP, et al. Prospective risk of pancreatic cancer in familial pancreatic cancer kindreds. Cancer Res 2004; 64:2634–8. **3.** Brandt A, Sundquist J, Hemminki K: Risk of incident and fatal melanoma in individuals with a family history of incident or fatal melanoma or any cancer. Br J Dermatol 165 (2): 342-8, 2011. **4.** Helgadottir H, Höiom V, Tuominen R, et al.: CDKN2A mutation-negative melanoma families have increased risk exclusively for skin cancers but not for other malignancies. Int J Cancer. 2015 May 5. doi: 10.1002/ijc.29595. [Epub ahead of print]. http://www.ncbi.nlm.nih.gov/pubmed/25943250 **5.** Canto MI, et al. International Cancer of the Pancreas Screening (CAPS) Consortium summit on the management of patients with increased risk for familial pancreatic cancer. Gut. 2013 62:339-47. **6.** Kefford RF et al. Counseling and DNA testing for individuals perceived to be genetically predisposed to melanoma: A consensus statement of the Melanoma Genetics Consortium. J Clin Oncol. 1999 17:3245-51. **7.** Coit DG et al. NCCN Clinical Practice Guidelines in Oncology®: Melanoma. V1.2017. January 15.

MANAGING **GASTRIC & PROSTATE CANCER** RISK FOR AN UNAFFECTED PATIENT BASED ON FAMILY HISTORY AND HEREDITARY CANCER STATUS



Gastric | Management Considerations	
General Population[1]	• No current screening guidelines exist
Familial Risk	• No current screening guidelines exist
Hereditary Risk[1]	• Upper endoscopy, possibly including targeted biopsies of the stomach beginning as early as age 15 every 2-3 years • Gastrectomy at age 18-40 years, or individualized to a younger age if a relative was diagnosed under age 25 • Treatment for Helicobacter pylori if present

Prostate | Management Considerations	
General Population[1]	• Risk benefit discussion with patient about screening with Digital Rectal Exam (DRE) and Prostate Specific Antigen (PSA) beginning at age 45
Familial Risk[4]	• Incorporate information about familial risk into risk benefit discussion with patient about screening with DRE and PSA beginning at age 45
Hereditary Risk[1,5]	• Recommend annual prostate cancer screening beginning at age 45

1. For the most up-to-date general population, gene-associated cancer risks, management criteria, and other syndrome-related cancers not listed here refer to the Gene Tables located at https://www.MyriadPro.com/myRisk/. Risks are for patients who have never had cancer. Patients with hereditary risk may have increased risk for other syndrome related cancers. **2.** Yaghoobi et al. (2010) Minireview: Family history and the risk of gastric cancer. British Journal of Cancer 102, 237 – 242. **3.** Kicinski M, Vangronsveld J, Nawrot TS: An epidemiological reappraisal of the familial aggregation of prostate cancer: a meta-analysis. PLoS One 6 (10): e27130, 2011. **4.** Carroll PR et al. NCCN Clinical Practice Guidelines in Oncology®: Prostate Cancer Early Detection. V2.2016. March 10. **5.** Daly MB et al. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High Risk Assessment: Breast and Ovarian. V2.2017. March 15.

* Prostate familial risk percentages are for one first-degree relative or second-degree relatives.

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CANCER RISK ASSESSMENT MAY IMPACT MANAGEMENT RECOMMENDATIONS FOR EVERY PATIENT YOU SEE TODAY

Today's Schedule

10:00 - Well-Woman Exam

10:15 - New OB Visit

10:30 - Contraception

10:45 - Problem Visit
Pelvic Pain

11:00 - Problem Visit
Irreg. Heavy Bleeding

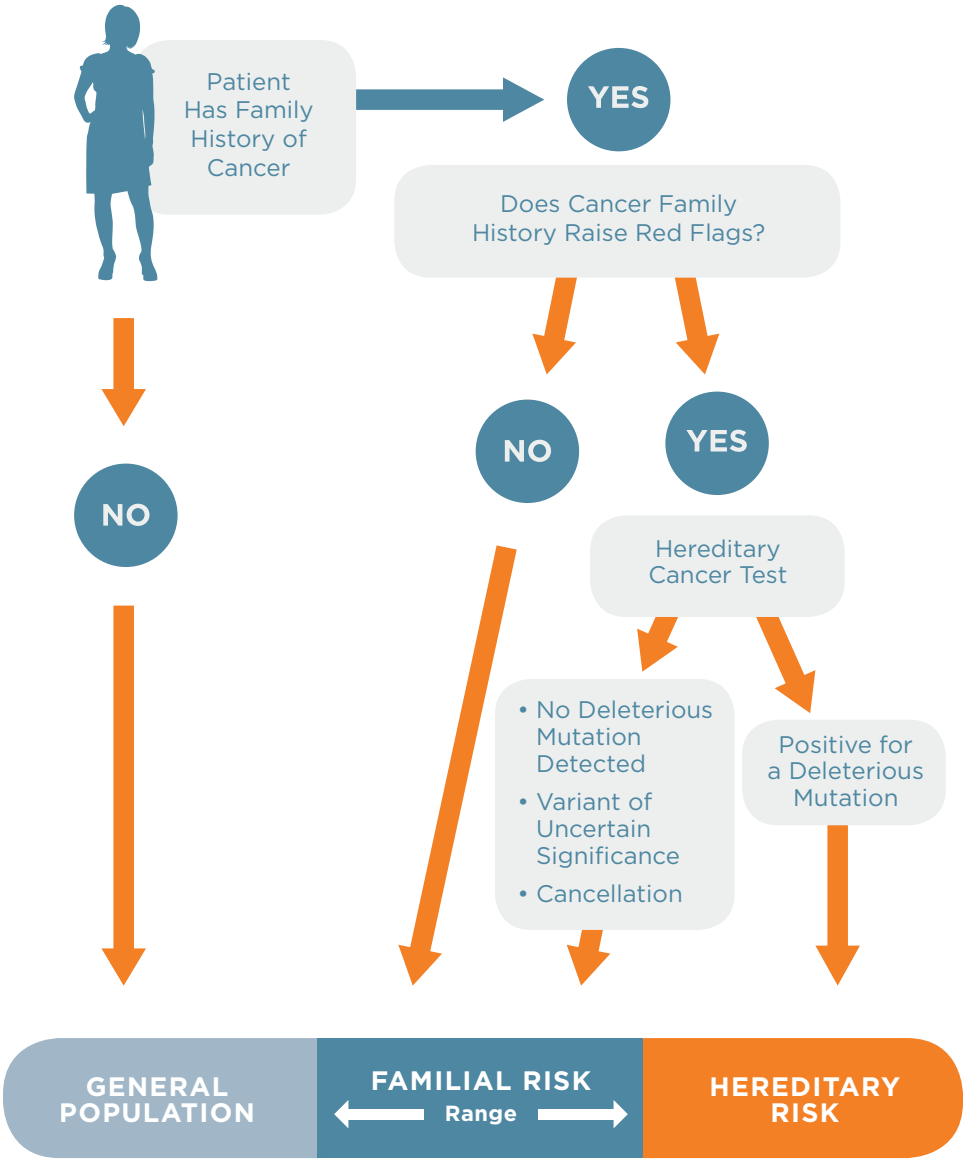
11:15 - Surgery Consult

11:30 - Well-Woman Exam

11:45 - Contraception

EVERY RESULT MATTERS

Stratifying a patient's cancer risk will enable you to identify those patients who are appropriate for hereditary cancer testing. The results, whether negative or positive, can be used to your patient's benefit. Combined with their cancer family history, the results can provide you with the valuable information you need to effectively make decisions and medically manage patients' risk on an individual basis.



Myriad myRisk® Hereditary Cancer Panel

- **Evaluates risk for 8 cancers** by analyzing multiple, clinically actionable genes, family history and other risk factors.
- **Provides medical management for positive or negative genetic results** based on professional societal guidelines for patients.

CONFIDENTIAL

52530322

Management Tool - Integrated BRACAnalysis®

Name: DOB: **May 05, 1970** Accession #: Report Date:

PROCEDURE	AGE TO BEGIN	FREQUENCY (Unless otherwise indicated by findings)	RELATED TO
FEMALE BREAST			
Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider. Periodic, consistent breast self-examination (BSE) may facilitate breast awareness.[1]	18 years	NA	*BRCA1*
Clinical breast examination[1]	25 years	Every 6 to 12 months	*BRCA1*
Breast MRI with contrast and/or Mammography[1]	Age 25 for MRI (preferred) or mammography. Age 30 for both MRI and mammography. Individualize to a younger age if a relative has been diagnosed younger than age 30.	Annually	*BRCA1*
Consider investigational screening studies within clinical trials.[1]	Individualized	NA	*BRCA1*
Consider risk-reducing mastectomy.[1]	Individualized	NA	*BRCA1*
Consider options for breast cancer risk-reduction agents (i.e. tamoxifen).[1]	Individualized	NA	*BRCA1*
OVARIAN			
Bilateral salpingo-oophorectomy[1]	35 to 40 years, upon completion of childbearing	NA	*BRCA1*
Consider transvaginal ultrasound and CA-125 measurement. Consider investigational screening studies within clinical trials.[1]	30 to 35 years	Individualized	*BRCA1*
Consider options for ovarian cancer risk-reduction agents (i.e. oral contraceptives).[1]	Individualized	NA	*BRCA1*
PANCREATIC			
Currently there are no specific medical management guidelines for pancreatic cancer risk in mutation carriers.	NA	NA	*BRCA1*

1. Daly M et al. NCCN Clinical Practice Guidelines in Oncology®: Genetic/Familial High-Risk Assessment: Breast and Ovarian. V 1.2017. September 19. Available at http://www.nccn.org.

Management: _____

KS AND MANAGEMENT ARE DETERMINED

Management Tool: **Page 3 of 5**

Management Tool: **Page 4 of 5**

Hereditary Cancer Test
Specimen Collection & Transportation Kit

MYRIAD myRisk® Hereditary Cancer

The Myriad Advantage: Best-In-Class Support

Myriad **Promise**™

Financial Support

Because patients and their families use test results to make life saving medical decisions, Myriad promises to provide affordable access to testing, a lifetime commitment to accurate results, and comprehensive support for ALL appropriate patients and their families.

If a patient encounters ANY financial hardship associated with their bill, Myriad will work directly with the patient toward their complete satisfaction.

Patients with questions regarding their Myriad bill or insurance Explanation of Benefits should contact Myriad rather than their health care provider. Myriad is here to help: **844-MYRIAD9** (844-697-4239) or **billinghelp@myriad.com**.

Patient Support

- Through mySupport360.com, Myriad connects your patients with a wealth of helpful information, expert guidance, and the ability to share their experiences with others.

Medical Support

- A team of highly trained medical specialists is available for consultation
- Support is accessible by phone, e-mail, and in person
- Medical Services: (800) 469-7423 x3850 helpmed@myriad.com

Visit **www.MyriadPro.com** for extensive medical education and resources

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RED FLAGS FOR HEREDITARY CANCER

An individual with a personal or family history of **any ONE of the following**:

MULTIPLE CANCERS A combination of cancers on the same side of the family	• **2 or more:** breast / ovarian / prostate / pancreatic cancer • **2 or more:** colorectal / endometrial / ovarian / gastric / pancreatic / other cancers (i.e., ureter/ renal pelvis, biliary tract, small bowel, brain, sebaceous adenomas) • **2 or more:** melanoma / pancreatic cancer
YOUNG CANCERS Any 1 of the following cancers at age **50 or younger**	• Breast cancer • Colorectal cancer • Endometrial cancer
RARE CANCERS Any 1 of these rare presentations at **any age**	• Ovarian cancer • Breast: male breast cancer or triple negative breast cancer • Colorectal cancer with abnormal MSI/IHC, MSI associated histology†† • Endometrial cancer with abnormal MSI/IHC • 10 or more gastrointestinal polyps*

Certain ancestries may have greater risk for hereditary cancer syndromes (e.g. Ashkenazi Jewish ancestry)

††Presence of tumor infiltrating lymphocytes, Crohn's-like lymphocytic reaction, mucinous/signet-ring differentiation, or medullary growth pattern.
*Adenomatous type.

Assessment criteria based on medical society guidelines. For these individual medical society guidelines, go to www.MyriadPro.com/guidelines.
Family members include first-, second-, and third-degree blood relatives on both your mother's and father's sides.

Hereditary Cancer Testing Provided by:
Myriad Genetic Laboratories, Inc., 320 Wakara Way, Salt Lake City, UT 84108

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