Risk Stratified Cancer Screening and Early Detection in Kansas

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- Lauren Nye, MD
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Objectives

- **Defining risk stratified cancer screening**
- **Cancer genetic risk assessment**
- **Risk assessment tools**
- **Presenting cancer screening guidelines from:**
  - United States Preventative Services Task Force (USPSTF)
  - National Comprehensive Cancer Network (NCCN)
  - American Cancer Society (ACS)
  - Professional Societies
- ***Focused on breast, cervical and colon cancer.***

Risk Assessment

- Standard guidelines are in place for "average" risk individuals.
- Separate guidelines apply for higher risk individuals.
  - typically provided by professional societies.
- Each individual needs a risk assessment so appropriate risk stratified cancer screening can be discussed.

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risk stratified cancer screening

Provider assessment of individual's cancer risk → **Patient-Provider** discussion of risk and cancer screening → **Patient** decision on cancer screening

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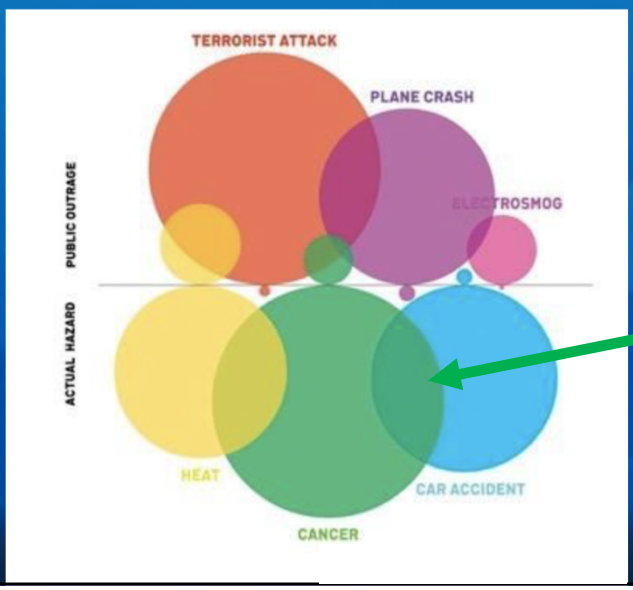
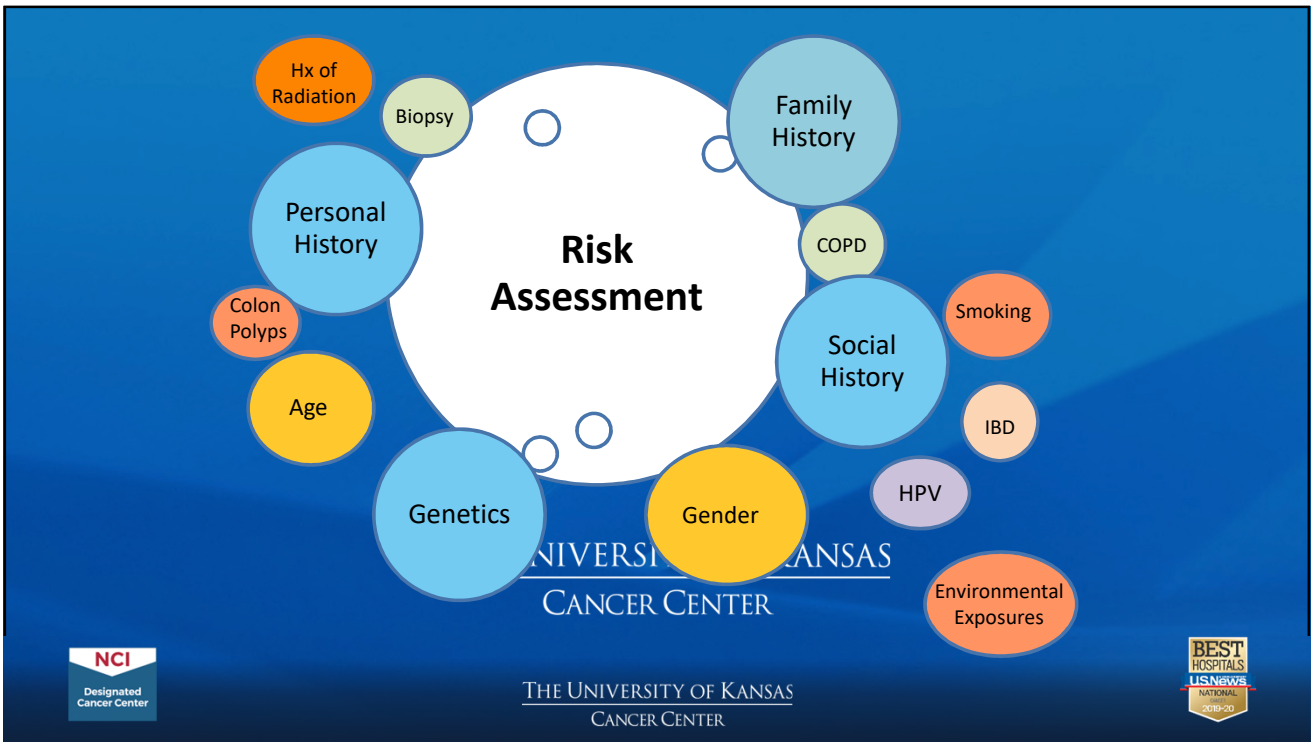
Components of Risk Analysis from the US Army Corp

https://www.iwr.usace.army.mil/Portals/70/docs/risk/Risk_Communication dft.pdf?ver 2018 07 03 134520 190

Putting Risk Into Context





Risk vs Benefit

- Benefit = Early Detection
  - Decreases morbidity
  - Some screening does not show a significant mortality benefit.
- Risk
  - False Positive
  - Cost
  - May lead to an invasive procedure with possible harm
  - (radiation)

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Cancer Genetic Risk Assessment

Evaluating an individual's likelihood of having an inheritable pathogenic variant (mutation) in their DNA that increases the individual's risk of cancer.

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Cancer Genetic Risk Assessment

- USPSTF updated recommendations (8/2019) recommends primary care physicians assess a women's personal and family history of breast, ovarian, tubal or peritoneal cancer with a familial risk assessment tool.
- NCCN recommends genetic testing for those with a relative with a mutation or family history that meets their individual guidelines.

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USPSTF Recommended Tools
Ontario Family History Assessment Tool
Manchester Scoring System
Referral Screening Tool
Pedigree Assessment Tool
7-Question Family History Screening Tool
IBIS instrument
BRCAPRO-LYTE

Focus only on HBOC

https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/brca-related-cancer-risk-assessment-genetic-counseling-and-genetic-testing1

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7 Question Family History Screening Tool

Table 5. Seven-Question Family History Screening[a,b]

No.	Questions
1	Did any of your first-degree relatives have breast *or* ovarian cancer?
2	Did any of your relatives have bilateral breast cancer?
3	Did any man in your family have breast cancer?
4	Did any woman in your family have breast *and* ovarian cancer?
5	Did any woman in your family have breast cancer before age 50 y?
6	Do you have 2 or more relatives with breast *and/or* ovarian cancer?
7	Do you have 2 or more relatives with breast *and/or* bowel cancer?

[a] See Ashton-Prolla et al,[25] Fischer et al.[26]
[b] One positive response initiates referral.

Ideal for patient completed tool.

Single positive triggers referral for genetic counseling.

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Pedigree Assessment Tool

Table 4. Pedigree Assessment Tool[a,b]

Risk Factor	Score for Every Family Member With Breast or Ovarian Cancer Diagnosis, Including Second-/Third-Degree Relatives
Breast cancer at age ≥50 y	3
Breast cancer at age <50 y	4
Ovarian cancer at any age	5
Male breast cancer at any age	8
Ashkenazi Jewish heritage	4
Total	

[a] See Hoskins et al.[23] Teller et al.[24]

[b] Score 8 or greater is the optimal referral threshold.

Ideal for provider team completed tool.

Requires Scoring (≥ 8) triggers referral for genetic counseling.

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National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2020
Hereditary Cancer Testing Criteria

NCCN Guidelines Index
Table of Contents
Discussion

TESTING CRITERIA FOR HIGH-PENETRANCE BREAST AND/OR OVARIAN CANCER SUSCEPTIBILITY GENES
(This often includes *BRCA1, BRCA2, CDH1, PALB2, PTEN,* and *TP53* among others. See GENE-A for a more complete list.)[a,b,c,d]

Testing is clinically indicated in the following scenarios:

1. Individuals with any blood relative with a known pathogenic/likely pathogenic variant in a cancer susceptibility gene
2. Individuals meeting the criteria below but with previous limited testing (eg, single gene and/or absent deletion duplication analysis) interested in pursuing multi-gene testing
3. *Personal history of cancer*
   - Breast cancer with at least one of the following:
     - Diagnosed at age ≤45 y; or
     - Diagnosed at age 46–50 y with:
       - Unknown or limited family history; or
       - A second breast cancer diagnosed at any age; or
       - ≥1 close blood relative[e] with breast, ovarian, pancreatic, or high-grade (Gleason score ≥7) or intraductal prostate cancer at any age
     - Diagnosed at age ≤60 y with triple-negative breast cancer;
     - Diagnosed at any age with:
       - Ashkenazi Jewish ancestry; or
       - ≥1 close blood relative[e] with breast cancer at age ≤50 y or ovarian, pancreatic, or metastatic or intraductal prostate cancer at any age; or
       - ≥3 total diagnoses of breast cancer in patient and/or close blood relatives[e]
     - Diagnosed at any age with male breast cancer
   - Epithelial ovarian cancer[f] (including fallopian tube cancer or peritoneal cancer) at any age
   - Exocrine pancreatic cancer at any age[g] (See CRIT-3)
   - Metastatic or intraductal prostate cancer at any age[h]
   - High-grade (Gleason score ≥7) prostate cancer with:
     - Ashkenazi Jewish ancestry; or
     - ≥1 close relative[e] with breast cancer at age ≤50 y or ovarian, pancreatic, or metastatic or intraductal prostate cancer at any age; or
     - ≥2 close relatives[e] with breast or prostate cancer (any grade) at any age.
   - A mutation identified on tumor genomic testing that has clinical implications if also identified in the germline
   - To aid in systemic therapy decision-making, such as for HER2-negative metastatic breast cancer[i]
4. *Family history of cancer*
   - An affected or unaffected individual with a first- or second-degree blood relative meeting any of the criteria listed above (except individuals who meet criteria only for systemic therapy decision-making)[j]
   - An affected or unaffected individual who otherwise does not meet the criteria above but has a probability >5% of a *BRCA1/2* pathogenic variant based on prior probability models (eg, Tyrer-Cuzick, BRCAPro, PennII)[k]

Criteria met → See GENE-1

If testing criteria not met, consider testing for other hereditary syndromes → If criteria for other hereditary syndromes not met, then cancer screening as per NCCN Screening Guidelines

Continued on next page

Footnotes on CRIT-2

NCCN Recommendations

https://www.nccn.org/professionals/physician_gls/pdf/genetics_bop.pdf

NCCN Recommendations

CRITERIA FOR THE EVALUATION OF LYNCH SYNDROME

- **Known LS pathogenic variant in the family**
- **Personal history of colorectal, endometrial, or other Lynch syndrome-associated cancer**
  - **An individual with colorectal or endometrial cancer at any age with tumor showing evidence of mismatch repair (MMR) deficiency, either by microsatellite instability (MSI) or loss of MMR protein expression[k]**
  - **An individual with colorectal or endometrial cancer and any of the following:**
    - **Diagnosed <50 y**
    - **Another synchronous or metachronous LS-related cancer[d]**
    - **≥1 first-degree or second-degree relative with LS-related cancer[d] diagnosed <50 y**
    - **≥2 first-degree or second-degree relatives with LS-related cancers[d] regardless of age**
  - **An individual with a colorectal tumor with MSI-high (MSI-H) histology (ie, presence of tumor-infiltrating lymphocytes, Crohn's-like lymphocytic reaction, mucinous/signet ring differentiation, or medullary growth pattern)**
- **Family history of any of the following:**
  - **≥1 first-degree relative with colorectal or endometrial cancer diagnosed <50 y**
  - **≥1 first-degree relative with colorectal or endometrial cancer and another synchronous or metachronous LS-related cancer[d]**
  - **≥2 first-degree or second-degree relatives with LS-related cancer,[d] including ≥1 diagnosed <50 y**
  - **≥3 first-degree or second-degree relatives**
- **Increased model-predicted risk for Lynch sy**
  - **An individual with a ≥5% risk[l] of having an** **odels (ie, PREMM5, MMRpro, MMRpredict)**

→ See Strategies For Evaluating LS (LS-1)

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https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf

PREMM 5

1 Patient information

Sex
- Male
- Female

Current age (years)

Has the patient had colorectal cancer?
- No
- Yes

Has the patient had any other Lynch syndrome-associated cancer?
Other Lynch syndrome-associated cancers include ovary, stomach, small intestine tract/bladder/kidney, bile ducts, brain, pancreas, and sebaceous gland skin tumors

2 Relatives: First-degree
*First-degree relatives include **parents, siblings, children,** family*

How many first-degree relatives have had colorectal cancer?
- None
- One
- Two or more

How many first-degree relatives have had endometrial (uterine) cancer?
- None
- One
- Two or more

Have any first-degree relatives had other Lynch syndrome-associated canc

3 Relatives: Second-degree
*Second-degree relatives are **grandparents, grandchildren, aunts, uncles, nieces, nephews,** only from affected side of family*

How many second-degree relatives have had colorectal cancer?
- None
- One
- Two or more

How many second-degree relatives have had endometrial (uterine) cancer?
- None
- One
- Two or more

Have any second-degree relatives had other Lynch syndrome-associated cancers?
Other Lynch syndrome-associated cancers include ovary, stomach, small intestine, urinary tract/bladder/kidney, bile ducts, brain, pancreas, and sebaceous gland skin tumors.

Overall predicted probability of *MLH1, MSH2, MSH6, PMS2, or EPCAM* mutation

22.6%

If the overall predicted probability is ≥ 2.5%

Referral for genetic evaluation is recommended. This may include tumor sample microsatellite instability (MSI) or immunohistochemistry (IHC) testing, genetic counseling, and/or germline genetic testing. (Kastrinos F, et al. Development and validation of the PREMM5 model for comprehensive risk assessment of Lynch syndrome. Journal of Clinical Oncology. 2017 May 10. Advance online publication. DOI: 10.1200/JCO.2016.69.6120. PREMM$_5$ JCO)

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https://premm.dfci.harvard.edu

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How will you include cancer genetic risk assessment in your work flow?

Taking a family history ➡ Screening tool for genetic risk ➡ Referral pattern for genetic risk assessment and testing ➡ Management plan for high risk individuals*

**negative genetic testing does NOT imply low risk*

Cancer Screening Guidelines

http://uspreventiveservicetaskforce.org

https://nccn.org ★

https://www.cancer.org

★ High Risk Guidelines Available

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Breast Cancer

- Gail Model
- IBIS/Tyrer Cuzick
- Defining Risk
- Screening Guidelines

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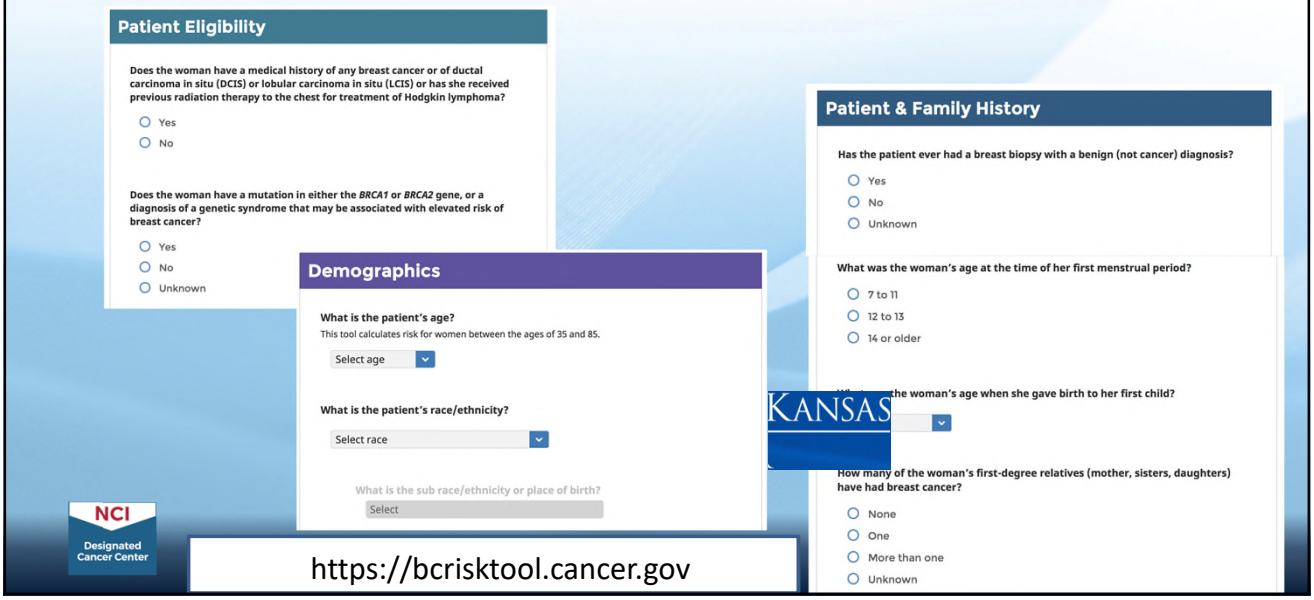
Breast Cancer Risk Assessment



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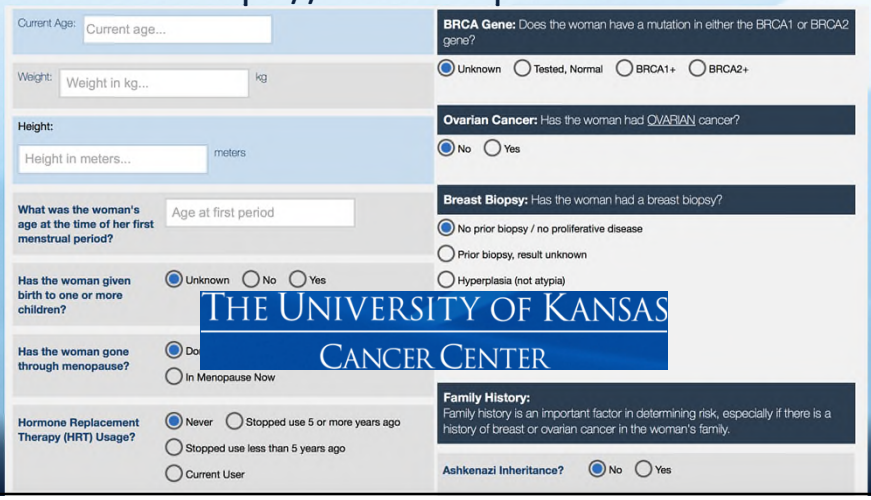
https://bcrisktool.cancer.gov

Breast Cancer Risk Assessment

IBIS Risk Assessment Tool (Tyrer-Cuzick)

https://ibis.ikonopedia.com



Breast Cancer Risk Assessment

Lifetime Risk:

Average to Moderate Risk: < 20%

High Risk: **≥ 20%**

5 year or short-term Risk:

Average to Moderate Risk: < 1.7% or < double average risk.

High Risk: **≥ 1.7% or double average risk.**

Breast Cancer Screening Guidelines			
	USPSTF	**NCCN**	**ACS**
Average Risk	Screening mammogram every 1 to 2 years for women 40 and older.	Annual screening mammogram (tomosynthesis) at age 40.	40-45: choice to start annual mammogram screening. 45-54: annual mammogram. 55 and older: option of annual vs every 2 year mammogram.
High Risk	N/A	Clinical breast exam very 6-12 months. Annual mammogram (tomosynthesis) Annual breast MRI. Starting age depends on risk.	Some women may need high risk screening with MRI in addition to mammogram.

Table 1. Estimated New DCIS and Invasive Breast Cancer Cases and Deaths among Women by Age, US, 2019

	DCIS cases		Invasive cases		Deaths	
Age	**Number**	**%**	**Number**	**%**	**Number**	**%**
<40	1,180	2%	11,870	4%	1,070	3%
40-49	8,130	17%	37,150	14%	3,250	8%
50-59	12,730	26%	61,560	23%	7,460	18%
60-69	14,460	30%	74,820	28%	9,920	24%
70-79	8,770	18%	52,810	20%	8,910	21%
80+	2,830	6%	30,390	11%	11,150	27%
All ages	**48,100**		**268,600**		**41,760**	

Estimates are ro[illegible]ot sum to 100 due to rounding

[illegible]veillance Research

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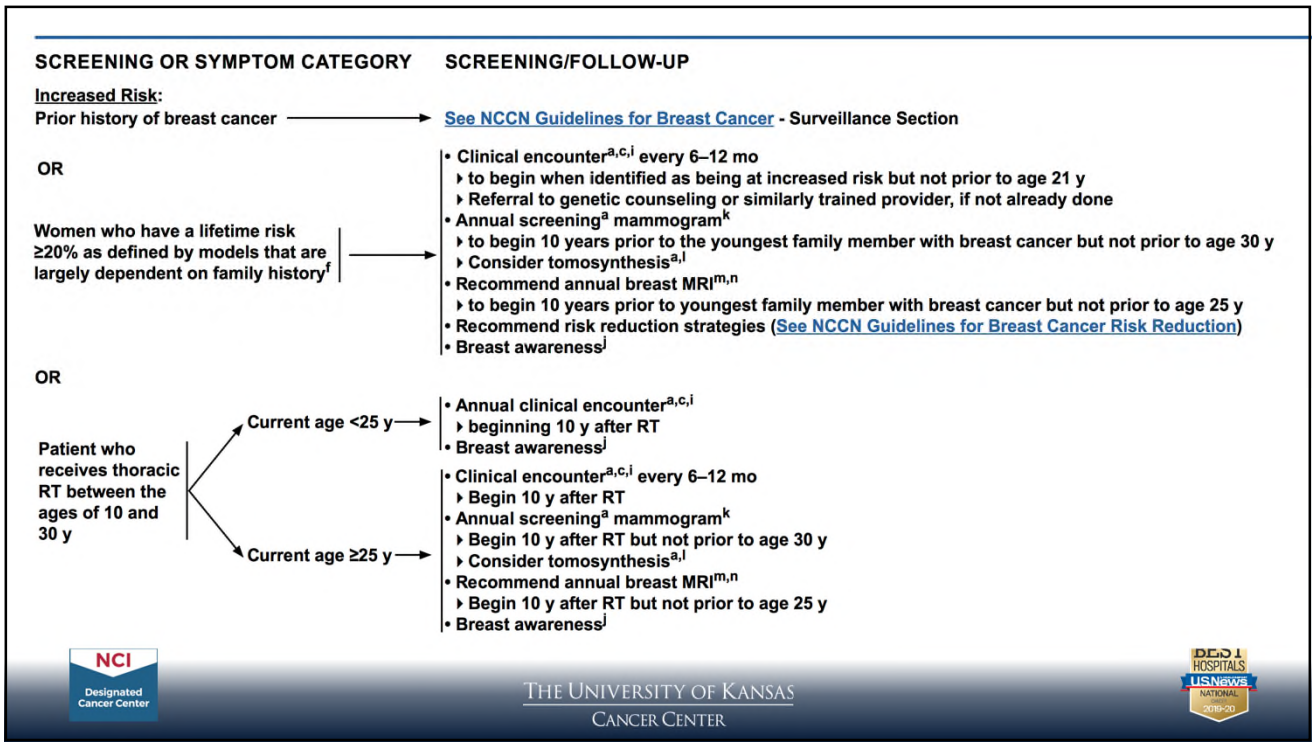
SCREENING OR SYMPTOM CATEGORY
SCREENING/FOLLOW-UP
Increased Risk:
Prior history of breast cancer
See NCCN Guidelines for Breast Cancer - Surveillance Section
OR
Women who have a lifetime risk ≥20% as defined by models that are largely dependent on family history[f]
• Clinical encounter[a,c,i] every 6–12 mo
▸ to begin when identified as being at increased risk but not prior to age 21 y
▸ Referral to genetic counseling or similarly trained provider, if not already done
• Annual screening[a] mammogram[k]
▸ to begin 10 years prior to the youngest family member with breast cancer but not prior to age 30 y
▸ Consider tomosynthesis[a,l]
• Recommend annual breast MRI[m,n]
▸ to begin 10 years prior to youngest family member with breast cancer but not prior to age 25 y
• Recommend risk reduction strategies (See NCCN Guidelines for Breast Cancer Risk Reduction)
• Breast awareness[j]
OR
Patient who receives thoracic RT between the ages of 10 and 30 y
Current age <25 y
• Annual clinical encounter[a,c,i]
▸ beginning 10 y after RT
• Breast awareness[j]
Current age ≥25 y
• Clinical encounter[a,c,i] every 6–12 mo
▸ Begin 10 y after RT
• Annual screening[a] mammogram[k]
▸ Begin 10 y after RT but not prior to age 30 y
▸ Consider tomosynthesis[a,l]
• Recommend annual breast MRI[m,n]
▸ Begin 10 y after RT but not prior to age 25 y
• Breast awareness[j]
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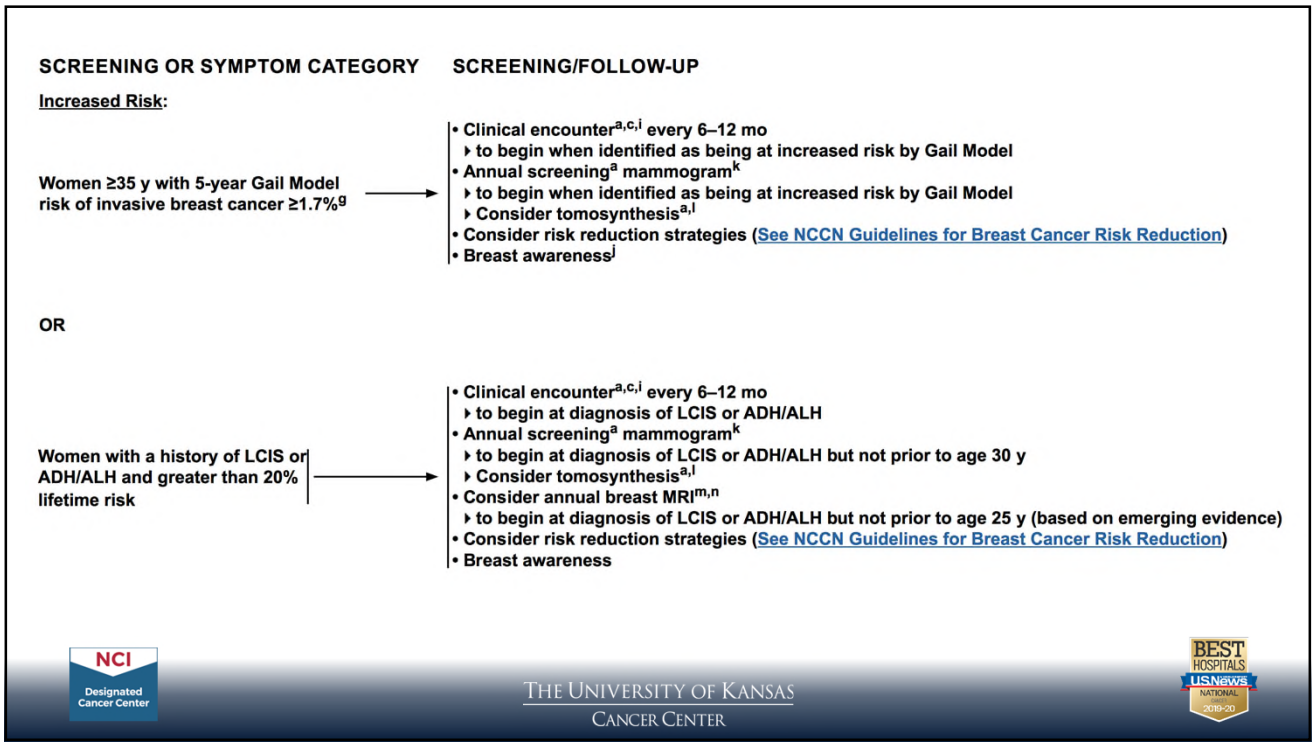
SCREENING OR SYMPTOM CATEGORY
SCREENING/FOLLOW-UP
Increased Risk:
Women ≥35 y with 5-year Gail Model risk of invasive breast cancer ≥1.7%[g]
• Clinical encounter[a,c,i] every 6–12 mo
▸ to begin when identified as being at increased risk by Gail Model
• Annual screening[a] mammogram[k]
▸ to begin when identified as being at increased risk by Gail Model
▸ Consider tomosynthesis[a,l]
• Consider risk reduction strategies (See NCCN Guidelines for Breast Cancer Risk Reduction)
• Breast awareness[j]
OR
Women with a history of LCIS or ADH/ALH and greater than 20% lifetime risk
• Clinical encounter[a,c,i] every 6–12 mo
▸ to begin at diagnosis of LCIS or ADH/ALH
• Annual screening[a] mammogram[k]
▸ to begin at diagnosis of LCIS or ADH/ALH but not prior to age 30 y
▸ Consider tomosynthesis[a,l]
• Consider annual breast MRI[m,n]
▸ to begin at diagnosis of LCIS or ADH/ALH but not prior to age 25 y (based on emerging evidence)
• Consider risk reduction strategies (See NCCN Guidelines for Breast Cancer Risk Reduction)
• Breast awareness
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Cervical Cancer Screening

- Screening Guidelines
- HPV Vaccination

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Cervical Cancer Screening

	USPSTF	ACS-ASCCP-ASCP
< 21	No screening	no screening
21-29	Cervical cytology alone every 3 years	Cervical cytology alone every 3 years
30-65	▪ Cytology alone every 3 years OR ▪ HPV testing alone every 5 years OR ▪ HPV and cytology “cotesting” every 5 years	▪ HPV and cytology “cotesting” every 5 years (preferred) ▪ Cytology alone every 3 years (acceptable)
> 65	No screening	No screening following adequate negative prior screening

Huh et al. Journal of Lower Genital Tract Disease • Volume 19, Number 2, April 2015

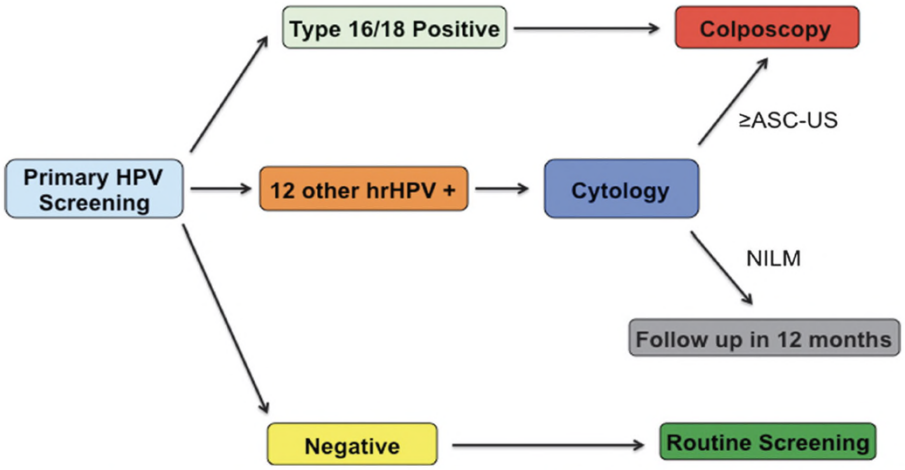

FIGURE 1. Recommended primary HPV screening algorithm. HPV, human papillomavirus; hrHPV, high-risk human papillomavirus; ASC-US, atypical squamous cells of undetermined significance; NILM, negative for intraepithelial lesion or malignancy.

HPV Vaccination

Children and adults aged 9 through 26 years. HPV vaccination is routinely recommended at age 11 or 12 years; vaccination can be given starting at age 9 years. Catch-up HPV vaccination is recommended for all persons through age 26 years who are not adequately vaccinated.

Adults aged >26 years. Catch-up HPV vaccination is not recommended for all adults aged >26 years. Instead, shared clinical decision-making regarding HPV vaccination is recommended for some adults aged 27 through 45 years who are not adequately vaccinated. HPV vaccines are not licensed for use in adults aged >45 years.

https://www.cdc.gov/vaccines/vpd/hpv/hcp/recommendations.html

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Colon Cancer Risk Assessment

Average Risk:

≥ 50 y/o

Increased Risk:

Adenoma or sessile serrated polyp
History of colorectal cancer
Inflammatory Bowel Disease
Family History

High Risk:

Lynch syndrome
Polyposis syndromes
Cowden Syndrome (PTEN)
Li Fraumeni Syndrome

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Colon Cancer Screening

	USPSTF	NCCN	ACS
Average Risk	Colorectal screening* beginning at age 50 until age 75.	50: colonoscopy or stool based test or flexible sigmoidoscopy or CT colonography	45 - 75: stool based test or colonoscopy. 76 – 85: discussion > 85: no longer recommended
High Risk	N/A	*Specific guidelines available depending on risk.*	N/A

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USPSTF Colorectal Screening*

Test	Interval
Colonoscopy	Every 10 years
CT Colonography	Every 5 years

https://www.cdc.gov/cancer/colorectal/basic_info/screening/tests.htm

CA CANCER J CLIN 2020;0:1–20

TABLE 1. Estimated Numbers of New Colorectal Cancer Cases and Deaths by Age, United States, 2020

	CASES						DEATHS	
AGE, YEARS	COLORECTUM	PERCENT	COLON	PERCENT	RECTUM	PERCENT	COLORECTUM[a]	PERCENT
Birth to 49	17,930	12%	11,540	11%	6,390	15%	3,640	7%
50 to 64	50,010	34%	32,290	31%	17,720	41%	13,380	25%
≥65	80,010	54%	60,780	58%	19,230	44%	36,180	68%
All ages	147,950	100%	104,610	100%	43,340	100%	53,200	100%

Note: Estimates are rounded to the nearest 10 and exclude in situ carcinoma.
[a]Deaths for colon and rectal cancers are combined because a large number of rectal cancer deaths are misclassified as colon.

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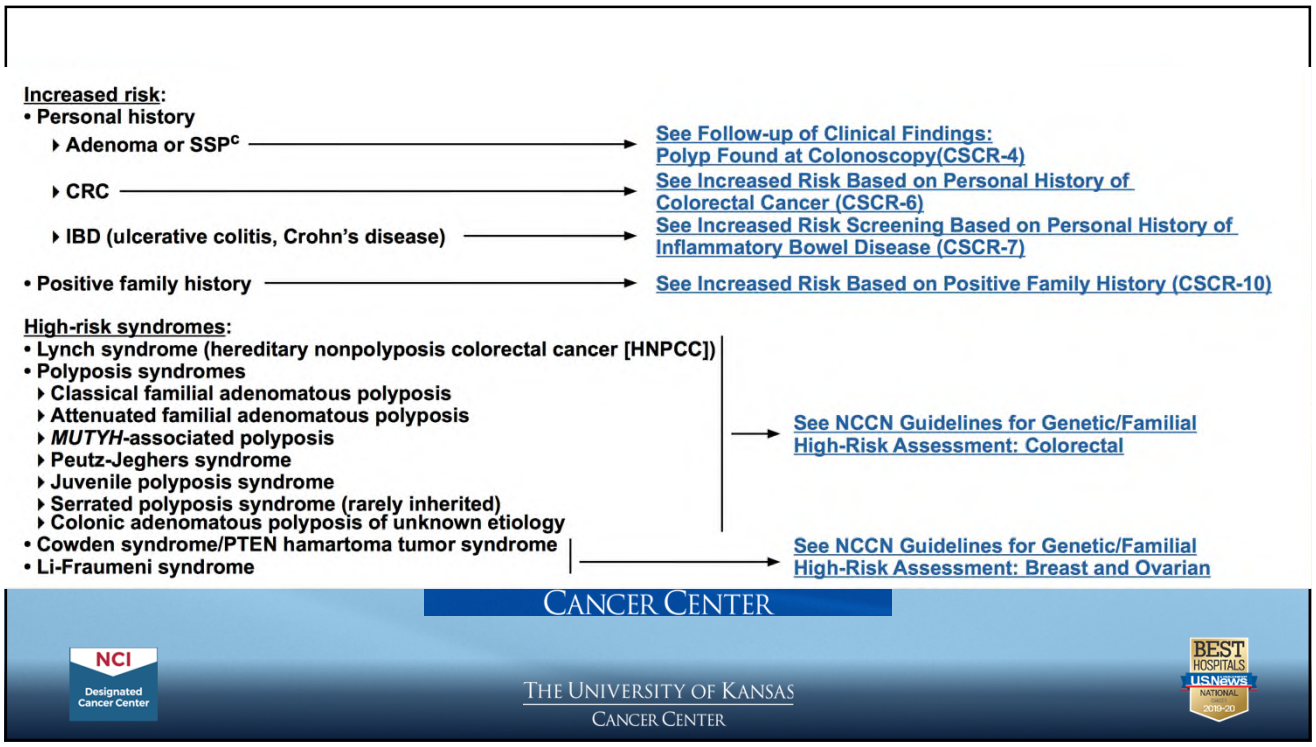
Increased risk:
• Personal history
Adenoma or SSP[c]
See Follow-up of Clinical Findings: Polyp Found at Colonoscopy(CSCR-4)
CRC
See Increased Risk Based on Personal History of Colorectal Cancer (CSCR-6)
IBD (ulcerative colitis, Crohn's disease)
See Increased Risk Screening Based on Personal History of Inflammatory Bowel Disease (CSCR-7)
• Positive family history
See Increased Risk Based on Positive Family History (CSCR-10)
High-risk syndromes:
• Lynch syndrome (hereditary nonpolyposis colorectal cancer [HNPCC])
• Polyposis syndromes
Classical familial adenomatous polyposis
Attenuated familial adenomatous polyposis
MUTYH-associated polyposis
Peutz-Jeghers syndrome
Juvenile polyposis syndrome
Serrated polyposis syndrome (rarely inherited)
Colonic adenomatous polyposis of unknown etiology
See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Colorectal
• Cowden syndrome/PTEN hamartoma tumor syndrome
• Li-Fraumeni syndrome
See NCCN Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian
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