High-Risk Breast Cancer Clinic

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The Gayle and Tom Benson Cancer Center

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Disclosures:

- Nothing to disclose

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Objectives:

- Why a High-Risk Breast Cancer Clinic?
- Referral process
- Risk calculators
  - Tyrer-Cuzick
  - Gail model
- Risk factors
  - Modifiable
  - Non-Modifiable
- Imaging
- Chemoprevention

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Why a High-Risk Breast Cancer Clinic?

- About 1 in 8 U.S. women (about 13%) will develop invasive breast cancer over the course of her lifetime.
- Breast cancer is the second most diagnosed cancer among American women, behind skin cancers.
- Breast cancer became the most common cancer globally as of 2021, accounting for 12% of all new annual cancer cases worldwide, according to the World Health Organization.
- The purpose of a High-Risk Breast Cancer Clinic is to identify women who are at high-risk, identify those who may benefit from supplemental screenings and formulate an individualized plan to help lower their risk.

Research shows screening and early detection of breast cancer leads to effective management and overall survival.

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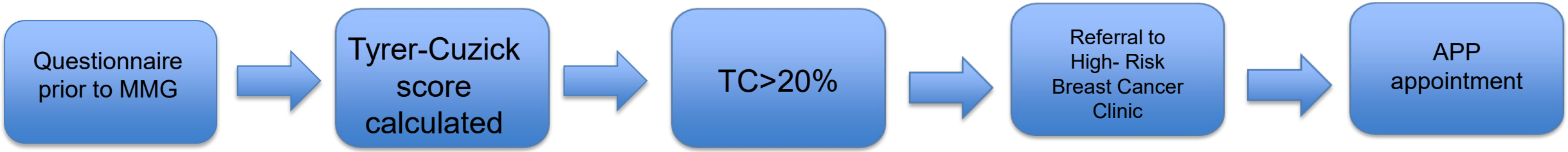
Referral Process



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APP Appointment Objectives:

- Calculation of Tyrer Cuzick and Gail Model Scores
  - Strategize an individualized plan
- Additional Imaging
  - Mammogram, MRI
- Risk Reduction Medication
  - Chemo Prevention
- Identify Modifiable and Non modifiable Risk factors
  - Lifestyle Modifications
- Additional Referrals

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Tyrer-Cuzick and Gail Model

Gail model	Claus model	BRCAPRO model	Tyrer–Cuzick model	BOADICEA model
• Age of the person • Age at menarche • Age at first live birth • Breast biopsies (AH) • Family history - First-degree relatives	• Age of the person • Age at menarche • Age at first live birth • Family history - First-degree relatives - Second-degree relatives	• Age of the person • Family history - First-degree relatives - Second-degree relatives - Third-degree relatives - Age at onset of breast cancer - Bilateral breast cancer - Ovarian cancer - Male breast cancer	• Age of the person • Body mass index • Age at menarche • Age at first live birth • Age at menopause • Hormone replace-ment therapy use • Breast biopsies (ADH, LCIS) • Family history - First-degree relatives - Second-degree relatives - Age at onset of breast cancer - Bilateral breast cancer - Ovarian cancer	• Age of the person • Family history - First-degree relatives - Second-degree relatives - Third-degree relatives - Age at onset of breast cancer - Bilateral breast cancer - Ovarian cancer - Male breast cancer

AH, atypical hyperplasia; LCIS, lobular carcinoma *in situ;* BOADICEA, breast and ovarian analysis of disease incidence and carrier estimation algorithm.

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Imaging

Average Risk

- Age 25 yo or above but <40: clinical encounter every 1-3 years
- 40 yo or above: annual clinical breast exam (CBE) and MMG
- Breast awareness

High Risk

- CBE every 6 months
- Mammogram with Tomo annually (to begin 10 years prior to when the youngest family member was diagnosed with breast cancer)
- MRI breast annually if TC = or > 20%
- If prior RT: 8 years after RT, begin annual CBE and MMG (not before age 30) and MRI breast (not prior to age 25).
- Breast awareness

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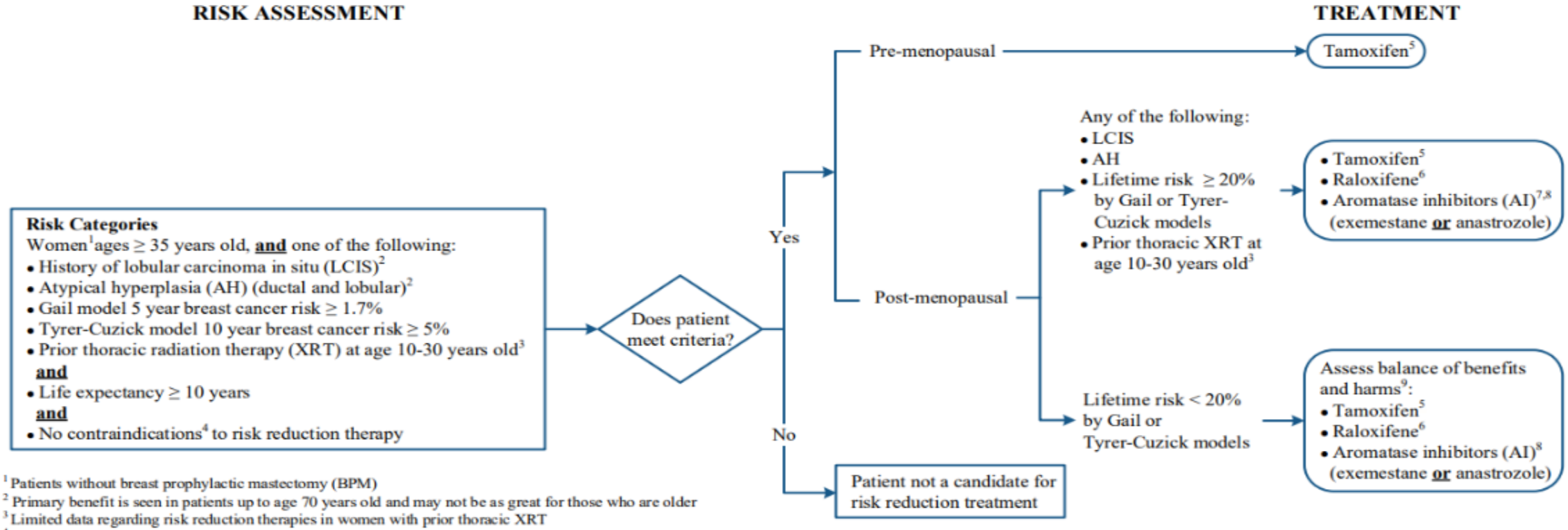
Breast Cancer Risk Reducing Therapy Algorithm



[1] Patients without breast prophylactic mastectomy (BPM)
[2] Primary benefit is seen in patients up to age 70 years old and may not be as great for those who are older
[3] Limited data regarding risk reduction therapies in women with prior thoracic XRT
[4] Prior history of a thromboembolic event is an absolute contraindication. Adequately treated endometrial hyperplasia or early-stage endometrial cancer is not a contraindication to the use of tamoxifen.
[5] Starting dose of tamoxifen is 20 mg by mouth once daily; may reduce to 5 mg once daily (or 10 mg every other day) if needed for patient tolerance
[6] Lower risk of uterine cancer but less long-term benefit
[7] Limited data regarding AIs in women with proliferative breast lesions
[8] Off-label (Not FDA approved)
[9] Tables that can be used to determine women for whom the benefits outweigh the risks can be found at Freedman, A. N., Yu, B., Gail, M. H., Costantino, J. P., Graubard, B. I., Vogel, V. G., … McCaskill-Stevens, W. (2011). Benefit/risk assessment for breast cancer chemoprevention with raloxifene or tamoxifen for women age 50 years or older. *Journal of Clinical Oncology, 29*(17), 2327.

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Chemoprevention

Endocrine therapy can reduce the risk of developing an estrogen receptor (ER) positive breast cancer (invasive and/or in situ)

1. Tamoxifen

2. Raloxifene

3. Aromatase Inhibitors

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Chemoprevention

Tamoxifen

- Used in premenopausal or postmenopausal women
  - Limited to pre- and postmenopausal individuals ≥35 years of age with a Gail Model 5-year breast cancer risk of ≥1.7% or a 10-year risk by IBIS/Tyrer-Cuzick of ≥5% or a history of LCIS.
- Daily for 5 years has shown to reduce risk of breast cancer by 49%
- Low dose tamoxifen (5 mg per day for 3 years) is an option only if patients is symptomatic on 20 mg dosing or if patient is unwilling to take standard-dose tamoxifen
- Tamoxifen has limited data in **BRCA 1/2** mutation carriers but limited retrospective data is suggestive of benefit in BRCA2 carriers
- High-risk postmenopausal individuals, data regarding the risk/benefit ratio for tamoxifen are influenced by age, presence of uterus, or comorbid conditions. There are insufficient data on ethnicity and race.

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Chemoprevention

Raloxifene

- Postmenopausal Women
  - Risk reduction are limited to postmenopausal individuals ≥35 years of age with a Gail Model 5-year breast cancer risk ≥1.7% or a 10-year risk by IBIS/Tyrer-Cuzick of ≥5% or a history of LCIS
- 60 mg daily for 5 years has shown to reduce risk of breast cancer.
  - Appears to be less efficacious in risk reduction than tamoxifen, consideration of toxicity may still lead to the choice of raloxifene
- There is no data for individuals who are carriers of BRCA 1/2 population and other pathogenic mutations

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Chemoprevention

Aromatase Inhibitor

- Postmenopausal Women
- 5 years have also shown risk reduction in terms of 50-60%
- **Exemestane**
  - A single large randomized study limited to postmenopausal individuals ≥35 years of age with a Gail Model 5-year breast cancer risk ≥1.7% or a 10-year risk by IBIS/Tyrer-Cuzick of ≥5% or a history of LCIS
  - 25 mg per day was found to reduce the relative incidence of invasive breast cancer by 65% from 0.55% to 0.19% with a median follow-up of 3 years
- **Anastrozole**
  - A single large randomized study limited to postmenopausal individuals 40 to 70 years of age with the following risk compared with the general population:
    - Aged 40 to 44 years - 4 times higher
    - Aged 45 to 60 years - ≥2 times higher
    - Aged 60 to 70 years - ≥1.5 times higher
  - 1 mg per day was found to reduce the relative incidence of breast cancer by 53% with a median follow-up of 5 years.

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Chemoprevention

- Currently, there is not adequate data to recommend longer courses of therapy more than 5 years for risk reduction.
- Tamoxifen and AIs have been shown to lower the risk of breast cancer incidence, however there is no survival benefit in patients who don't have breast cancer.
- Risk reduction therapy in patients <35 yo is unknown.
- Exemestane and anastrozole can be used in postmenopausal females who are highly motivated towards risk reduction and who have significant contraindications to selective estrogen receptor modulators (SERMs).

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Chemo Prevention Side Effects

Tamoxifen and Raloxifene

- Hot flashes
- Invasive endometrial cancer*
- Cataracts
- Increased risk of thrombosis and pulmonary embolism
- Hair thinning
- Mid abdominal weight gain

Aromatase Inhibitors

- Hot flashes
- Joint pain
- Possible adverse effects include osteoporosis, hypercholesterolemia

* Tamoxifen only and in women > 49 years of age (2.3/1000 compared to 0.9/1000)

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Risk Factors

Non-Modifiable
Family History
Increasing age
Ethnicity/Race
Prior estrogen and progesterone hormone
Reproductive History • Younger age at menarche • Nulliparity/Lower parity • Older age at first live birth • Older age at Menopause
History LCIS/AH (ductal and/or lobular)
Number of prior breast biopsies
Breast Density
Prior thoracic radiation therapy <30 y of age

Modifiable
Lifestyle factors • Increased body mass index (BMI) • Alcohol intake • Smoking • HRT use • Regular exercise

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Referrals

- Weight loss
- Nutrition
- Genetics
- Women’s Health

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Thank You

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