



# Women's Health Update

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# Table of Contents

- ❖ Menopause transition definition
- ❖ Vasomotor symptoms of menopause
- ❖ Novel, non-hormonal treatment
- ❖ Testosterone use in postmenopausal women
- ❖ Use it or lose it: why perception matters
- ❖ Update on breast cancer screening guidelines

# Menopause

## Pre-menopause:

- Diagnosis: Women aged 40-49 with  $\geq 3$  consecutive months of amenorrhea or a mean cycle length  $\geq 42$  days

## Menopause:

- Diagnosis: 12 consecutive months of amenorrhea without a pathologic cause
- Supporting the diagnosis: useful in women without a uterus
  - Elevated FSH
  - Estradiol  $< 20$

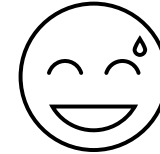
# Vasomotor Symptoms of Menopause



Hot flashes with  
Vasodilation



Shivering



Sweating

**These symptoms affect 80% of women during peri-menopause or menopause**

**Affecting women for approximately 7.4 years**

**Symptoms during the day can lead to decreased quality of life**

**Symptoms at night can affect sleep and mood**

# Novel, non-hormonal treatment

# Fezolinetant



FDA approved for the treatment of vasomotor symptoms in menopause

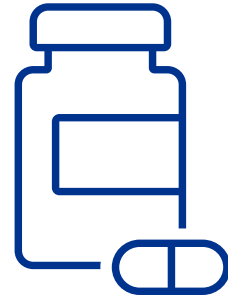


NK3R antagonist: blocks the binding of neurokinin B to KNDy neurons which affects thermoregulation

# Fezolinetant by Chavez et al.



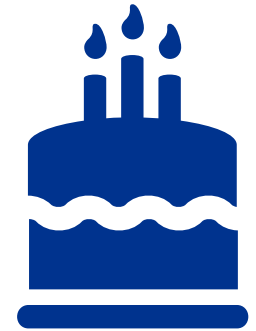
**2260 people  
assigned to  
Fezolinetant**



**1042 people  
assigned to  
placebo**

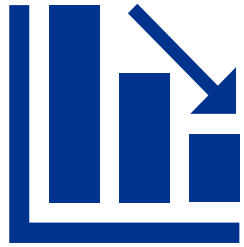


**Follow up  
period: 12-  
55 weeks**



**Mean Age:  
53.3-54.9  
years**

# Fezolinetant by Chavez et al. Efficacy Endpoints



**Primary efficacy endpoint: reduction of moderate-severe vasomotor symptoms from baseline over 4 and 12 weeks**



**Secondary efficacy endpoints: change in sleep disturbance, hot flashes and quality of life**



# Fezolinetant by Chavez et al. Safety Endpoints



**Thrombocytopenia**



**GI disorders  
& nausea**



**Fracture**



**Breast Disorders**



**Disordered  
proliferative  
pattern**



**Depression**



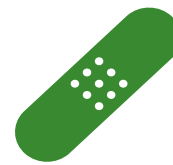
**Reproductive  
Disorders**



**MSK tissue  
disorders**



**Headache**



**ALT or AST  
>3x ULN**



**ALK >ULN**



**All  
cause  
mortality**

# Fezolinetant by Chavez et al. Continued

## **Pooled analysis significant outcomes:**

- Daily frequency of VMS in week 4 (p-value: 0.02) and week 12: (p-value: 0.01)
- Quality of life at week 12: (p-value: 0.01)
- Sleep disturbance: (p-value: 0.01)

## **Pooled analysis insignificant outcomes:**

- GCS scale (p-value: 0.23)
- TEAE's (p-value: 0.36), serious TEAE's (p-value: 0.52)
- Permanent discontinuation of treatment due to TEAE's (p-value: 0.35)
- Reduction in reproductive system and breast disorders (p-value: 0.04)

# Notable Comparators

Paroxetine: efficacy  
40-65%

Dose dependent  
effect and side effect  
limitations

No improvement in  
sleep disturbance

Venlafaxine: not FDA  
approved

Dose dependent  
effect and side effect  
limitations

Exercise, Acupuncture,  
Relaxation Therapy,  
Phytoestrogens and  
Black Cohosh

No  
significant reduction  
of VMS

5 alternative neurokinin  
receptor antagonists:  
currently in phase III  
clinical trials

Rise in  
transaminase levels

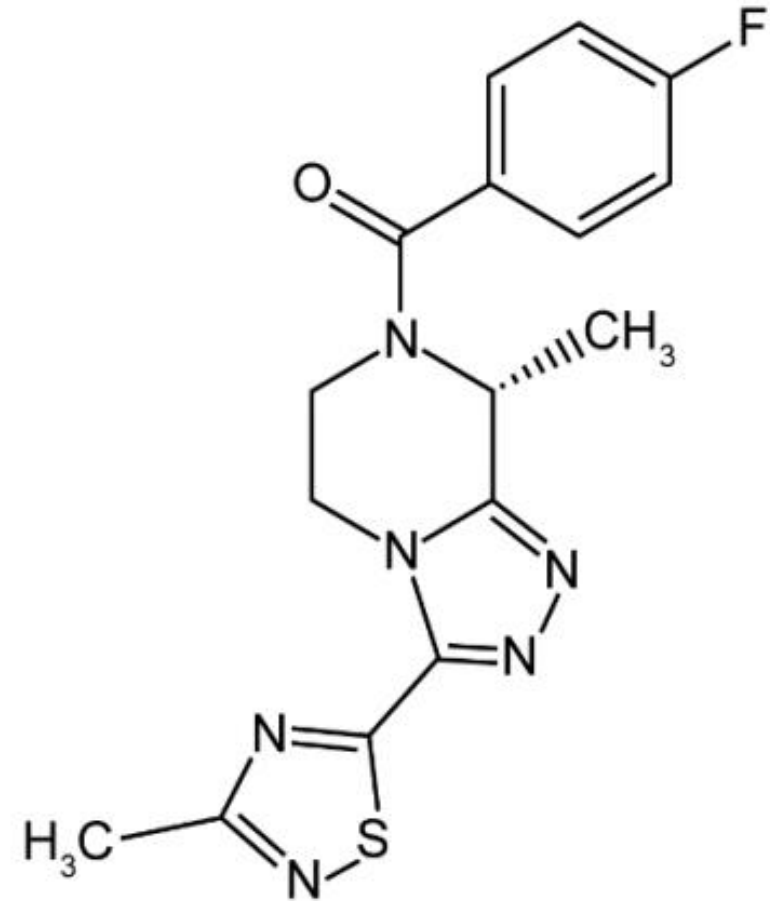
# Fezolinetant Dosing

FDA approved: 45 mg daily

- Taken with or without food
- Missed doses: take the missed dose then return to normal daily schedule

Chavez et al studied: 30 mg daily, 45 mg daily, 90 mg BID

- No significant difference in effect size attributable to dose
- 45 mg dosing demonstrated a significant impact on sleep compared with 30 mg dosing
- No difference in drug related TEAE's in 90 mg BID v. placebo



# Fezolinetant

- **Chavez et al. Limitations:**
  - Heterogeneity
  - Baseline - week 4 without statistical significance
  - Healthy women only
  - Lack of Diversity: highly white population
- **Contraindications to Use:**
  - Known Cirrhosis
  - Severe Renal Impairment or ESRD
  - Use with CYP1A2 inhibitors



## Fezolinetant in Summary

- Safe and effective for treatment of vasomotor symptoms in menopause
- FDA approved 45 mg daily dosing
- Do not use in women with known ESRD, cirrhosis or interacting medications
- Monitor LFT's while patients are on this medication

# Testosterone Use in Menopausal Women

# Background



## Global Position Statement

2019: Authors representing 10 societies conducted an extensive literature review regarding the use of testosterone in women

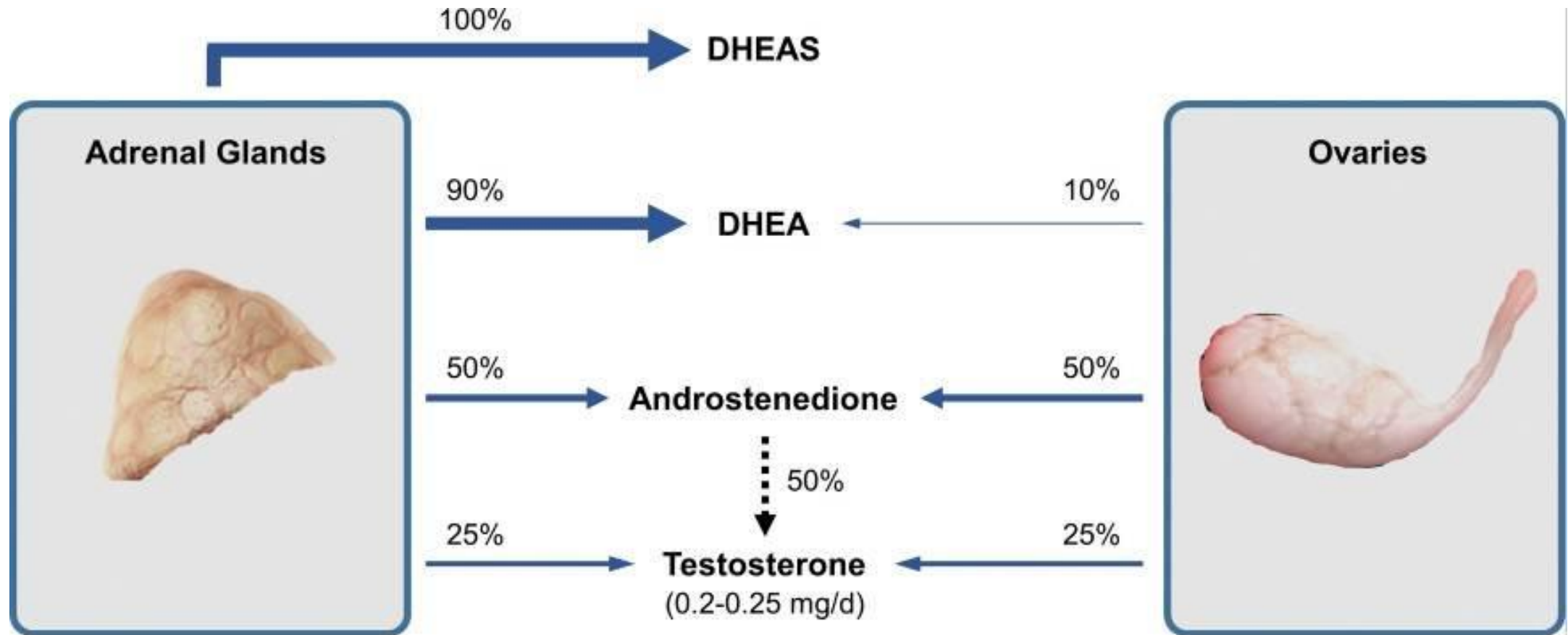
The sole indication for testosterone: Hypoactive Sexual Desire Disorder

Why is there controversy?

**There are no FDA approved prescriptions of Testosterone for women**

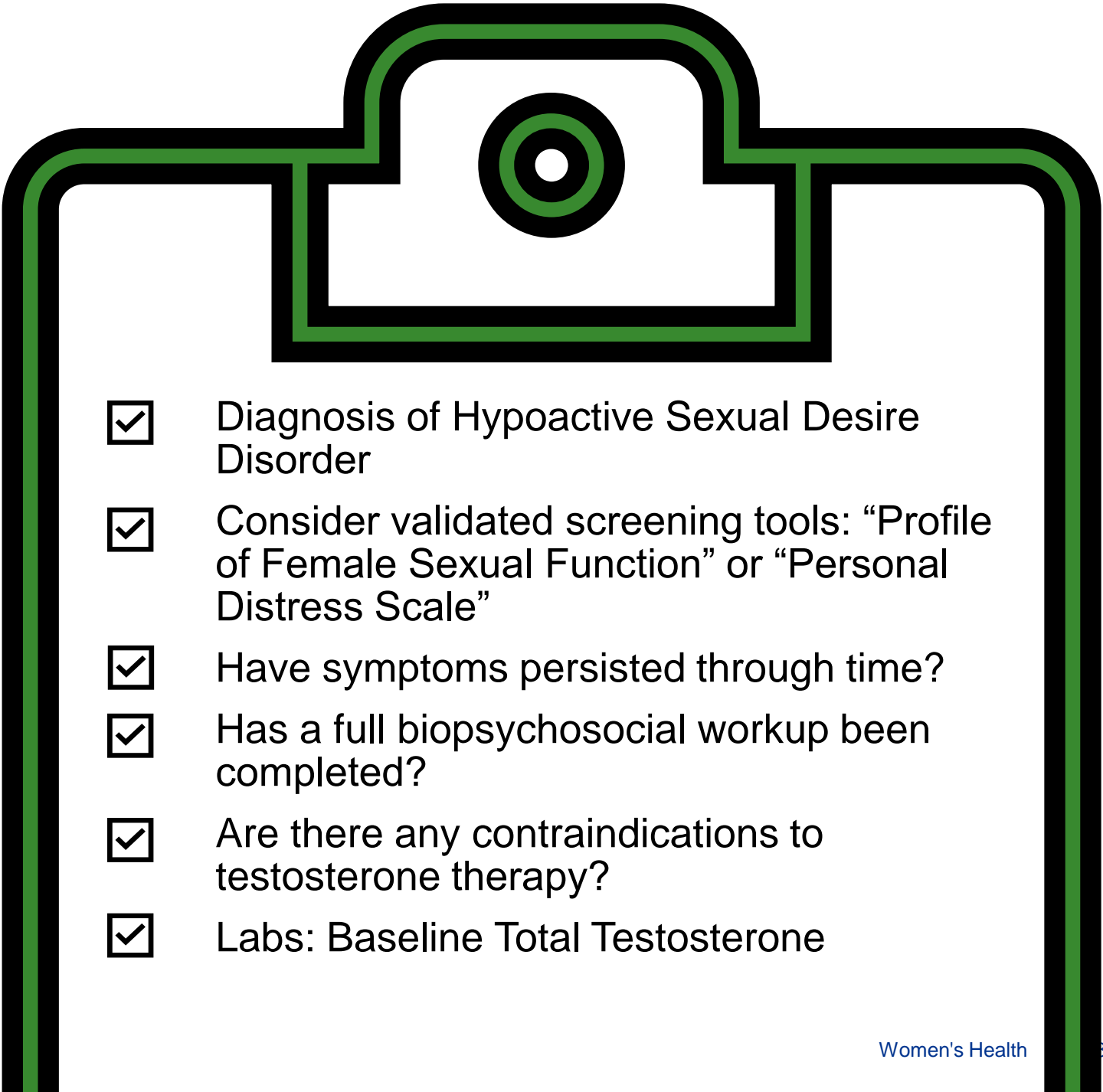


# Pathophysiology



Source: Parish et al.

# Intake & Assessment

- 
- Diagnosis of Hypoactive Sexual Desire Disorder
  - Consider validated screening tools: “Profile of Female Sexual Function” or “Personal Distress Scale”
  - Have symptoms persisted through time?
  - Has a full biopsychosocial workup been completed?
  - Are there any contraindications to testosterone therapy?
  - Labs: Baseline Total Testosterone

## Initial Dosing

- Options for Dosing – Transdermal Patch or Gel

### Patch

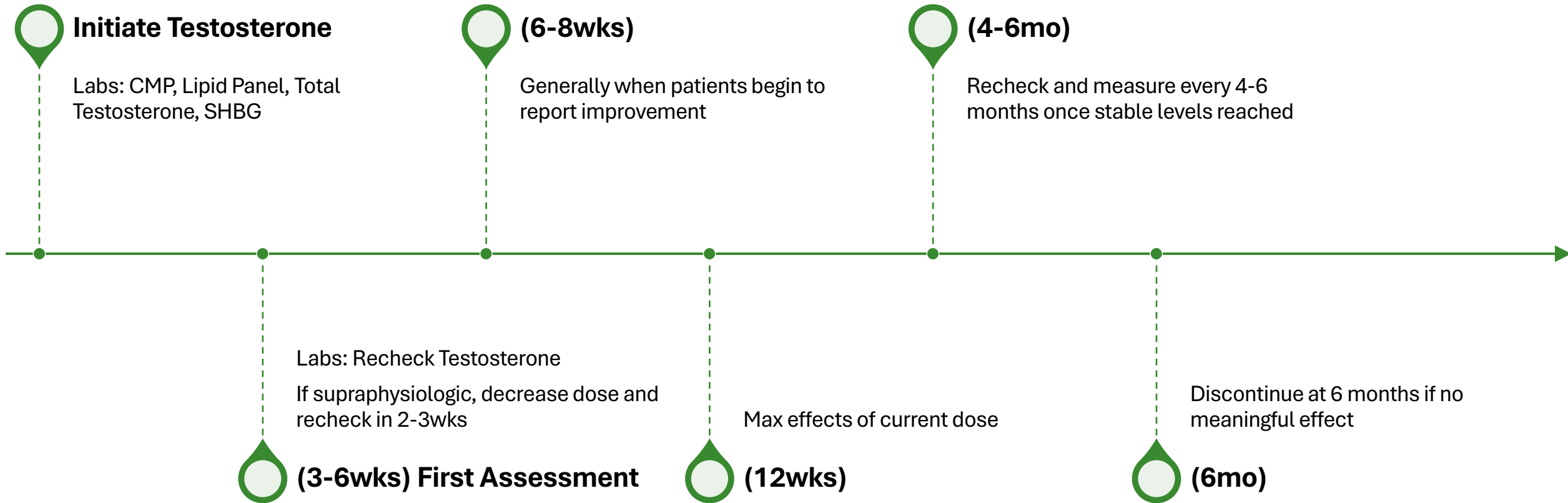
Initial Dose: 300  $\mu$ g / 24 hours  
(~1/10th of a 2mg patch)

### Gel

Initial Dose: 1%  
Testosterone  
(~1/10th of a tube/packet)

- Counsel the patient regarding use
  - **Consent**
  - **Application**
  - **Risk of transference**
  - **Alternatives on the market --> generally not recommended**

# Monitoring



# Safety & Side Effects

- Expected Side Effects
  - Increase in hair growth
  - Increase in acne
- Unexpected Side Effects
  - Abnormal uterine bleeding
- No Expected changes
  - Lipid Profiles
  - Carbohydrate metabolism
  - Renal/liver function
  - Cardiometabolic markers
  - Mammographic breast density\*
  - Risk for endometrial cancer/hyperplasia
  - Bone mineral density
  - Memory/cognitive performance/mood

# Barriers & Limits

- Testosterone remains off label in the United States and elsewhere
- Limited studies in women
- Studies thus far have been heterogenous in design
- Alternatives on the market



## Testosterone in Summary

- Indication: Hypoactive Sexual Desire Disorder
- No FDA approved prescriptions for women
- Dosing: patch 300 mcg/day or gel 1/10 of a tube
- Dose for physiologic levels of testosterone in women
- Expected side effects: increased hair growth and acne

# Use it or lose it: why perception matters



# Use It or Lose It

“The sexual stuff is sometimes very complex; it’s not always a quick fix,” says Streicher, an associate clinical professor of obstetrics and gynecology at [Northwestern University’s Feinberg School of Medicine](#). “A lot of people expect that they can come in and say, ‘I have no libido, can you give me something for that?’ The answer is yes, we can work on that, but there are often a lot of different things that are going to impact it.”

## Use it or lose it

The first thing women should know — and this is something that’s not spoken of frequently — is that there is a “use it or lose it” phenomenon when it comes to menopause, sex and the vagina. “One of the risk factors for vaginal dryness, thinning and loss of elasticity is lack of use,” Streicher says. In other words, if you’re not having sex regularly, it could increase the odds of sex becoming painful when you become sexually active again.

# Some alternatives our patients see

**Supplements for Menopause Symptoms**

**Read: natural, not effective**

**Black cohosh:** may help reduce hot flashes and mood swings

**Chasteberry:** may help reduce hot flashes and improve mood

**Ginseng:** may help reduce hot flashes

**St. John's wort:** may treat hot flashes in perimenopausal or postmenopausal women

**Flax seeds:** may help treat hot flashes and improve moods and sexual health

**Red clover:** may help reduce hot flashes and improve mood

**Root and rhizomes:** may help reduce hot flashes and improve sleep

**verywell**

## BENEFITS OF BHRT VS. HRT

Compounded bioidentical hormones offer many benefits to both men and women. Here are a few reasons we strongly prefer BHRT over synthetic hormones.



Made from plant sources

**Read:  
natural, effective,  
tailored**

Customized in a compounding pharmacy



Improves quality of life, including sleep, energy & mood

<https://www.herbazest.com/wellness/top-5-herbs-to-relieve-menopause-symptoms> | <https://www.longevitamemedical.com/blog/bhrt-vs-hrt-why-choose-bioidentical-hormone-replacement>

# Why Perception Matters

## What's wrong with conventional treatments?

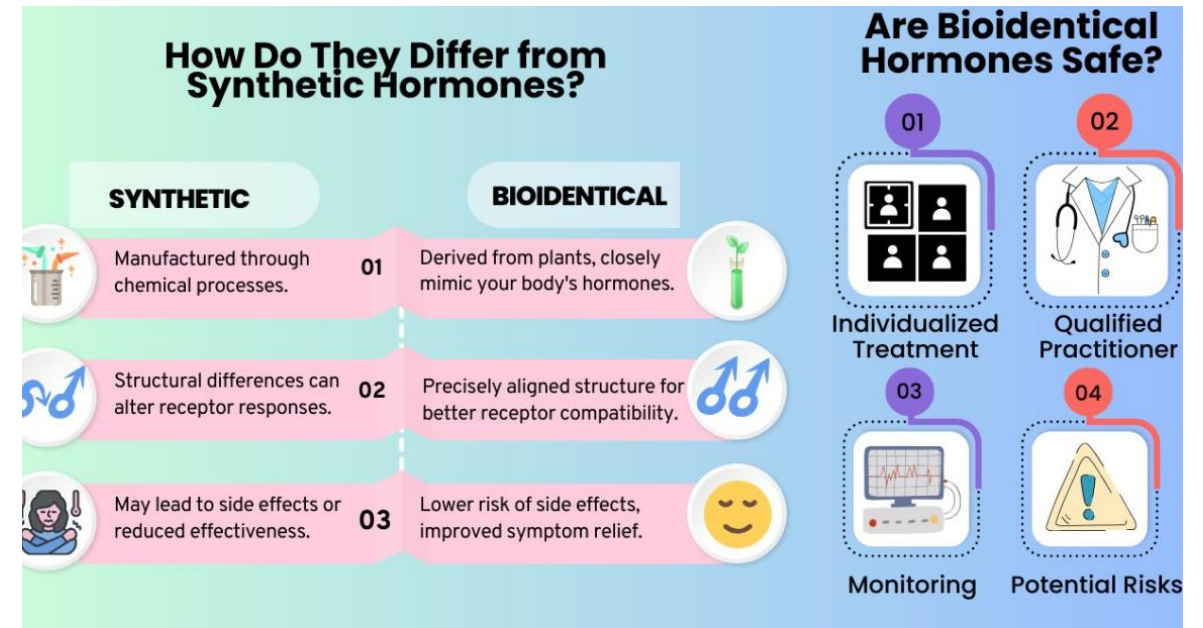
- Fear and uncertainty about safety of HRT
- Distaste for conjugated estrogens

## What about alternative therapies?

- They don't really work

## The draw of compounded bioidentical hormone therapy (CBHT)

- Effective
- "Safer" than conventional HRT
- Individualized treatment
- Enhanced clinical experience



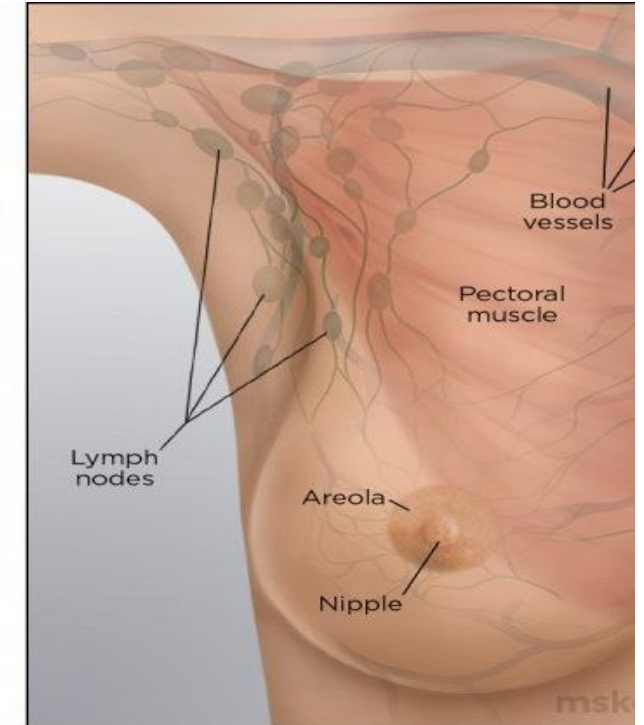
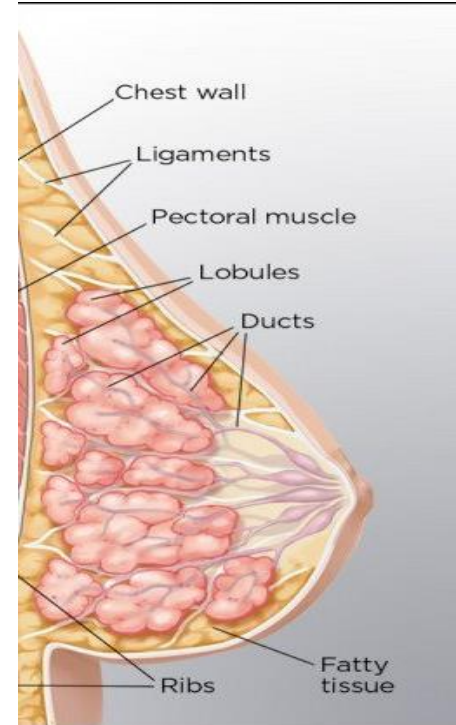
<https://amazing-meds.com/bhrt-bioidentical-hormone-replacement-therapy/>

“...[A]n important take home message of this study is that women are not only seeking alternatives to conventional pharmaceuticals, but alternatives to conventional care.... In short, the clinical context of CBHT appears to explicitly invite women to participate [in] shared decision-making in ways the standard clinical context does not.”

# Breast cancer screening guidelines

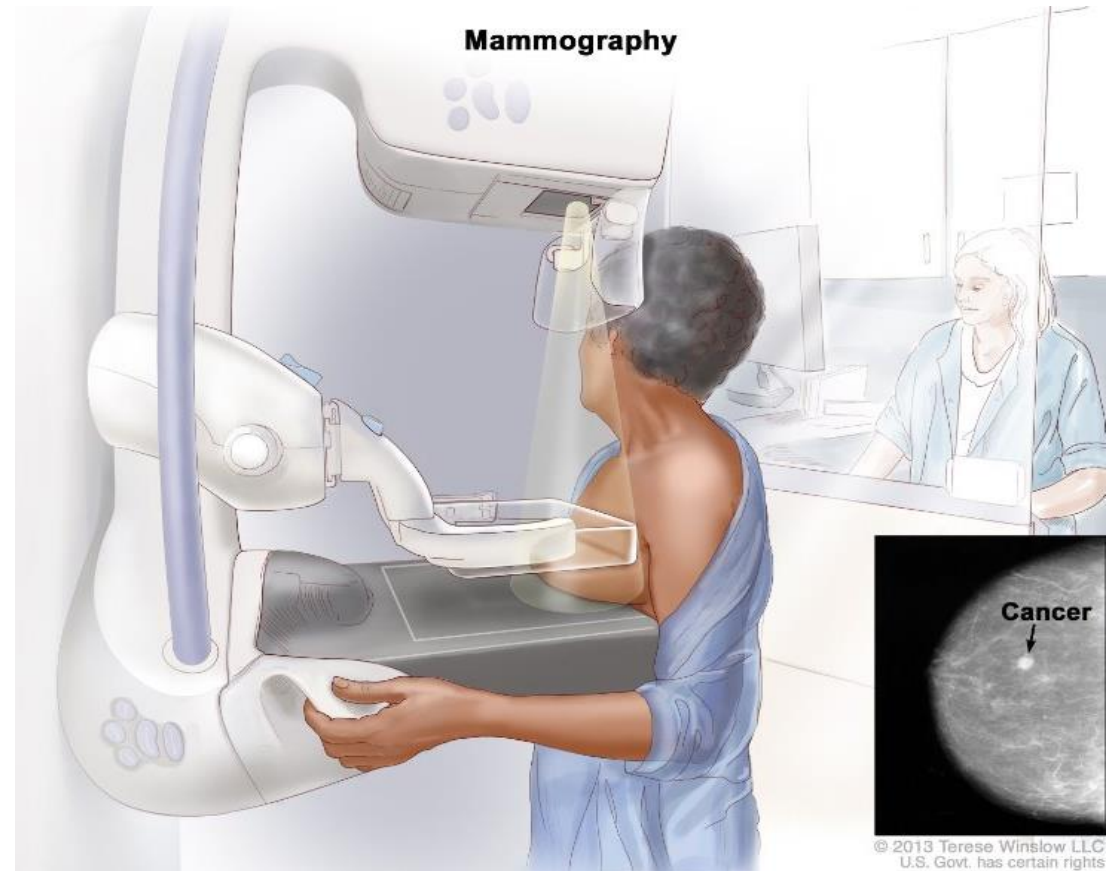
# Breast cancer screening – USPSTF 2024 update

- Moderate certainty for biennial screening mammography in women aged **40-74** with moderate net benefit
- Biennial vs annual screening
- Insufficient evidence to determine screening **over age 75**
- Insufficient evidence to determine supplemental screening regardless of breast density



# Mammography

- Only imaging technique shown to decrease mortality
- Types
  - Film
  - Digital 2D
  - Digital breast tomosynthesis (3D)
- Mammogram report



## BI-RADS assessment categories

Assessment	Management	Likelihood of cancer
Category 0: Incomplete – Need additional imaging evaluation and/or prior mammograms for comparison	Recall for additional imaging and/or comparison with prior examination(s)	N/A
Category 1: Negative	Routine mammography screening	Essentially 0% likelihood of malignancy
Category 2: Benign	Routine mammography screening	Essentially 0% likelihood of malignancy
Category 3: Probably benign	Short-interval (6-month) follow-up or continued surveillance mammography	>0 but ≤2% likelihood of malignancy
Category 4: Suspicious	Tissue diagnosis*	>2 but <95% likelihood of malignancy
Category 4A: Low suspicion for malignancy		>2 to ≤10% likelihood of malignancy
Category 4B: Moderate suspicion for malignancy		>10 to ≤50% likelihood of malignancy
Category 4C: High suspicion for malignancy		>50 to <95% likelihood of malignancy
Category 5: Highly suggestive of malignancy	Tissue diagnosis*	≥95% likelihood of malignancy
Category 6: Known biopsy-proven malignancy	Surgical excision when clinically appropriate	N/A

BI-RADS: Breast Imaging-Reporting and Data System.

\* Practice guidelines recommend biopsy for all BI-RADS 4 and 5 lesions. If there are clinical factors (eg, age, comorbidities, etc) for which the patient, in consultation with the clinician, chooses to defer biopsy, the reasoning should be documented in the medical record.



MAMMOGRAPHIC FINDINGS:

Breast Composition: Heterogeneously dense. This breast composition may limit the sensitivity of mammography.

Mass: No significant or suspicious mass.

Asymmetry/Architectural Distortion: None of significance.

Calcifications: None of significance.

No significant new findings since the previous mammogram.

Stable bilateral surgical changes.

IMPRESSION:

BIRADS ASSESSMENT: Benign / CATEGORY 2

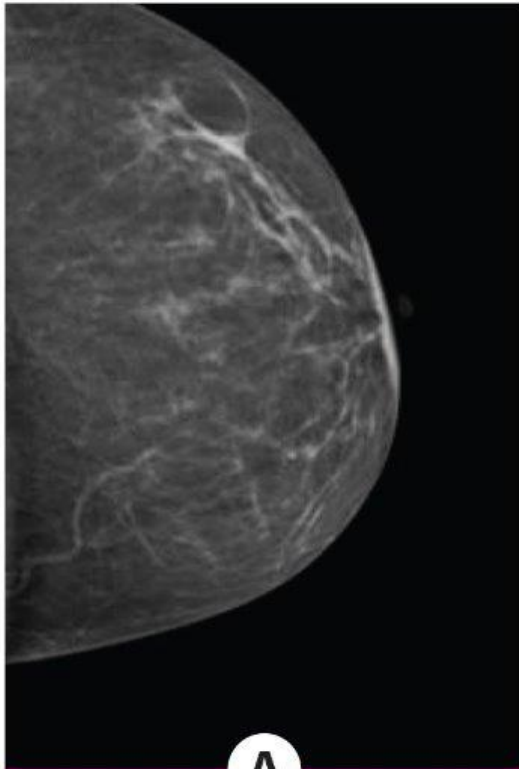
RECOMMENDATION: Routine screening mammography, in one year per ACR (American College of Radiology) and SBI (Society of Breast Imaging) guidelines or diagnostic mammography if clinically indicated.

Estimated Lifetime Breast Cancer Risk: Average risk: Less than 15%.

The Tyrer-Cuzick (IBIS) Model Version 8 risk assessment tool incorporates a number of variables, including gynecologic health, personal history of breast biopsies, breast density and family history, to identify patients that may be at higher than average risk of developing breast cancer. Patients and their clinicians can use this information to tailor breast cancer screening recommendations on an individual basis.

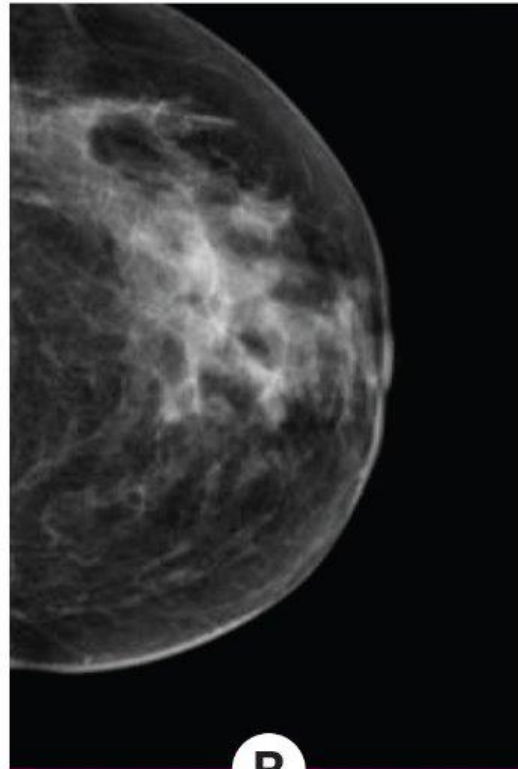
These images were also analyzed using computer-aided detection equipment.

A letter of notification will be sent to the patient.



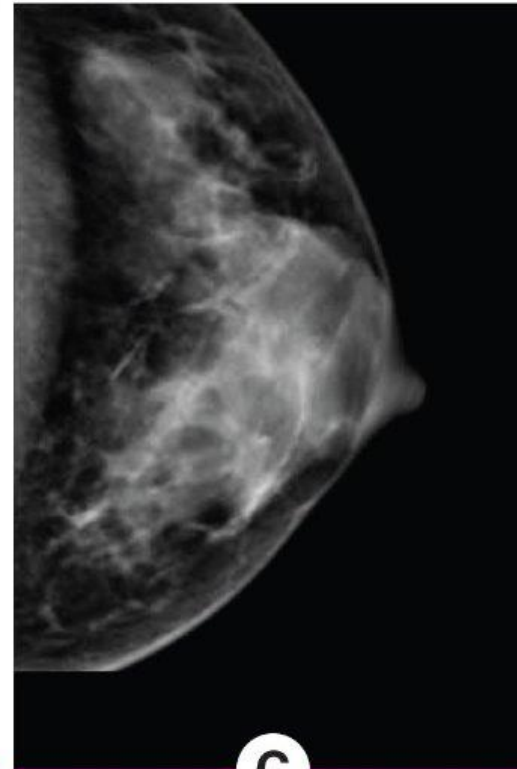
**A**

Almost entirely fatty (least amount of fibroglandular tissue)



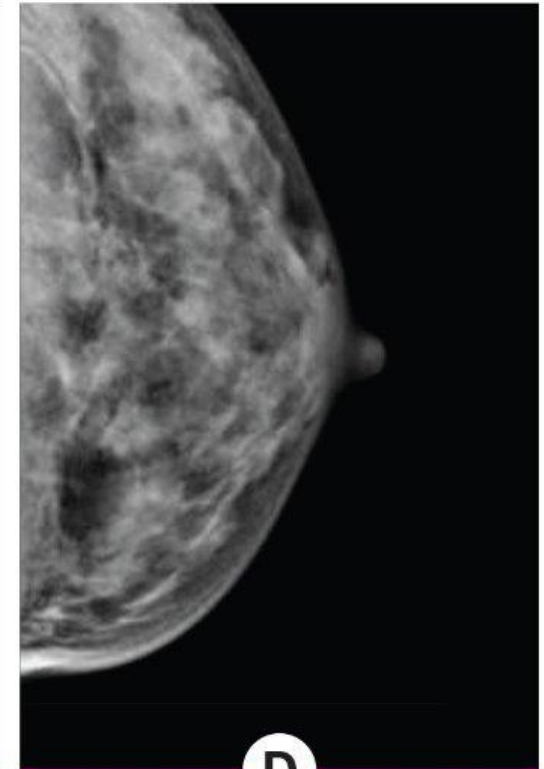
**B**

Scattered fibroglandular tissue



**C**

Heterogeneously dense



**D**

Extremely dense (most amount of fibroglandular tissue)

# Breast density

- Associated with: BRCA1/BRCA2, hormone therapy, younger age, lower BMI, alcohol consumption
- Decreases with age
- Can obscure underlying breast lesions
- Increased risk of breast cancer in dense tissue but no increased risk of mortality from breast cancer with dense breasts
- Breast density reporting

## Gail model

Age Valid for women 35-85 years old.	<input type="text"/>	years
First menstrual period	<input type="radio"/> Unknown <input type="radio"/> 7-11 years old <input type="radio"/> 12-13 years old <input type="radio"/> >13 years old	
First live birth	<input type="radio"/> Unknown <input type="radio"/> No births <input type="radio"/> <20 years old <input type="radio"/> 20-24 years old <input type="radio"/> 25-29 years old <input type="radio"/> ≥30 years old	
First-degree relatives with breast cancer Include only mother, sisters and daughters	<input type="radio"/> Unknown	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> >1
Previous breast biopsy	<input type="radio"/> Unknown	<input type="radio"/> 0 <input type="radio"/> 1 <input type="radio"/> >1
Race/ethnicity	<input type="radio"/> White <input type="radio"/> African-American <input type="radio"/> Hispanic <input type="radio"/> Asian-American <input type="radio"/> American-Indian/Alaskan Native <input type="radio"/> Unknown	

## Tyrer-Cuzick model (IBIS)

Have you given birth to one or more children?

Yes  No

Select your stage of menopause

- Premenopausal - Regular occurring menstrual cycles
- Perimenopausal - Irregular cycles and early menopause symptoms with less than 12 months since the last menstrual period
- Postmenopausal - No menstrual periods for 12+ months, marking the end of reproductive years
- I don't know

Have you ever used Hormone Replacement Therapy?

Note: HRT includes estrogen only or combined estrogen and progesterone but does not include hormonal birth control.

- Never
- Previous user (more than 5 years ago)
- Previous user (less than 5 years ago)
- Current user

Do you have a mutation in either the BRCA1 or BRCA2 gene?

Not Tested  Negative  BRCA1  BRCA2

Have you had a breast biopsy?

If you have had a breast biopsy and are unsure about which result to select below, this information should be displayed on your pathology report.

- No prior biopsy / No proliferative disease
- Prior biopsy, result unknown
- Hyperplasia (not atypia) ⓘ
- Atypical Hyperplasia
- Lobular Carcinoma in Situ (LCIS)

Have you had ovarian cancer?

Yes  No

Select your Breast Density

If you are unsure about which breast density category you fall under, this information should be displayed on your last mammography report. If you have not had a mammogram in the past, or are unsure about which breast density category you fall under, select the "I don't know" option below.

- A - Almost entirely fatty
- B - Scattered fibroglandular density
- C - Heterogeneously dense
- D - Extremely dense
- I don't know

Do you have any Ashkenazi inheritance?

Yes  No  I don't know

Increased breast density

Lifetime risk

Average  
<15%

Intermediate  
15-19%

High  
>20%

Continue  
recommended  
screening

Yearly screening

Yearly mammogram  
+ yearly breast MRI

## In Summary

- Risk assessment by age 30
- 40-75 -> mammogram every 1-2 years
- Dense breasts -> assess risk (Gail, Tyrer-Cuzick)
- High risk >20% -> yearly mammogram + breast MRI

# Women's Health Take Home Points

- Fezolinetant is a novel therapy for VMS of Menopause that is highly effective, safe in women who cannot/do not want hormonal therapy
- Off-label testosterone can be used in women with HSDD after addressing biopsychosocial needs and any genitourinary symptoms of menopause
- Perception matters - women turn to alternative remedies for a variety of reasons; setting goals for treatment and asking their "why" can create a shared decision making
- USPSTF updated their breast cancer guidelines to start mammograms every other year at age 40. Utilize breast density and risk calculators to identify those at higher risk who need more frequent and/or additional screening

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