# The Q-Spot™: The Menopause Blueprint

# Statistics You Need To Know

## Chapter 1

### Demographics & Life Expectancy

- **Worldwide trends**:
  - 1990 → 471 million women aged ≥50.
  - 2015 → 861 million (↑82.6%, about 2.4% per year)
- **U.S. trends**:
  - 2020 → ~64 million women aged ≥50.
  - 2060 → ~90 million projected.
  - Life expectancy for U.S. females: **81.2 years** (unchanged since 2012).
  - Probability of survival from age 50 to 80: **67.2%**.
  - Average additional years lived after 50: **33.3 years**
  - Many U.S. women spend **up to 40% of life in postmenopause**.
- **Canada**:
  - 2016 → 39% of women aged ≥50.
  - 2038 projection → 43%.
  - Life expectancy increased from **60.6 years (1920–22)** to **83.6 years (2009–11)**

### Age at Menopause

- Natural menopause usually occurs between **ages 40–58**.
- **Early menopause**: Final menstrual period (FMP) before **45**.
- **Late menopause**: FMP after **54**
- **Premature menopause / Primary ovarian insufficiency (POI)**: before **40**.
  - Estimated **650,000 women in 2020**, increasing to **730,000 by 2060**

### Reproductive Aging & Ovarian Reserve

- **Oocyte decline**:

  - Fetus (~20 weeks gestation): **6–7 million oocytes**.
  - At birth: **1–2 million**.
  - At puberty: **300,000–500,000**.
  - Only **400–500 ovulated** in lifetime; rest lost via apoptosis
- **Markers of ovarian aging**:
  - **AMH (antimüllerian hormone)** declines with age; peaks around **24.5 years**.
  - **FSH** rises with diminished ovarian reserve (day 3 FSH often used).
  - **Antral follicle count (AFC)** and AMH are complementary.
  - Hormonal contraceptives may lower AMH by **~30–50%**

## STRAW+10 Staging System

- **Seven stages total** (−5 to +2):
  - **Reproductive (−5 to −3a)**: normal to late reproductive phase.
  - **Menopause transition (−2, −1)**:
    - Early (persistent ≥7-day difference in cycle length).
    - Late (≥60 days amenorrhea). Average duration **1–3 years**.
  - **Postmenopause (+1a to +2)**:
    - +1a: first year after FMP.
    - +1b: second year.
    - +1c: 3–6 years after FMP (FSH/estradiol stabilize).
    - +2: ≥5–8 years after FMP, lasting remainder of life

## Hormonal Changes

- **Estradiol**: declines, but can fluctuate with "LOOP" cycles (1 in 4 early transition cycles).
- **FSH**: rises; STRAW+10 recognizes **≥25 IU/L** as marker of late transition.
- **Progesterone**: declines with increased anovulation.
- **SHBG**: declines ~40% during transition → free androgen index ↑ by ~80%.
- **Testosterone**: generally stable across transition; may increase slightly after age 70

# Chapter 2

## Vulvovaginal & Urinary Changes

- Vaginal atrophy increases vaginal **pH**, decreases lactobacilli, and predisposes women to **urinary tract infections (UTIs)**, urgency, frequency, and dysuria
- Pelvic floor changes and hormone receptor effects contribute to **pelvic organ prolapse**, with some evidence that **local estrogen** can help prevent it

## Obesity & Weight

- **Obesity prevalence (2013–2014, U.S., BMI ≥30):**
  - **Women:** 40.4%
  - **Men:** 35%
- **Severe obesity (BMI ≥40):**
  - **Women:** 9.9%
  - **Men:** 5.5%
- **Abdominal (central) obesity prevalence (2011–2012):**
  - **Women:** 64.7%
  - **Men:** 43.5%
  - Up from 55.4% (women) and 37.1% (men) in 1999–2000

## Body Composition & Fat Distribution

- Menopause is associated with **increased abdominal/visceral fat** and **decreased lean body mass**, independent of age
- Visceral adiposity increases risk for:
  - **Type 2 diabetes**
  - **Metabolic syndrome**
  - **Hepatic steatosis**
  - **Aortic plaque**

# Chapter 3

## Prevalence of Vasomotor Symptoms (VMS)

- VMS (hot flashes and night sweats) are the **most commonly reported symptoms** of the menopause transition.
- By 2025, **21 million US women** and **1.1 billion women worldwide** are expected to experience menopause-related VMS
- The **SWAN study** found that **60–80%** of women experience VMS during the menopause transition

## Racial/Ethnic Variations

- In SWAN's survey of 16,065 women aged 40–55 years:
  - Black women: **46%**
  - Hispanic women: **35%**
  - White women: **31%**
  - Chinese women: **21%**
  - Japanese women: **18%**

    Japanese women were least likely to describe symptoms as bothersome
- Black women also report a **longer duration** of VMS than white women

## Timing Across the Transition

- Prevalence increases with menopausal stage:
  - Premenopause: ~**20–40%**
  - Perimenopause: **60–80%**
  - Postmenopause: ~**42%**

## Duration of VMS

- **Penn Ovarian Aging Study**: moderate–severe VMS lasted a **median of 10 years**
- **SWAN**: frequent VMS lasted a **median of 7 years**, including **4.5 years after the final menstrual period**
- Most Black women experience symptoms for **more than a decade**

### Symptom Trajectories

- Australian longitudinal study (n > 5,000 women) identified **four groups**:
  - **Mild:** 42%
  - **Moderate:** 18%
  - **Early severe:** 11%
  - **Late severe:** 29%

# Chapter 4

### Depression & Mood

- **Lifetime prevalence of major depressive disorder (MDD)** in U.S. women: **~21%**
- **12-month prevalence of MDD** in U.S. women: **~8%**
- During the menopause transition, women are at **2–4× greater risk** of developing a first episode of depression compared with premenopause
- Risk is highest in **late perimenopause** and **early postmenopause**

### Anxiety

- Anxiety symptoms (irritability, nervousness, unexplained fear, heart pounding) tend to **surge in late perimenopause**, even in women without baseline anxiety
- This represents a **"window of vulnerability"** for a subgroup of women during the menopause transition.

### Sleep Disturbances

- Women are **more likely than men** to experience insomnia or sleep complaints
- Common problems: **difficulty initiating sleep, maintaining sleep, and frequent awakenings**.
- Sleep complaints are often linked to **depression, anxiety, pain, vasomotor symptoms, or primary sleep disorders** (e.g., OSA, restless legs syndrome)
- Depressed midlife women show:
  - **Less time in bed**
  - **Shorter total sleep time**

- **Longer sleep-onset latency**
- **Lower sleep efficiency**

### Hormonal Effects

- Estrogen plays a **modulatory role in mood**:
  - Enhances serotonin and norepinephrine transmission.
  - Reduces serotonin degradation via **monoamine oxidase inhibition**.
  - Increases tryptophan hydroxylase (rate-limiting for serotonin synthesis).
  - Stimulates **BDNF (brain-derived neurotrophic factor)**, which is neuroprotective

**Exam focus:**

- Prevalence stats (MDD lifetime and 12-month rates).
- The **2–4× increased risk** of new depression during the transition.
- The **timing of highest risk** (late perimenopause/early postmenopause).
- The "window of vulnerability" for anxiety.
- Gender differences in sleep complaints and the role of estrogen in mood regulation.

# Chapter 5

### Prevalence of Vulvovaginal Atrophy (VVA) / GSM

- VVA is highly prevalent, affecting **20% to 84% of menopausal women** (wide range due to study differences)
- **PEPI study (US, women aged 40–65):**
  - Symptoms consistent with VVA in **57% of sexually active women**

**48%** of menopausal women reported vaginal discomfort.

  - Among those: **85% reported vaginal dryness** and **52% reported pain with intercourse**
- Women with **female sexual dysfunction** are ~**4× more likely** to have VVA symptoms than women without sexual dysfunction

### Impact on Quality of Life

- GSM symptoms (dryness, irritation, pain) **worsen with prolonged estrogen deficiency** beyond menopause, unlike vasomotor symptoms which often improve over time
- GSM can:
    - Limit clothing choices and activities (e.g., cycling, tight clothing).
    - Cause significant **sexual distress**, sometimes leading women to stop penetrative sex altogether

### Special Populations

- Women with **primary ovarian insufficiency**, **hypothalamic amenorrhea**, prolonged lactation, or those on **GnRH agonists** may also present with bothersome VVA
- **Cancer survivors** (chemo, pelvic radiation, ovarian surgery, aromatase inhibitors) are at especially high risk for severe and persistent GSM symptoms

**Exam focus:**

- Remember the **20–84% prevalence range**, with **~57% in sexually active midlife women** (PEPI study).
- Know the **VIVA survey stats** (48% discomfort, 85% dryness, 52% dyspareunia).
- GSM **worsens over time**, unlike VMS.
- **Cancer treatments** and **low estrogen states at any age** can trigger GSM.

# Chapter 6

### Alzheimer's Disease & Dementia

- **Alzheimer disease (AD)** accounts for **well over half of all dementia cases**
- Dementia is more common in women, partly due to **longer life expectancy**, but also due to:
    - Greater vulnerability to **genetic risks** (e.g., ApoE genotype).
    - Higher prevalence of **modifiable risk factors** (obesity, inactivity, etc.)
- Up to **50% of AD cases worldwide** are attributable to **seven modifiable risk factors**:
    - Diabetes mellitus
    - Midlife hypertension

- Midlife obesity
- Smoking
- Depression
- Cognitive inactivity/low educational attainment
- Physical inactivity

## Cognition Across the Menopause Transition

- **Common complaints:** difficulty concentrating and remembering things, especially in **late perimenopause and early postmenopause**
- **SWAN study:** decline in **processing speed** during late perimenopause, not fully explained by age, VMS, depression, anxiety, or sleep disturbance
- **Penn Ovarian Aging Study:** memory significantly declined from premenopause to postmenopause

## Surgical Menopause

- Memory for verbal information may be compromised **immediately after surgical menopause** and in the **longer term if menopause occurs before the natural age**
- **Hysterectomy (with or without oophorectomy) before age 50** has been linked to **early onset dementia**, though absolute risk before age 65 remains **rare**
- **Oophorectomy before age 46** is associated with increased risk of cognitive decline or dementia in later life

## Hormone Therapy (HT) and Cognition

- **WHIMS trial (women ≥65):**
  - **Estrogen + progestin therapy (EPT)** doubled risk of dementia.
  - **Estrogen therapy (ET) alone** did not significantly increase dementia risk
  - Conclusion: **HT should not be started after age 65** for dementia prevention
- **Early postmenopause RCTs (KEEPS, WHIMSY, ELITE):**
  - No cognitive harm or benefit from HT
- Small trials suggest **ET may prevent memory decline** if started soon after surgical menopause

**Exam focus:**

- AD = **>50% of dementia**, more common in women.
- **50% of AD cases preventable** via 7 modifiable risks.
- **Late perimenopause = processing speed decline.**
- **Surgical menopause before 46 → ↑ dementia risk.**
- **WHIMS:** EPT doubled dementia risk in women ≥65; **ET alone not significant.**
- **HT should NOT be used to improve cognition or prevent dementia.**

# Chapter 7

## Cardiovascular Disease (CVD) in Women

- **CVD is the leading cause of death in U.S. women** – responsible for **1 in every 3 deaths** .
- By age **65**, **1 in 3 women** has some form of CVD .
- **Coronary heart disease (CHD):**
  - Accounts for **~20% of deaths** in women.
  - Median age at first myocardial infarction (MI): **70 years** for women vs **66 years** for men .
- **Stroke:**
  - Women account for **nearly 60% of stroke deaths**.
  - At age 55, lifetime risk of stroke is **1 in 5 for women**, **1 in 6 for men** .

## Risk Factors

- **Hypertension**:
  - Affects **~50% of women by age 60**, **~75% by age 75** .
- **Diabetes mellitus (DM):**
  - **2–4× greater risk** of CHD and stroke in women compared with women without DM.
  - Women with DM lose the usual female advantage in CVD protection .
- **Dyslipidemia:**
  - After menopause, women experience an increase in **total cholesterol, LDL-C, and triglycerides**, plus a decrease in HDL-C .
- **Metabolic syndrome:**
  - Prevalence in U.S. midlife women: **22% to 39%**.
  - Associated with a **2× risk of CVD events** .

### Special Populations & Timing

- **Premature menopause (<40 years)** and **early menopause (<45 years)** are linked to **higher CVD risk and mortality**, especially if untreated with hormone therapy .
- **Timing hypothesis:** Initiating menopausal hormone therapy (MHT) **before age 60 or within 10 years of menopause** may lower CHD and all-cause mortality, but not when initiated later .

**Exam Focus Points:**

- CVD is the **#1 killer of women** – 1 in 3 deaths.
- **Stroke risk:** 1 in 5 for women vs 1 in 6 for men at age 55.
- **Hypertension prevalence:** ~50% at 60, ~75% at 75.
- **Metabolic syndrome prevalence:** 22–39% in midlife women, doubles CVD risk.
- **Diabetes:** wipes out female CVD protection (2–4× risk).
- **Timing hypothesis:** MHT <60 years or <10 years since menopause may reduce CHD risk.

# Chapter 8

### Prevalence of Osteoporosis & Low Bone Mass

- **NHANES data:**
  - **15.4%** of U.S. women ≥50 years had osteoporosis (T-score ≤ –2.5 at femoral neck).
  - **51.4%** had low bone mass (osteopenia).
- Prevalence rises from **6.8% in women aged 50–59** to **34.9% in women ≥80**
- In 2010: **10.2 million adults** in U.S. had osteoporosis, and another **43 million had low bone density**, most of them postmenopausal women
- Canadian data (CaMos): **15.8% of women ≥50 years** had osteoporosis

### Fractures

- **>2 million osteoporosis-related fractures per year in the U.S.**, including:
  - **700,000+ vertebral fractures**
  - **300,000 hip fractures**

    - **400,000 hospital admissions**
- **Lifetime fracture risk: 40–50% of postmenopausal women** will experience an osteoporotic fracture
- **Hip fractures:**
    - Mean age at occurrence: **82 years**.
    - Associated with a **5–8× higher mortality in first 3 months**.
    - **>20% excess mortality within 1 year** (persisting for up to 10 years).
    - **25% require long-term care**, and **50% lose mobility**
- **Vertebral fractures:** linked with **10% excess mortality** within 1 year, plus pain, deformity, and loss of function

### Ethnic Differences in Risk

- **Whites and Hispanics**: highest fracture risk.
- **American Indians, Asians, Blacks**: progressively lower fracture risk

### Trends

- Hip fracture rates **decreased after 1997** (possibly linked to alendronate introduction), but appear to have **plateaued or risen again since 2008**, coinciding with declining osteoporosis medication use

**Exam Focus Points:**

- **15.4% osteoporosis / 51.4% low bone mass** in U.S. women ≥50.
- Prevalence rises sharply with age: **~7% at 50–59 → ~35% at ≥80**.
- **10.2M with osteoporosis + 43M with low bone mass** in U.S. (2010).
- **>2 million fractures/year**; **40–50% lifetime risk** for postmenopausal women.
- **Hip fracture stats**: avg age 82, 5–8× mortality in 3 months, 20%+ 1-year mortality, 25% LTC, 50% mobility loss.
- **Ethnic order of fracture risk:** White/Hispanic > American Indian > Asian > Black.

# Chapter 9

### Overall Cancer Risk

- Women have a **1 in 3 lifetime chance** of developing cancer
- Obesity prevalence in U.S. adults (2015–2016 NHANES): **39.8%**.
    - **Non-Hispanic Black women:** 54.8%
    - **Hispanic women:** 50.6%
    - **Non-Hispanic white women:** 38%
- Obesity significantly increases risk for **breast, uterine, ovarian, and colorectal cancers**

## Breast Cancer

- **Most common cancer in women** in the U.S. and worldwide
- After WHI reported ↑ breast cancer incidence in women on combined estrogen-progestin therapy (EPT), **HT use declined**, and so did breast cancer incidence
- In recent years, U.S. breast cancer incidence has **slightly increased**, but **mortality has steadily decreased** (due to early detection and improved therapy)
- There are now **>3.5 million breast cancer survivors** in the U.S.
- **Most breast cancers (95%)** are diagnosed at **stages I–III**, while **5% present with de novo metastatic disease**

## Colorectal Cancer

- **3rd most common cancer in U.S. women**.
- Estimated **64,010 new female cases in 2017**.
- **3rd leading cause of cancer death** in women: ~**23,110 deaths in 2017** (after lung and breast).
- Lifetime risk: **~4.2%** of Americans will develop it.
- 5-year survival rate: **64.5%**

## Lung Cancer

- In WHI: postmenopausal women on EPT had a **nonsignificant increase** in incidence (219 cases vs 184 placebo) and deaths (153 vs 132 placebo)
- Women account for the **majority of lung cancer deaths** in midlife.

**Exam Focus Points**:

- **1 in 3 lifetime cancer risk for women**.

- **Obesity rates by ethnicity** and its link to breast/uterine/ovarian/colorectal cancers.
- **Breast cancer = most common cancer**; **>3.5M survivors in U.S.**
- **WHI link between EPT and breast cancer**.
- **95% localized/regional breast cancer vs 5% metastatic**.
- **Colorectal cancer = 3rd most common**; **4.2% lifetime risk**; **64.5% 5-year survival**.
- **Lung cancer + HT (EPT nonsignificant risk in WHI)**.

# Chapter 10

## Effectiveness

- Estrogen therapy (ET) or estrogen-progestogen therapy (EPT) **reduces vasomotor symptom (VMS) frequency by ~75%** and significantly decreases severity
- About **50% of women experience return of VMS** when HT is discontinued

## Use & Undertreatment

- HT use **dropped sharply in the early 2000s** after WHI results on risks were released
- In some countries (e.g., Bangladesh, 2016 survey of >1,500 women), **0% were using prescription therapies for VMS** despite proven efficacy

## Cardiovascular & Thromboembolic Risk

- **Venous thromboembolism (VTE):**
  - WHI showed increased risk with **oral estrogen + progestin (EPT)**
  - Transdermal estrogen appears to have **lower VTE risk** compared to oral
- **Stroke:** Risk increases with oral estrogen; transdermal and lower-dose regimens show lower associated risk
- **Timing hypothesis:** Cardiovascular outcomes are more favorable when HT is started **before age 60 or within 10 years of menopause**

## Women's Health Initiative (WHI) Findings

- **EPT (conjugated equine estrogen + medroxyprogesterone acetate):**
  - ↑ risk of breast cancer, CHD, stroke, and VTE.

    - ↓ risk of fractures and colorectal cancer.
- **ET (conjugated equine estrogen alone, women with hysterectomy):**
    - No ↑ breast cancer risk; possible ↓ risk.
    - ↑ risk of stroke and VTE.
- Both arms showed increased risk when therapy was started in older women (>65).

**Exam Focus Points**:

- **75% reduction** in VMS frequency with HT.
- **50% recurrence of VMS** when HT is stopped.
- **Oral EPT = ↑ VTE, stroke, CHD, breast cancer.**
- **Transdermal estrogen = lower VTE/stroke risk.**
- **Timing hypothesis:** safer if <60 years or <10 years from menopause.
- **WHI key takeaways:**
    - EPT → ↑ breast cancer, CHD, stroke, VTE.
    - ET alone → ↑ stroke/VTE, no ↑ in breast cancer.

# Chapter 11

## Paroxetine (only FDA-approved nonhormone therapy)

- Paroxetine salt **7.5 mg** or standard **10–25 mg/day**:
    - **Reduces VMS frequency and severity** for up to **24 weeks**.
    - Improves **sleep disturbances associated with VMS**.
    - Well tolerated, with **no serious adverse events** in trials
- In survivors of gynecologic cancer, paroxetine significantly reduced VMS after **4 and 16 weeks**
- Pooled data: paroxetine **reduced hot flash–related nighttime awakenings** and **increased sleep duration by week 4**, with benefits sustained up to **24 weeks**

## Other SSRIs and SNRIs

- Effective agents include:
    - **Citalopram (10–20 mg/day)**
    - **Escitalopram (10–20 mg/day)**
    - **Desvenlafaxine (100–150 mg/day)**

    - **Venlafaxine (37.5–150 mg/day)**
- **Pooled analysis of 899 women:** after 8 weeks, hot flash reduction was:
    - Escitalopram: **1.4 VMS/day** fewer
    - Venlafaxine: **1.8 VMS/day** fewer
    - Low-dose oral estradiol (0.5 mg): **2.4 VMS/day** fewer
    - → Suggests SSRIs/SNRIs are **nearly as effective as low-dose estrogen**.

## Global & CAM (Complementary and Alternative Medicine) Use

- **Australian survey (women aged 40–65):** high use of complementary and alternative medicines (CAM) for menopause
- CAM includes herbs, phytoestrogens, acupuncture, exercise, and mind-body practices. Effectiveness varies and evidence is weaker than for HT or SSRIs/SNRIs.

**Exam Focus Points:**

- **Paroxetine 7.5 mg = only FDA-approved nonhormone VMS therapy**.
- Reduces VMS and improves sleep up to 24 weeks.
- SSRIs/SNRIs (citalopram, escitalopram, venlafaxine, desvenlafaxine) **reduce hot flashes almost as effectively as low-dose estrogen**.
- CAM therapies are widely used globally, but with mixed efficacy evidence.