SWAN Fact Sheet: Bone Health over the Menopause Transition*

Osteoporotic fractures usually occur in older postmenopausal women, however, bone loss leading to osteoporosis begins before menopause. The SWAN study followed a cohort of initially pre- and early perimenopausal women through the transition into postmenopause, and longitudinally tracked their bone health; we list below the major findings.

- A period of fast bone loss starts one year before the final menstrual period. This is generally (but not always) when there has been no menses for 3 or more months but some bleeding in the last year [1].Bone loss is fast for around 3 years, and continues in postmenopause, but more slowly [2].
- During the period of fast loss, bone density declines on average about 2% each year, with greater declines in the spine than in the hip. Over 10 years, cumulative bone density decline is around 10% [2].This is accompanied by loss of bone quality and strength (the ability to resist breakage or fracture)[3,4].
- Women who lose more bone density during the menopause transition have more fractures in postmenopause [5].
- Women with earlier menopause have lower bone density in postmenopause and more fractures [6].
- Several SWAN findings demonstrate the importance of looking beyond bone density:
    - Women who are obese have greater bone density than women without obesity [7], but it does not necessarily translate to more bone strength [8]. Obese women had as many fractures as non-obese women in SWAN, but compared to non-obese women with similar bone density, obese women had significantly more fractures [8].
    - Bone density is higher in women with type 2 diabetes than in women without diabetes; yet, bone strength is lower in diabetic women [9] and they experience more fractures than women without diabetes [10]. This may be due to lower bone quality [11], earlier menopause, and faster bone lossin diabetic women [10].
    - A higher level of C-reactive protein, a marker of inflammation, that has been related to life stresses and adversity, is associated with greater bone density, but not with greater bone strength. SWAN women with higher levels of C-reactive protein had more fractures than women with lower levels of C-reactive protein [12]. In addition, increase in C-reactive protein level over time was associated with faster decline in bone density [13].

What can you do to maximize bone health?

- In premenopausal and early perimenopausal women, physical activity, be it doing housework or sports and regular exercise, is associated with greater bone density and bone strength [14,15]. Thus, women who are physically active enter the menopause transition (when bone is lost) with greater bone reserves.
- Vitamin D sufficiency (25-hydroxyvitamin D levels >20 ng/ml) increased over time in SWAN women [16]. SWAN women with adequate vitamin D levels had fewer fractures than women with low levels [17].
- Working with your health care provider to control body weight, blood glucose, and chronic inflammation is important for overall health. Whether doing so also lessens bone loss cannot be learned from SWAN; clinical trials of the effects of lowering glucose, inflammatory markers, and weight on bone loss are needed.

For more information, please check out:

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SWAN Fact Sheet: Memory and Cognition During and After the Menopause Transition*

Many areas of the brain, such as the hippocampus and prefrontal cortex, are rich in estrogen receptors. This has led researchers to hypothesize that falling estrogen levels during the menopause transition might cause difficulties with memory and other aspects of cognition. The SWAN study followed a cohort of women through the menopause transition, and longitudinally tracked their performance on tests of verbal memory, working memory and cognitive processing speed; we list below the major findings.

- About two-thirds of women reported memory complaints such as forgetfulness during the menopause transition [1].
- In premenopause, objective measures of both verbal memory and processing speed improved with repeat testing, demonstrating the ability to improve with practice. In perimenopause however, this improvement with practice was not seen, consistent with the women's perception of memory and cognition difficulties. This perimenopausal decrement appears to be time-limited, as improvement with practice was seen again in early postmenopause [2].
- Sleep and mood problems increase during the menopause transition. Lack of sleep is linked to poor memory and difficulty focusing one's thoughts; depression and anxiety impair effort and performance on cognition testing.
    - SWAN women with depressive symptoms did perform less well on tests of processing speed, and women with anxiety symptoms showed smaller practice-related improvements in verbal memory scores.
    - During the menopause transition, self-reported measures of sleep and hot flashes were not associated with decrements in memory, processing speed, or practice-related improvements [3].
    - In early postmenopause however, women with sleep difficulties such as greater wakefulness and sleep fragmentation, scored lower on cognitive processing speed [4].
- After menopause (which occurs on average at age 52) cognitive processing speed fell, but declines in verbal and working memory scores did not typically start until later, after ages 58 and 61 years, respectively [5,6].
- Women with high blood pressure, elevated glucose, and obesity, and women who reported financial hardship experienced faster declines in cognitive processing speed [6,7,8].

What can you do?

- Address sleep problems by modifying your sleep habits or talking with a health professional to come up with possible solutions. Many sleep apps are available to improve sleep. For more information, refer to the SWAN sleep fact sheet.
- Other studies have found that objectively measured hot flashes are associated with memory difficulties. If you are experiencing hot flashes, discuss them with your health care provider. Refer to the SWAN hot flashes fact sheet.
- Address mood and anxiety symptoms during the menopause transition; discuss them with your healthcare provider.
- If memory changes come on suddenly, you should report them to your primary health care provider.
- Working with your health care provider to control blood pressure, glucose and weight is important for overall health. Whether controlling these conditions also lessens cognitive decline is being tested in ongoing clinical trials.

For more information, please check out:

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3. Greendale GA, Wight RG, Huang MH, Avis N, Gold E, Joffe H, Seeman T, Vuge M, and Karlamangla AS. Menopause-associated symptoms and cognitive performance: Results from the Study of Women's Health Across the Nation. *Amer J Epidemiol* 2010; 171(11): 1214-1224
4. Swanson LM, Hood MM, Hall MH, Kravitz HM, Matthews KA, Joffe H, Thurston RC, Butters MA,Ruppert K, Harlow SD. Associations between sleep and cognitive performance in a racially/ethnically diverse cohort: the Study of Women's Health Across the Nation. *Sleep*. 2021 Feb;44(2):zsaa182.
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SWAN Fact Sheet: Hot Flash Fact Sheet*

Did you know that:

- Most (up to 80%) of women will have some hot flashes or night sweats as they go through menopause and a few women will have very disruptive hot flashes.[1]
    - Some women have hot flashes when they are having periods, other women's hot flashes start when their periods stop, other women will have hot flashes both before and after their periods stop.[2]
    - Hot flashes can be very variable, even in the same woman, in how often they occur and how severe they are.
- Hot flashes differ in severity. Many women have few or mild hot flashes but about 10% of women will have ***more than 7 hot flashes a day***.
- Hot flashes can disrupt a woman's life by[3]:
    - Interfering with sleep
    - Making it harder to concentrate
    - Making one's mood worse
    - Reducing one's energy
    - Causing women to reduce/withdraw from social activities
- Hot flashes often start ***before*** a woman's periods stop; almost 30% of women will have hot flashes in their 30's[4,5] when they are still getting regular menstrual periods.
- Frequent hot flashes can last 7 or more years for about half of women.[6]
- Hot flashes may last longer if they started early or if a woman is also experiencing anxiety, stress, or depressive symptoms.[6,7]
- Hot flashes vary by race and ethnicity:[6,7]
    - Native American and Black women have the most frequent and most bothersome hot flashes of all groups studied to date[8].
    - Hispanic/Latinx women have similar rates of hot flashes than White women, but fewer than Black women
    - Chinese and Japanese women have the fewest hot flashes
- Hot flashes begin in the brain: special chemical messengers in the brain send signals to blood vessels to flush, which causes hot flashes.[9] Blocking these messengers stops hot flashes.
- Hormones are the most effective treatment for hot flashes that occur after menopause, however:
    - Non-hormonal treatments, such as SSRI or SNRI antidepressants, hypnosis, or cognitive behavioral therapy may be helpful for women who cannot or who do not wish to take hormones.[10]
    - Treatments that block hot flash chemical messengers in the brain may become available within the year and will provide a new non-hormonal way to treat hot flashes.

For more information, please see:

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Fact Sheet: Sleep during the Menopausal Transition*

What kinds of sleep changes do women experience during the menopausal transition?

- For many women, especially those with good sleep before perimenopause, sleep doesn't get worse during this time. [1]
- But, about half of women report sleep problems during perimenopause, compared to 30% in premenopause.
- Sleep problems start to get worse in early perimenopause, are highest in late perimenopause, then become stable or get better in postmenopause. [1]
- Difficulty staying asleep is the most common problem in perimenopause and can last into postmenopause. Waking up too early also gets worse in perimenopause, but then often gets better in postmenopause. [1]
- Changes in hormones during perimenopause can cause sleep problems. Hot flashes/flushes and night sweats cause wake ups during the night. But, even women who don't have hot flashes say their sleep is worse during perimenopause. One potential reason is that the brain becomes more active during sleep during this time, which makes sleep lighter and leads to worse sleep quality.[1-4]
- Seasons also play a role: perimenopausal women have more problems sleeping in the summer than winter, when they also have more hot flashes and night sweats. [5]

What else should you know about sleep during the menopausal transition?

- Women are at higher risk for sleep apnea once they begin the menopausal transition, which maybe related to hormonal changes and weight gain. Tell your doctor if you experience snoring or wake up gasping for air, which can be symptoms of sleep apnea. [6]
- Sleep differs among women with different racial/ethnic heritage. For instance, in SWAN:
    - Black, Chinese, Japanese, and Hispanic/Latinx women had shorter sleep relative to White women.
    - Black and Hispanic/Latinx women had more interrupted sleep relative to White women.
    - Black, Chinese, and Japanese women had poorer sleep quality relative to White women.
    - Race/ethnic differences in sleep may be related to race/ethnic differences in healthproblems, hot flashes/night sweats, waist size, physical inactivity, stress, financial strain,and emotional health.
- Staying active by playing sports or exercising may help with staying asleep during the night,improve sleep quality and insomnia, and make sleep deeper. [8]
- Sleep often will get better! As women get into their 60's and are further into postmenopause, theysleep longer and spend less time awake during the night than they did during perimenopause. [9]

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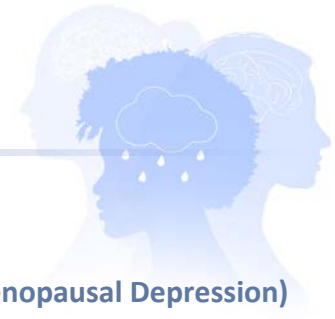

SWAN Fact Sheet:

Depression in Women – From Midlife and Across the Menopause Transition (Perimenopausal Depression)

Does the menopausal transition affect a woman's mood?

- It is not uncommon for some women to experience psychological and emotional symptoms, or mood swings during the menopausal transition (MT). These can be caused by many factors.
- Depressive symptoms, such as periodic feelings of sadness, feeling down, tired, and helpless or hopeless are not uncommon and can affect up to a quarter of women even prior to the menopause transition. Studies have shown that the percentage of women experiencing depressive symptoms during the perimenopause is higher, but the exact percentages vary widely across study populations and countries. Far fewer women will experience long lasting and severe depressive symptoms, called major depression (see below).
- The menopausal transition is the time in midlife when women begin to experience changes in the amount, duration, and timing of their menstrual flow, and then begin to skip menstrual periods. Women are more vulnerable to developing depressive symptoms during the transition, especially just before their final menstrual period.
- Changes in female hormones across the MT can contribute to depressive symptoms; symptoms may be worse when estrogen levels vary more widely and progesterone is no longer produced.
- Classic depressive symptoms often occur in combination with, and may be a result of, other menopause symptoms such as hot flashes and night sweats, but they also may be due to sleep disturbance. They may also occur in response to psychosocial challenges like relationship problems, changes in income, or other stressful events. It can be difficult to sort out all the issues that contribute to mood disturbances.
- Some women may experience depressive symptoms for the first time during midlife. For these women, stressful life events, a history of anxiety disorder, and limitations in physical health seem to be more important risk factors for this first episode of depressive symptoms than menopause.
- A clinical diagnosis of depression, also called Major Depressive Disorder (MDD) is a mood disturbance that includes persistent feelings of sadness, feeling down, lack of energy, and loss of interest or pleasure in activities once enjoyed to the point where these symptoms also affect eating, sleeping, and daily activities, lasting for at least 2 weeks.
- Women who have had MDD prior to menopause may be more vulnerable to having depressive symptoms or MDD during the perimenopause and in the early post-menopausal years.

What can you do to prevent or alleviate depression during the menopausal transition and post menopause?

- Be aware of depressive symptoms and mounting stressors or other psychological or physical challenges.
- Adopt healthy behaviors and preventive practices (e.g. eat a healthy diet, exercise, get good sleep, practice mindfulness, and meditation therapies, spend time with friends) to reduce stress.
- Tell your healthcare provider about depressive symptoms or find a healthcare professional referral so that they can provide treatment strategies and solutions. Effective non-medication and medication treatments are available.
- There is some evidence that estrogen therapy has an antidepressant effect comparable to traditional antidepressant medications. However, women who haven't had a hysterectomy generally are prescribed hormonal therapy that combines estrogen plus progesterone, and research on the effect of combined HT on depressive symptoms is sparse.

To find out more, please check out:

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Urinary Incontinence (UI)

- In midlife, about 15% of women have episodes of urine leakage that occur at least weekly, while about 10% have leakage that occurs daily; 25% of women wear protective undergarments for leakage protection.

- UI is not a menopause symptom.

    - Compared to women in the pre- or post-menopause, women in the peri-menopause are as likely to report resolution of infrequent UI (leakage once per month or less) as new onset of infrequent UI.

    - Developing weekly or more frequent UI or reporting having worsening of existing urine leakage in midlife is not associated with menopause or with changes in estrogen levels during the menopause transition. Rather, more troublesome leakage is associated with aging, and other factors, such as weight gain and diabetes.

- Weight gain, in particular gain in the waist-to-hip ratio, is associated with development or worsening of stress UI (leakage with coughing, sneezing, jumping) in midlife. Women who did not gain weight in midlife were less likely to develop or have worsening UI.

- Weight gain and the development of diabetes are associated with development of urgency UI (leakage with a sense of urgency). Women who do not gain weight or develop diabetes are less likely develop or have worsening of UI.

- White women have the highest risk of reporting UI before the onset of menopause. Black and Hispanic women have the highest risk of reporting worsening of UI during and after the menopausal transition.

- Women are more likely to seek treatment for leaking urine the longer they have this condition and the more frequent the episodes of leaking.

- Women who do not seek treatment for urine leakage often report inaccurate beliefs about UI (such as leaking is a normal consequence of aging) or motivational barriers (their provider never asked about them having a leakage problem) as reasons for not seeking treatment.

Sexual Functioning and Vaginal Health

- Vaginal dryness is related to sexual health. The prevalence of vaginal dryness increases across the menopause transition, from about 15% in premenopausal women to about three times that in late perimenopause and postmenopause.

- Women who have their ovaries removed are 2-3 times as likely to develop vaginal dryness as women who go through natural menopause.

- Women who have less frequent sexual intercourse over time, or have breaks from sexual intercourse, are **NOT** more likely to develop sexual pain than women who have consistent or more frequent sexual intercourse during midlife and beyond.

- For women who have a natural menopause, sexual functioning (a measured combination of sexual desire, emotional satisfaction, ability to climax, arousal, and sexual pain) declines the most in the time frame of 20 months prior to the final menstrual period until 1 year later.

- For women who undergo a hysterectomy (with or without removal of both ovaries) in midlife, sexual functioning begins to decline after surgery.

- Vaginal dryness and pain with intercourse are most related to the menopausal transition. Other aspects of sexual health such as desire, arousal and emotional satisfaction are more related to factors such as older age, fair or poor health, depressive symptoms, and anxiety.

- For women who have a natural menopause, using sexual lubricants in the perimenopausal period is associated with better sexual functioning.

- Being over- or under-weight is **NOT** associated with changes in sexual function across the menopausal transition.

- Breast cancer survivors and women without a history of cancer show similar declines in being sexually active, sexual intercourse frequency, and desire over time. However, among sexually active women, more cancer survivors report vaginal dryness and pain with intercourse.

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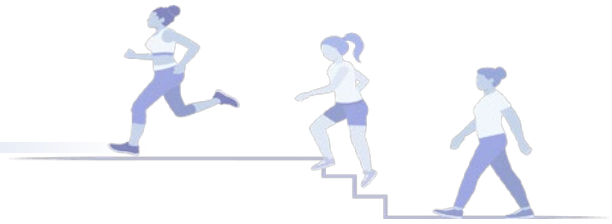

SWAN Fact Sheet: Physical Functioning over the Menopause Transition

Women and Physical Functioning

- Physical functioning is one's ability to do common tasks like walking, climbing stairs, bending and lifting things.
- In the United States, women tend to live longer than men but have more disability and experience more difficulty in physical functioning.
- The midlife (40-64 years) is an important time for changes in physical functioning for women.

What have we learned from SWAN so far?

- Nearly 1 in 5 women ages 40-55 years reported some limitations in physical functioning. Difficulties in physical functioning increase with age such that by 56-66 years of age, nearly 50% of women had physical functioning limitations.[1-3]
- Improvement in physical functioning is also common during the midlife.[2] Among SWAN women, the proportion of women whose functioning improved ranged from 14% to 55% depending on race-ethnicity and body size.[2]
- The menopausal transition is an important period with respect to physical functioning. Women who were either peri- or postmenopausal have poorer physical functioning as compared to premenopausal women.[1,4-6] These differences are related to changes in estrogen (specifically estradiol), the hormone that declines rapidly during the menopausal transition.[7]
- During the menopausal transition, women tend to gain fat mass and lose lean mass.[8] Women with more lean mass and less fat mass have better physical functioning including faster walking speed, more leg strength, and faster stair climbing speed.[9,10]

Measures of physical functioning are important markers of healthy aging.

- In SWAN, poor physical functioning was related to worse cardiovascular health and diabetes risk.[11-14]
- Many midlife women have chronic conditions such as knee osteoarthritis, peripheral nerve impairment and depressive symptoms.[16,17] These conditions are associated with worse physical functioning and more disability.[16,18,19]

Social determinants of health are social factors that are strongly related with health factors. Investigating these factors helps us better understand reasons for group differences. SWAN has identified several social factors related to physical functioning.

- In SWAN, there were differences in the performance of standard physical functioning tasks (i.e., stair climb, walking on a flat surface, rising from a chair) across racial and ethnic groups such that average physical functioning scores were higher for Japanese women relative to White women and were lower among Black and Hispanic women .[15,20,21]
- Differences in physical functioning in midlife women were partially explained by differences in socioeconomic status, body mass index, pain, and physical activity.[20,21]

What may help maintain or improve physical function during midlife?

- In SWAN, not smoking, participation in regular physical activity and a healthy diet were associated with better physical function.[22]
- In SWAN, women who ate more fruits, vegetables, and fiber and less fat had better physical function.[23]
- Women who participated in high levels of physical activity, like running or walking very quickly, or in moderate levels of physical activity, like walking briskly or vacuuming had better physical functioning than women with low physical activity.[24]

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