Personalizing Women's Health Through Menopause and Beyond

"Overview of the Menopause Transition: Highlights from the Study of Women's Health Across the Nation (SWAN)"

Joel S. Finkelstein, M.D.
Associate Professor of Medicine
Harvard Medical School
Endocrine Unit
Massachusetts General Hospital

Background

- The menopause is a universal experience of women in midlife.
- Relatively little is known about differences in menopausal symptoms and physiology among women.
- Most information on the menopause is derived from studies of Caucasian women.
- It is unclear if many midlife changes are due to the menopause or aging (or both).

Outline of presentation

- Describe SWAN (The Study of Women's Health Across the Nation)
- Discuss midlife changes commonly linked to the menopause transition
  - Novel findings from SWAN for changes known to be related to the menopause transition
  - Determine whether other common midlife change are due to the menopause transition or to aging.
- Speculate from an evolutionary perspective why some midlife changes are clearly linked to the menopause transition while others appear to be due primarily to aging.

SWAN: Overview

- SWAN is a multi-center study funded by the National Institutes of Health to examine a wide variety of issues as women traverse the menopause.

SWAN: Overview

- SWAN is a multi-center study funded by the National Institutes of Health to examine a wide variety of issues as women traverse the menopause.
- SWAN investigates a broad range of physiological, psychological, and social issues for women at mid-life.

SWAN: Overview

- SWAN is a multi-center study funded by the National Institutes of Health to examine a wide variety of issues as women traverse the menopause.
- SWAN investigates a broad range of physiological, psychological, and social issues for women at mid-life.
- A unique feature of SWAN is that a wide variety of racial and ethnic groups are included
  - African-Americans (n=935)
  - Caucasians (n=1,550)
  - Chinese (n=250)
  - Hispanics (n=286)
  - Japanese (n=281)

SWAN: Overview

- SWAN is a multi-center study funded by the National Institutes of Health to examine a wide variety of issues as women traverse the menopause.
- SWAN investigates a broad range of physiological, psychological, and social issues for women at mid-life.
- A unique feature of SWAN is that a wide variety of racial and ethnic groups are included
  - African-Americans (n=935)
  - Caucasians (n=1,550)
  - Chinese (n=250)
  - Hispanics (n=286)
  - Japanese (n=281)
- **Broad goals of SWAN are to describe characteristics of the transition, separate effects of chronologic vs ovarian aging, and describe ethnic variations in menopause and mid-life experiences.**

SWAN: Participating Sites

- Massachusetts General Hospital
- New Jersey Medical School
- Rush-Presbyterian St. Luke's Medical Center Chicago
- University of California at Davis
- University of California at Los Angeles
- University of Michigan
- University of Pittsburgh

- Coordinating Center - University of Pittsburgh
- Core Laboratory - University of Michigan

SWAN: Study design

Phase I: Cross-sectional study (n=16,000)

- 15 minute telephone interview to obtain data on a variety of topics in women aged 40-55 (irrespective of menstrual status) and determine eligibility for the cohort.

SWAN: Study design

Phase I: Cross-sectional study (n=16,000)

- 15 minute telephone interview to obtain data on a variety of topics in women aged 40-55 (irrespective of menstrual status) and determine eligibility for the cohort.

Phase II: Longitudinal cohort study (n=3,302)

- Common core protocol at all 7 study sites for pre-menopausal women age 42 to 52.
- Each site recruited 450 women, half Caucasian and half of the site's targeted minority group.

SWAN: Menopause status definitions

- Premenopause: bleeding within last 3 months with no change in regularity in past year
- Early perimenopause: bleeding within last 3 months with some change in regularity in past year
- Late perimenopause: no bleeding within last 3 months but some bleeding in last 11 months
- Postmenopause: no bleeding for at least 12 consecutive months

SWAN: Eligibility for Longitudinal Study

- Age 42 to 52 at last birthday
- Pre- or early perimenopausal status and not currently pregnant
- No use of oral contraceptives or other female reproductive hormones in past 3 months
- Self-identified ethnicity belonging to one of the site's targeted ethnic groups

SWAN: Core Protocol

The SWAN cohort study core protocol includes:

- Multiple questionnaires to assess medical history, reproductive history, menstrual history, family history, symptoms, medications, diet, physical activity, mood, QOL, sexual function, cognitive function, social support, CAM use, etc.

SWAN: Core Protocol

The SWAN cohort study core protocol includes:

- Multiple questionnaires to assess medical history, reproductive history, menstrual history, family history, symptoms, medications, diet, physical activity, mood, QOL, sexual function, cognitive function, social support, CAM use, etc.
- Measurement of height, weight, waist:hip ratio, and BP

SWAN: Core Protocol

The SWAN cohort study core protocol includes:

- Multiple questionnaires to assess medical history, reproductive history, menstrual history, family history, symptoms, medications, diet, physical activity, mood, QOL, sexual function, cognitive function, social support, CAM use, etc.
- Measurement of height, weight, waist:hip ratio, and BP
- A single fasting blood sample between days 2-5 of the menstrual cycle for reproductive hormones, lipids, insulin, glucose, CRP, PAI-1, hemostatic factors, etc.

SWAN: Core Protocol

The SWAN cohort study core protocol includes:

- Multiple questionnaires to assess medical history, reproductive history, menstrual history, family history, symptoms, medications, diet, physical activity, mood, QOL, sexual function, cognitive function, social support, CAM use, etc.
- Measurement of height, weight, waist:hip ratio, and BP
- A single fasting blood sample between days 2-5 of the menstrual cycle for reproductive hormones, lipids, insulin, glucose, CRP, PAI-1, hemostatic factors, etc.
- Monthly menstrual calendar with symptom assessment

SWAN: Core Protocol

The SWAN cohort study core protocol includes:

- Multiple questionnaires to assess medical history, reproductive history, menstrual history, family history, symptoms, medications, diet, physical activity, mood, QOL, sexual function, cognitive function, social support, CAM use, etc.
- Measurement of height, weight, waist:hip ratio, and BP
- A single fasting blood sample between days 2-5 of the menstrual cycle for reproductive hormones, lipids, insulin, glucose, CRP, PAI-1, hemostatic factors, etc.
- Monthly menstrual calendar with symptom assessment
- Spine, hip, and total body BMD by DXA

SWAN: Core Protocol

The SWAN cohort study core protocol includes:

- Multiple questionnaires to assess medical history, reproductive history, menstrual history, family history, symptoms, medications, diet, physical activity, mood, QOL, sexual function, cognitive function, social support, CAM use, etc.
- Measurement of height, weight, waist:hip ratio, and BP
- A single fasting blood sample between days 2-5 of the menstrual cycle for reproductive hormones, lipids, insulin, glucose, CRP, PAI-1, hemostatic factors, etc.
- Monthly menstrual calendar with symptom assessment
- Spine, hip, and total body BMD by DXA
- Body composition by DXA and bioelectrical impedance

SWAN: Core Protocol

The SWAN cohort study core protocol includes:

- Multiple questionnaires to assess medical history, reproductive history, menstrual history, family history, symptoms, medications, diet, physical activity, mood, QOL, sexual function, cognitive function, social support, CAM use, etc.
- Measurement of height, weight, waist:hip ratio, and BP
- A single fasting blood sample between days 2-5 of the menstrual cycle for reproductive hormones, lipids, insulin, glucose, CRP, PAI-1, hemostatic factors, etc.
- Monthly menstrual calendar with symptom assessment
- Spine, hip, and total body BMD by DXA
- Body composition by DXA and bioelectrical impedance
- **White blood cells for DNA**

SWAN: Daily Hormone Study

- **At each site, 90-180 women (n = 990) collected a daily morning urine sample for 1 menstrual cycle (or 50 days depending on which comes first) each year.**
- **Urine samples were analyzed for sex steroid metabolites, gonadotropins, and creatinine.**

SWAN: Selected Cohort Study Topics

- **Menopause symptoms**
- **Bone loss and bone turnover**
- **Cardiovascular disease predictors**
- **Physical and psychological health**
- **Health status and health care utilization**
- **Complementary and alternative medicine use**
- **Dietary habits and effects on health**
- **Body composition**
- **Cognitive function**
- **Sexual function and activity**
- **Sleep disturbances**
- **Menstrual bleeding patterns**
- **Reproductive hormone profiles**

What can we learn from SWAN?

- **Descriptive data about the menopause transition**
  - **Age of menopause and factors that modify it**
  - **Hormone profiles**
- **Develop predictive models for midlife events**
  - **Use of Mullerian Inhibiting Substance to predict the FMP**
- **Details about changes known to be related to menopause**
  - **Bone loss**
  - **Vasomotor symptoms**
- **Distinguish if other midlife changes are due to menopause or aging**
  - **Weight, body composition, and lipids**
  - **Mood, cognition, and sexual desire**
- **Develop hypotheses regarding mechanisms and causation of effects**

Age at FMP in SWAN

- **Median age of natural FMP was 51.4 years in cross sectional survey and 53 years in longitudinal cohort study (adjusted for multiple covariates including race/ethnicity, BMI, smoking, education, parity, prior use of OCPs).**

Variables in multivariable model:

- **Baseline FSH**
- **Baseline estradiol**
- **Education**
- **Prior OCP use**
- **Diabetes**
- **Height**
- **Weight**
- **Marital status**

Variables not in multivariable model:

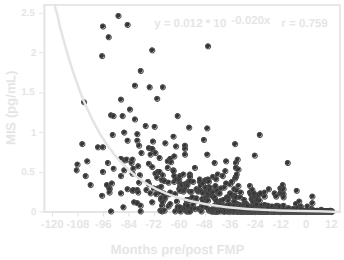
- **Race/ethnicity**
- **Smoking**
- **Parity**
- **Income**
- **Self-reported health**
- **Heart disease**
- **Genistein intake**

Predicting FMP with MIS (AMH) and age in SWAN

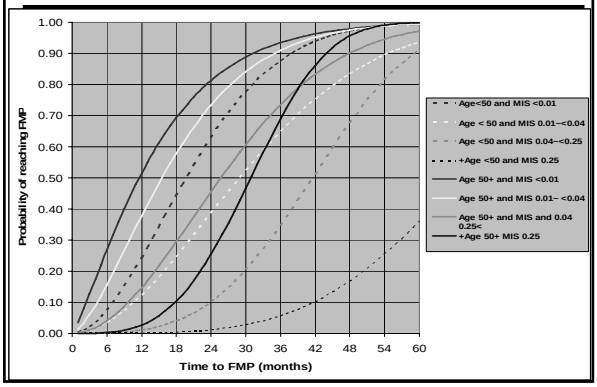
- **A major unmet goal of menopause research is to predict when a woman will stop menstruating.**
- **Because MIS (Mullerian Inhibiting Substance) is made by granulosa cells, we hypothesized that MIS levels would decline progressively as follicles are lost each month and thus provide a stable marker of ovarian aging.**

Predicting FMP with MIS (AMH) and age in SWAN

- Serum MIS was measured annually for up to 11 years in 184 women who underwent a "clean" transition. Data were censored once a woman reported 12 months without bleeding.



Predicting FMP with MIS (AMH) and age in SWAN



Changes often attributed to the menopause transition

<u>Cleary established</u>
- Vasomotor flushes
- Bone loss
- Vaginal dryness
- Decreased breast density

<u>Relationship unclear</u>
- Weight gain
- Increase in body fat
- Decrease in lean mass
- Increase in LDL
- Increase in BP
- Increase in vascular ds
- Increase in depression
- Decrease in cognitive fx
- Increase in incontinence
- Decrease in libido
- Difficulty sleeping

Criteria for a menopause effect

- The change should occur with ovariectomy (or GnRH agonist administration) and should be preventable with hormone replacement.

Criteria for a menopause effect

- The change should occur with ovariectomy (or GnRH agonist administration) and should be preventable with hormone replacement.
- The natural menopause transition should be associated with an alteration in the rate of change compared with premenopausal years.

Criteria for a menopause effect

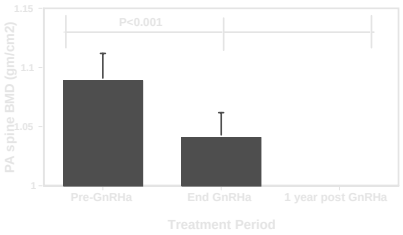
- The change should occur with ovariectomy (or GnRH agonist administration) and should be preventable with hormone replacement.
- The natural menopause transition should be associated with an alteration in the rate of change compared with premenopausal years.
- The change should occur in the majority of women as they go through the menopause transition.

Criteria for a menopause effect

- The change should occur with ovariectomy (or GnRH agonist administration) and should be preventable with hormone replacement.
- The natural menopause transition should be associated with an alteration in the rate of change compared with premenopausal years.
- The change should occur in the majority of women as they go through the menopause transition.
- There should a plausible biologic mechanism linking ovarian hormones to the observed changes.

Effects of GnRH agonists on spine BMD

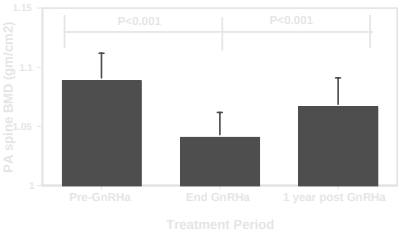
Spine BMD in 23 women with endometriosis (mean age 34 yr) before (left), after 12 months of GnRHa (nafarelin acetate 200 mcg BID) therapy (middle), and 1 year after stopping GnRHa therapy (right).



Finkelstein et al., JCEM 84:1214, 1999

Effects of GnRH agonists on spine BMD

Spine BMD in 23 women with endometriosis (mean age 34 yr) before (left), after 12 months of GnRHa (nafarelin acetate 200 mcg BID) therapy (middle), and 1 year after stopping GnRHa therapy (right).



Finkelstein et al., JCEM 84:1214, 1999

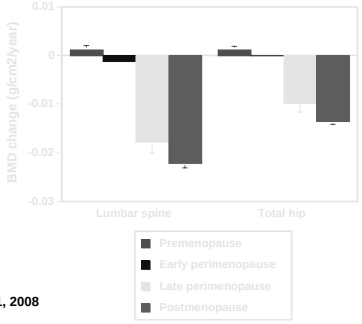
Ethnic variation in bone density in SWAN

- 2277 African-American, Caucasian, Chinese or Japanese women age 42-52
- Pre- or early perimenopausal
- Unadjusted BMD:
- AA > Caucasian > Chinese/Japanese
- Weight-matched BMD:
- AA > or = Chinese/Japanese > Caucasian

Finkelstein et al., JCEM 87:3057-67, 2002

BMD across the menopause transition in SWAN

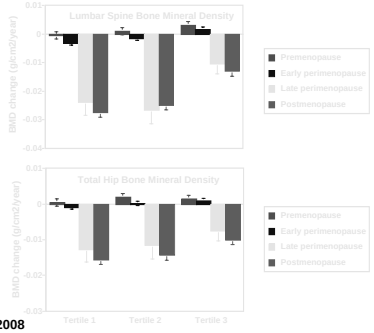
Annual rate of change of spine and total hip BMD by menopause status in 1902 African-American, Caucasian, Chinese, and Japanese women age 42-52 at baseline followed for up to 5 years



Finkelstein et al., JCEM 93:861, 2008

BMD across the menopause transition in SWAN

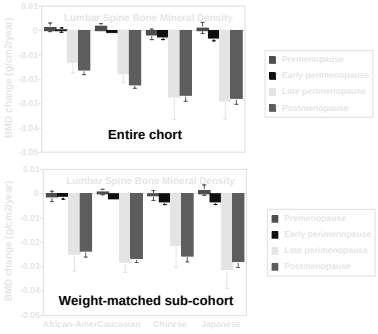
Annual rate of change of spine (upper panel) and total hip (lower panel) BMD by tertiles of body weight and menopause status in 1902 African-American, Caucasian, Chinese, and Japanese women.



Finkelstein et al., JCEM 93:861, 2008

BMD across the menopause transition in SWAN

Annual rate of change of spine by menopause status and ethnicity in 1902 African-American, Caucasian, Chinese, and Japanese women in the whole cohort (upper panel) and in a sub-cohort in which ethnic groups were matched for weight (lower panel).

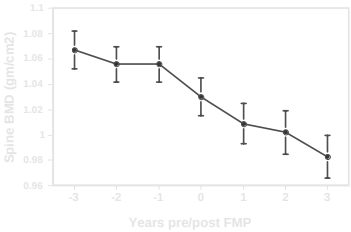


Finkelstein et al., JCEM 93:861, 2008

BMD across the menopause transition in SWAN

Spine BMD in relation to years from the final menstrual period (FMP) in 112 women age 42-52 at baseline followed for 7 years.

All women had "clean" transitions and contributed data at each time point.

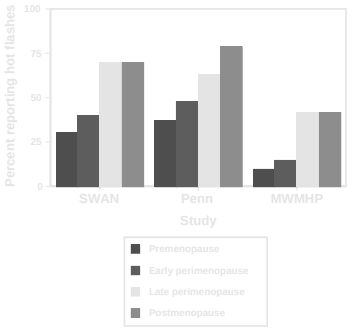


Prevalence of vasomotor symptoms across the menopause transition

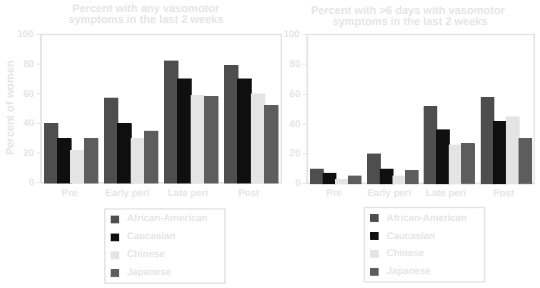
SWAN = Study of Women's Health Across the Nation. (n=3302)
VMS in past 2 weeks

Penn = Penn Ovarian Aging Study(n=236)
VMS in past month

MWMHP = Melbourne Women's Midlife Health Project (n=172)
VMS in past 2 weeks



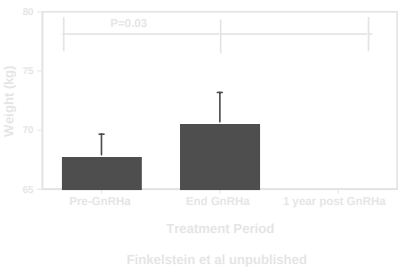
Vasomotor symptoms across the menopause transition in SWAN



Adapted from Gold et al., Am J Public Health 96:1226, 2006

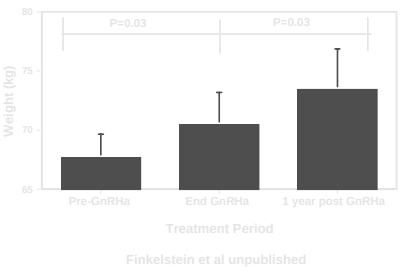
Effects of GnRH agonists on weight

Body weight in 35 women with endometriosis (mean age 34 yr) before (left), after 12 months of GnRHa (nafarelin acetate 200 mcg BID) therapy (middle), and 1 year after stopping GnRHa therapy (right).

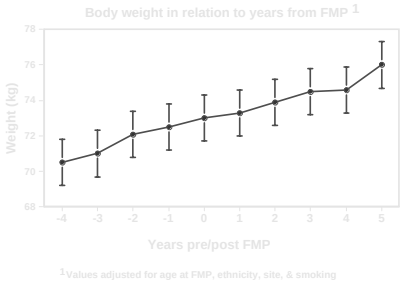


Effects of GnRH agonists on weight

Body weight in 35 women with endometriosis (mean age 34 yr) before (left), after 12 months of GnRHa (nafarelin acetate 200 mcg BID) therapy (middle), and 1 year after stopping GnRHa therapy (right).

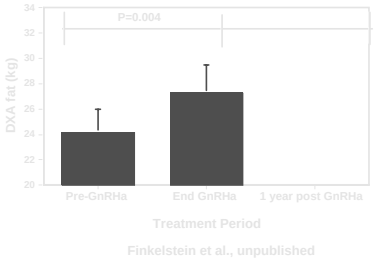


Body weight across the menopause transition in SWAN



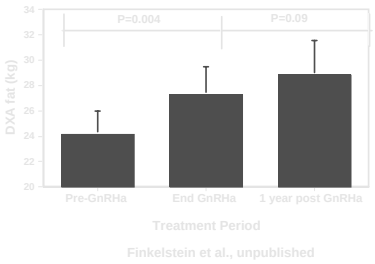
Effects of GnRH agonists on body composition

Body fat by DXA in 35 women with endometriosis (mean age 34 yr) before (left), after 12 months of GnRHa (nafarelin acetate 200 mcg BID) therapy (middle), and 1 year after stopping GnRHa therapy (right).



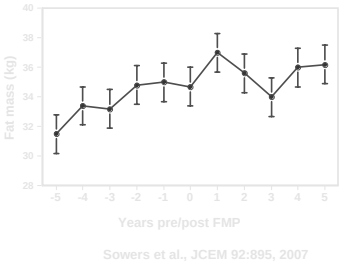
Effects of GnRH agonists on body composition

Body fat by DXA in 35 women with endometriosis (mean age 34 yr) before (left), after 12 months of GnRHa (nafarelin acetate 200 mcg BID) therapy (middle), and 1 year after stopping GnRHa therapy (right).



Fat mass across the menopause transition in SWAN

Fat mass by BIA in relation to years from the final menstrual period (FMP) in 543 African-American or Caucasian women age 42-52 at baseline followed for up to 6 years

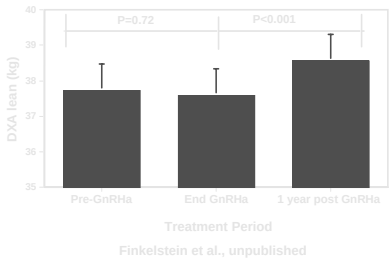


Effects of GnRH agonists on body composition

Lean mass by DXA in 35 women with endometriosis (mean age 34 yr) before (left), after 12 months of GnRHa (nafarelin acetate 200 mcg BID) therapy (middle), and 1 year after stopping GnRHa therapy (right).

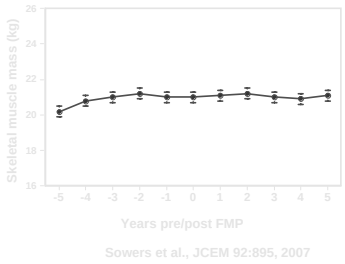
Effects of GnRH agonists on body composition

Lean mass by DXA in 35 women with endometriosis (mean age 34 yr) before (left), after 12 months of GnRHa (nafarelin acetate 200 mcg BID) therapy (middle), and 1 year after stopping GnRHa therapy (right).



Muscle mass across the menopause transition in SWAN

Lean mass by bio-electrical impedance (BIA) in relation to years from the final menstrual period (FMP) in 543 African-American or Caucasian women age 42-52 at baseline followed for up to 6 years.



Sowers et al., JCEM 92:895, 2007

Effect of the menopause transition on body composition

- Multiple studies report increases in fat mass with GnRHa therapy.
- Increases tend to be in truncal and visceral fat.
- Effects of GnRHa therapy on lean mass are variable.
- HT counteracts menopause-related changes in body composition.
- Biological plausibility exists for changes in fat since estrogen steers differentiation of pluripotent stem cells away from adipocytes.

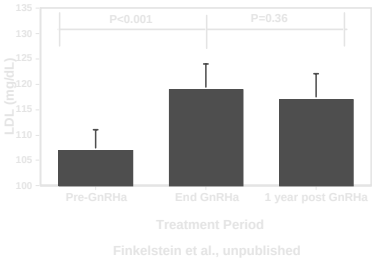
Effects of GnRH agonists on lipids

LDL cholesterol in 35 women with endometriosis (mean age 34 yr) before (left), after 12 months of GnRHa (nafarelin acetate 200 mcg BID) therapy (middle), and 1 year after stopping GnRHa therapy (right).

Finkelstein et al., unpublished

Effects of GnRH agonists on lipids

LDL cholesterol in 35 women with endometriosis (mean age 34 yr) before (left), after 12 months of GnRHa (nafarelin acetate 200 mcg BID) therapy (middle), and 1 year after stopping GnRHa therapy (right).



Finkelstein et al., unpublished

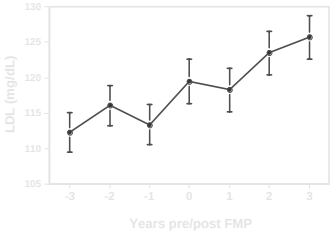
Effect of hysterectomy/GnRHa on LDL

- LDL increased 18% in 31 premenopausal women 18 months after TAH/BSO
  - Farish et al., BJOG 97:78, 1990
- No change in LDL in 10 women treated with GnRHa + low dose norethindrone for 48 weeks or in 18 controls (RCT)
  - Surrey et al., Fertil Steril 63:747, 1995
- No change in LDL in 15 premenopausal women 6 months after TAH/BSO.
  - Goldman et al., Eur J Obstet Gynecol Reprod Biol 66:133, 1996
- No change in LDL in 30 premenopausal women 6 months after TAH/BSO versus 44 controls who underwent TAH alone
  - Cheung et al., Climacterc 1:33, 1998

LDL across the menopause transition in SWAN

LDL cholesterol levels in relation to years from the final menstrual period (FMP) in 112 women age 42-52 at baseline followed for 7 years.

All women had "clean" transitions and contributed data at each time point.



Carotid IMT across the menopause transition

- Age-adjusted carotid IMT (intima-media thickness) was related to years since TAH/BSO but not to years since TAH.
  - Dwyer et al., Am J Epidemiol 156:438, 2002
- Carotid IMT was lower in 70 surgically menopausal women who received HT than in 65 women those who did not.
  - Mihmanli et al., Maturitas 42:37, 2002
- In the HERS study, HT had no significant effect on the progression of carotid IMT.
  - Byington et al., Arterioscler Thromb Vasc Biol 22:1692, 2002
- In SWAN, a cross-sectional analysis in 483 women found no significant association between menopause status and IMT after adjustment for age.
  - Wildman et al., Menopause 15:414, 2008

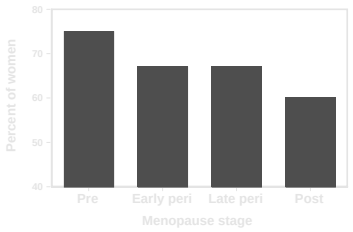
Sexual desire across the menopause transition

- Women had fewer sexual thoughts as they went through the menopause transition.
  - McCoy et al., Maturitas 7:203, 1985
- Advancing menopause status was associated with lower sexual desire.
  - Avis et al., Menopause 7:297, 2000
- Sexual desire declined exponentially from late peri- to postmenopause and the prevalence of sexual dysfunction increased from 42% to 88%.
  - Dennerstein et al., Fertil Steril, 2001

Sexual desire across the menopause transition in SWAN

Percent of women reporting sexual desire at various stages of the menopause transition in SWAN.

Analyses adjusted for age, psychosocial health and physical health variables.



Effect of hysterectomy on depression

- Prevalence of "psychologic distress" fell from 55 to 32% after TAH/BSO
  - Ryan et al., Br J Psychiatry 154:516, 1989
- Women who underwent TAH/BSO reported fewer stress symptoms and a more optimistic attitude c/w premenopausal controls
  - Everson et al., Health Psychol 14:435, 1995
- Psychologic symptoms, including depression, improved similarly after TAH or TAH/BSO (RCT).
  - Thakar et al., BJOG 111:1115, 2004
- TAH/BSO is associated with a decrease in depressive symptoms c/w TAH or TAH + unilateral OOX (RR=0.36)
  - Rohl et al., Am J Obstet Gynecol 199:22, 2008

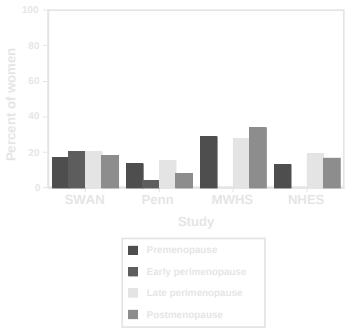
Depressive symptoms across the menopause transition

SWAN = Study of Women's Health Across the Nation. (n=3302)
CES-D >16

Penn = Penn Ovarian Aging Study(n=236)
CES-D >16

MWHS = Mass Women's Health Study (n=2352)
symptom checklist

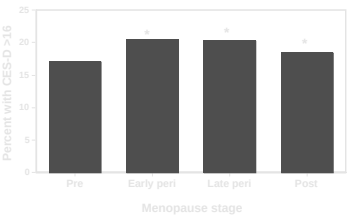
NHES = National Health Examination Study (n=394)
CES-D >16



CES-D score across the menopause transition in SWAN

Prevalence of Center for Epidemiologic Studies Depression Scale (CES-D) scores ≥16 in relation to menopause status in 3302 multi-ethnic women age 42-52 at baseline followed for up to 5 years.

Values are adjusted for age, site, ethnicity, hot flashes, smoking, social support, perceived health, medication use, and SES.



*Odds ratio significantly different from premenopausal

Adapted from Bromberger et al.,J Affective Dis 103:267, 20

Ovarian hormones and cognitive function

- Estrogens, androgens, or both had no effective on cognitive function. Women who underwent TAH scored better than women who had TAH/BSO.
  - Sherwin, Psychoneuroendocrinology 13:345, 1988
- Cognitive function (MMSE) was similar in former, current, and never HRT users.
  - Low et al., Maturitas 54:86, 2006
- Effects of menopause status on cognitive function (National Adult Reading Test) are explained by premenopausal cognitive function.
  - Kok et al., Menopause 13:19, 2006
- CEE alone or with MPA lowered cognitive performance (MMSE) in women participating in the WHI Memory Study (WHIMS).
  - Espeland et al., JAMA 291:2959, 2004

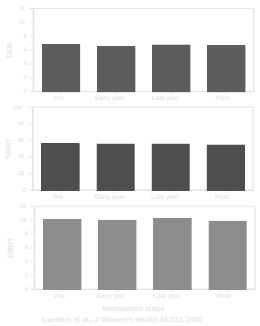
Cognitive function tests in SWAN

- **Symbol Digit Modalities Test (SDMT)**
  - Evaluates processing speed, working memory, and executive functioning (maximum score = 110)
- **Digit Span Backward (DSB)**
  - Assesses working memory (maximum score = 12)
- **East Boston Memory Test (EBMT)**
  - Evaluates immediate and delayed verbal memory (maximum score = 12)

Cognitive function across the menopause transition in SWAN

DSB, SDMT, and EBMT scores in 1657 pre (n=149), early peri (n=945), late peri (n=222), or postmenopausal (n=341) women at the 4th annual SWAN visit.

Values are adjusted for age, site, race/ethnicity, hot flashes, BMI, education, poor health, poor sleep, somatic symptoms, and dysphoric mood symptoms.

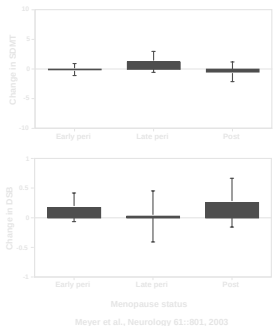


Luetters et al., J Women's Health 16:331, 2007

Cognitive function across the menopause transition in SWAN

Changes in DSB and SDMT scores in 868 African-American or Caucasian women by menopause status over a 5 year period. Premenopausal status is the reference group.

Values are adjusted for age, time since baseline, race/ethnicity, education, income, and self-reported health.



Meyer et al., Neurology 61:801, 2003

Changes often attributed to the menopause transition

Link is clearly established

- Vasomotor flushes
- Bone loss
- Vaginal dryness
- Decreased breast density

Changes often attributed to the menopause transition

Link is clearly established

- Vasomotor flushes
- Bone loss
- Vaginal dryness
- Decreased breast density

Evidence favors a link

- Decreased libido
- Increase in body fat

Changes often attributed to the menopause transition

Link is clearly established
- Vasomotor flushes
- Bone loss
- Vaginal dryness
- Decreased breast density

Evidence favors a link
- Decreased libido
- Increase in body fat

Evidence is equivocal
- Increase in LDL
- Difficulty sleeping
- Increase in vascular ds

Changes often attributed to the menopause transition

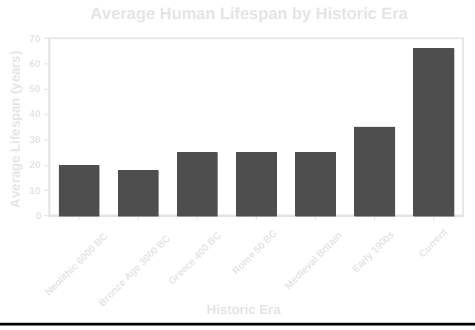
Link is clearly established
- Vasomotor flushes
- Bone loss
- Vaginal dryness
- Decreased breast density

Evidence favors a link
- Decreased libido
- Increase in body fat

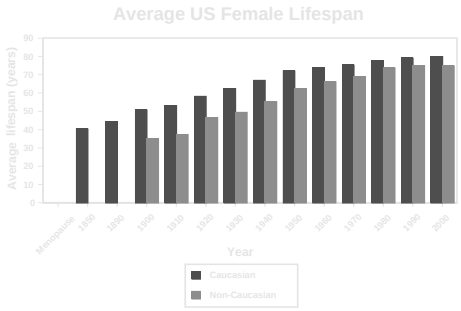
Evidence is equivocal
- Increase in LDL
- Difficulty sleeping
- Increase in vascular ds

Evidence is largely against
- Increase in weight
- Increase in BP
- Decrease in lean mass
- Increase in coagulation
- Increase in depression
- Decrease in cognition
- Increase in incontinence

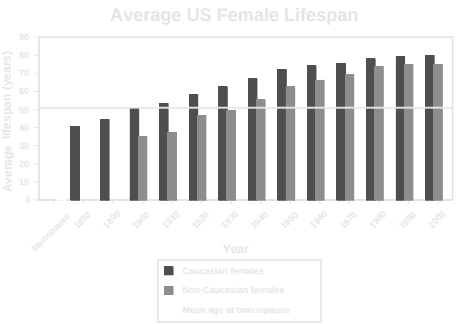
The menopause transition: An evolutionary perspective



The menopause transition: An evolutionary perspective



The menopause transition: An evolutionary perspective



The menopause transition: An evolutionary perspective

- Evolution did not plan for a prolonged menopause--if it planned for any menopause at all!

The menopause transition: An evolutionary perspective

- Evolution did not plan for a prolonged menopause--if it planned for any menopause at all!
- As far as evolution is concerned, we exist to reproduce, ensure the survival of our offspring, and then we can die.

The menopause transition: An evolutionary perspective

- Vaginal lubrication and libido
  - Are unnecessary once a woman is no longer reproductively competent. Evolution does not care about sexual pleasure.

The menopause transition: An evolutionary perspective

- Vaginal lubrication and libido
  - Are unnecessary once a woman is no longer reproductively competent. Evolution does not care about sexual pleasure.
- Glandular breast tissue
  - No longer needed once a woman is done nursing her young.

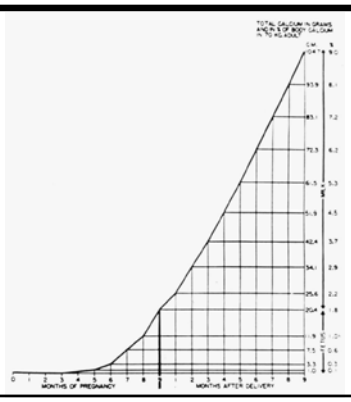
The menopause transition: An evolutionary perspective

- Vaginal lubrication and libido
  - Are unnecessary once a woman is no longer reproductively competent. Evolution does not care about sexual pleasure.
- Glandular breast tissue
  - No longer needed once a woman is done nursing her young.
- Increased body fat
  - A useful adaptation to deal with the energy requirements of nursing a neonate as fat is the most efficient energy source

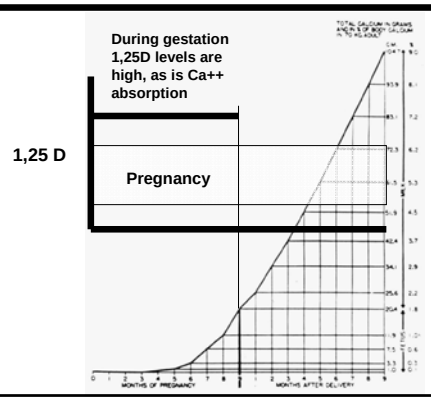
The menopause transition: An evolutionary perspective

- Vaginal lubrication and libido
  - Are unnecessary once a woman is no longer reproductively competent. Evolution does not care about sexual pleasure.
- Glandular breast tissue
  - No longer needed once a woman is done nursing her young
- Increased body fat
  - A useful adaptation to deal with the energy requirements of nursing a neonate as fat is the most efficient energy source
- Estrogen-deficiency bone loss
  - What does it have to do with reproduction?

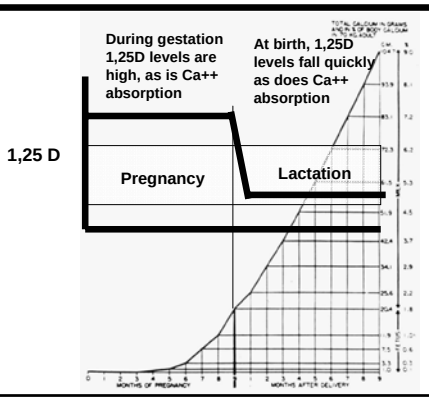
Mineralization of the fetal skeleton



1,25D during pregnancy and lactation



1,25D during pregnancy and lactation



The menopause transition: An evolutionary perspective

- Vaginal lubrication and libido
  - Are unnecessary once a woman is no longer reproductively competent. Evolution does not care about sexual pleasure.
- Glandular breast tissue
  - No longer needed once a woman is done nursing her young
- Increased body fat
  - A useful adaptation to deal with the energy requirements of nursing a neonate as fat is the most efficient energy source
- Estrogen deficiency bone loss
  - Evolution's way of mobilizing calcium for the neonate
- **Hot flashes**
  - Are they an accident of evolution?

The menopause transition: An evolutionary perspective

- Vaginal lubrication and libido
  - Are unnecessary once a woman is no longer reproductively competent. Evolution does not care about sexual pleasure.
- Glandular breast tissue
  - No longer needed once a woman is done nursing her young
- Increased body fat
  - A useful adaptation to deal with the energy requirements of nursing a neonate as fat is the most efficient energy source
- Estrogen deficiency bone loss
  - Evolution's way of mobilizing calcium for the neonate
- **Hot flashes**
  - I doubt it but I don't know why they are conserved.

Acknowledgments

The MGH SWAN Staff

- Sherri-Ann M. Burnett-Bowie, MD
- Robert M. Neer, MD
- Hang Lee, PhD
- Jason Wyland, PA
- Claudia Chae, MD
- Hadine Joffe, MD
- Laura Chappell-Campbell, BA
- Kathryn Faloba, BA
- Catherine Sullivan, BA
- Erin Donnelly, BA
- Laura Flynn, BA

The SWAN Bone Committee

- Robert M. Neer, MD
- Sarah E. Brockwell, PhD
- Gail A. Greendale, MD
- MaryFran Sowers, PhD
- Bruce Ettinger, MD
- Jane A. Cauley, PhD
- Janet Johnston, PhD
- Michelle Danielson, PhD
- Joan C. Lo, MD

Acknowledgments

The Study of Women's Health Across the Nation (SWAN) has grant support from the National In[illegible] Aging (NIA), the N[illegible] of Research o[illegible] 12535; AG012531; [illegible] content of this pres[illegible] necessarily represent t[illegible]