MAYO CLINIC | School of Continuous Professional Development

19TH ANNUAL

WOMEN'S HEALTH UPDATE 2023

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MAYO CLINIC | School of Continuous Professional Development

CARDIOVASCULAR HEALTH AT MIDLIFE AND MENOPAUSE

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DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

- Nothing to disclose

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

All relevant financial relationships have been mitigated.

ALARMING FACTS:

- CVD remains the leading killer of women in US
  - Only half of women know CVD is their #1 killer, that is down to one-third in Black and Hispanic women
- 1 woman dies every 80 seconds = 1,080 per day = 400,000 per/yr

<u>Unequal Standards of Care</u>:

- Women are more likely to die in the year following a heart attack than a man
- Women are 50% more likely to be given the wrong diagnosis of a heart attack
- 64% of women who die of sudden heart disease have no prior symptoms

CDC.gov – Heart Disease Facts
www.womensheartalliance.org

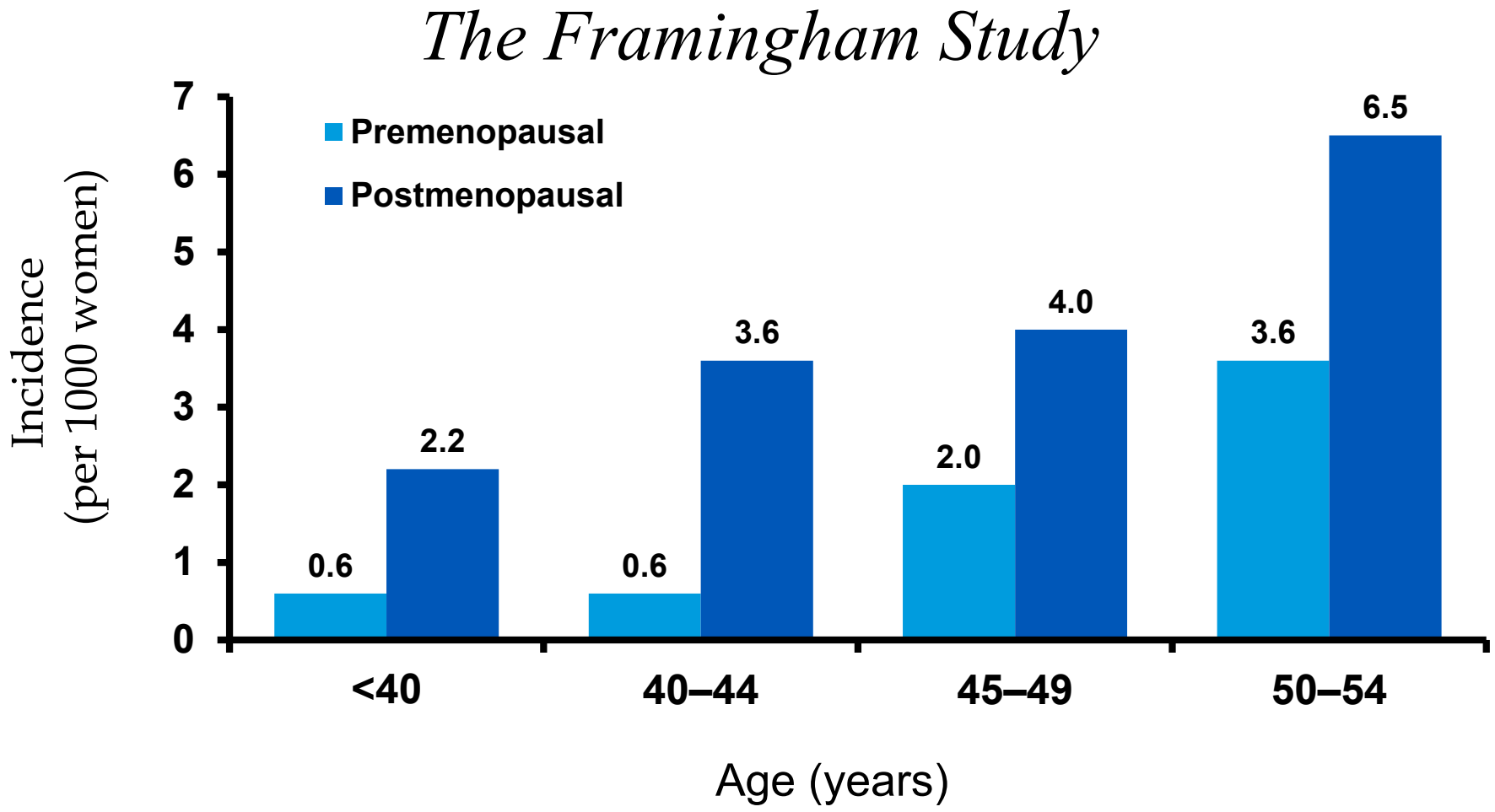
MENO-CARD
Women's Cardiovasculars Risk at Midlife

- The menopause transition is a period of accelerated CVD risk.
- SWAN study demonstrated that lipoproteins (total cholesterol, LDL-C, and apolipoprotein B levels) increase dramatically from the year before to the year after the FMP. This is independent of the effect of aging alone.
- Adverse changes in body fat deposition and increases in metabolic syndrome risk have been related to the menopause transition independently of aging.
- Only 7% of women during the menopause transition report a physical activity level that matches the current recommendation, and <20% consistently maintain a healthy eating diet.

El Khoudary S. et al. Circulation 2020;142:e506-e532.

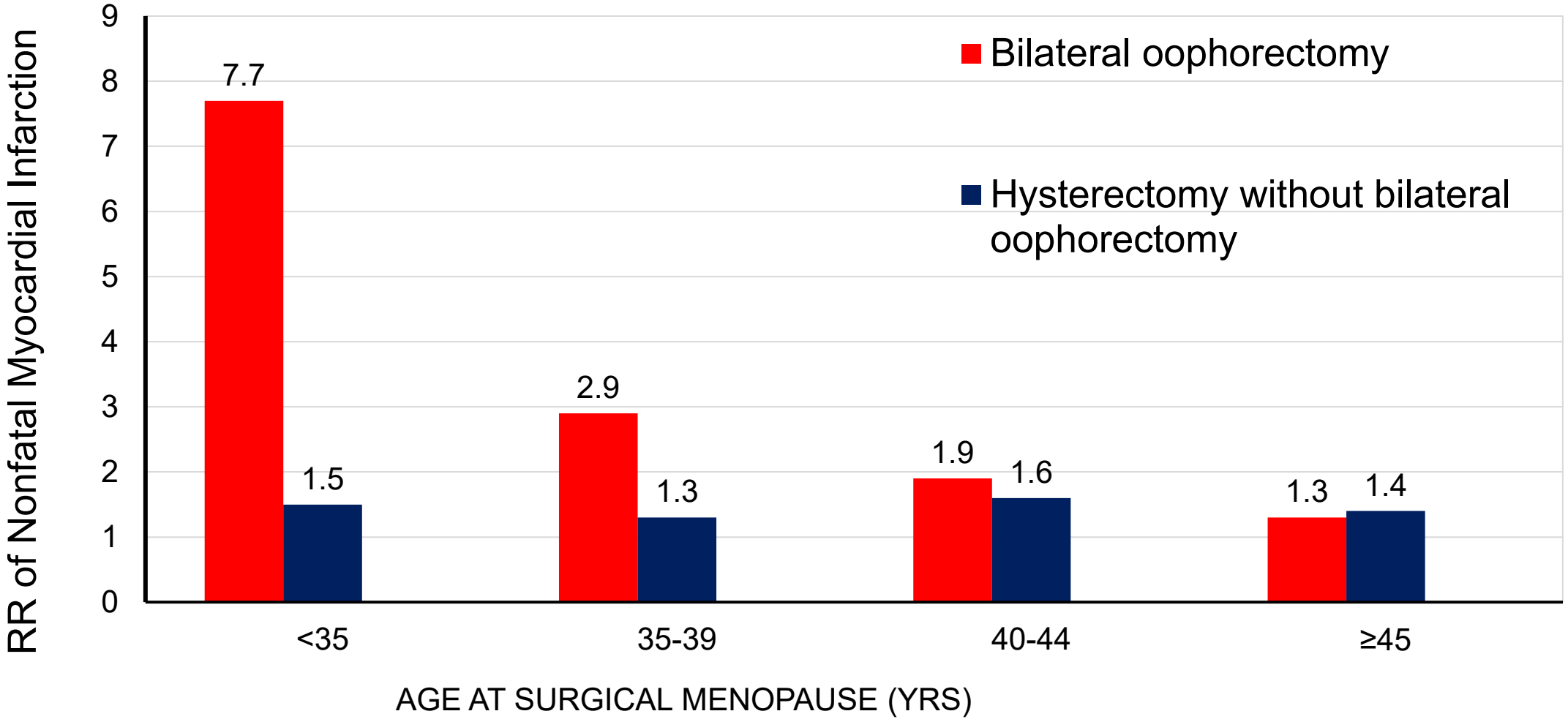
Menopause Characteristics Relevant to CVD Risk

INCIDENCE OF CVD: RELATION TO MENOPAUSE STATUS



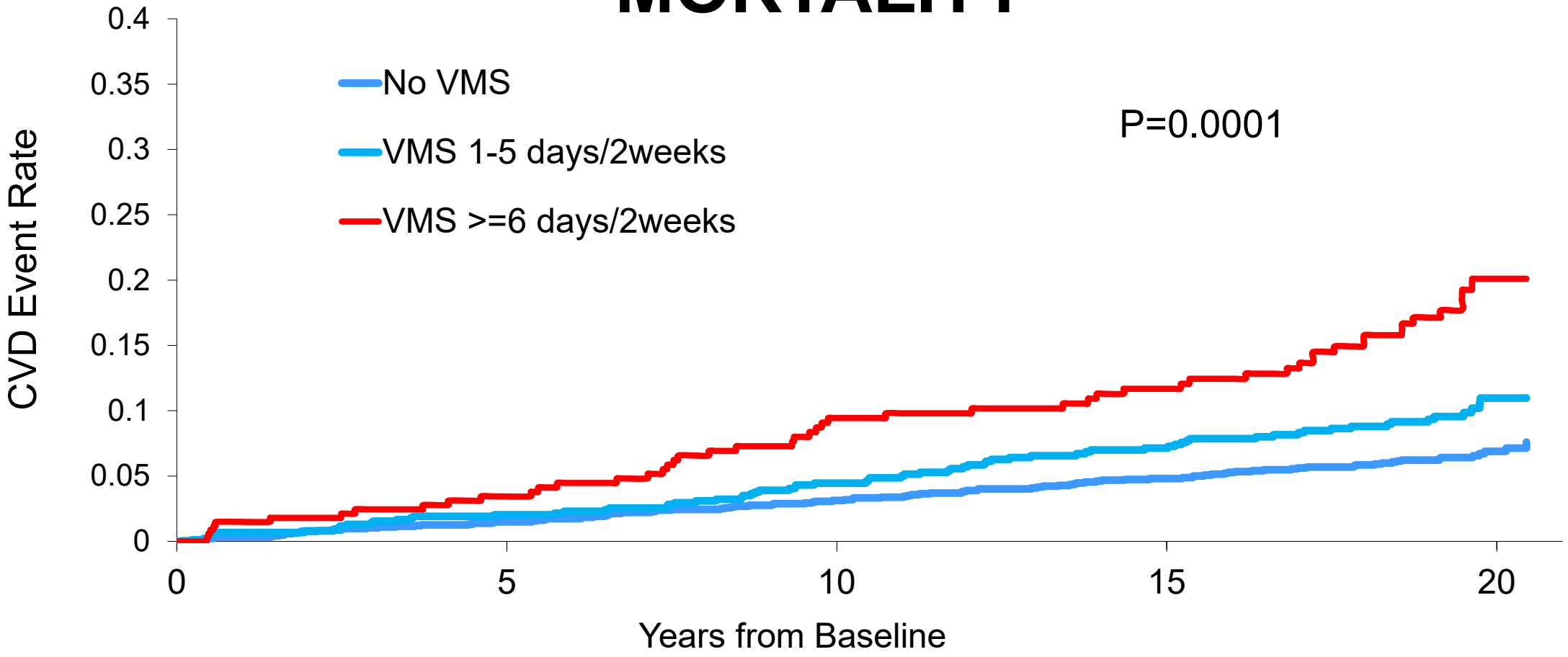
Kannel WB, et al. *Ann Intern Med.* 1976;85:447-52.

SURGICAL MENOPAUSE: THE YOUNGER THE WOMEN, THE GREATER THE CONCERN



Rosenberg L, et al, Am J Obstet Gynecol, 1981;139:47-51

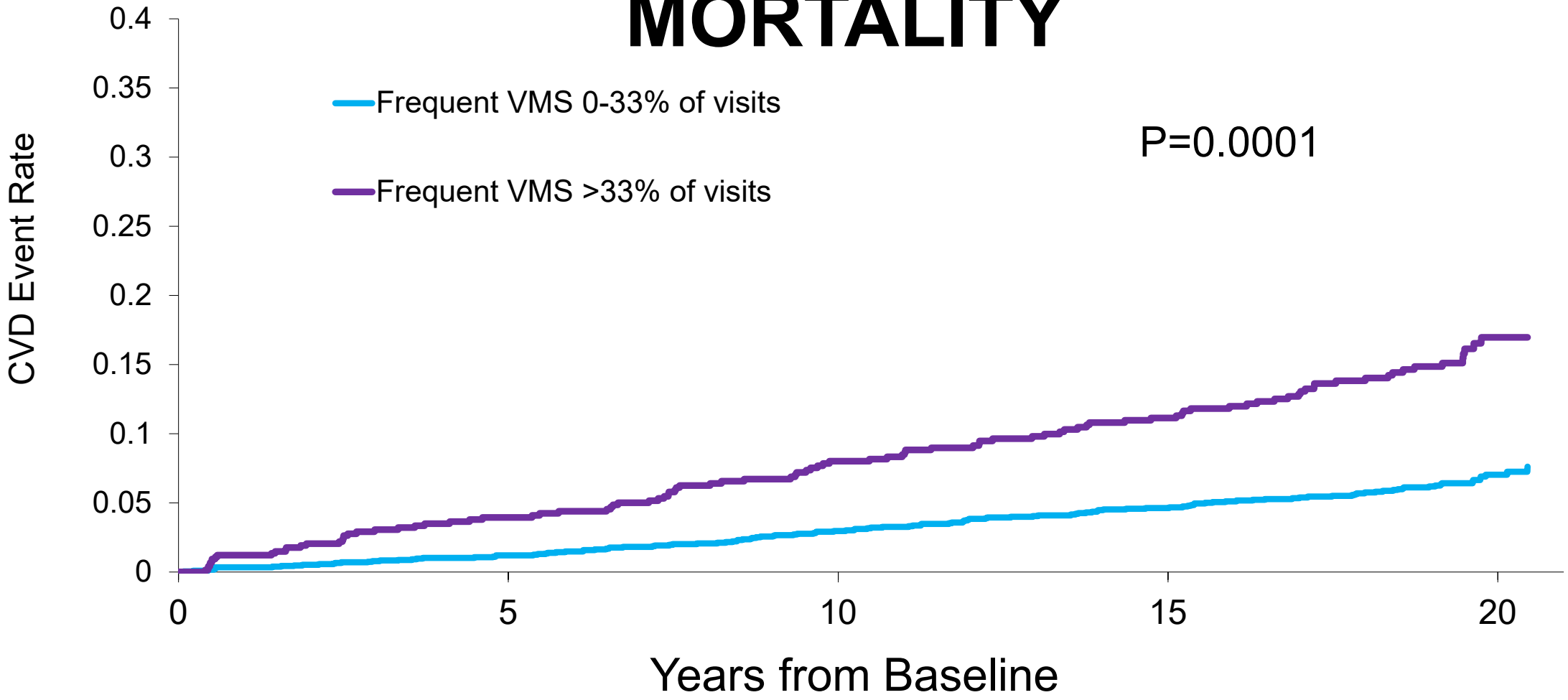
SWAN: MORE VASOMOTOR SYMPTOMS LINKED TO INCREASED CVD / CVD MORTALITY



N=3083, 231 events

Thurston et al., JAHA,2021;10:e017416

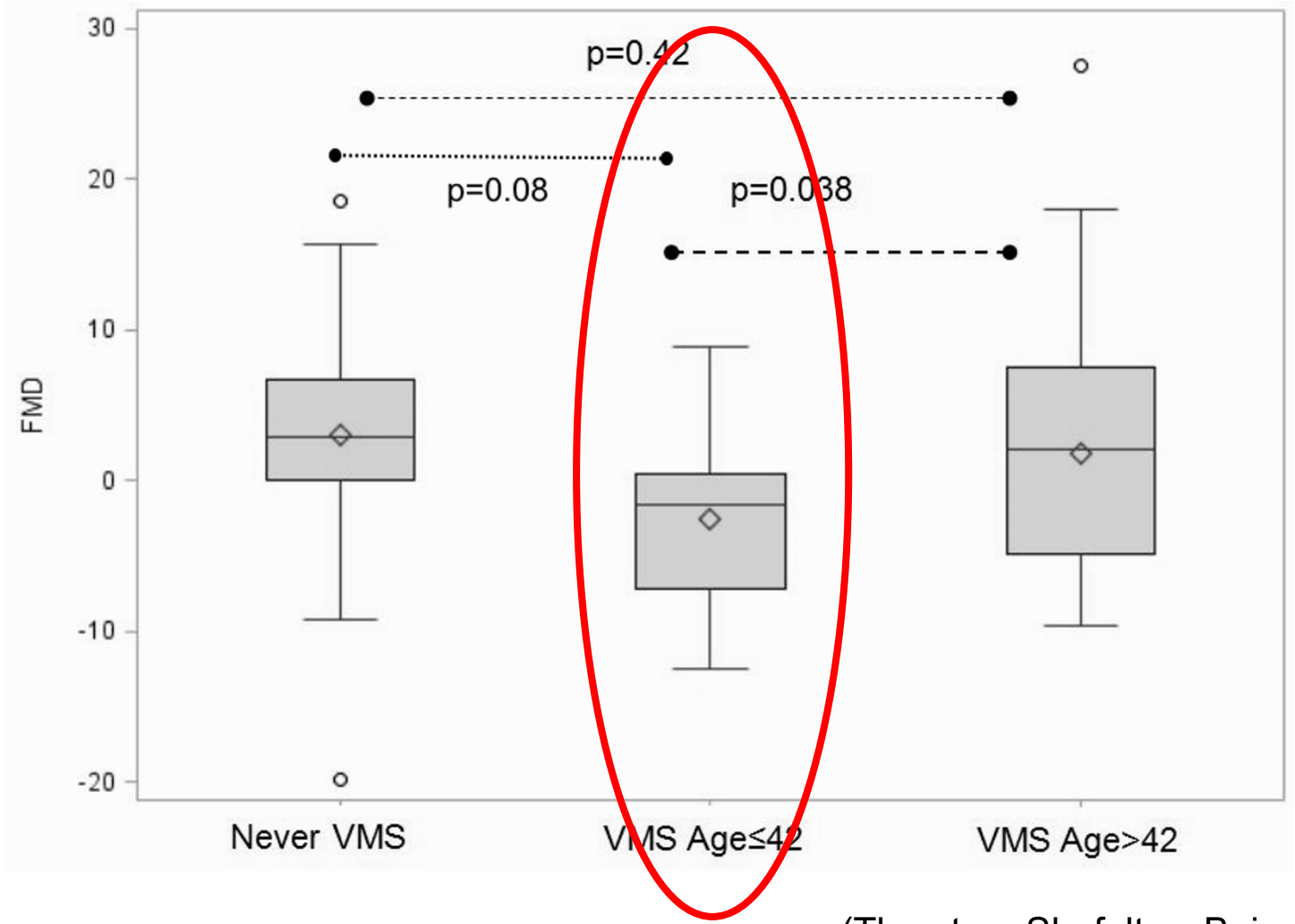
SWAN: MORE PERSISTENT VMS LINKED TO GREATER RISK OF CVD / CVD MORTALITY



N=3083, 231 events

Thurston et al., JAHA,2021;10:e017416

WISE: Early Onset VMS Associated with Lower FMD



(Thurston, Shufelt,….Bairey Merz, 2017, *Menopause*)

Summary of Menopause Characteristics

Menopause characteristics	CVD Risk
Earlier age at natural menopause	↑CVD
BSO during the premenopausal period	↑ CVD
Hysterectomy, regardless of ovarian status	↔
Vasomotor symptoms	↑ CVD risk factors, CVD & endothelial dysfunction

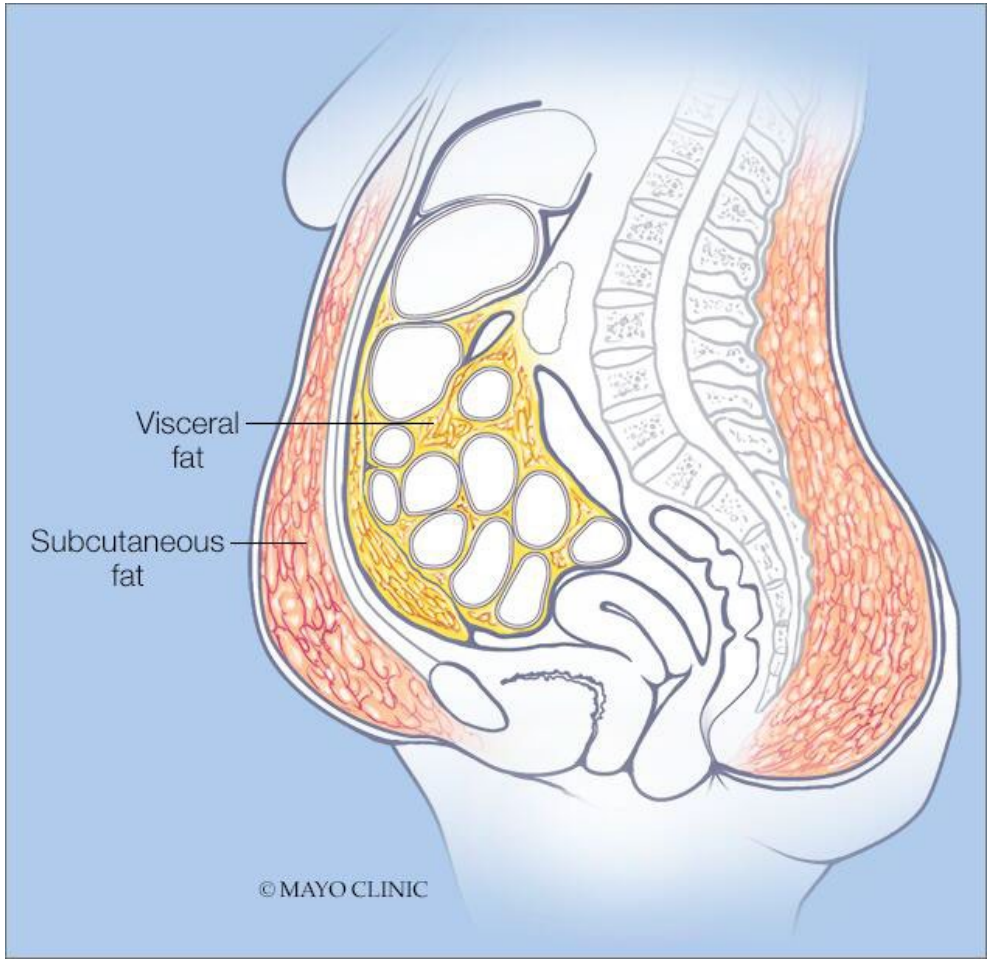
Cardiometabolic changes:

Ovarian aging vs

Chronological aging

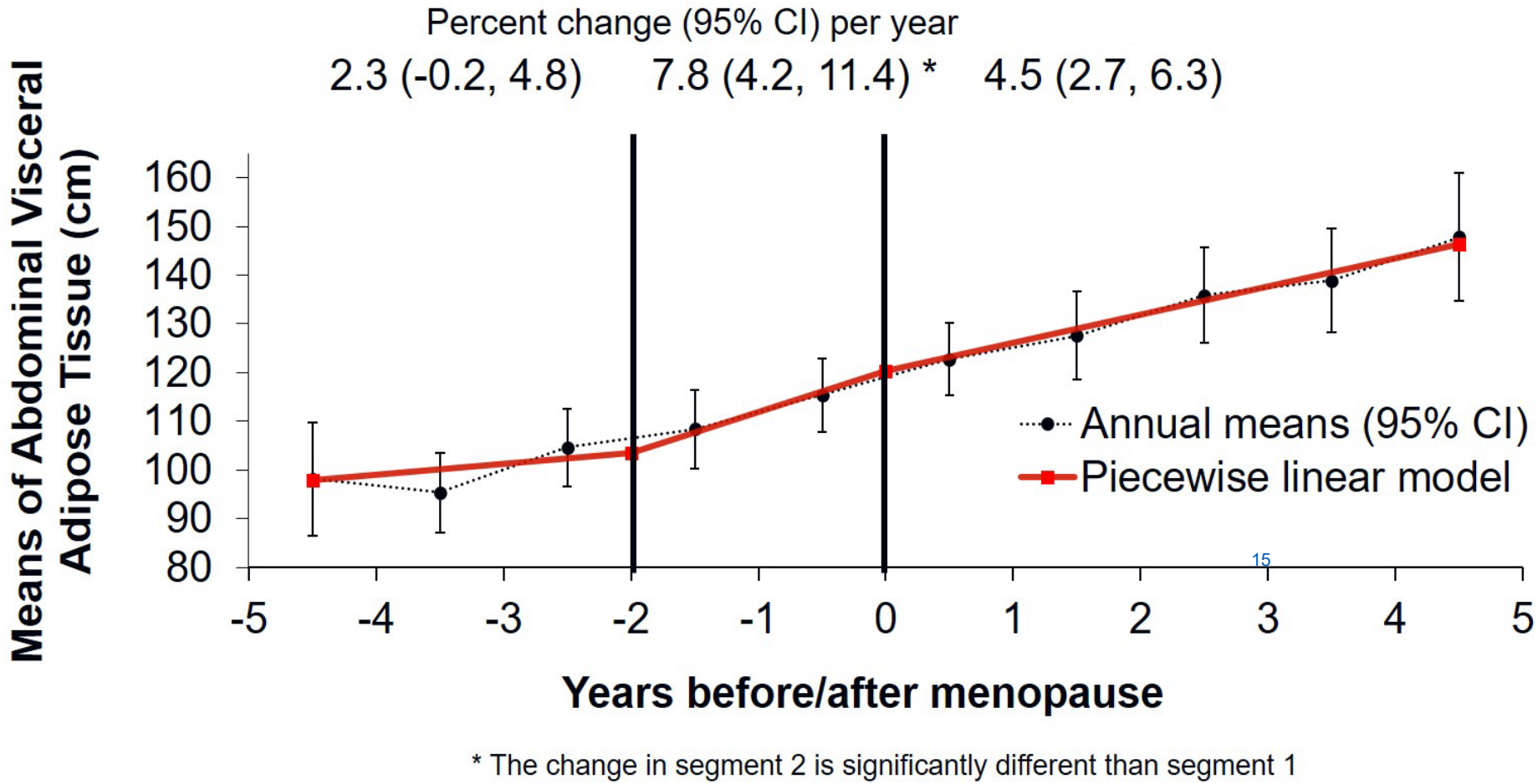
Body Composition and Fat Distribution

- Weight gain is common during midlife → by aging rather than by menopause
- A shift from lean mass to fat mass, with ovarian as well as chronologic aging
- Greater visceral adipose tissue in the abdomen after menopause



Abdulnour J et al. Menopause. 2012 Jul;19(7):760-7.;
Janssen I et al. Obesity (Silver Spring). 2010;18(3):604-10
Lovejoy JC et al. Int J Obes (Lond). 2008;32(6):949-58;
Sowers et al. JCM 2007; 92:895-901

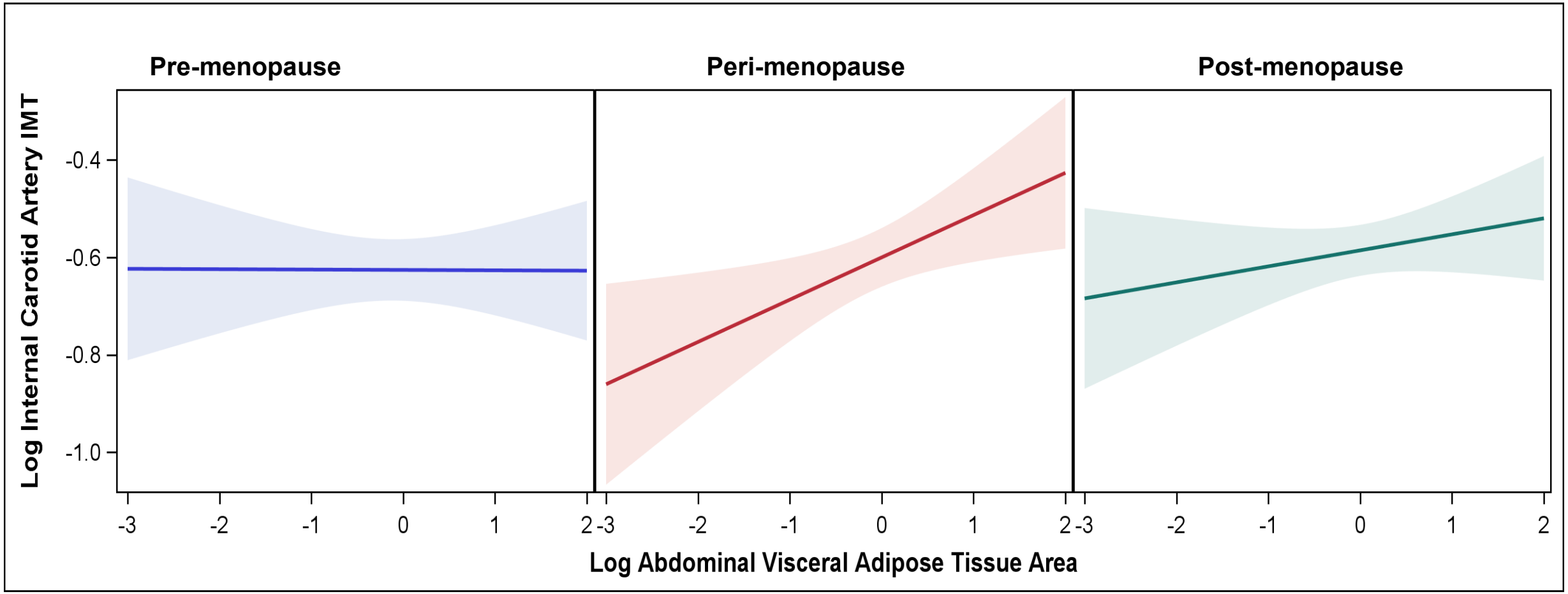
Abdominal Visceral Fat Accelerates in Perimenopause



* The change in segment 2 is significantly different than segment 1

Samargandy S et al. Menopause. 2021 Mar 1;28(6):626-633.

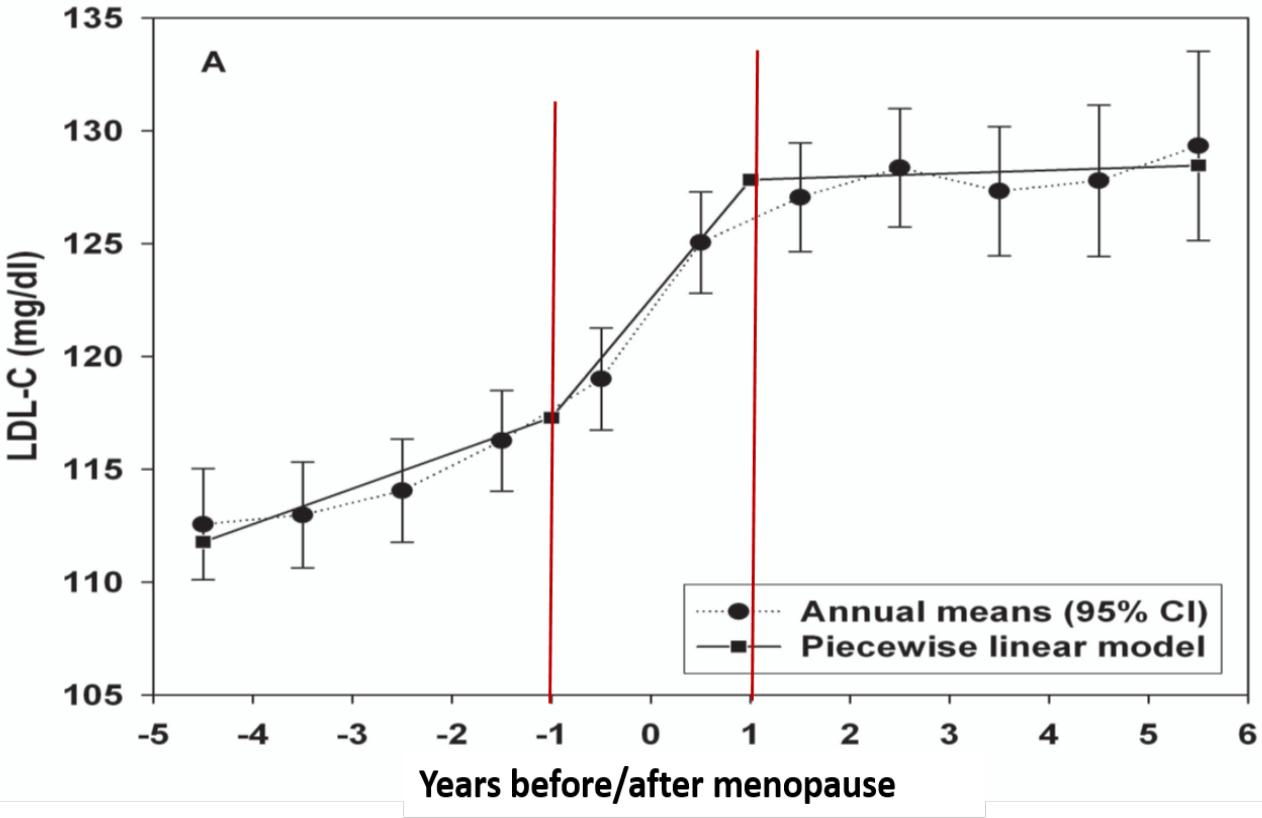
Shift of Fat Distribution



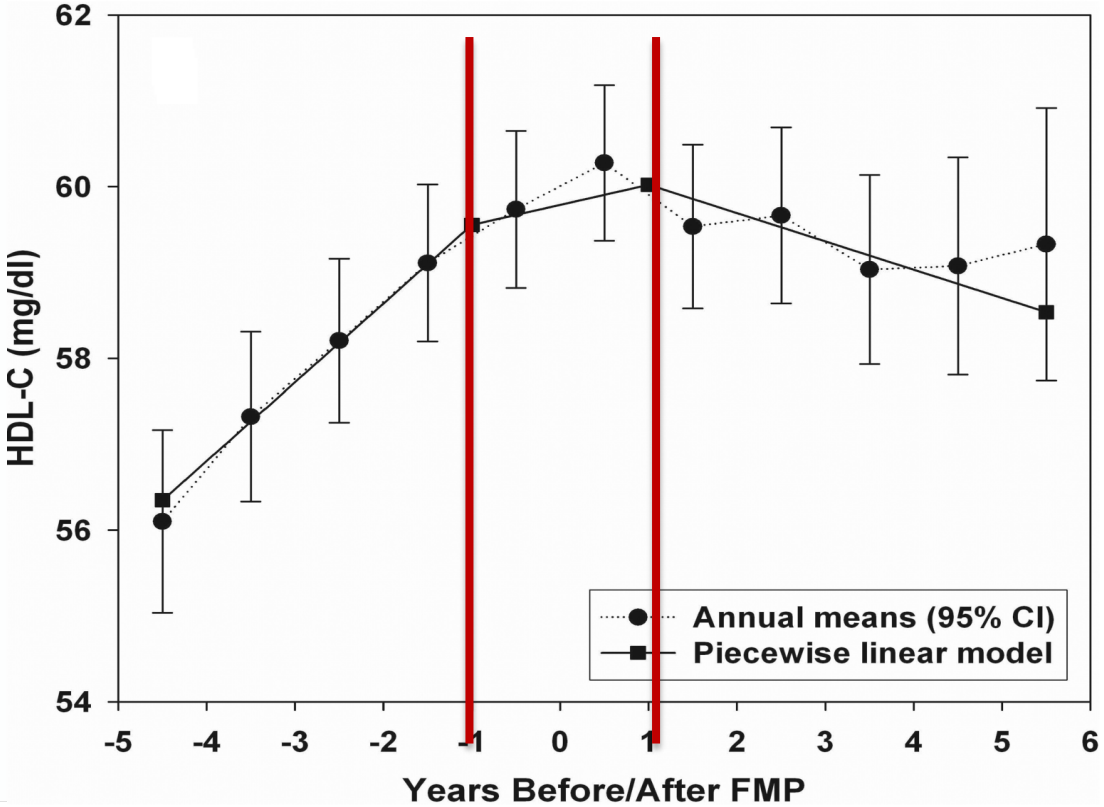
Samargandy S, et al. Menopause. 2021 Mar 1;28(6):626-633

Cholesterol and Menopause Transition

LDL-C



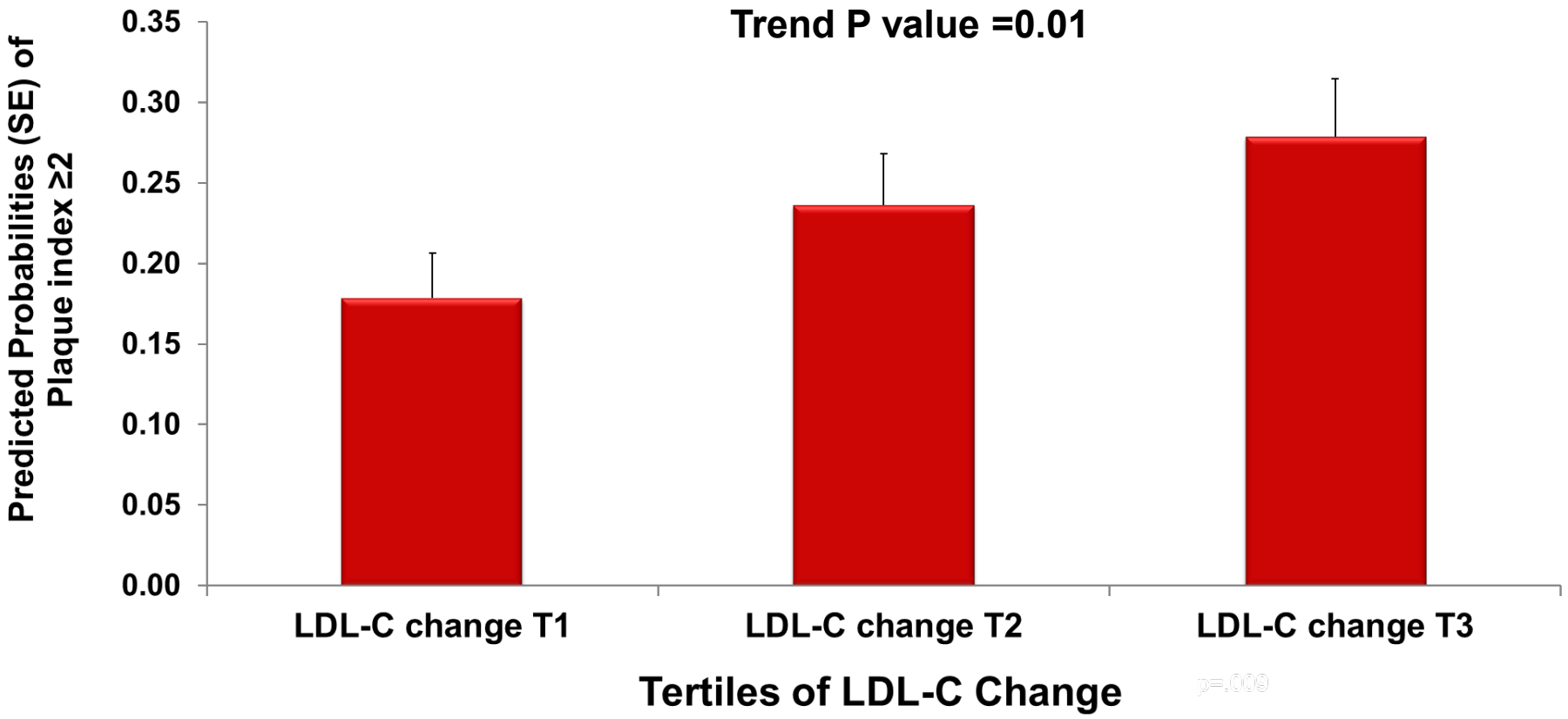
HDL-C



N=1054, age:42-57 at baseline, 10 annual examination over the MT

Matthews et al. J Am Coll Cardiol. 2009;54(25):2366-73

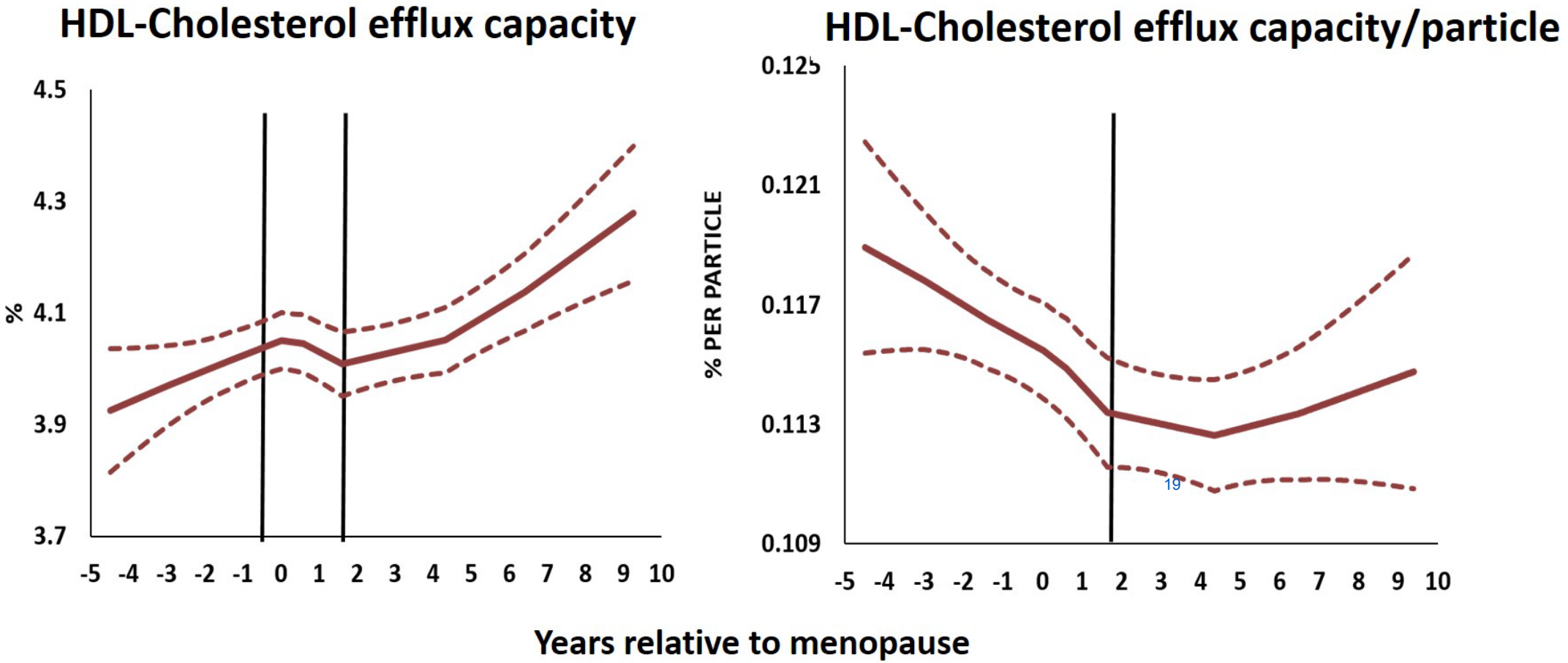
Increase in LDL-C around the Final Menstrual Period is Related to Greater Risk of Carotid Plaque Presence



N=863, age:42-57 at baseline, 8 years around FMP

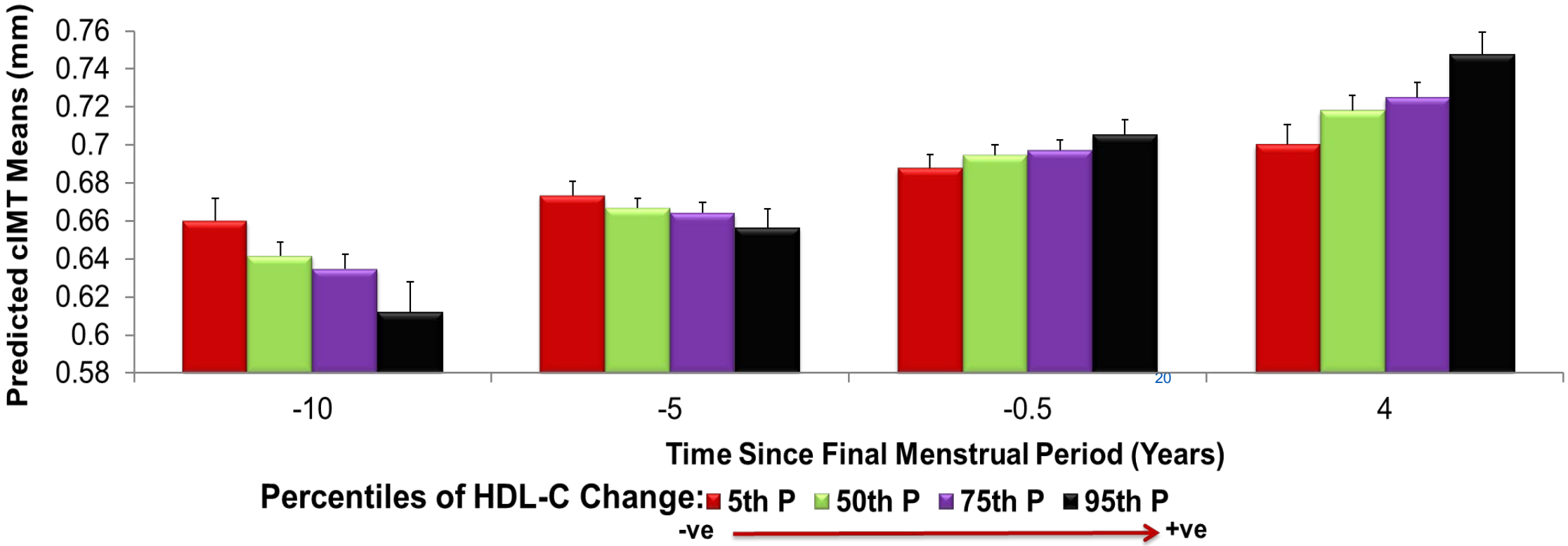
Matthews et al. Stroke. 2017 Jan;48(1):70-76

HDL Function over the Menopause Transition



El Khoudary SR et al. Arterioscler Thromb Vasc Biol. 2021;41(2):951-961.

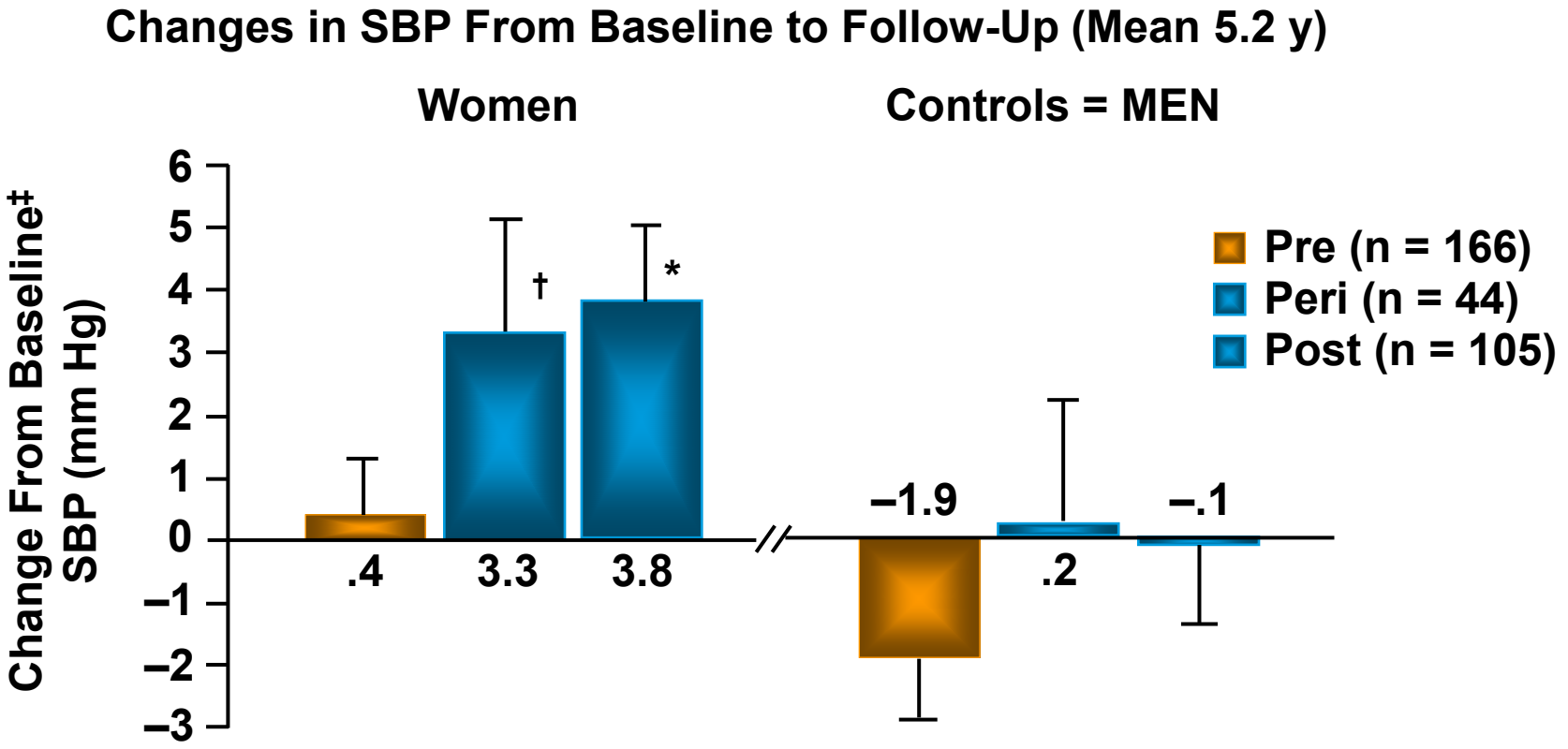
↑HDL-C before Menopause is Associated with ↓ cIMT, Whereas an Increase after Menopause is Associated with ↑ cIMT



N=213, up to 5 scans over 9 years of follow-up

El Khoudary et al. J Clin Lipidol. 2016 Jul-Aug;10(4):962-9.

BLOOD PRESSURE AND MENOPAUSE: AGE OLD DEBATE

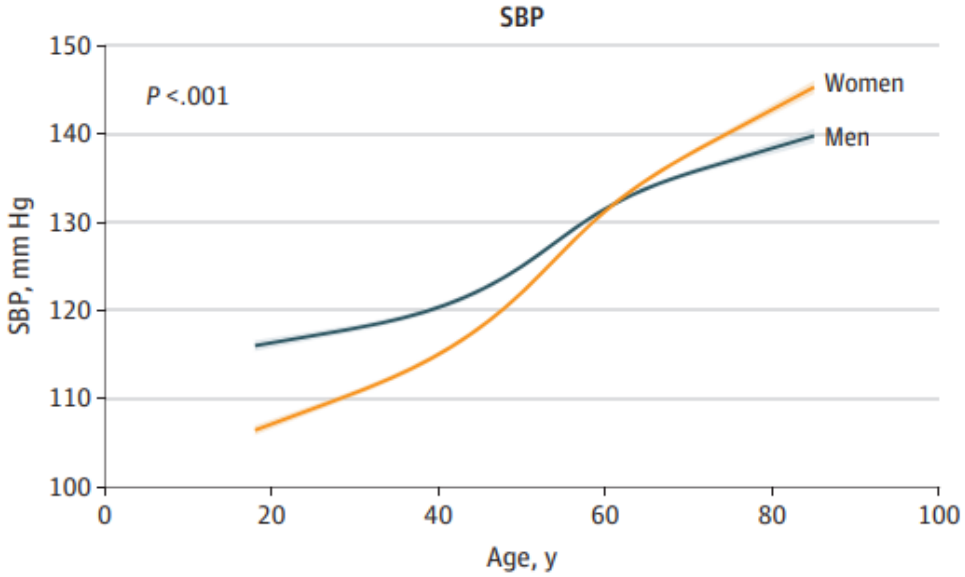


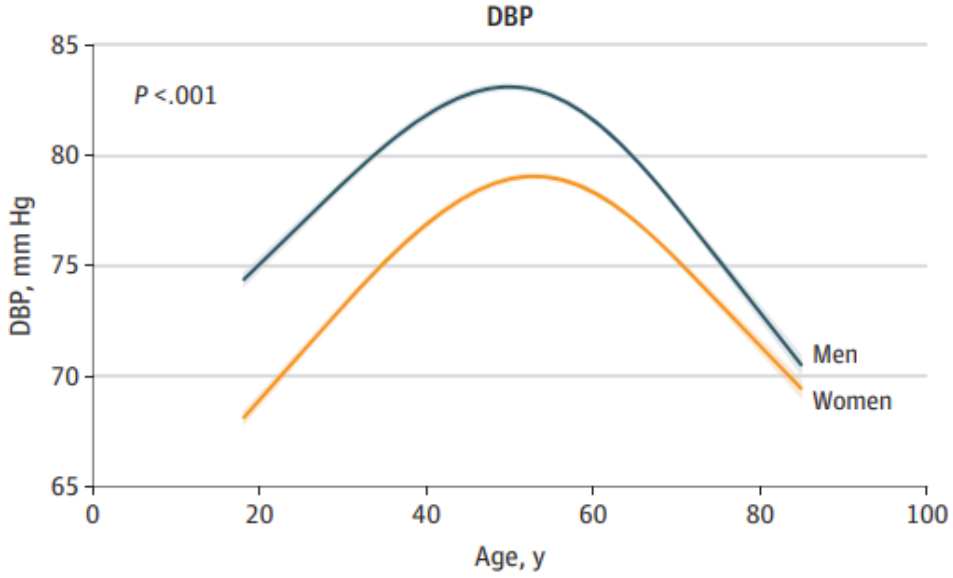
*$P \leq .05$; †$P = .07$. ‡Baseline SBP: Pre = 121.4 ± 1.3 mm Hg; Peri = 122.0 ± 1.8 mm Hg; Post = 126.5 ± 1.7 mm Hg.
Controls were men matched by age and BMI.

Staessen JA, et al. *J Hum Hypertens*. 1997;11:507–514.

BLOOD PRESSURE

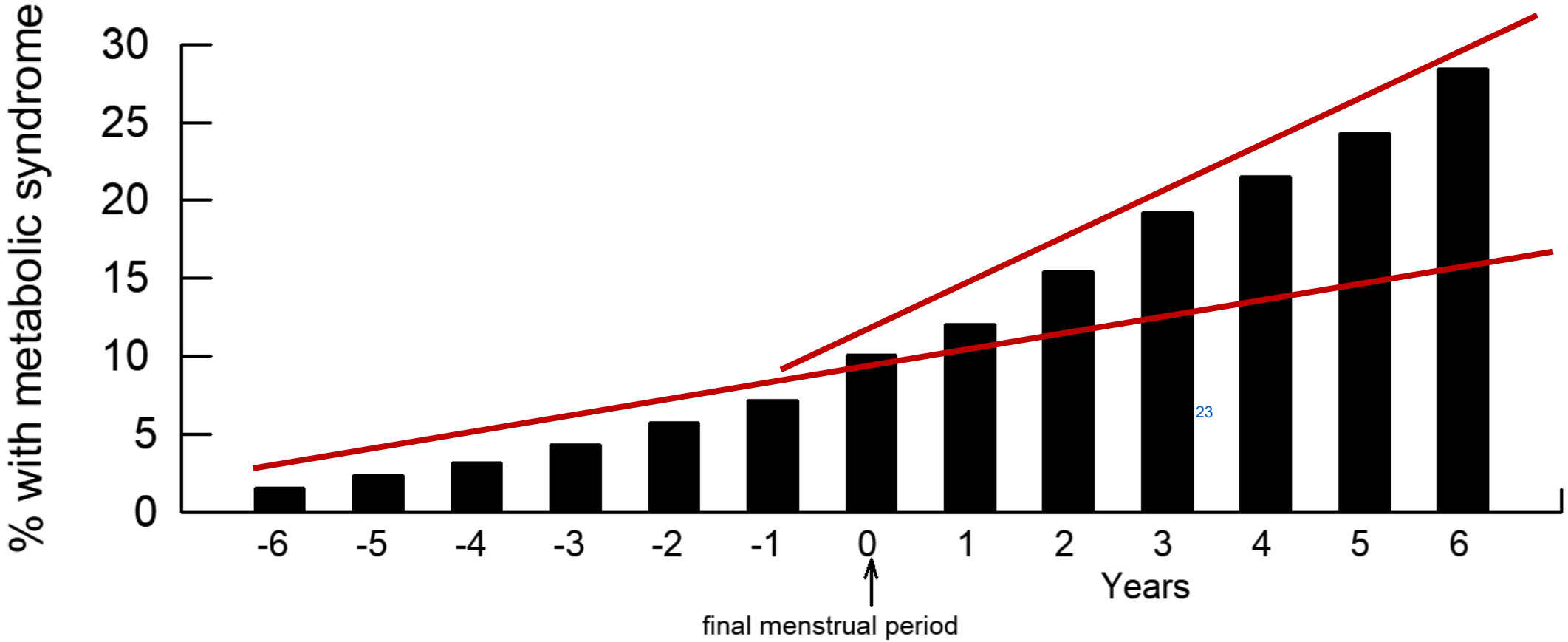
- SWAN has not found an association with menopausal transition and blood pressure beyond age
- Gender differences in BP elevation over the life course
- Women compared to men: BP may be lower in early years but rises more steeply in later years





Hongwei, Ebinger, Bairey Merz, et al. JAMA Cardiol. doi:10.1001/jamacardio.2019.5306

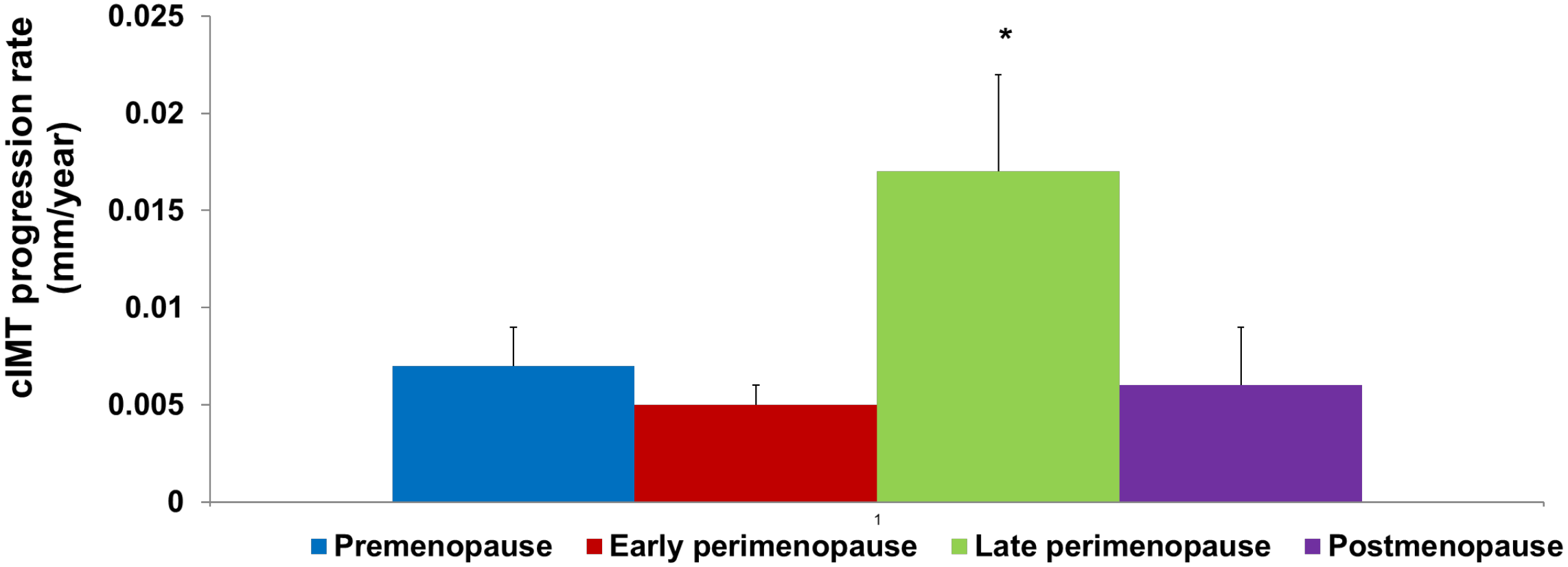
Metabolic Syndrome Increases Over the Menopause Transition



N=949, age 42-52 at baseline, 9 years of follow-up

Janssen et al. Arch Intern Med. 2008 Jul 28;168(14):1568-75.

Progression of Carotid Intima-media Thickness Accelerates in Late Perimenopause (Structural changes)

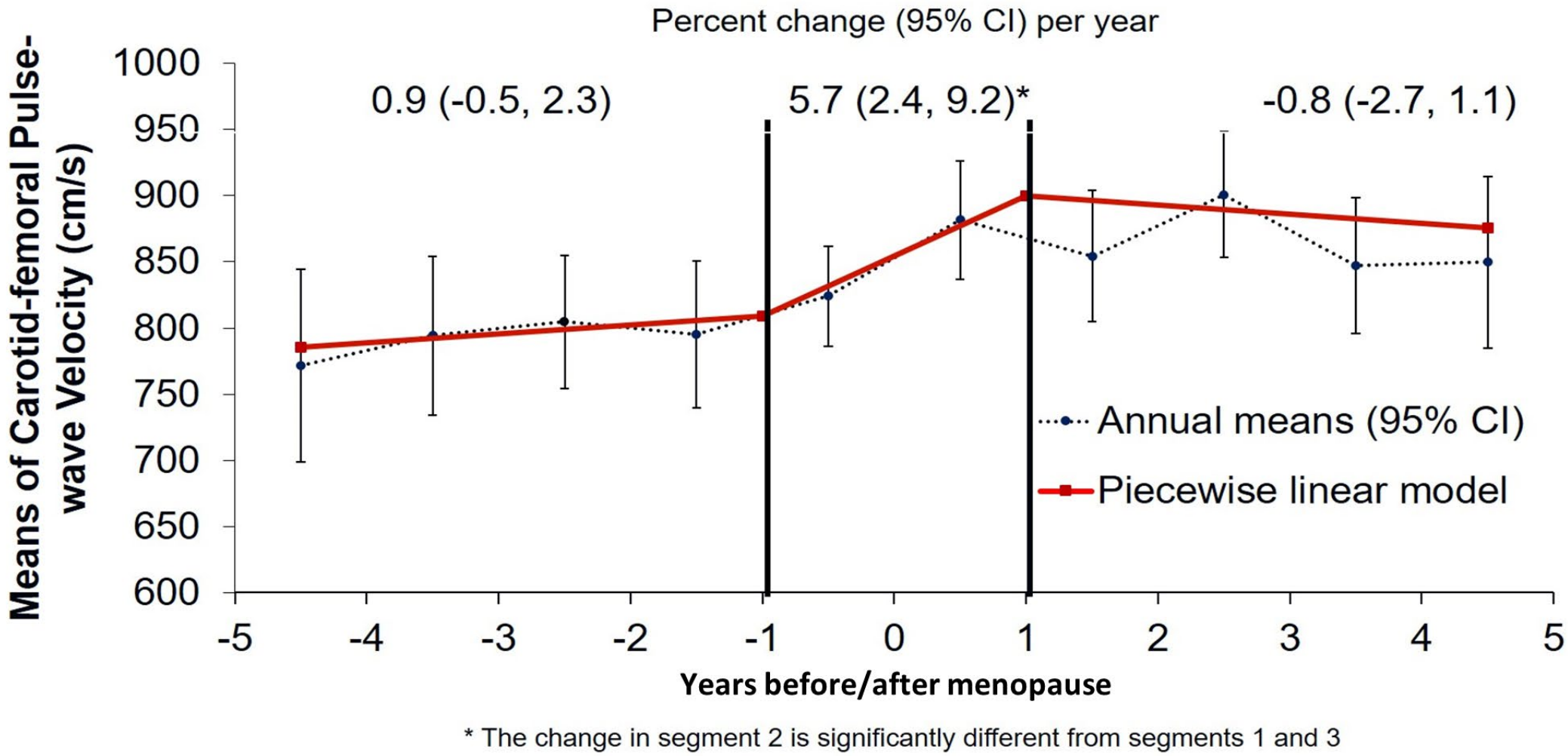


* Adjusted for age and race. Rate of change in late peri- differs from pre- and early peri- menopausal stages, P<0.05

N=249, age:42-57 at baseline, 9 years of follow-up

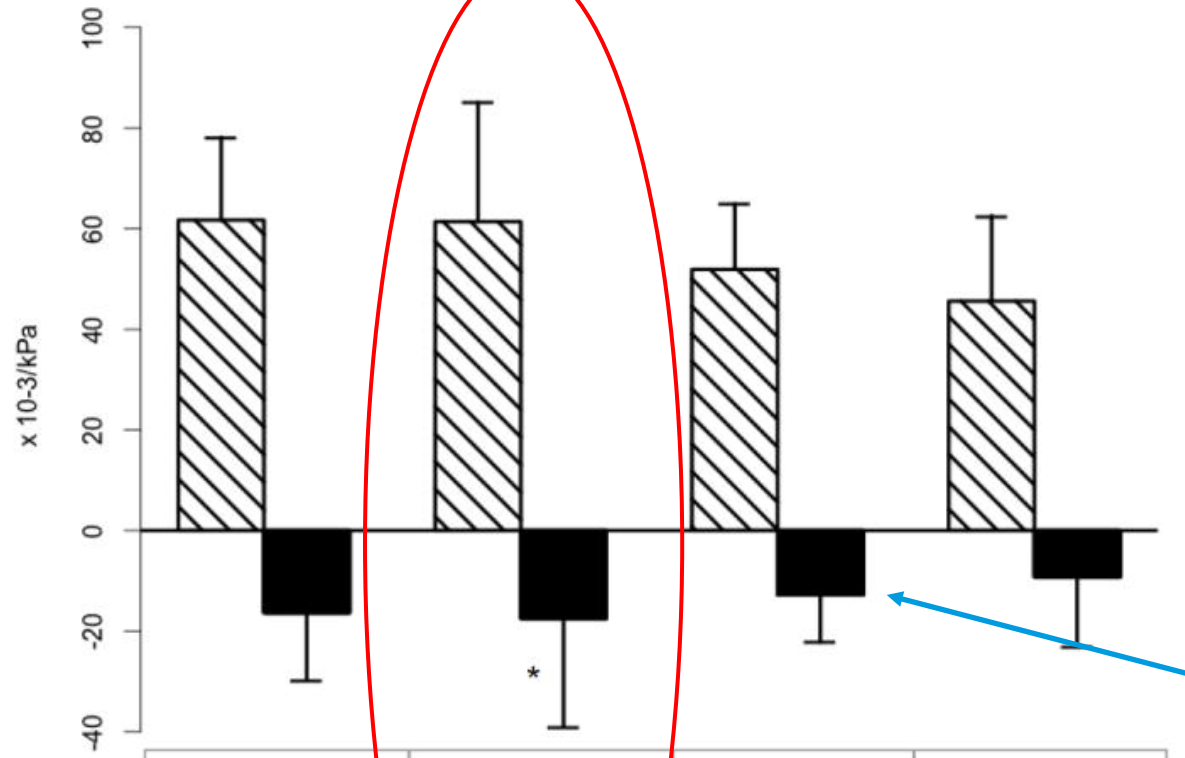
El Khoudary et al. Menopause. 2013 Jan;20(1):8-14.

Progression of Arterial Stiffness Accelerates in Perimenopause (Functional changes)



Samargandy S et al. ATVB. 2020;40:1001-1008.

Arterial distensibility decreases during menopause (Functional changes)



*p=0.016 vs. Post	Pre n=17	Tran/No HT n=23	Tran/HT n=28	Post n=93
Baseline DI	61.7 ± 16.5	61.4 ± 23.7	51.9 ± 13.0	45.6 ± 17.0
3-year ΔDI	-16.4 ± 13.3	-17.5 ± 21.4	-12.8 ± 9.4	-9.3 ± 13.8

Menopausal transition is associated with reduced vascular compliance

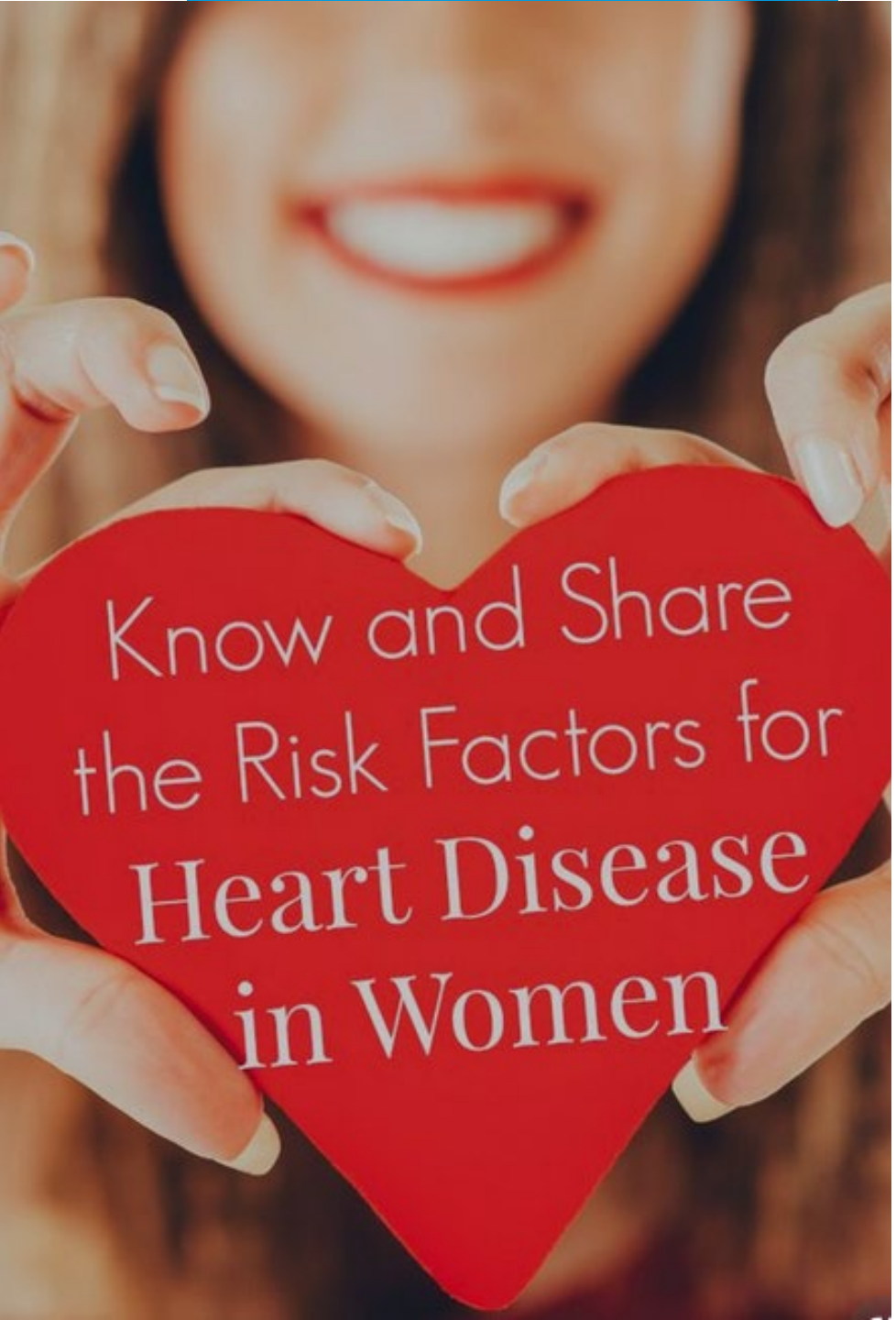
Loss of distensibility has been associated with the development of CVD, hypertension, and stroke in healthy individuals.

HT appears to have an impact on arterial distensibility only if taken during the MT period of menopause

Shufelt CL et al. Menopause. 2016;23(2):150-7.

Summary of Cardiometabolic Changes

MORE RELATED TO:	Ovarian aging	Chronological aging
Central/visceral fat increases and lean muscle mass decreases	X	
Weight gain, Reduced energy expenditure		X
Metabolic syndrome risk	X	
Blood Pressure		X
Decrease in HDL and function	X	
Increases in lipids (LDL-C and apolipoprotein B)	X	
Vascular Remodeling and Function	X	



SUMMARY

- Awareness that Menopause transition is a period of symptomatic, hormonal, and physiological changes relevant to CVD risk
- Lipids, vascular health, metabolic syndrome, visceral adiposity are associated with ovarian aging and an aggressive prevention-based approach for women at MT, to include
- Research should focus on women who are undergoing the MT & consider how to integrate women's reproductive aging into the study design