Exercise, Hormones, and Disease Prevention

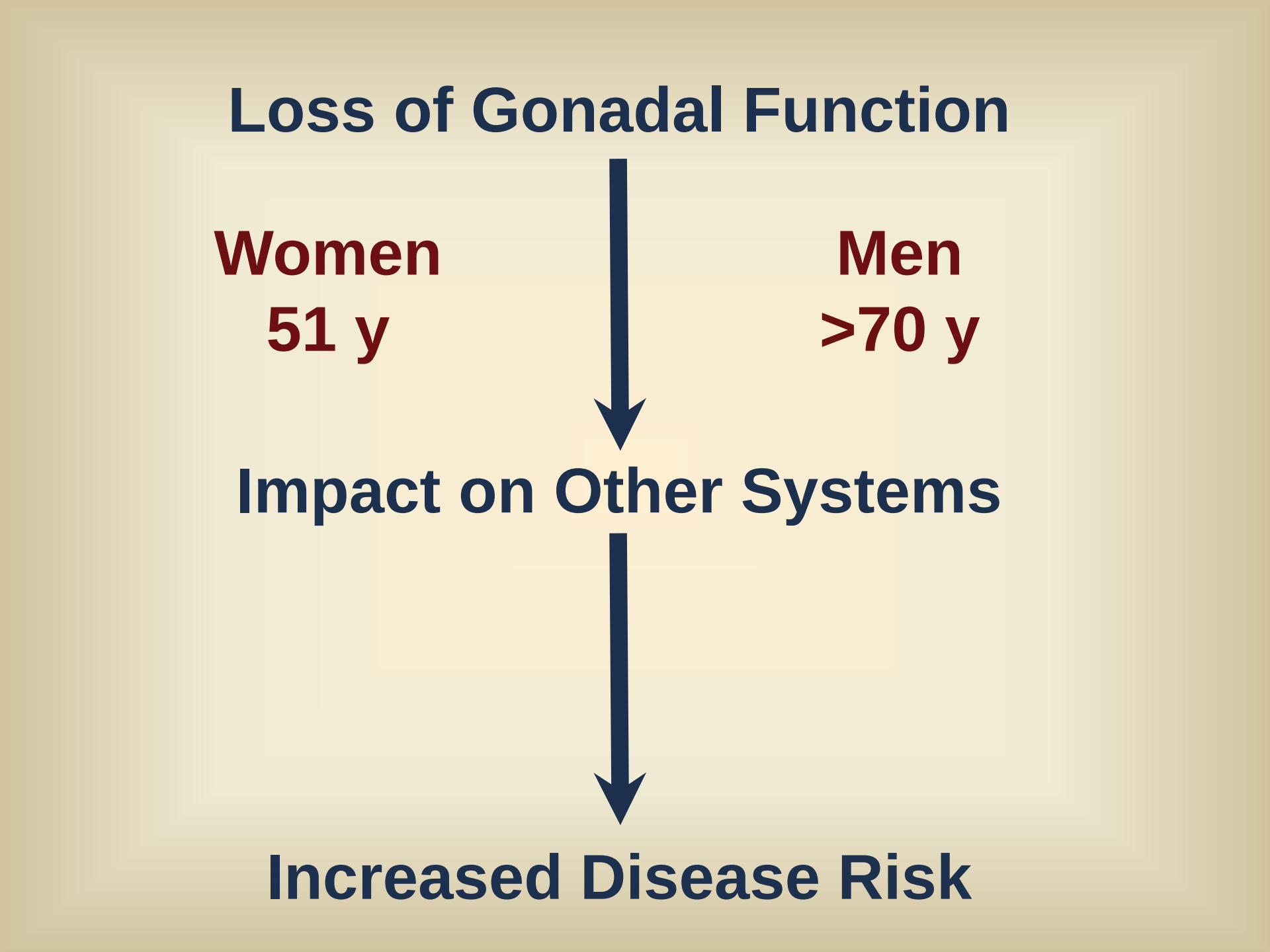
Wendy M Kohrt, PhD
Professor of Medicine and Obstetrics & Gynecoloegy
Division of Geriatric Medicine
Nancy Anschutz Chair in Women's Health Research
University of Colorado – Anschutz Medical Campus

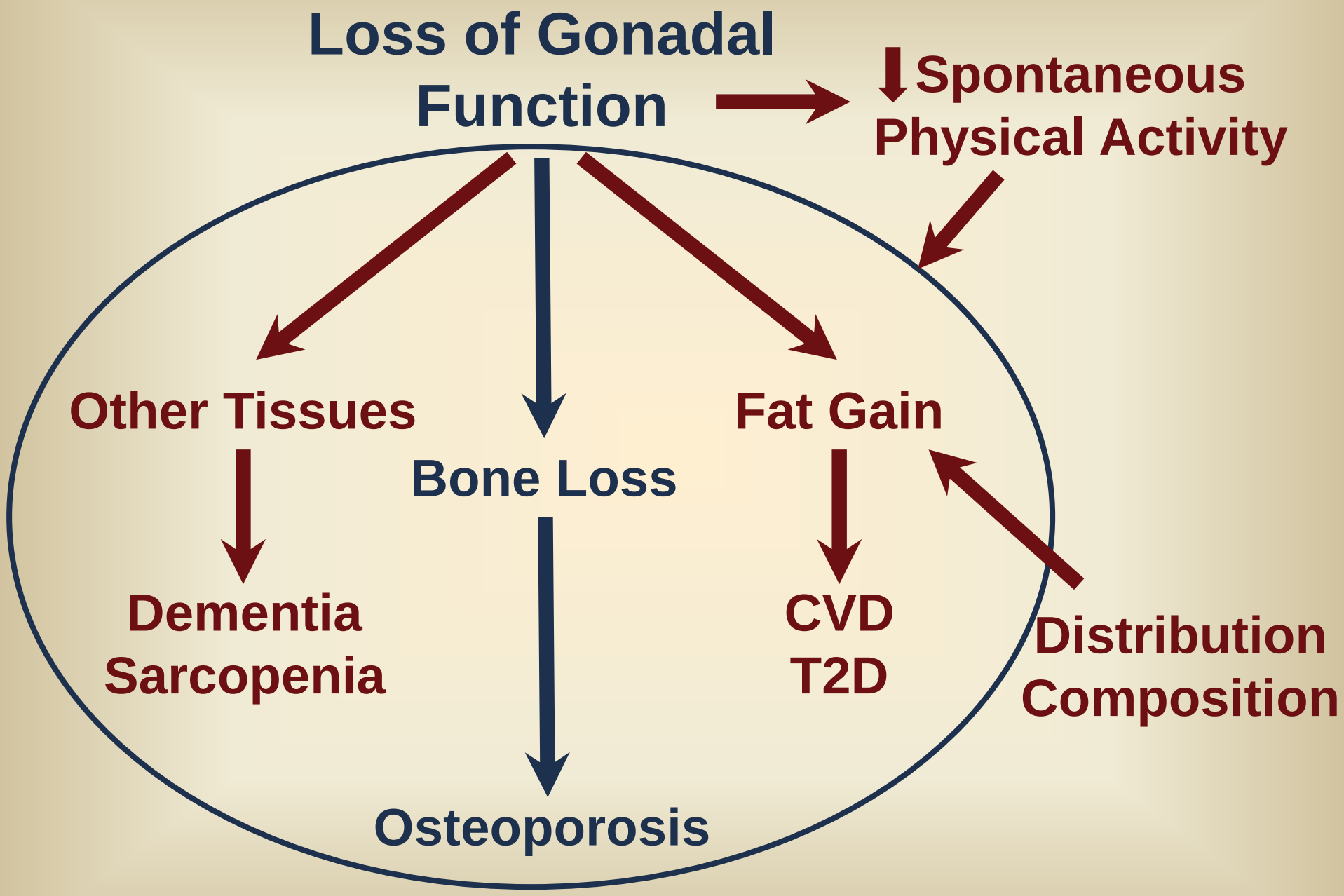
Outline

1. Potential consequences of the loss of gonadal function – working model

2. Metabolic consequences of the loss of estrogens – preclinical
   - Mitigation by exercise

3. Metabolic consequences of the loss of estrogens – clinical
   - Mitigation by exercise


Loss of Gonadal Function
Women
51 y
Men
>70 y
Impact on Other Systems
Increased Disease Risk


Loss of Gonadal Function
Spontaneous Physical Activity
Other Tissues
Bone Loss
Fat Gain
Dementia
Sarcopenia
Osteoporosis
CVD
T2D
Distribution
Composition

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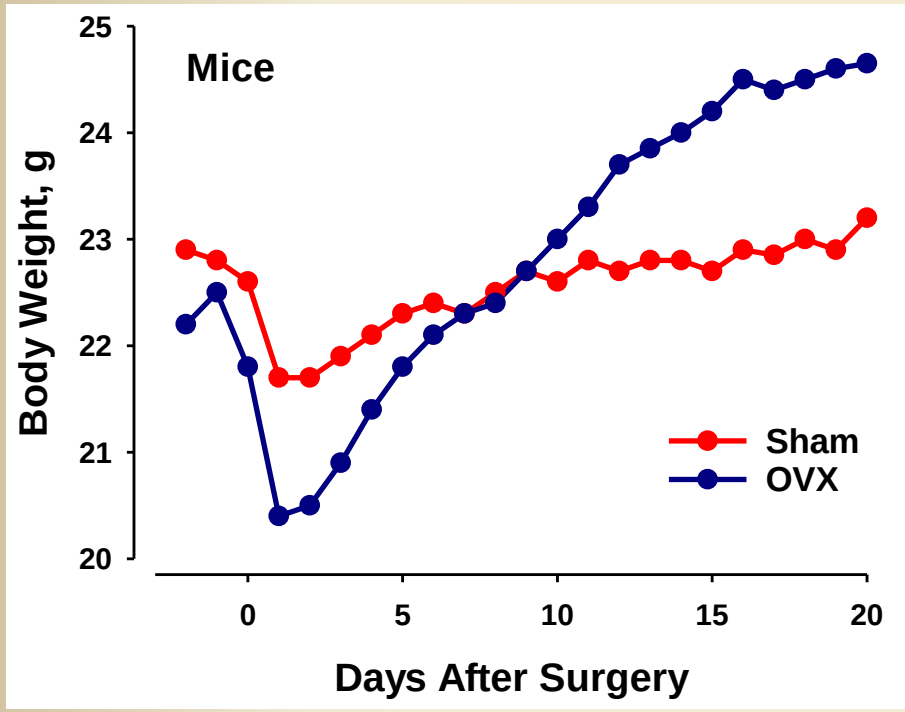
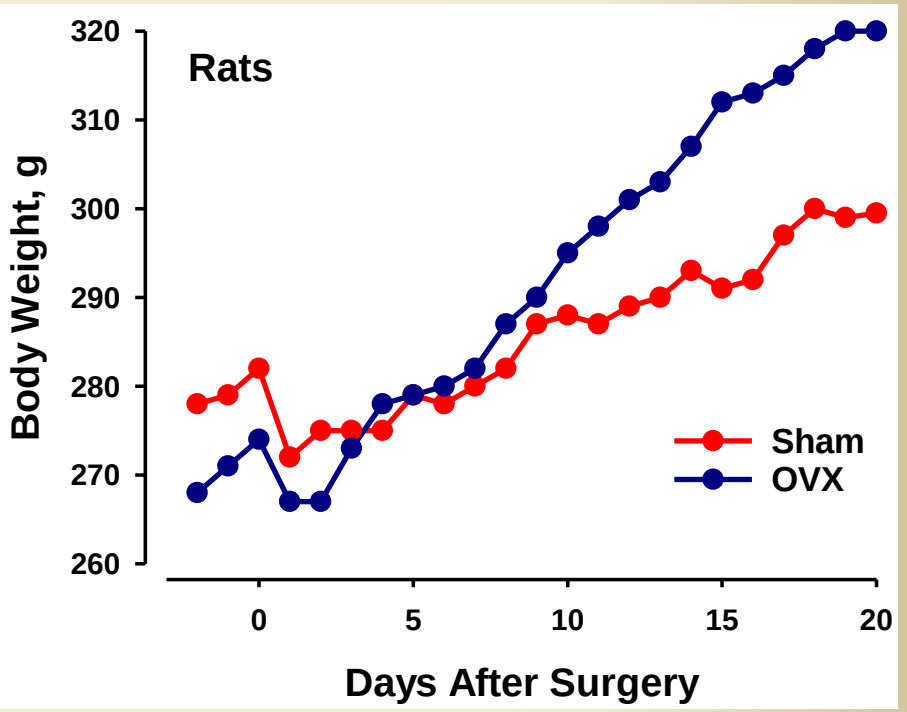
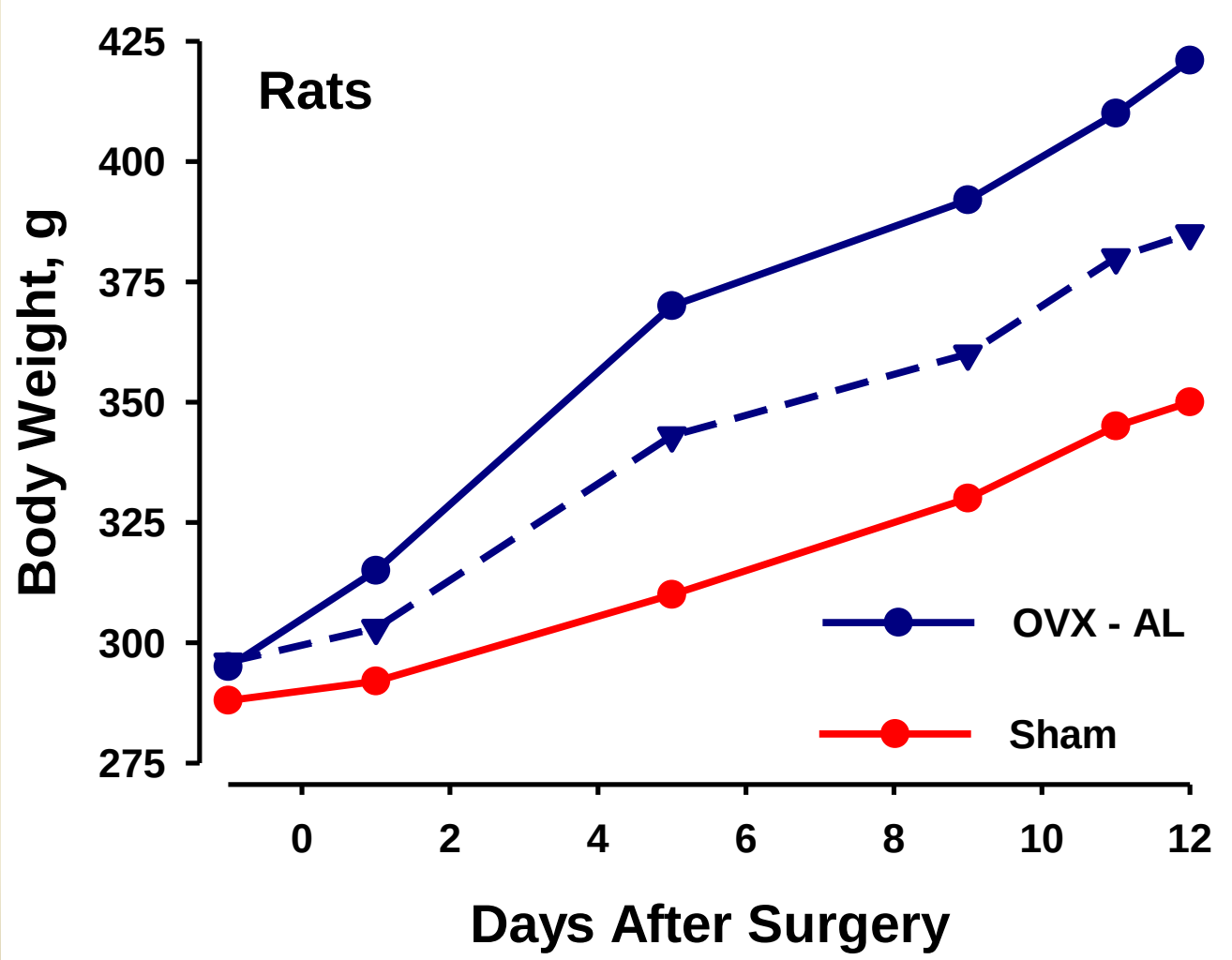
Body Weight in Mice and Rats OVX vs Sham





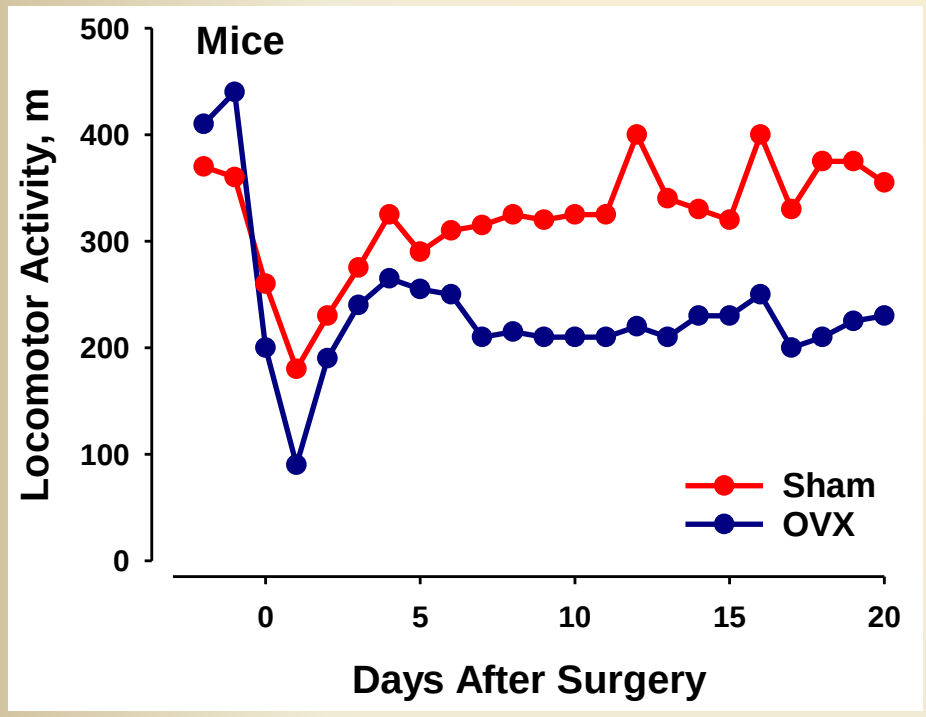
Adapted from: Witte MM et al. *General Compar Endocrinol* 166:520, 2010

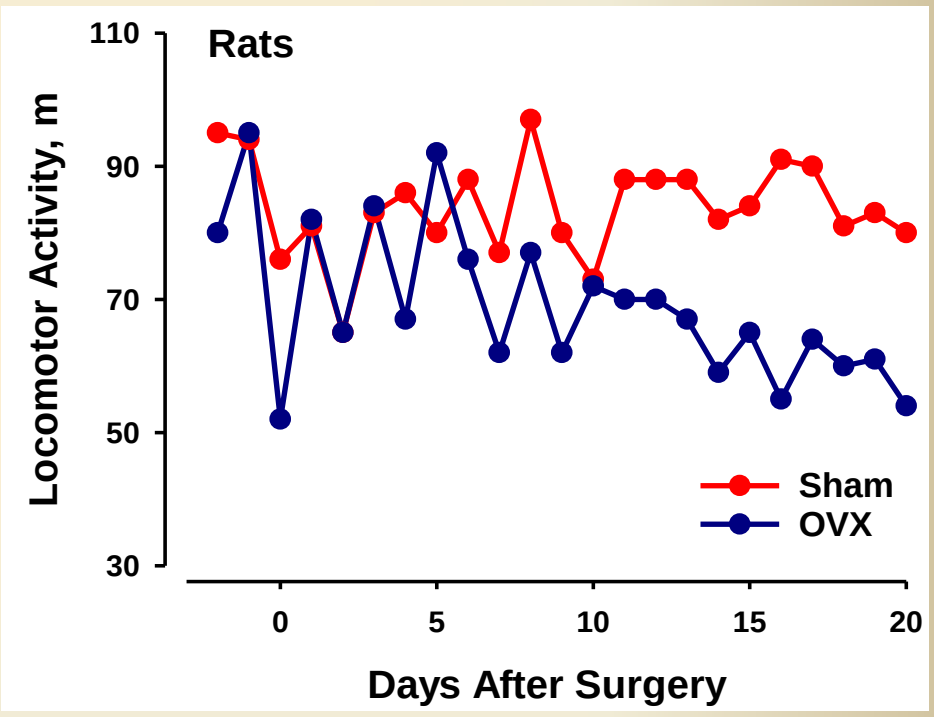
Body Weight in Rats
OVX-AL vs OVX-PF vs Sham



Adapted from: Witte MM et al. *General Compar Endocrinol* 166:520, 2010

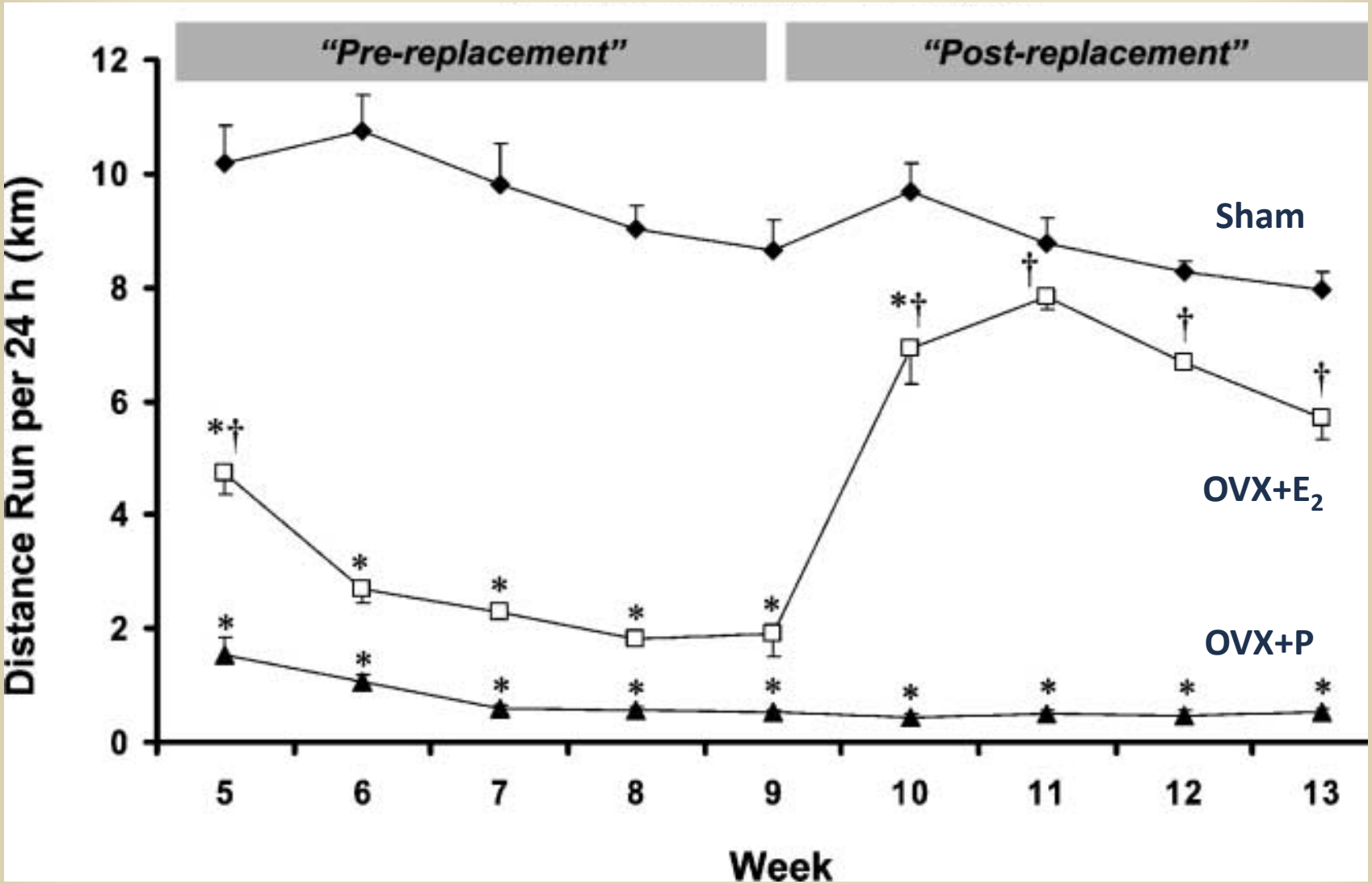
Locomotor Activity in Mice and Rats OVX vs Sham





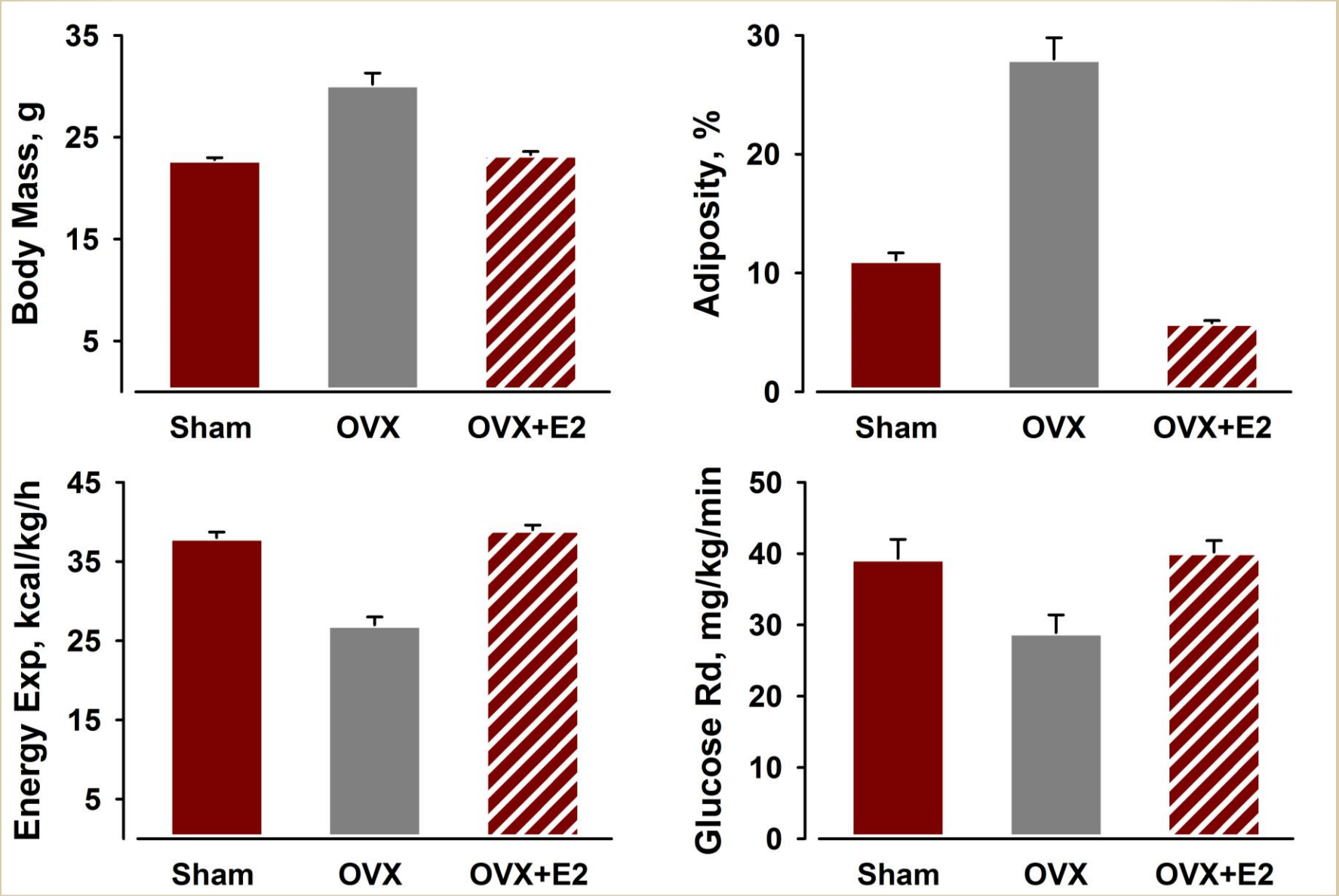
Adapted from: Witte MM et al. *General Compar Endocrinol* 166:520, 2010

Wheel-running Distance in Sham and OVX Mice



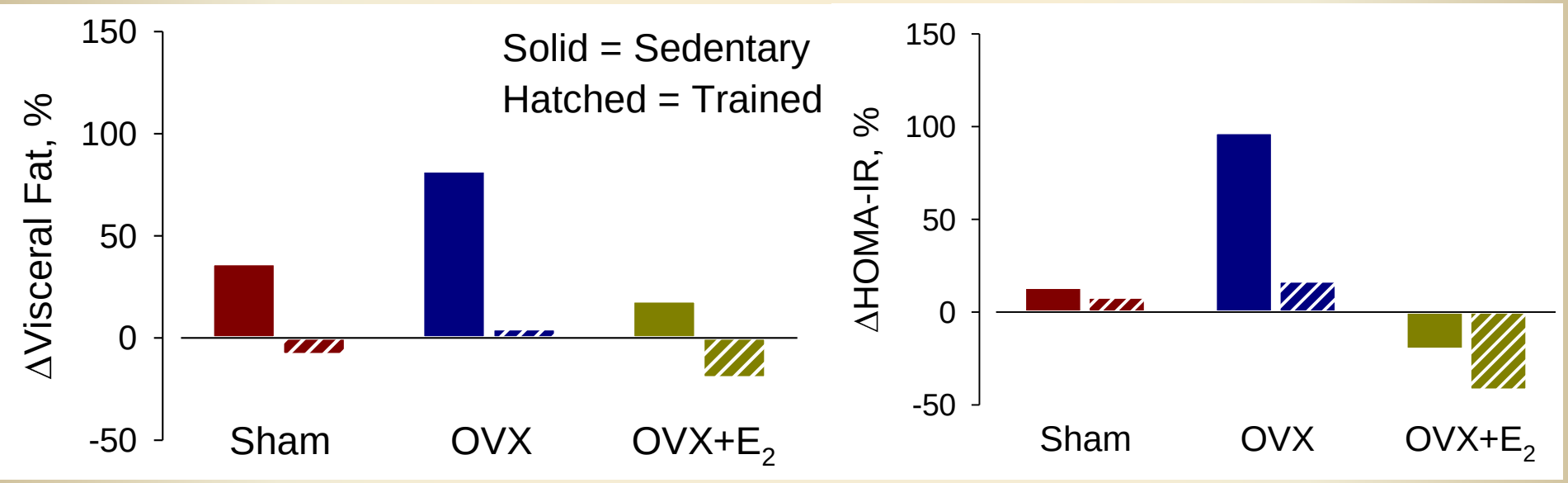
From: Gorzek JF et al. *Med Sci Sports Exerc* 39:248, 2007

Effects of OVX and E_2 Add-back in Mice



From: Camporez JP et al. *Endocrinol* 154:1021, 2013

Effects of Programmed Exercise on Adiposity and Insulin Action



Adapted from: Pighon A et al. *Climacteric* 13:238, 2010

Effects of OVX:

- decreased physical activity
- decreased resting metabolic rate
- increased energy intake (some species)
- increased abdominal fat gain
- metabolic dysfunction

Prevented by E_2 treatment and by exercise

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Ovarian Hormone Suppression ($GnRH_{AG}$; 5 months) With Placebo or E_2

2-group model	$GnRH_{AG}$+PL n=35	$GnRH_{AG}$+E_2 n=35
Age, y	36 ± 2	35 ± 2
Wt, kg	74 ± 3	76 ± 3
BMI, kg/m^2	28 ± 2	28 ± 1
FM, kg	28 ± 2	28 ± 3
FFM, kg	46 ± 1	48 ± 1

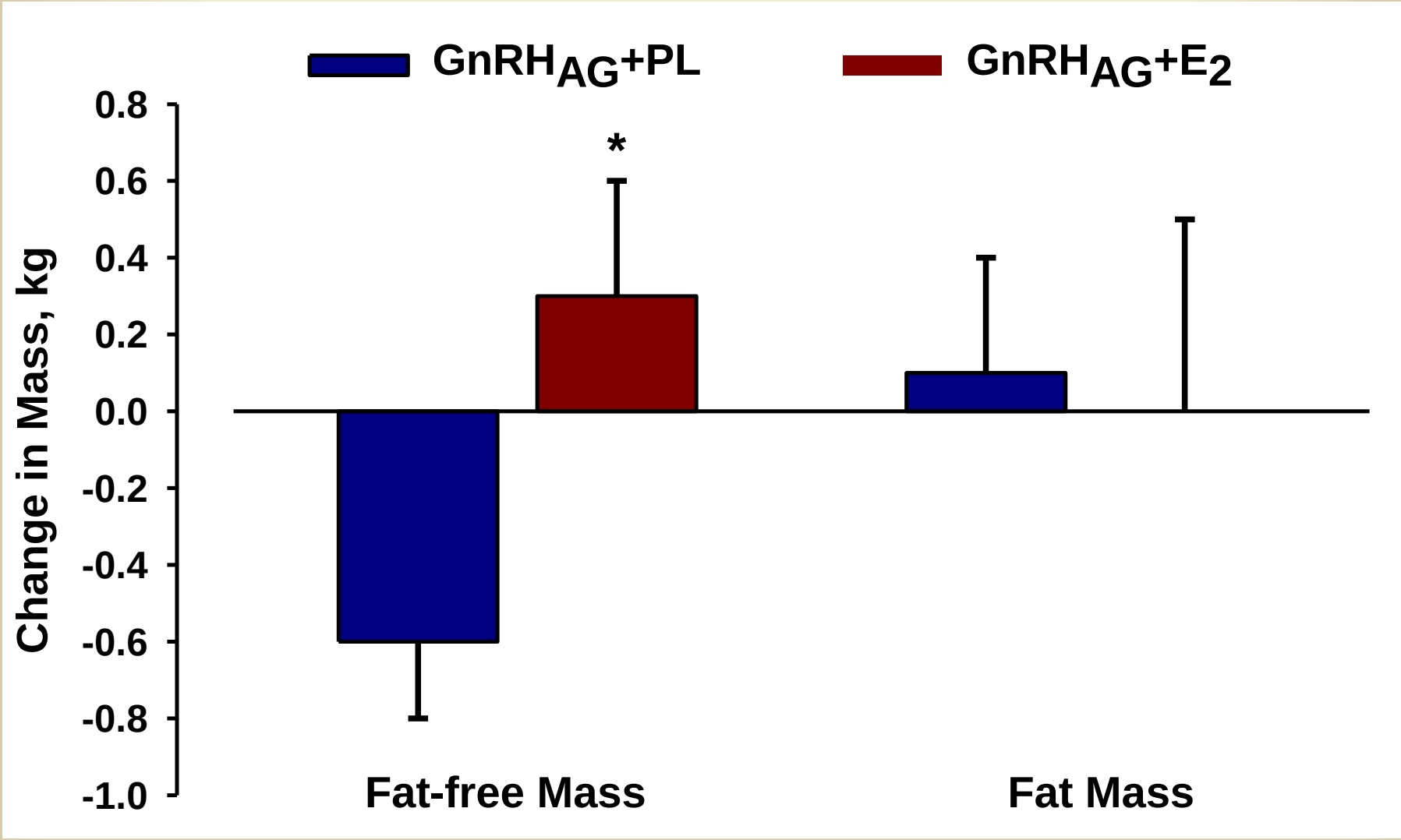
Shea K et al. *Menopause* 22:1045, 2015

Ovarian Hormone Suppression ($GnRH_{AG}$; 5 months) + Placebo or E_2, ± Resistance Exercise

4-group model	$GnRH_{AG}$+PL n=35		$GnRH_{AG}+E_2$ n=35	
	-Ex n=23	+Ex n=12	-Ex n=23	+Ex n=12
Age, y	36 ± 2	36 ±2	34 ± 2	36 ±2
Wt, kg	74 ± 4	75 ± 4	76 ± 4	78 ± 5
BMI, kg/m^2	28 ± 1	28 ± 2	28 ± 1	29 ± 2
FM, kg	27 ± 3	28 ± 3	28 ± 3	28 ± 3
FFM, kg	47 ± 1	47 ± 2	48 ± 1	50 ± 2

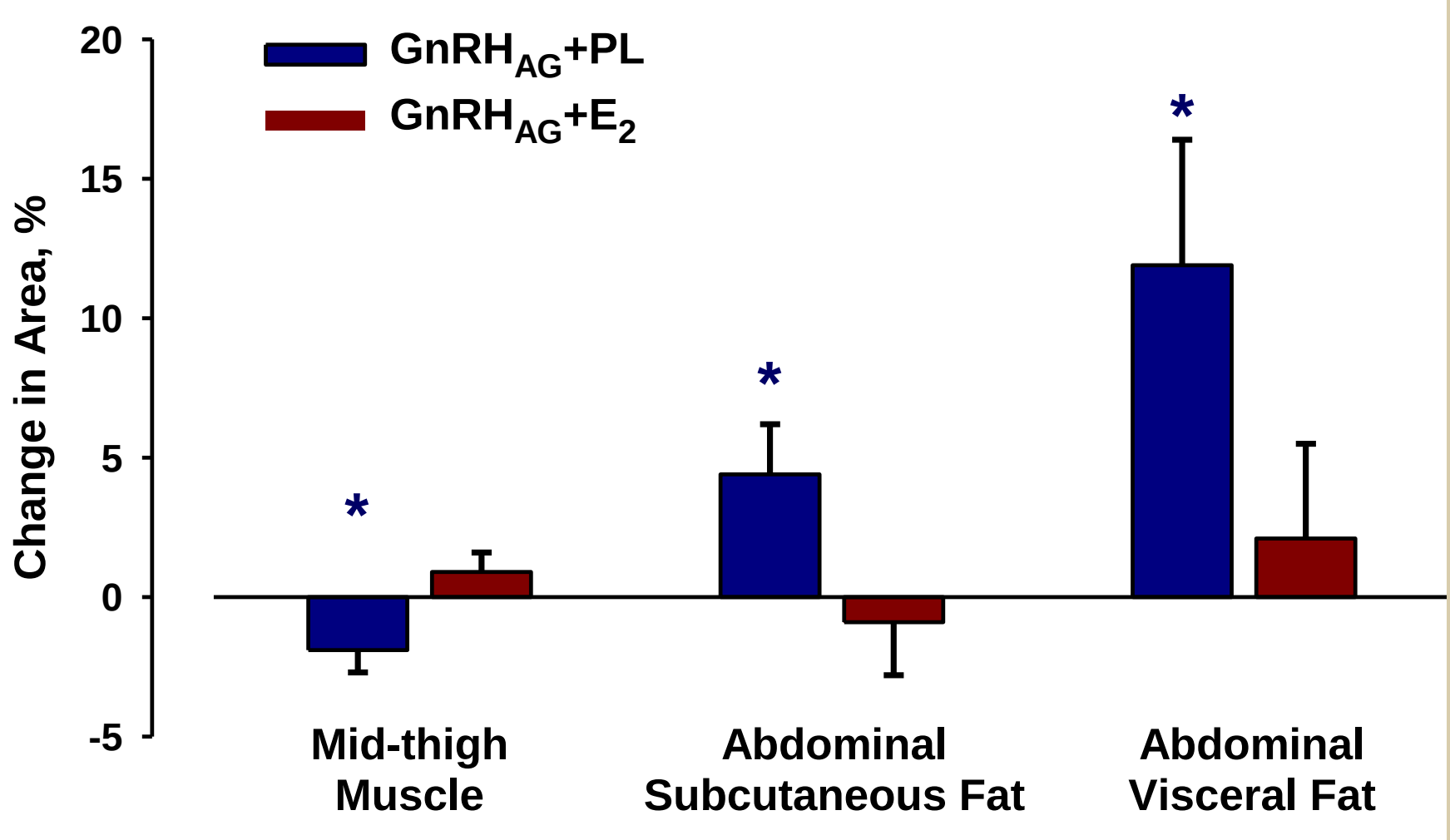
Shea K et al. *Menopause* 22:1045, 2015

$GnRH_{AG}$+PL vs $GnRH_{AG}$+E_2
5-mo Changes in Body Composition (DXA)



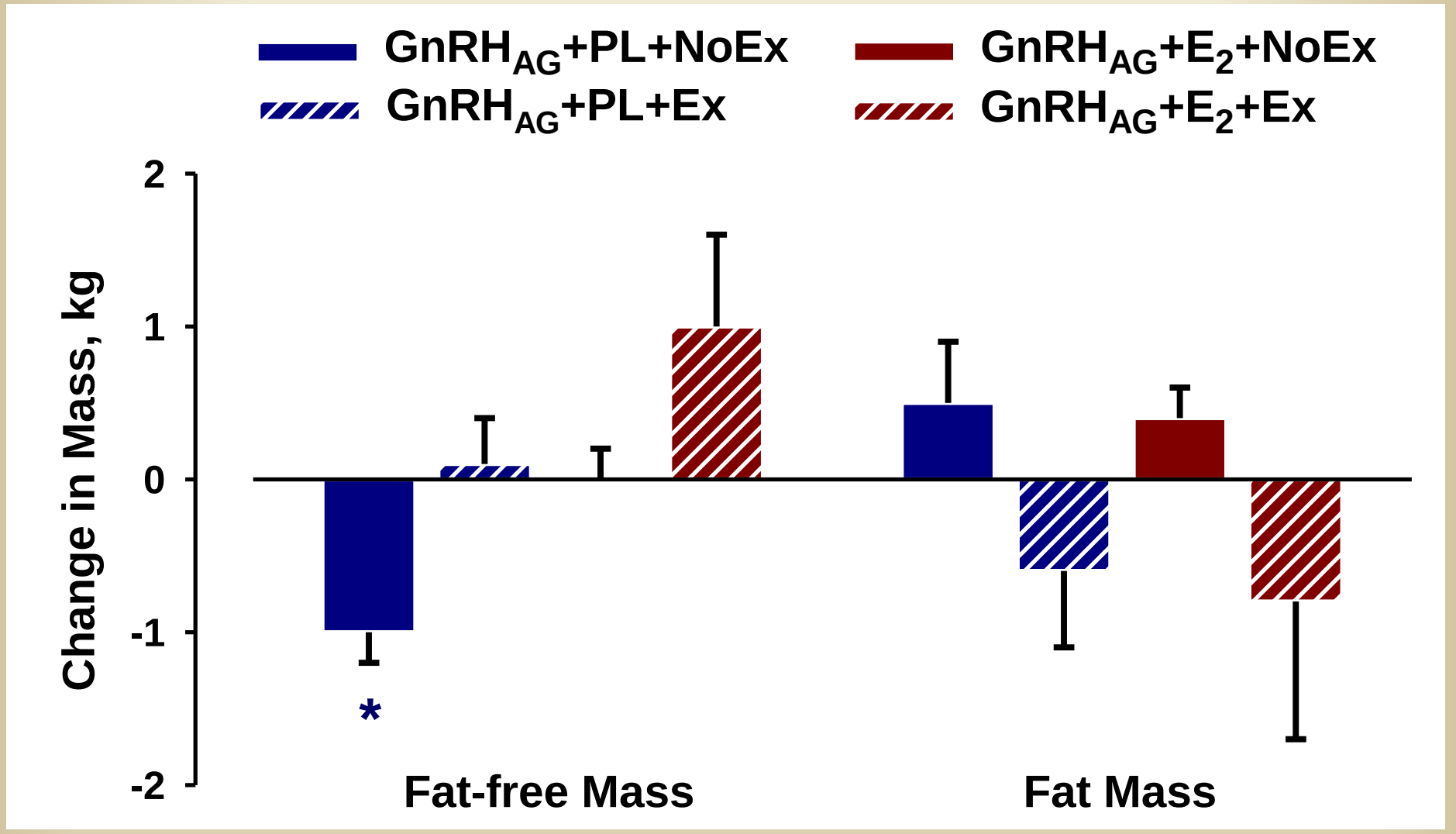
Shea K et al. *Menopause* 22:1045, 2015

$GnRH_{AG}$+PL vs $GnRH_{AG}$+E_2
5-mo Changes in Body Composition (CT)



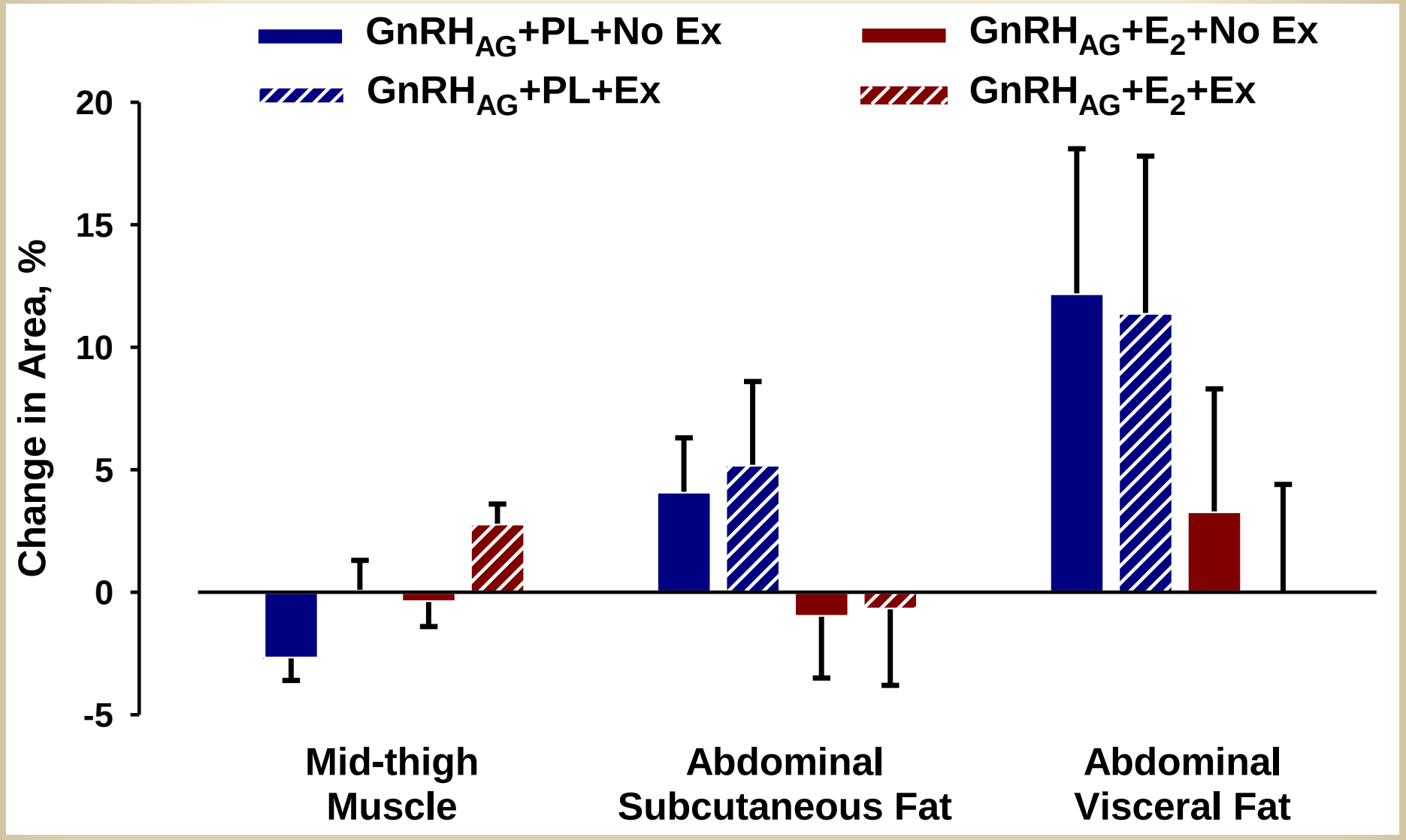
Shea K et al. *Menopause* 22:1045, 2015

$GnRH_{AG}$, +/- E_2, +/- Exercise Training
5-mo Changes in Body Composition (DXA)



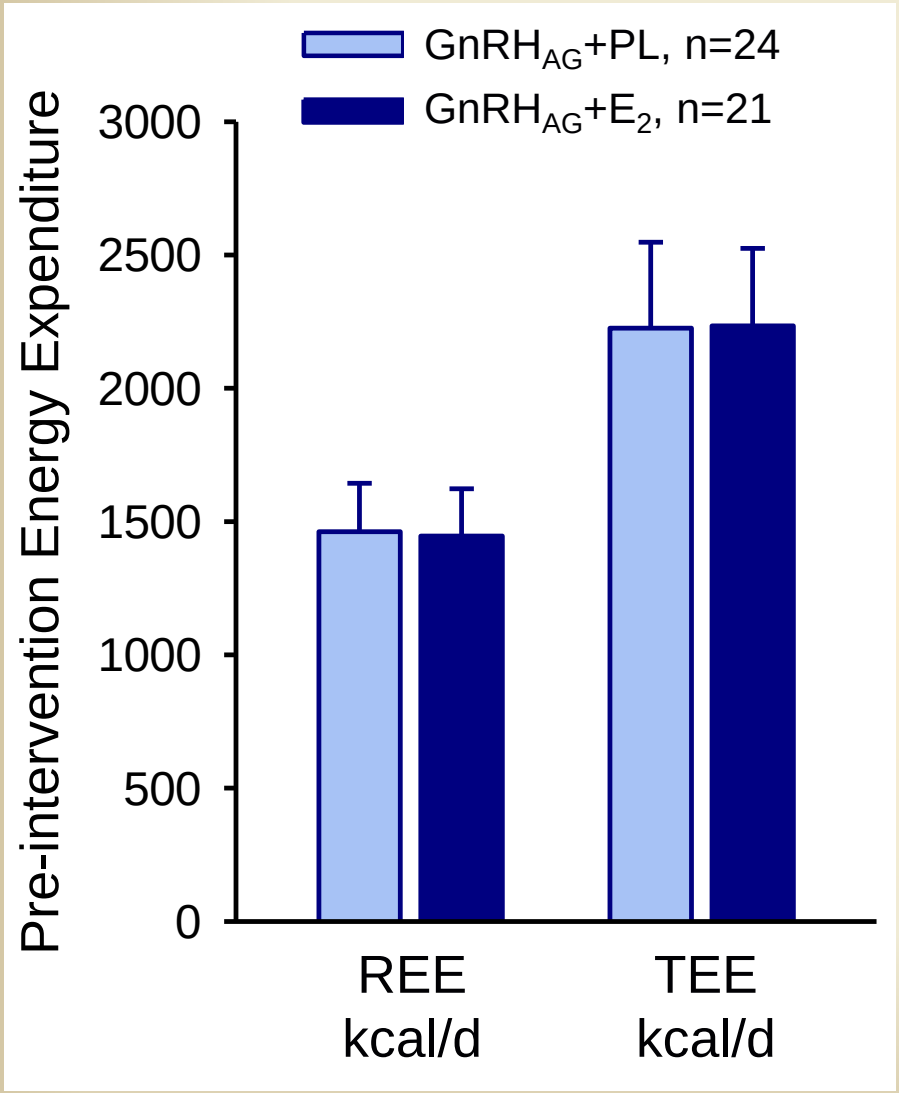
Shea K et al. *Menopause* 22:1045, 2015

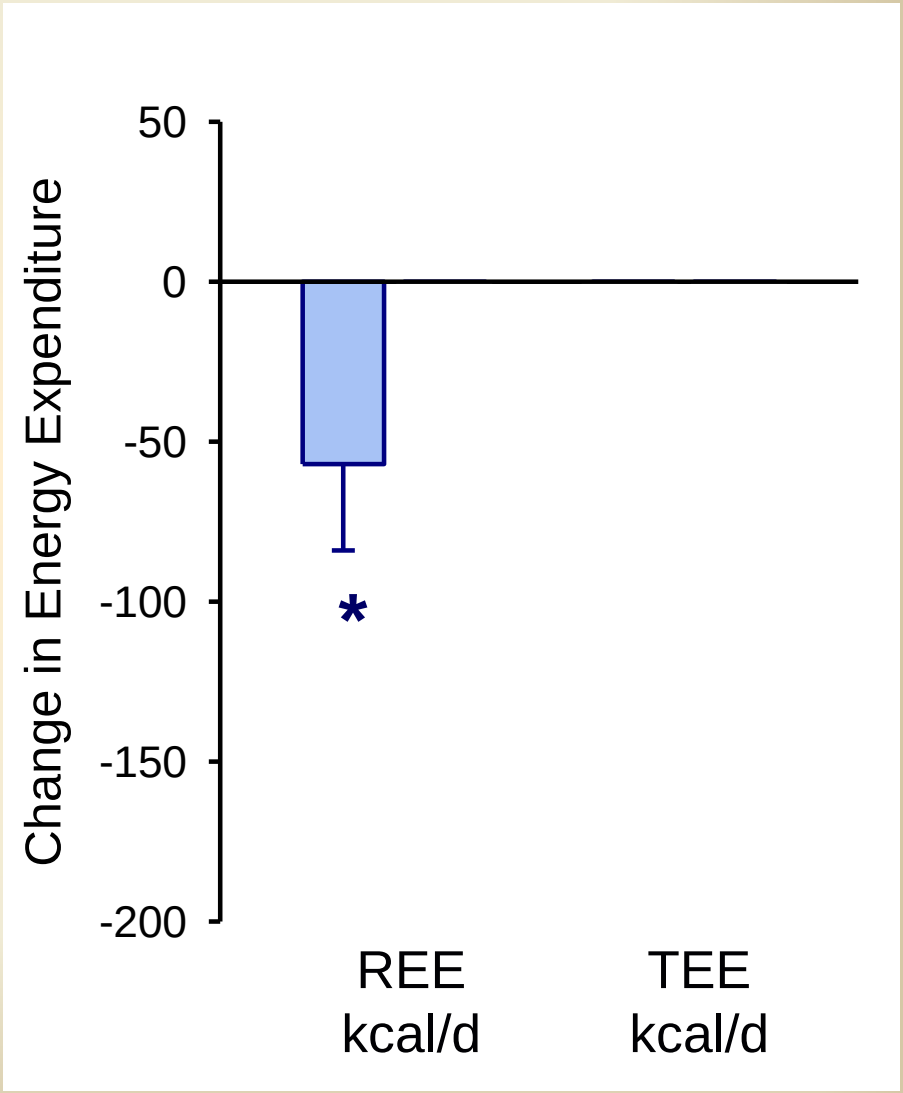
$GnRH_{AG}$+PL vs $GnRH_{AG}$+E_2
5-mo Changes in Body Composition (CT)



Shea K et al. *Menopause* 22:1045, 2015

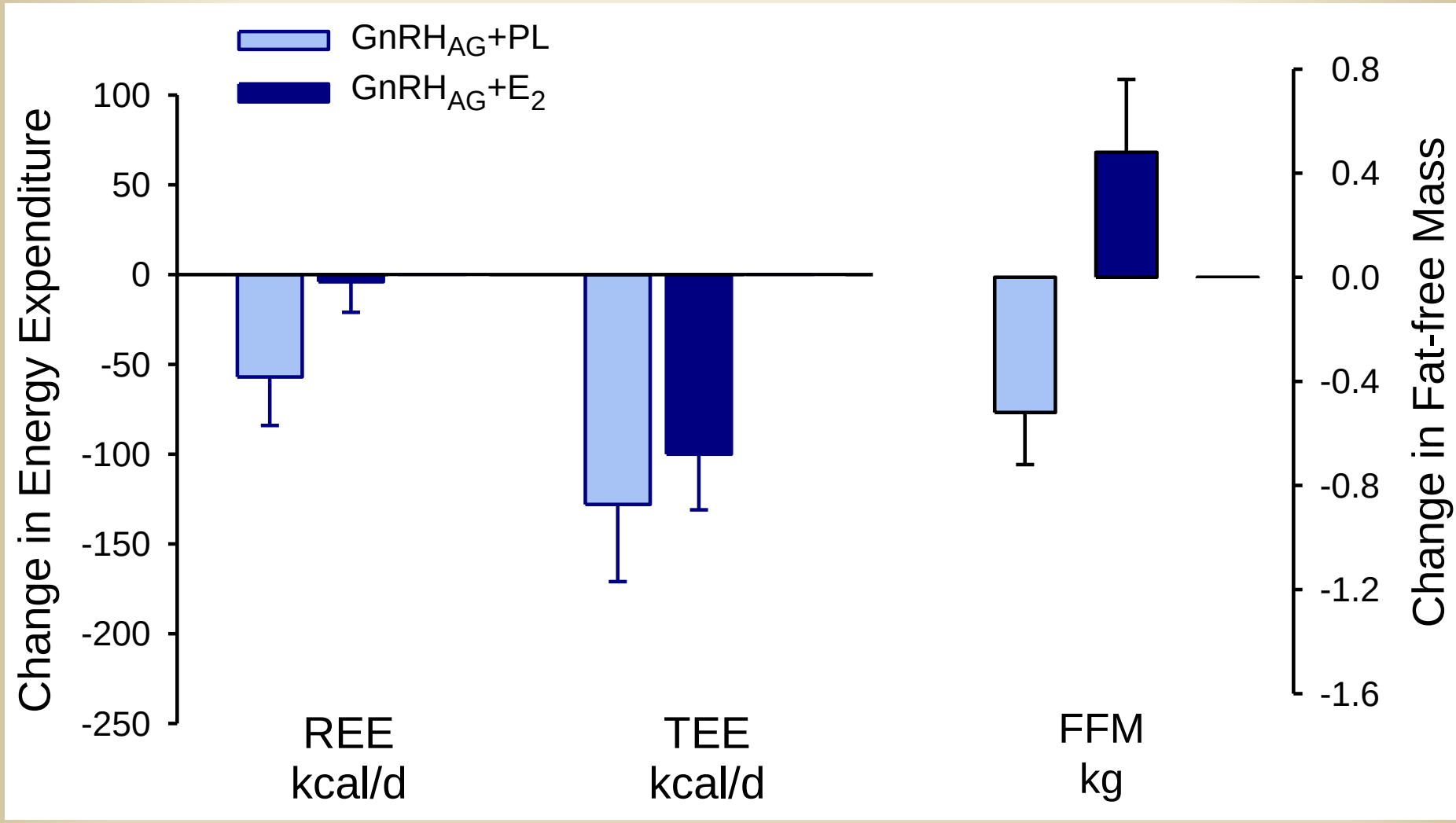
$GnRH_{AG}$+PL vs $GnRH_{AG}$+E_2
5-mo Changes in Energy Expenditure





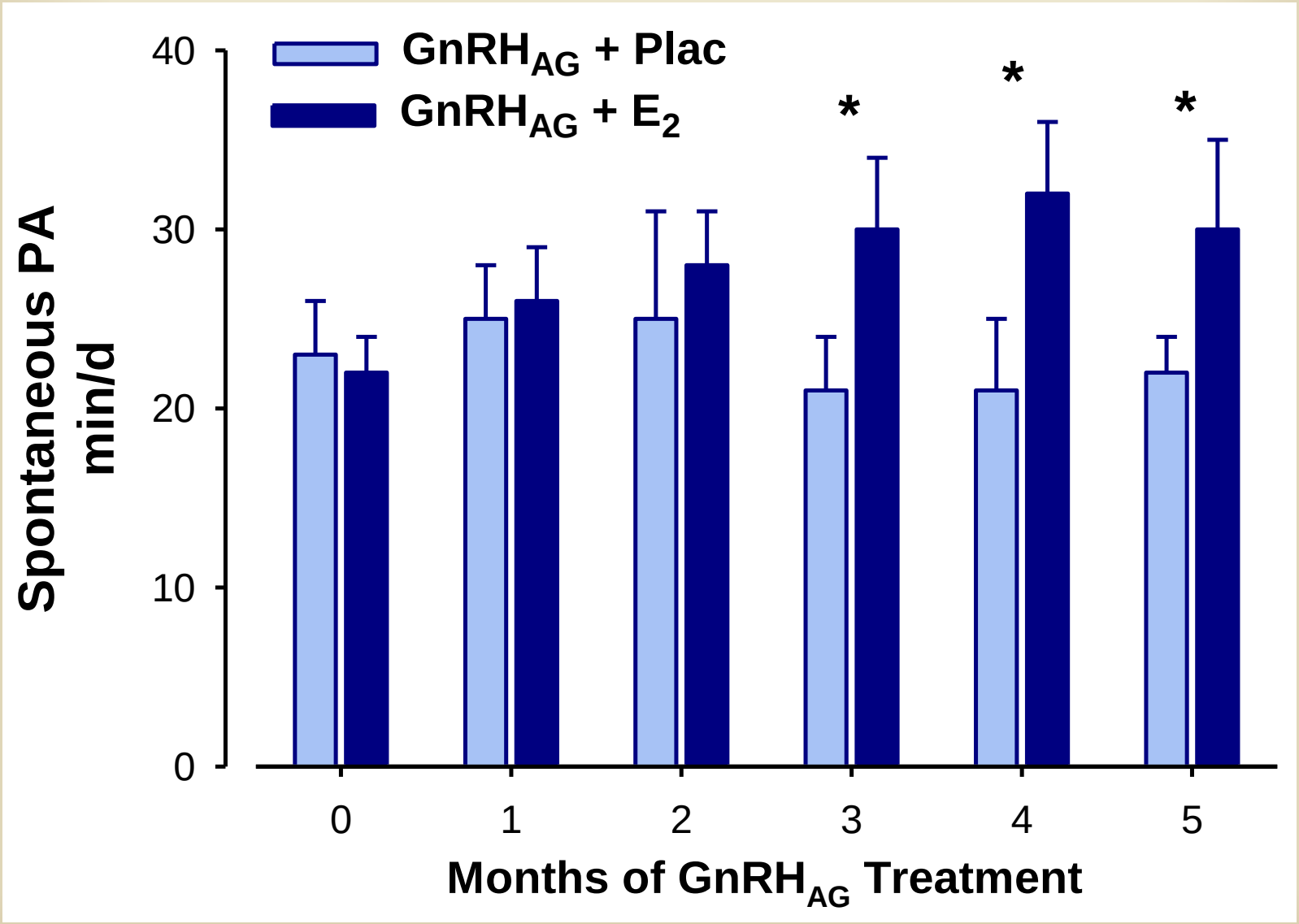
Melanson EL et al. *J Appl Physiol* 119:975, 2015

$GnRH_{AG}$+PL vs $GnRH_{AG}$+E_2 vs $GnRH_{AG}$+PL+Ex
5-mo Changes in Energy Expenditure



Melanson EL et al. *J Appl Physiol* 119:975, 2015

$GnRH_{AG}$+PL vs $GnRH_{AG}$+E_2
5-mo Changes in Spontaneous Physical Activity



Melanson EL et al, *Med Sci Sports Exerc* in press

Ovarian Suppression – Body Composition

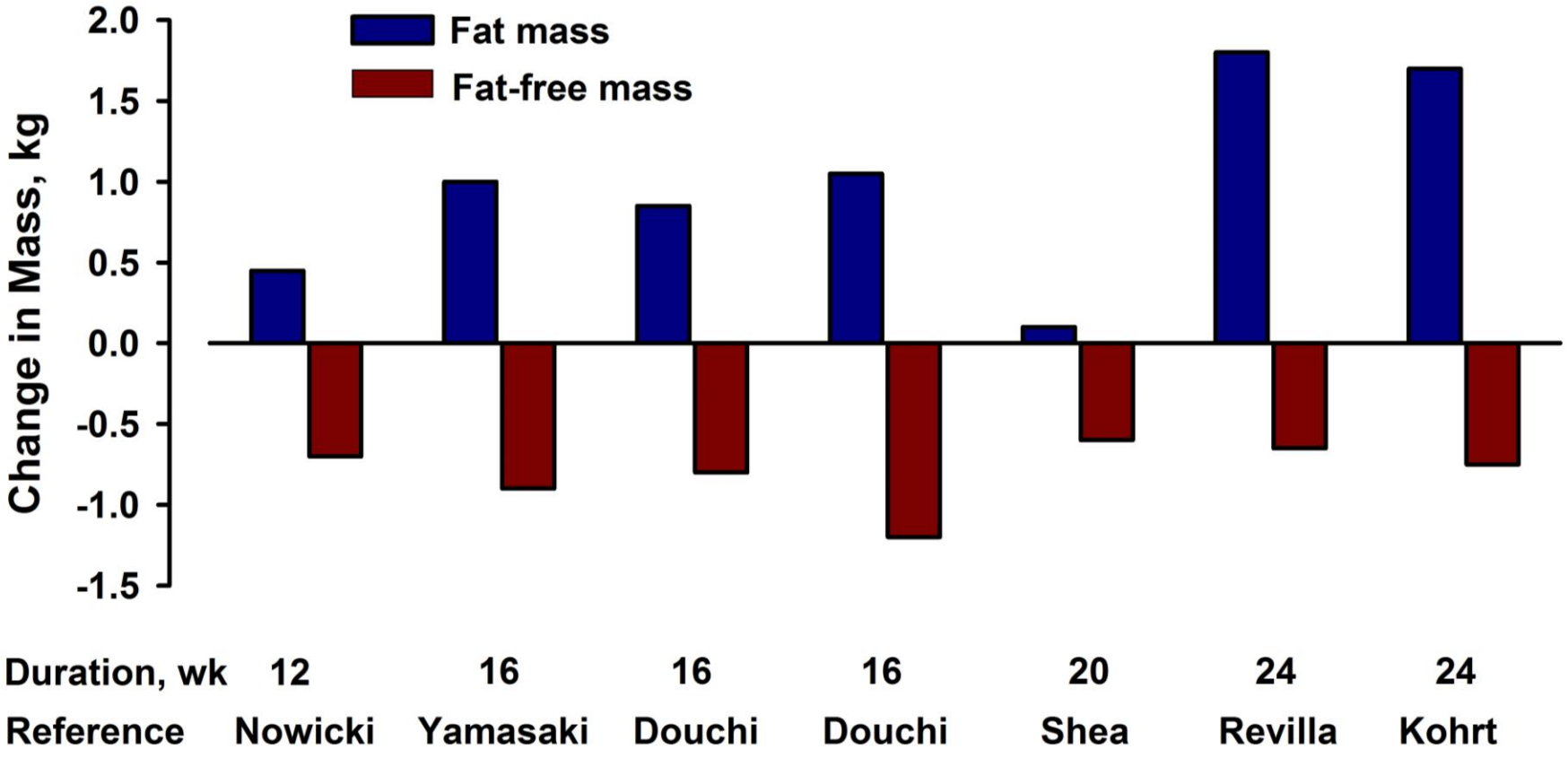


Figure 4. Changes in fat mass and fat-free mass in response to 12 to 24 weeks of gonadotropin releasing hormone therapy.

Estrogen Status and Energy Homeostasis

- Preclinical (OVX) and clinical studies ($GnRH_{AG}$) provide consistent evidence for the role of estrogens in the regulation of energy balance
- The loss of estrogens (OVX, $GnRH_{AG}$) promotes fat gain through multiple system-level mechanisms
  - decreased resting metabolic rate
  - decreased physical activity
  - increased energy intake (some species)

Estrogen Status and Energy Homeostasis

- Mitigation by Exercise -

- In animals, exercise prevents the effects of OVX to increase abdominal adiposity and metabolic dysfunction
- In women, *resistance* exercise attenuates the loss of lean mass during ovarian suppression, but not the increase in abdominal adiposity or decrease in RMR.
- *Endurance* exercise may attenuate total fat gain, but not in central regions, and may not attenuate the loss of lean mass.

Investigations in Metabolism, Aging, Gender, and Exercise

IMAGE

medschool.ucdenver.edu/image

W Kohrt, PhD
R Schwartz, MD
R Boxer, MD
S Creasy, PhD
K Gavin, PhD
K Hildreth, MD
K Jankowski, PhD
H Lum, MD
E Melanson, PhD
K Moreau, PhD
Y-M Park, PhD
C Rynders, PhD
C Swanson, MD
S Wherry, PhD

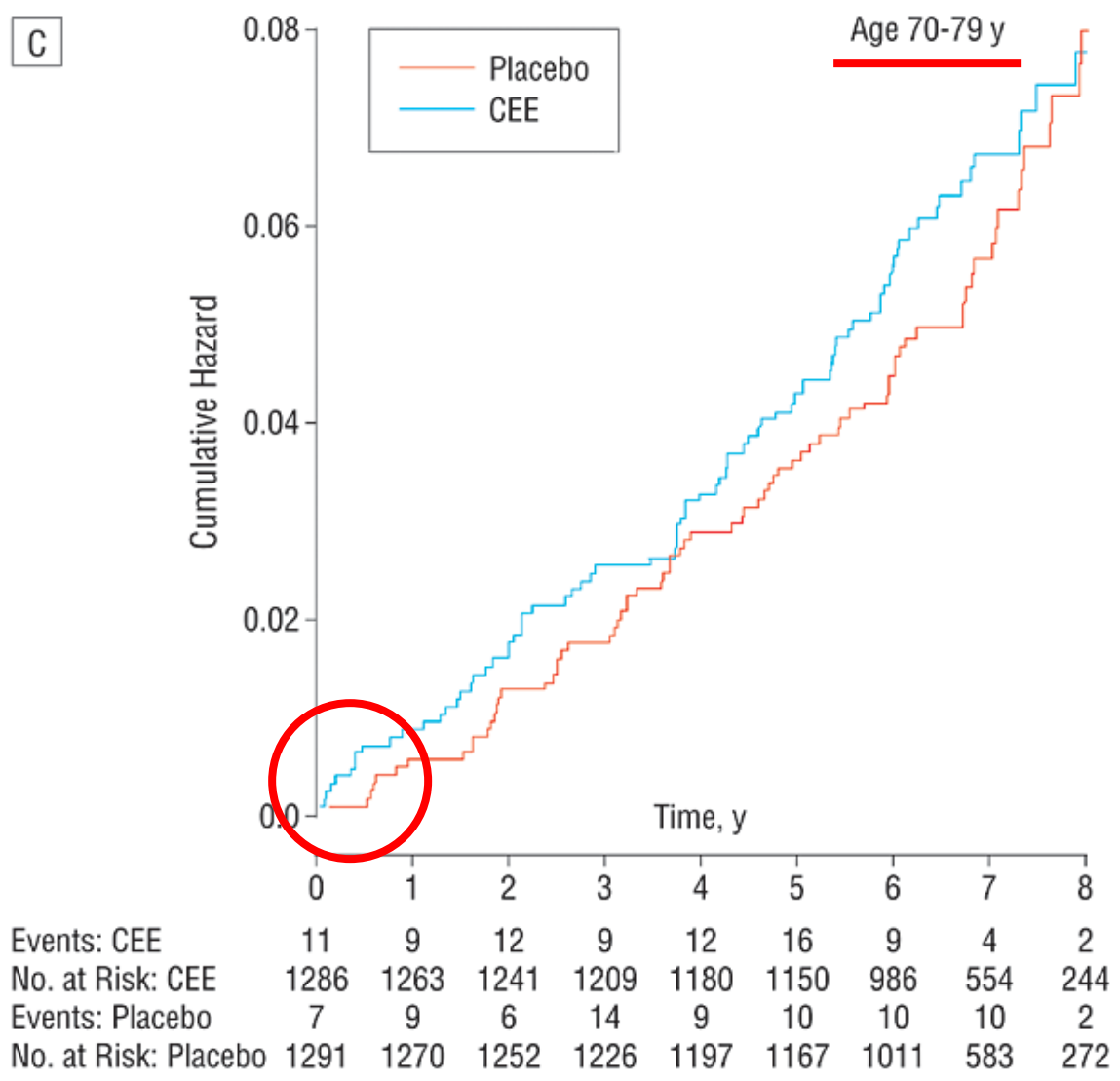
NIH
R01 AG018198
R21 DK092718
P50 HD073063
U01 TR001082
P30 DK048520

GRECC

Center for Women's Health Research

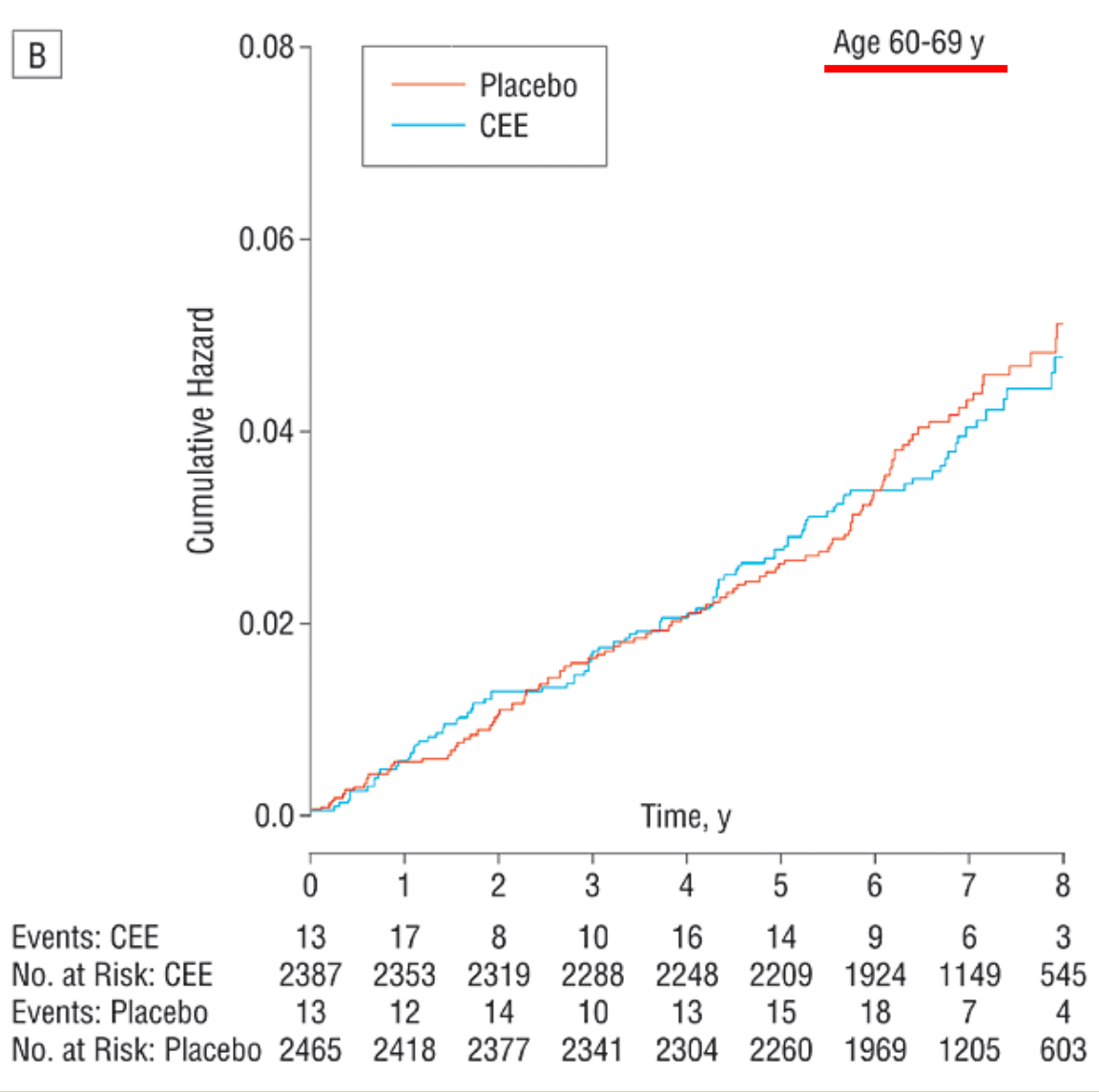
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Menopausal HT and CVD Risk



Hsia J et al. Arch Intern Med 166:357-365, 2006

Menopausal HT and CVD Risk



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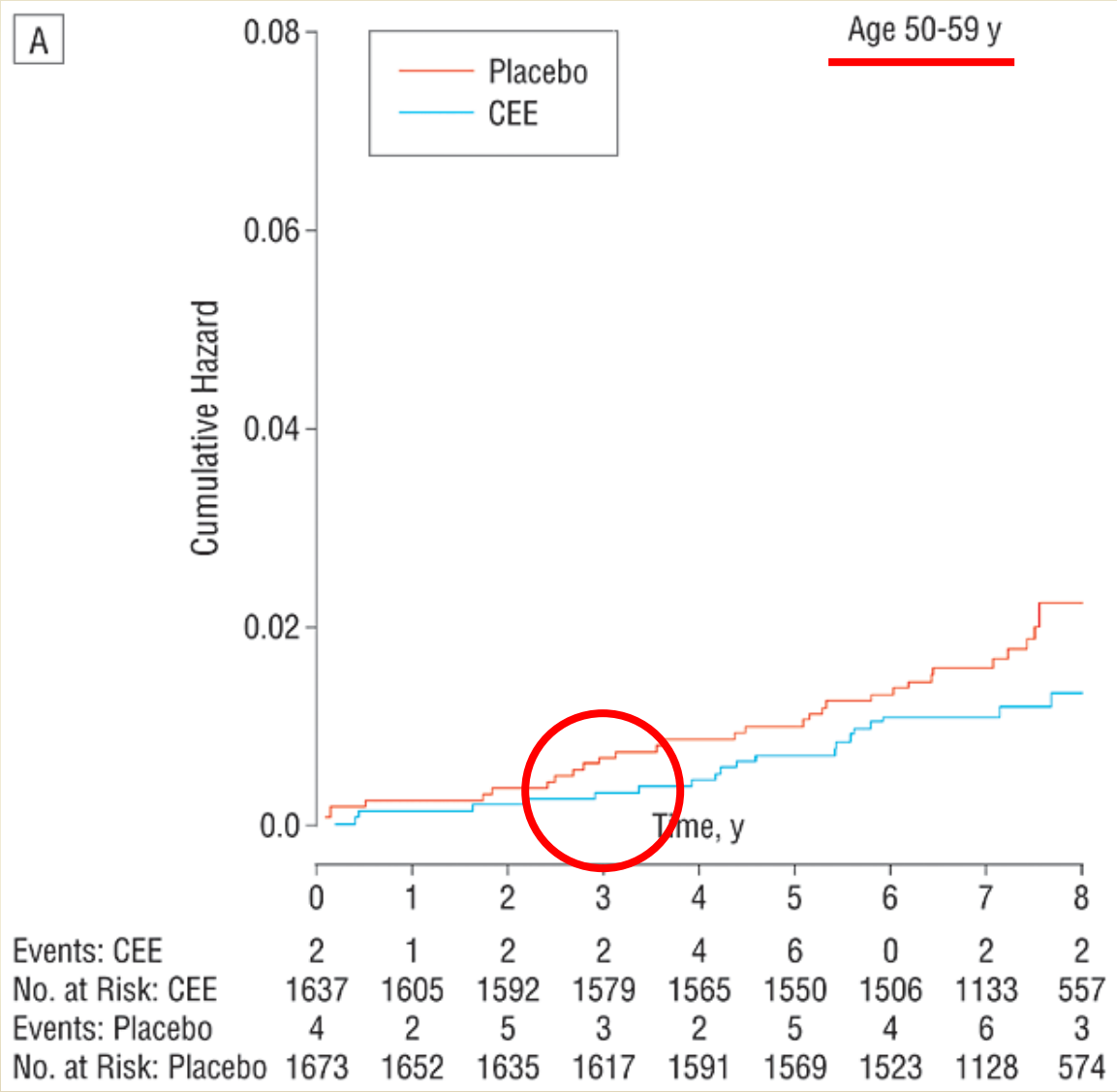
Menopausal HT and CVD Risk



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