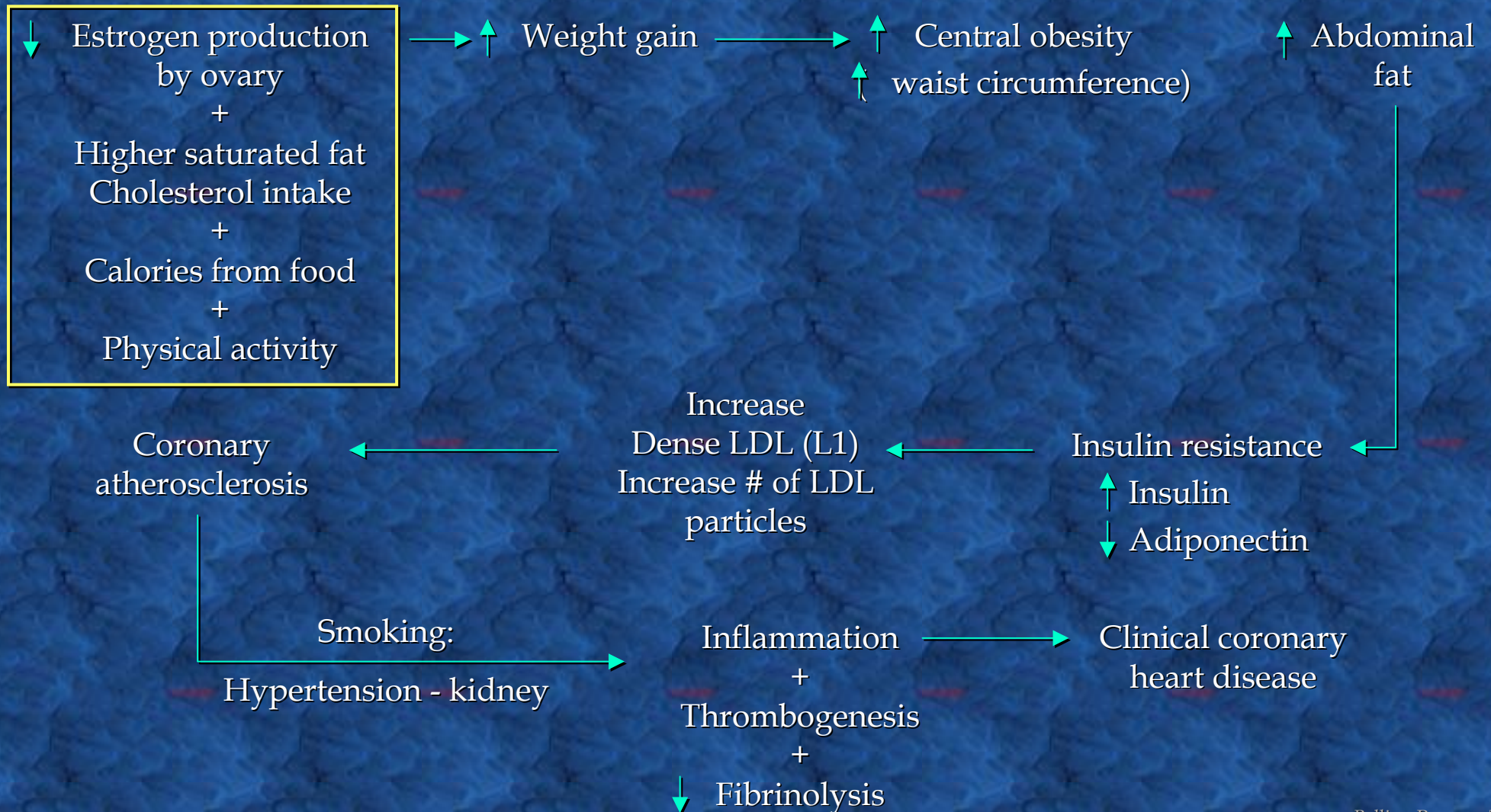


Obesity and Premenopausal Risk Factors

Lewis H. Kuller, MD, DrPH
University of Pittsburgh

Development of Atherosclerosis of Coronary Arteries Among Postmenopausal Women



Obesity and Premenopausal Protection

- I. Increase in weight for pre- to postmenopause: 1-2 pounds/year, 45-55 on average, increase in % body fat
- II. Increase in central obesity or abdominal visceral fat pre- to postmenopausal may be due, in part, to estrogen deficiency; thinner women have more menopausal symptoms

- III. Substantial international variation in both extent of atherosclerosis and coronary heart disease mortality among early postmenopausal women cannot be explained by estrogen deficiency alone
- IV. Increase in LDLc from peri- to postmenopause, in part, is related to weight gain and obesity, diet, and decreased estrogen production
- V. Weight gain and obesity, especially central obesity, associated with increased LDL particles and smaller LDL particles, both associated with increased risk of coronary atherosclerosis and heart attack

- VI. Obesity postmenopausal eliminates beneficial lipid effects of hormone therapy (LDLc, HDLc) associated with increase in triglycerides and number of LDL particles
- VII. Obesity postmenopausal and increased waist circumference associated with insulin resistance (increased insulin, decreased adiponectin, increased blood glucose); estrogen therapy decreased risk of diabetes
- VIII. Insulin resistance key risk factor for diabetes mellitus

- IX. Diabetes is a major risk factor for cardiovascular disease among women. Increased blood pressure postmenopausal is associated more with aging and weight gain, salt retention, vascular stiffness, increased production of angiotensinogen by fat cells? (role of estrogen?)
- X. Weight gain, obesity postmenopause associated with increased blood estrogen levels, estrone, estradiol, decreased SHBG, decreased testosterone
- XI. Increased BMI is postmenopausal major risk factor for breast, uterine cancer

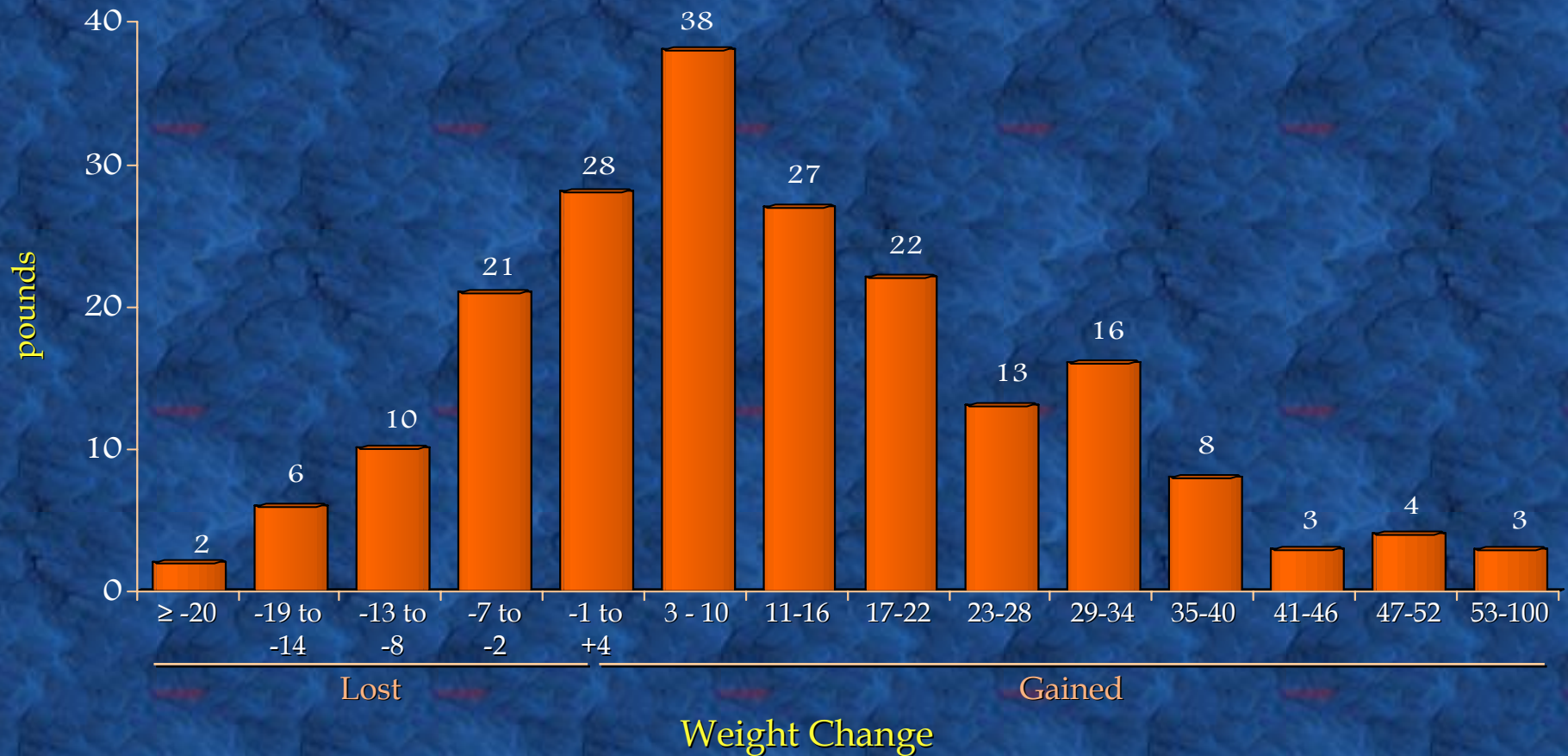
- XII. Increased bone and muscle mass associated with BMI among peri- and postmenopausal women and decreased risk of osteoporotic fracture
- XIII. Higher bone mineral density, increased risk of breast cancer, higher estrone, estradiol in blood, increased risk of breast cancer
- XIV. Obesity is major determinant of venous thrombosis, ie, postmenopausal women (increased risk of thrombosis?)
thrombosis

XV. Obesity, especially central obesity, is associated with substantial increase in inflammatory markers, interrelationship with adipokines, leptin, adiponectin

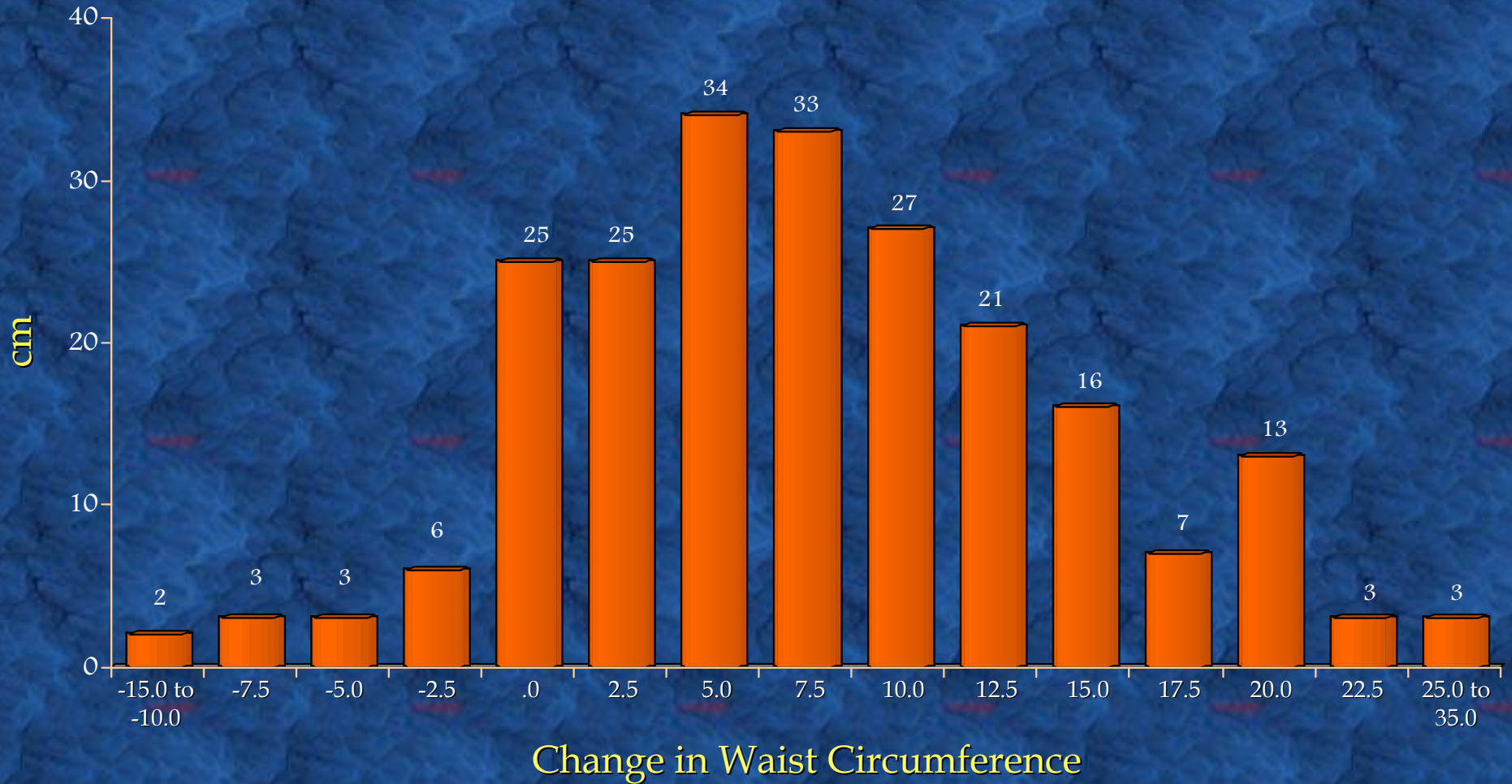
XVI. Weight loss peri- to postmenopause:

- a. decrease in LDL particles, small LDL
- b. decrease in insulin resistance – diabetes
- c. decrease in bone mineral density, muscle mass
- d. decrease in estrogen levels?

Change in Weight by Baseline to 12th Postmenopausal Exam: *Healthy Women Study*

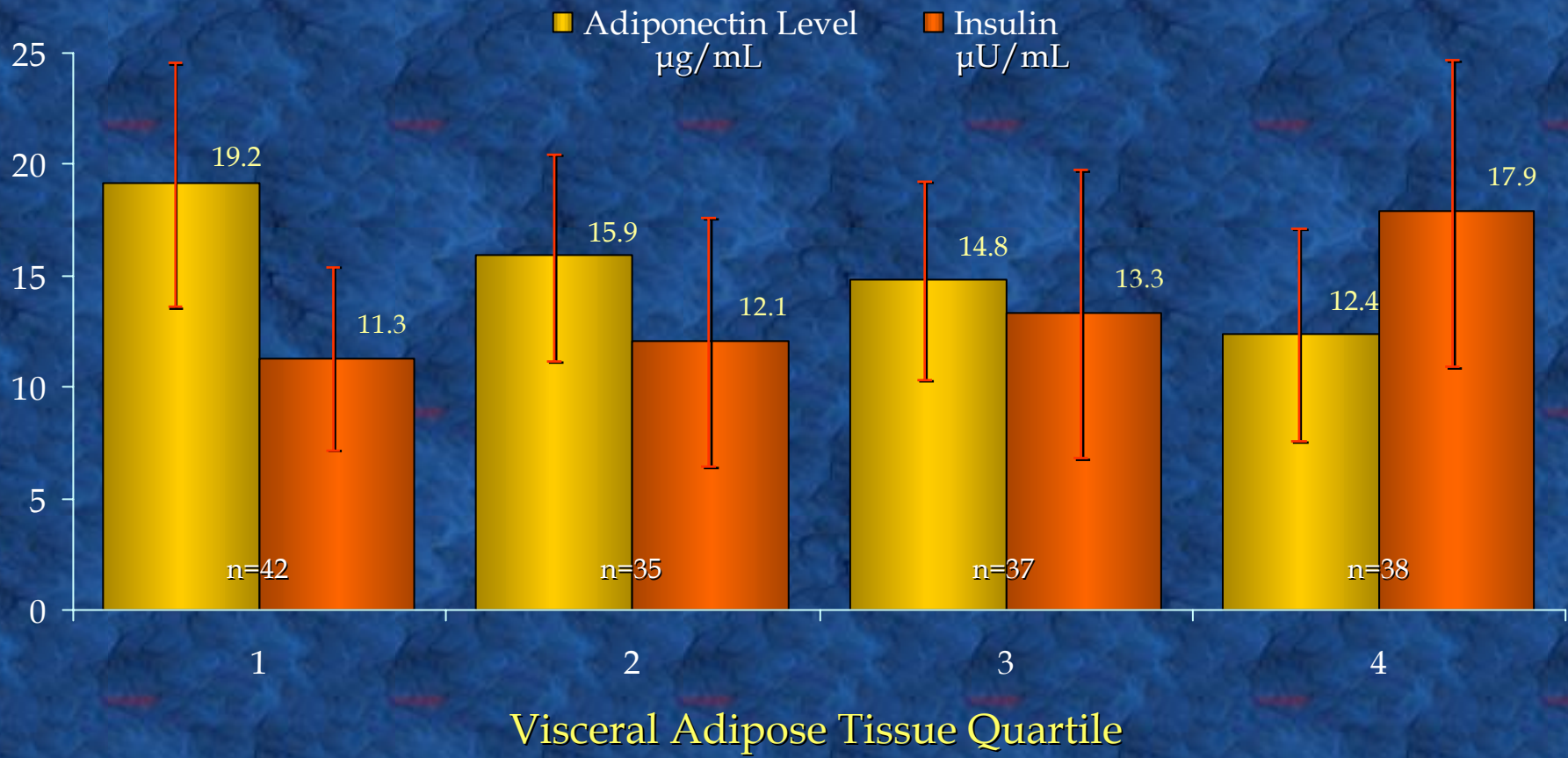


Change in Waist Circumference From 1st to 8th Post in the Healthy Women Study, N=221

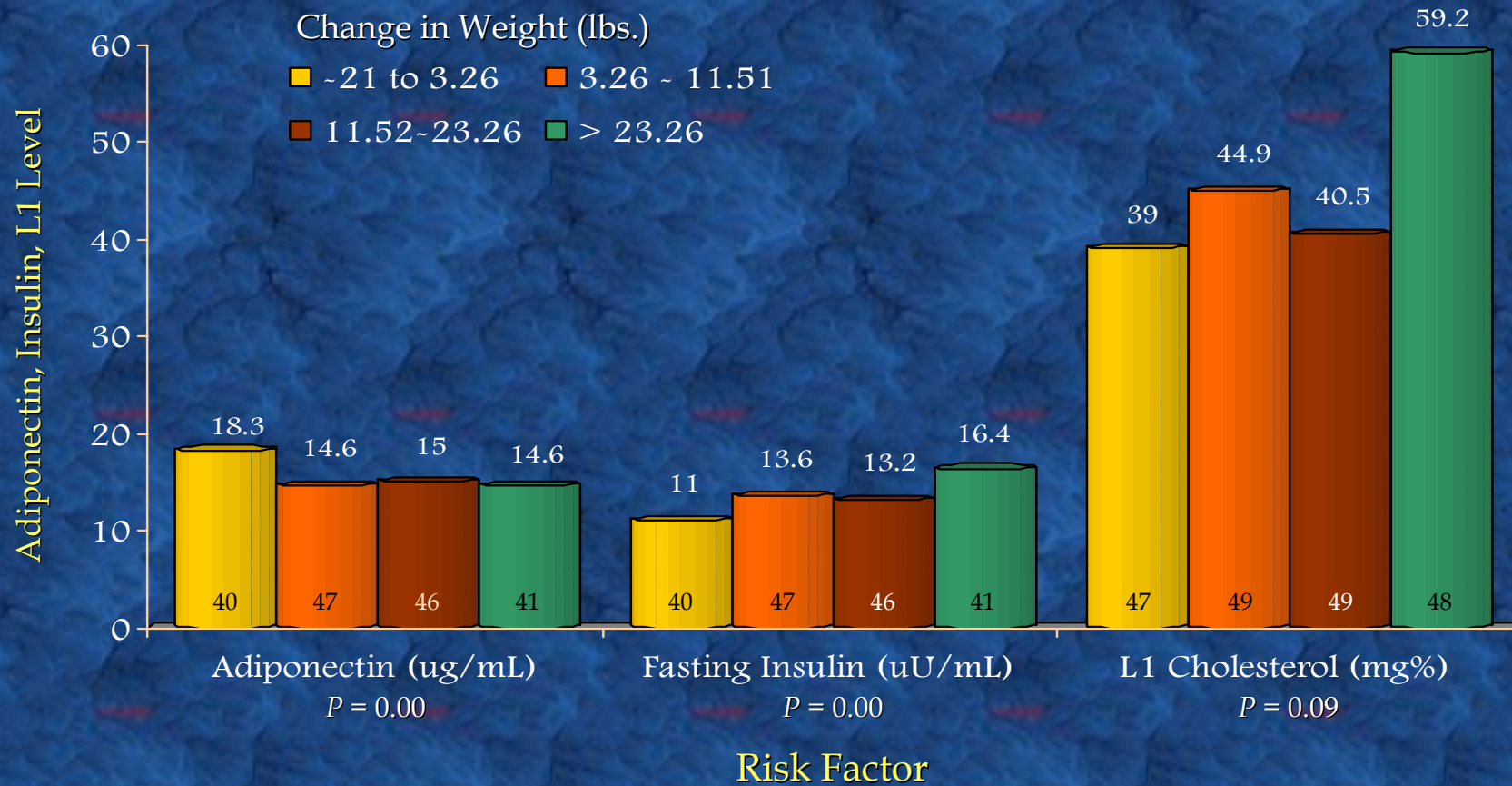


Relationship of Adiponectin and Insulin Level to Amount of Visceral Adipose Tissue Based on CT: 8th Post

$P = 0.0000$



Relationship of Weight Change (Baseline to 12th Postmenopausal Exam) to Adiponectin, Insulin and L1 Cholesterol Levels: *Healthy Women Study*

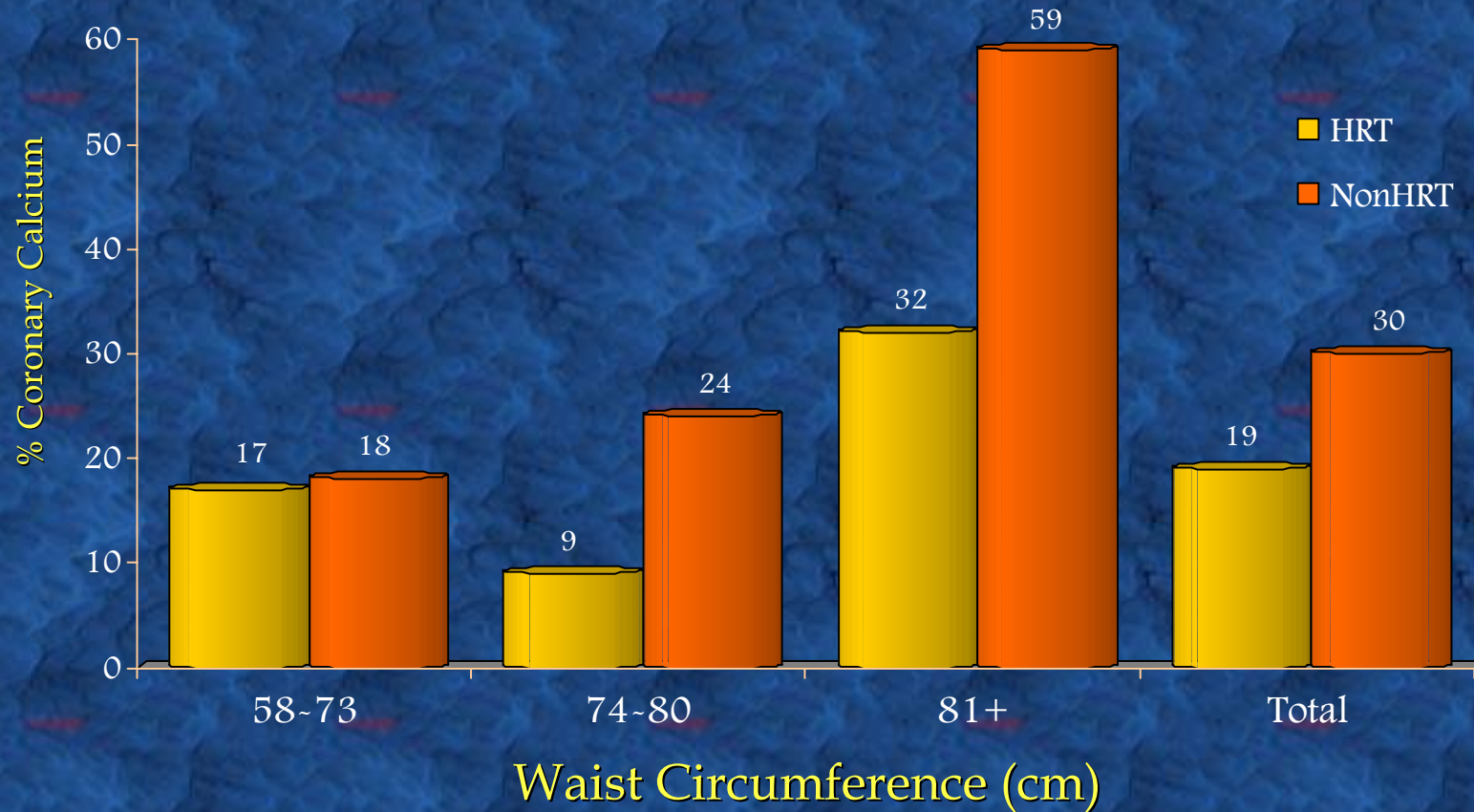


Risk Factors for Coronary Calcium (Baseline Healthy Women Study, n=359) – Coronary Calcium = 169, No Calcium = 190

	Coronary Calcium		P
	No	Yes	
Age at baseline	48	48	--
Systolic blood pressure	106	110	0.001
LDLc	101	116	< .0001
HDLc	61	58	< .01
Triglycerides	73	89	< 0.001
Cigarette smoking %	19	35	< 0.001
BMI	23.7	25.8	< 0.001
Education % College graduate	56.3	42.6	< 0.009

No association, alcohol intake, physical activity, fasting or 2 hr glucose, diastolic blood pressure (weak)

Relationship Between Waist Circumference at Baseline and Presence of Coronary Calcium in the WHLP Study by HRT Use at 78 Month Visit (Post-menopausal Women)



Baseline BMI by Heart Femoral Pulse Wave Velocity (WOMAN Study)

