Menopausal Changes in Body Fat Distribution and Metabolic Syndrome

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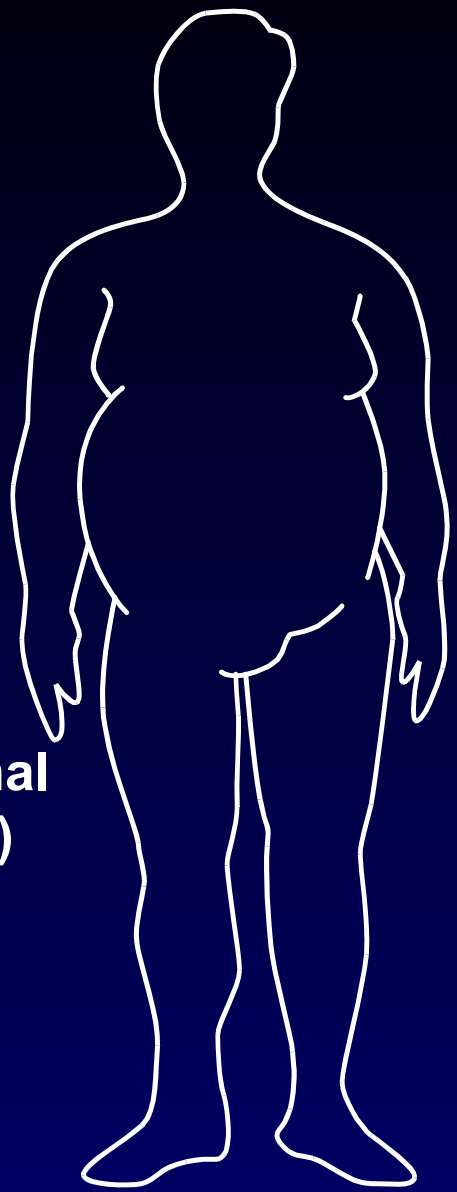
Menopause

- Changes in Metabolism
  - body fat distribution
  - insulin resistance
- Midlife Cholesterol Study

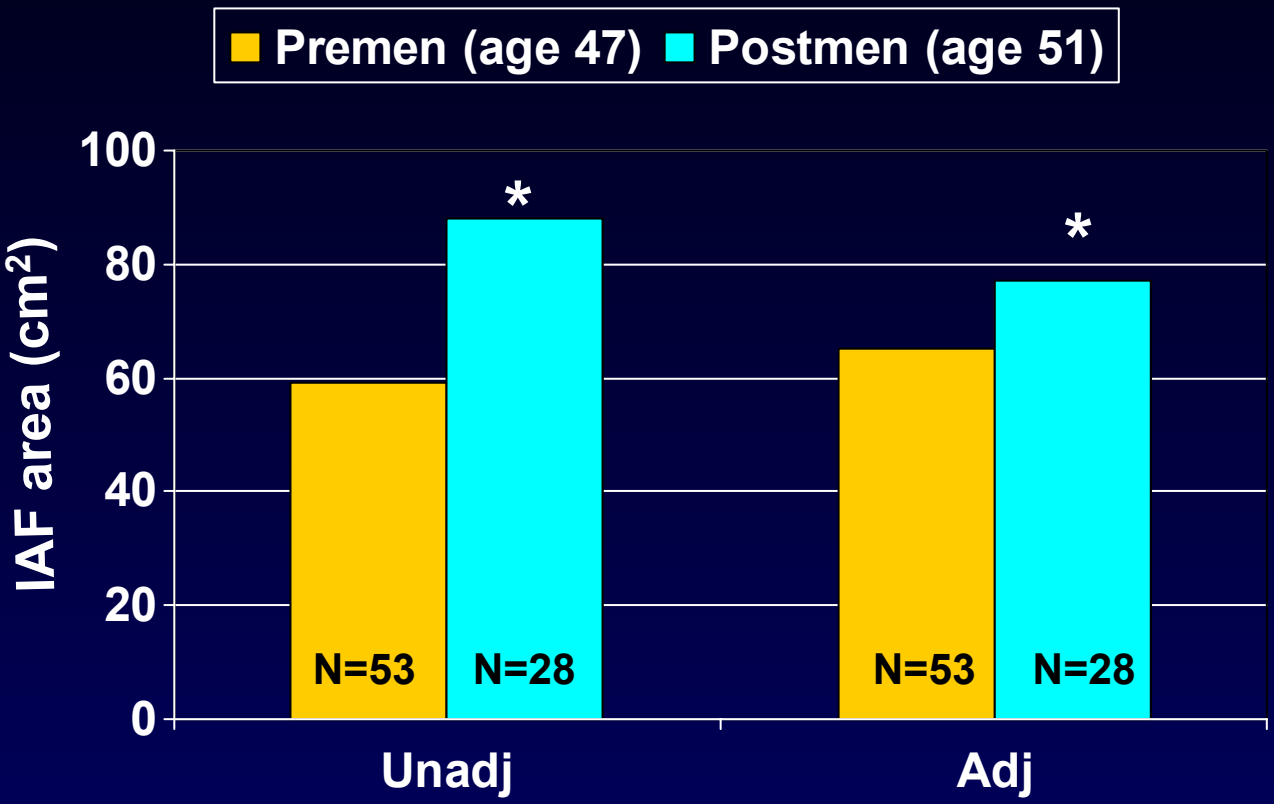
Patterns of Body Fat Distribution



Abdominal
(Android)

Lower Body
(Gynoid)

Pre- vs. Postmenopausal Comparison of IAF



* p<0.05

Adjusted for age and total body fat mass

Toth et al. Int J Obesity24: 226, 2000

Menopausal Changes in Body Composition

- ± Weight
- ↑ Total body fat (%)
- ↓ LBM
- ↑ Abdominal adiposity
  - ↑ Waist circumference
  - ↑ Truncal fat (DEXA scan)
  - ↑ IAF (CT scan)

Do Adipocyte-Derived Proteins Change with Menopause?

• Adipocyte LPL	±	Mauriege JCEM 2000, Ferrara JCEM 2002
• Leptin	±	DiCarlo et al. Gyn Endo 2002
• Adiponectin	↑	Gavrila et al. JCEM 2003
• PAI-1	↑	Pfeilschifter et al. Endo Rev 2002
• TNF- α	↑	Pfeilschifter et al. Endo Rev 2002
• IL-6	↑	Pfeilschifter et al. Endo Rev 2002

Prevalence of Metabolic Syndrome Changes with Menopause

Features of the Metabolic Syndrome

- Central obesity
- Insulin Resistance
- Dyslipidemia
  - Elevated TG
  - Small dense LDL
  - Reduced HDL
- High Blood pressure
- Hypercoaguable state
- Proinflammatory state

NCEP ATP III: Identification of the Metabolic Syndrome

Positive diagnosis based on the presence of three or more of the following:

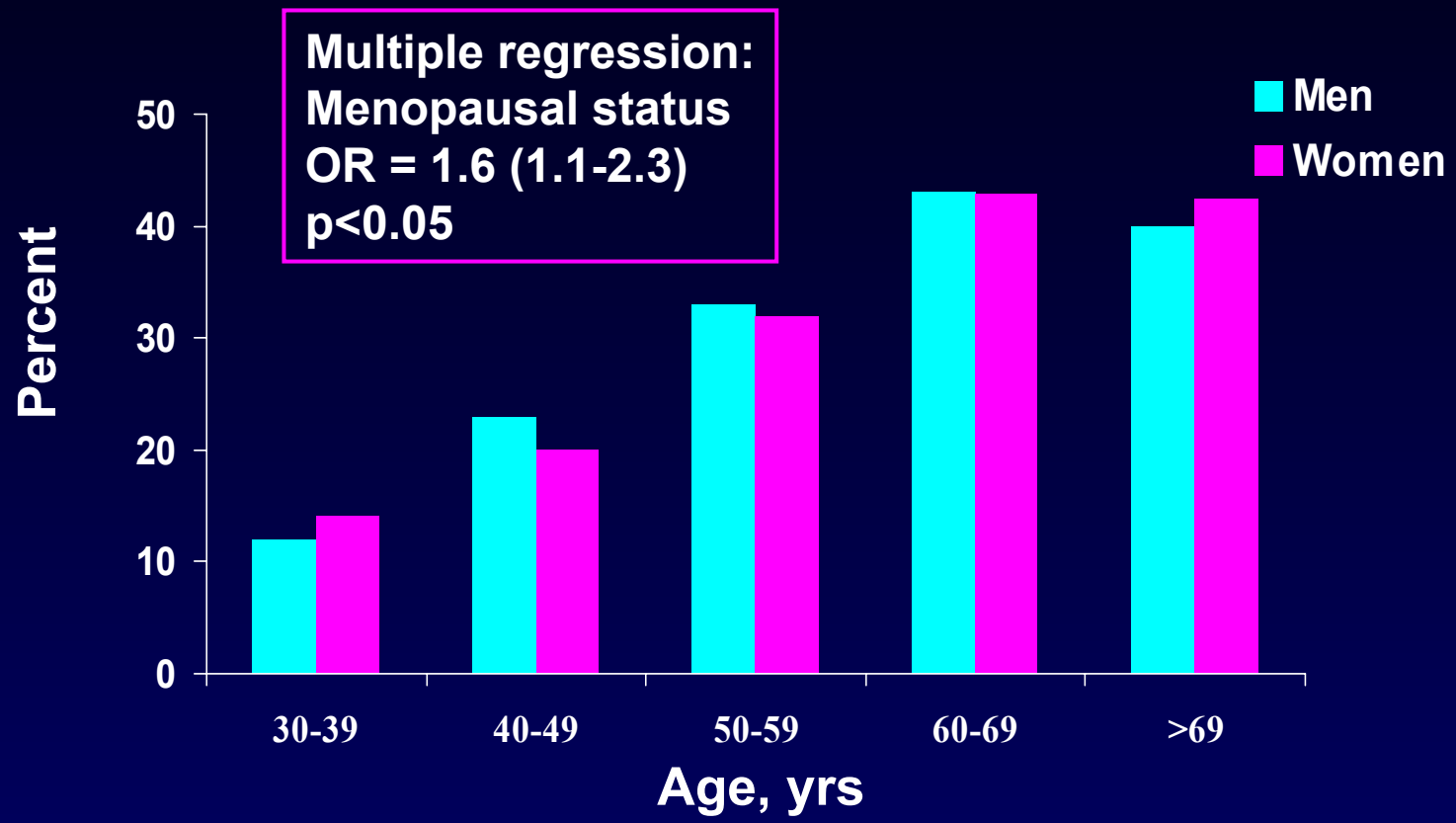
Risk Factor	Defining Level
Abdominal obesity (waist circumference[†])	
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/≥85 mm Hg
Fasting glucose	≥110 mg/dL

[†]Some male patients can develop multiple metabolic risk factors when waist circumference is only marginally increased (e.g., 94–102 cm [37–40 inches]).

NCEP ATP III. *JAMA.* 2001;285(19):2486-2497.

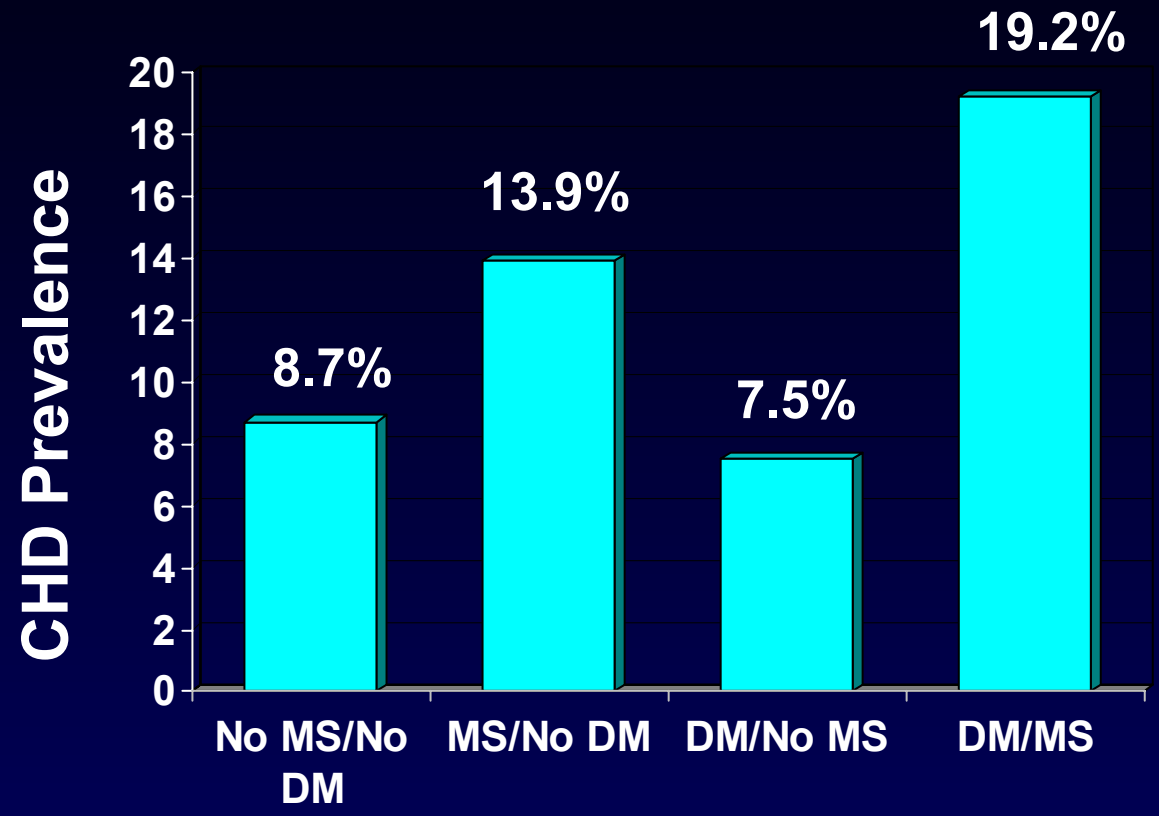
Metabolic Syndrome: *Prevalence by ATP III Criteria* (NHANES III Population)

Overall 22% for age 20 years and older



Ford ES, et al. *JAMA.* 2002;287(3):356-359.
Park et al. Arch Intern Med. 2003;163:427-436

Age-adjusted Prevalence of CHD in US Population (>50 y) - NHANES III

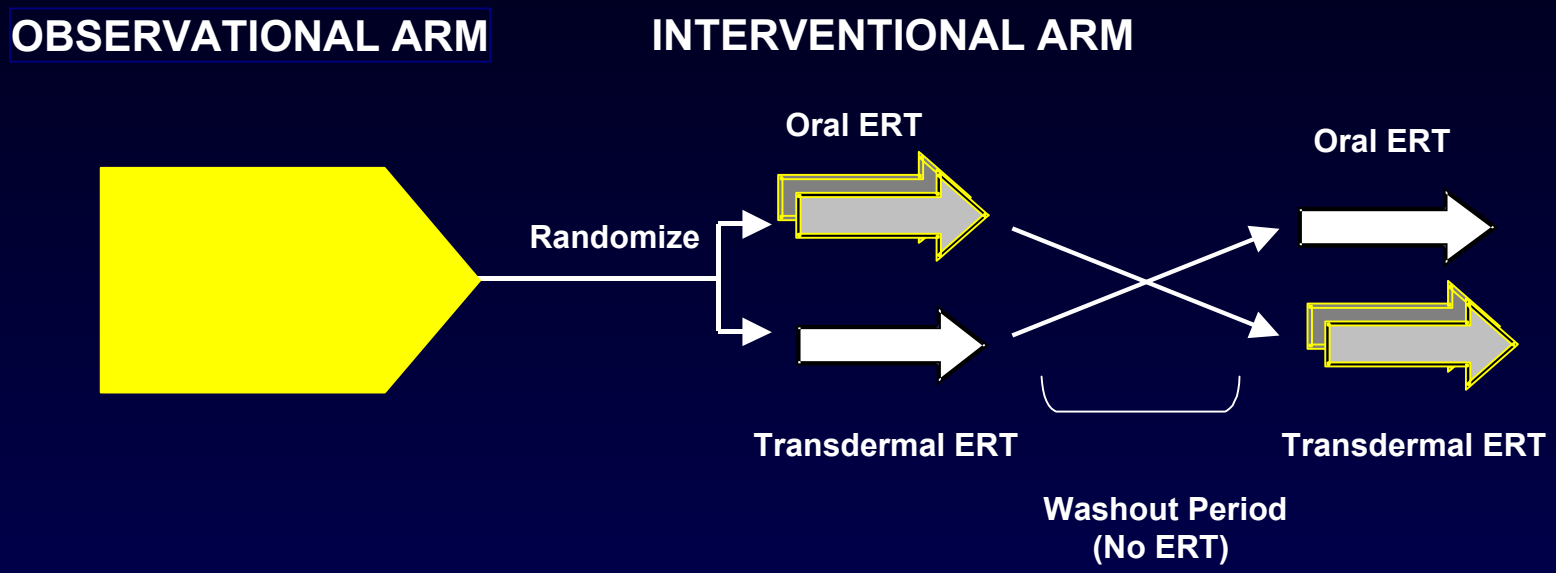


N= 3,510

% of population = 54.2% 28.7% 2.3% 14.8%

Alexander et al. Diabetes 52:1210, 2003

Midlife Cholesterol Study



Premenopausal → Postmenopausal

N = 120

Midlife Cholesterol Study

- Endpoint measures
  - LDL size
  - Fasting lipids
  - Hepatic lipase, LPL, CETP, PLTP
  - Visceral adiposity
  - Fasting insulin and glucose
  - Fibrinolytic/inflammatory factors (PAI-1, tPA, CRP, IL-6, SAA)

Summary: Postmenopause

- Fasting lipids (↑LDL, ↑TG, ↓HDL,↑sdLDL)
- Body fat distribution (↑ IAF)
- ↑ Insulin and glucose levels
- ↑ Prevalence of Metabolic Syndrome

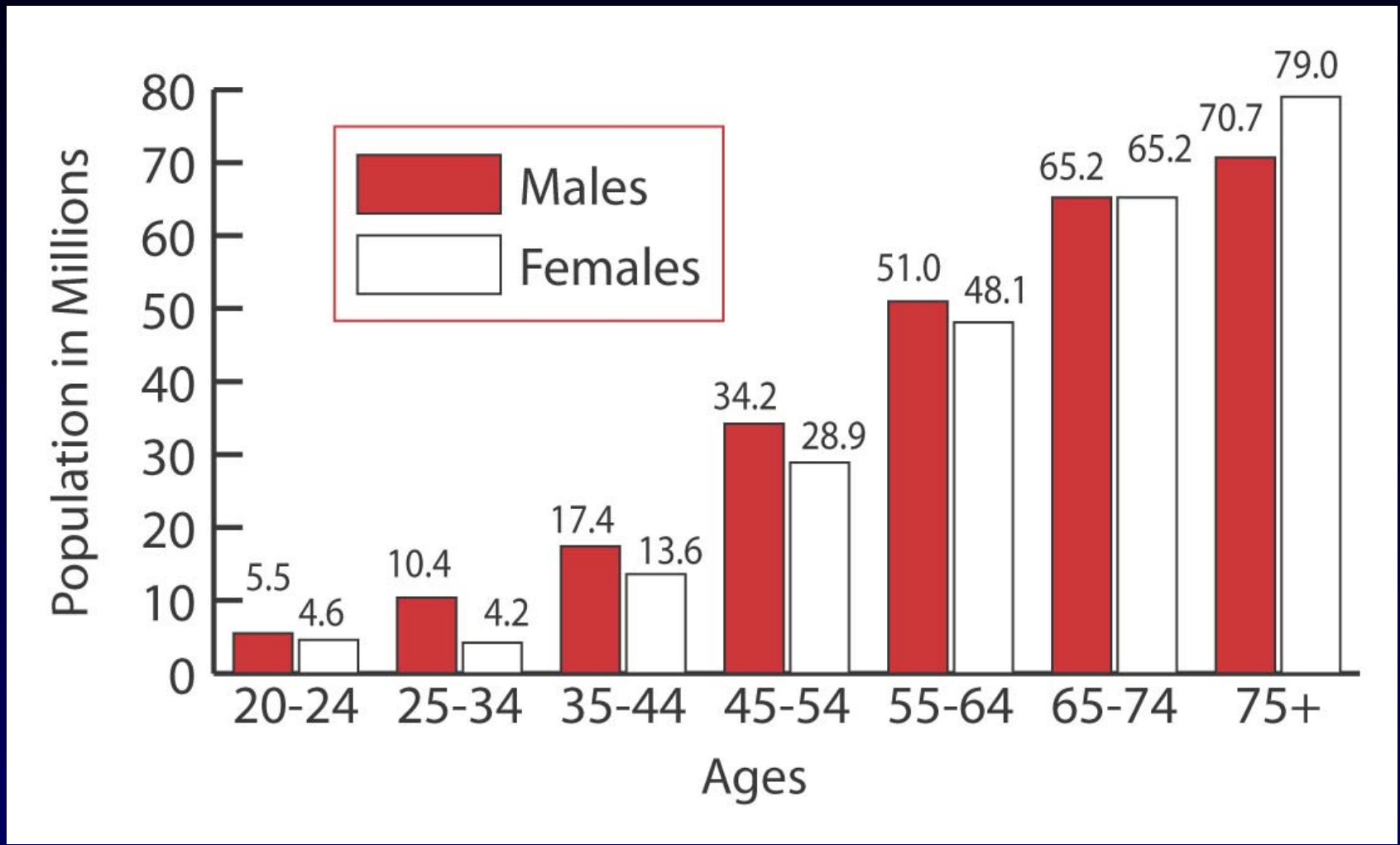
Limitations of current data

- Most data cross-sectional
- Difficult to control for aging and BMI in cross-sectional studies
- Lack of control groups in prospective studies (women who remain premen during follow-up)
- Only one small prospective study assessing IAF by CT scan

Relationship of Menopausal Status and Adiposity - Summary of Research Agenda

Prevalence of Cardiovascular Diseases in Americans Age ≥ 20 by Age and Sex

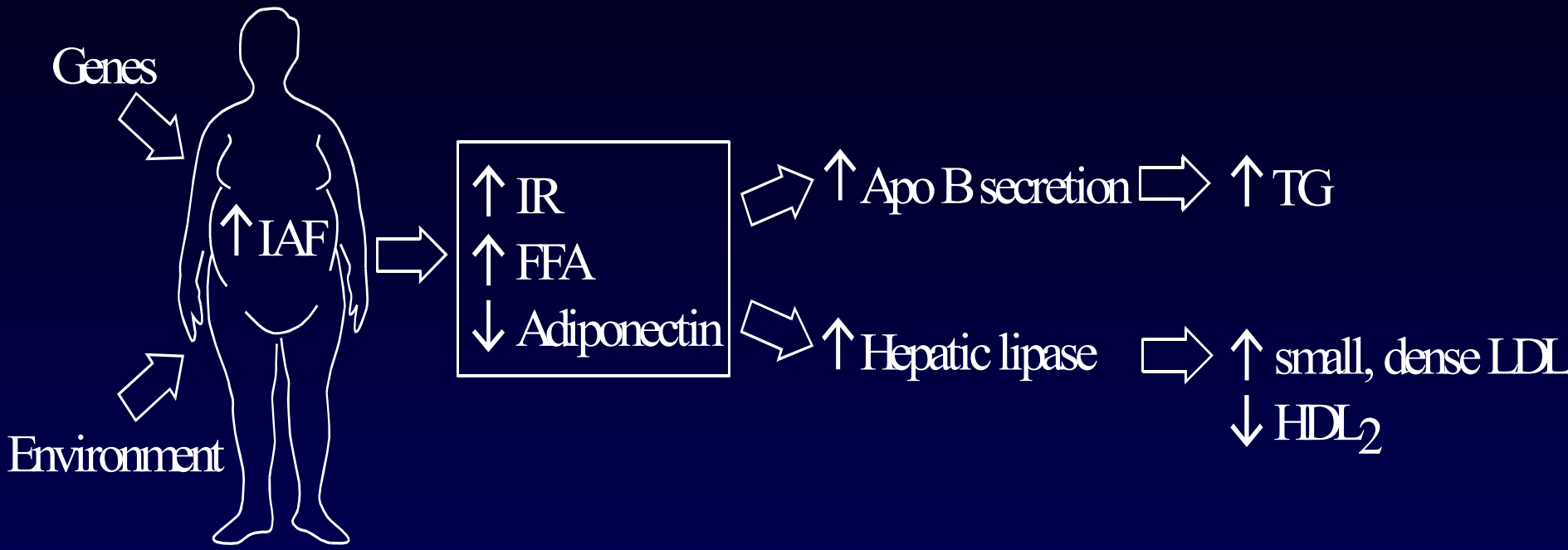
United States: 1988-94



Summary: Postmenopause

- Fasting lipids (↑LDL, ↑TG, ↓HDL,↑sdLDL)
- Body fat distribution (↑ IAF)
- ↑ insulin and glucose levels
- ↑ thrombotic/inflammatory factors
  - PAI-1, CRP, IL-6

Influence of the Menopause on Metabolism



Carr, MC. J Clin Endocrinol Metab 88:2404-11, 2003.

Research Questions

- Does abdominal fat preferentially increase with menopause?
- What factors influence this shift in body fat distribution (upstream)? (genetic, nutritional, physical inactivity, SES)
- Does the shift in body fat account partially or entirely for the changes in metabolism (lipid, insulin resistance/DM)?
- What is the mechanism by which HRT blocks the accumulation of central adipose tissue?