Gender

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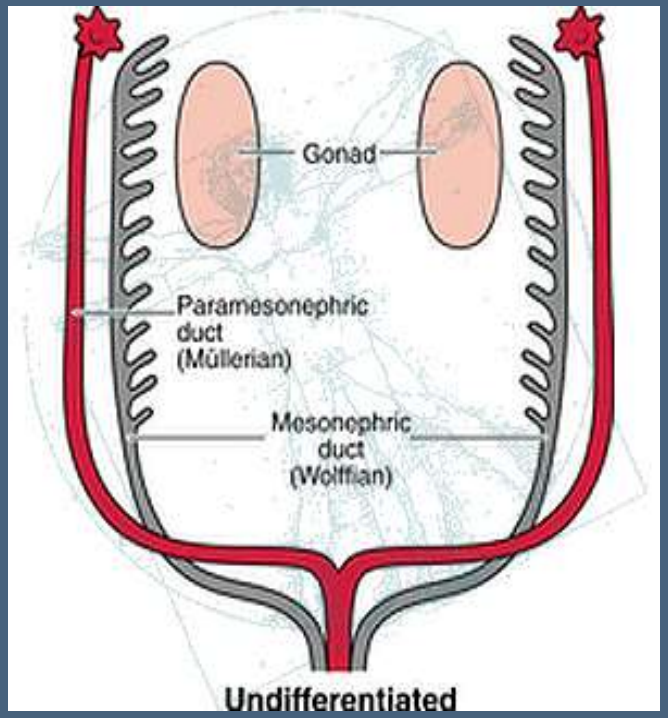
Gender

- The combination of our biological sex with the impact of our environment on our health and behavior as men or women.

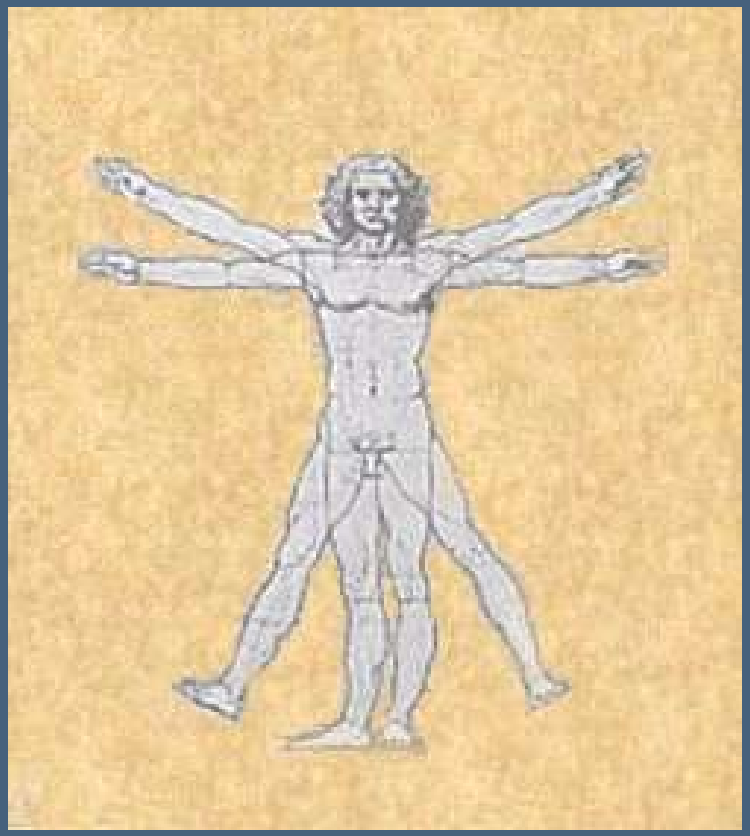
Jmhg 2004; 1:12-19

Does Sex Matter?

National Academy of Sciences
Institute of Medicine 2001



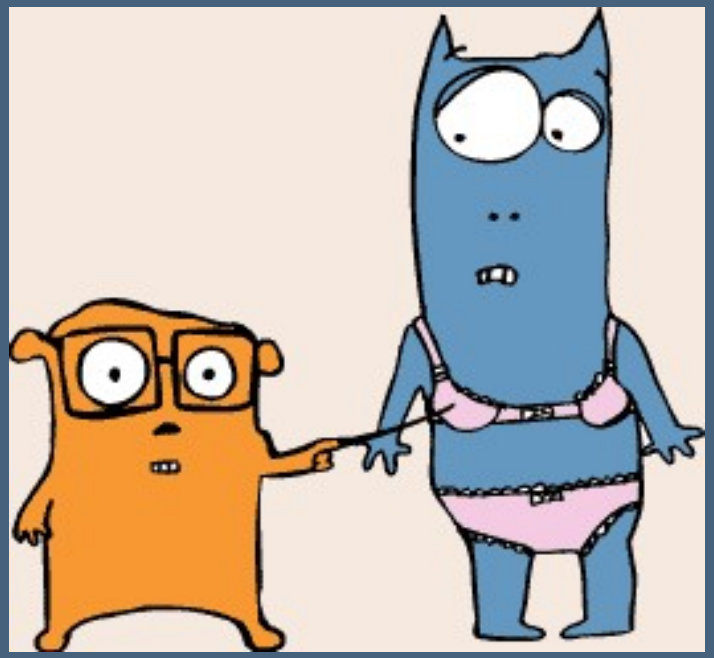
Differences in Gene Expression before differentiation of fetal gonads



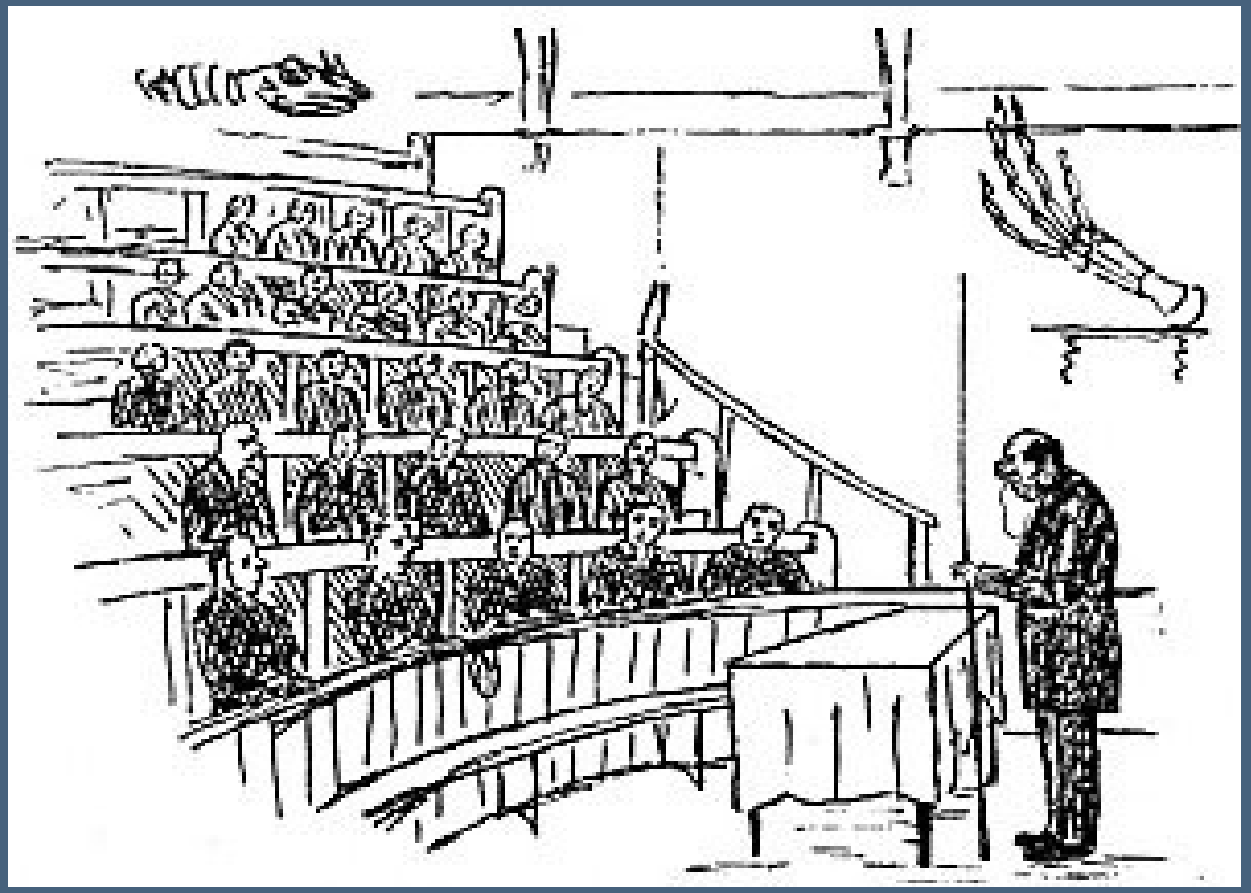
- 2/3 of all diseases that affect both men and women have been exclusively studied in men.

“Women are more than just boobs and tubes”

-chairwomen of Partnership for Gender-Specific Medicine

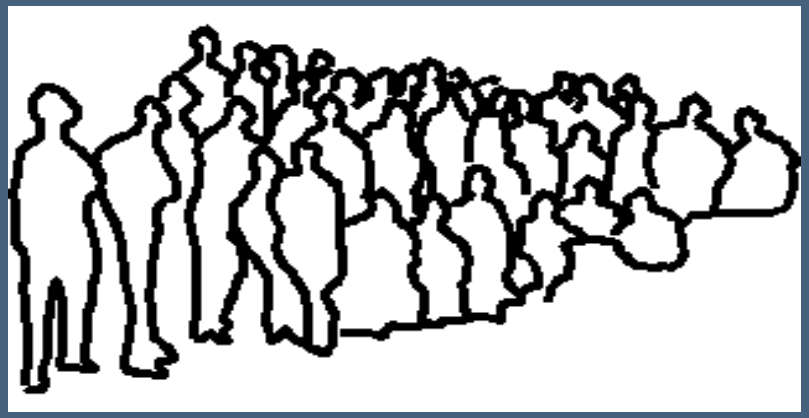


Information



Research on Clinical Subjects

- Aftermath of WW-II
  - Nuremberg Trials
  - Tuskegee Study
  - Brooklyn Jewish Chronic Disease Hospital
- National Research Act 1974
- Institutional Review Boards



Women as Clinical Subjects

Perceived greater risk

Women

- Fear damage to reproductive ability

Researchers

- Fear complexities of menstruation

Men are Homogenous

- Prescott 1978
  1) 56% reduce variability
  2) 28% limited resources
  3) 15% lack of interest

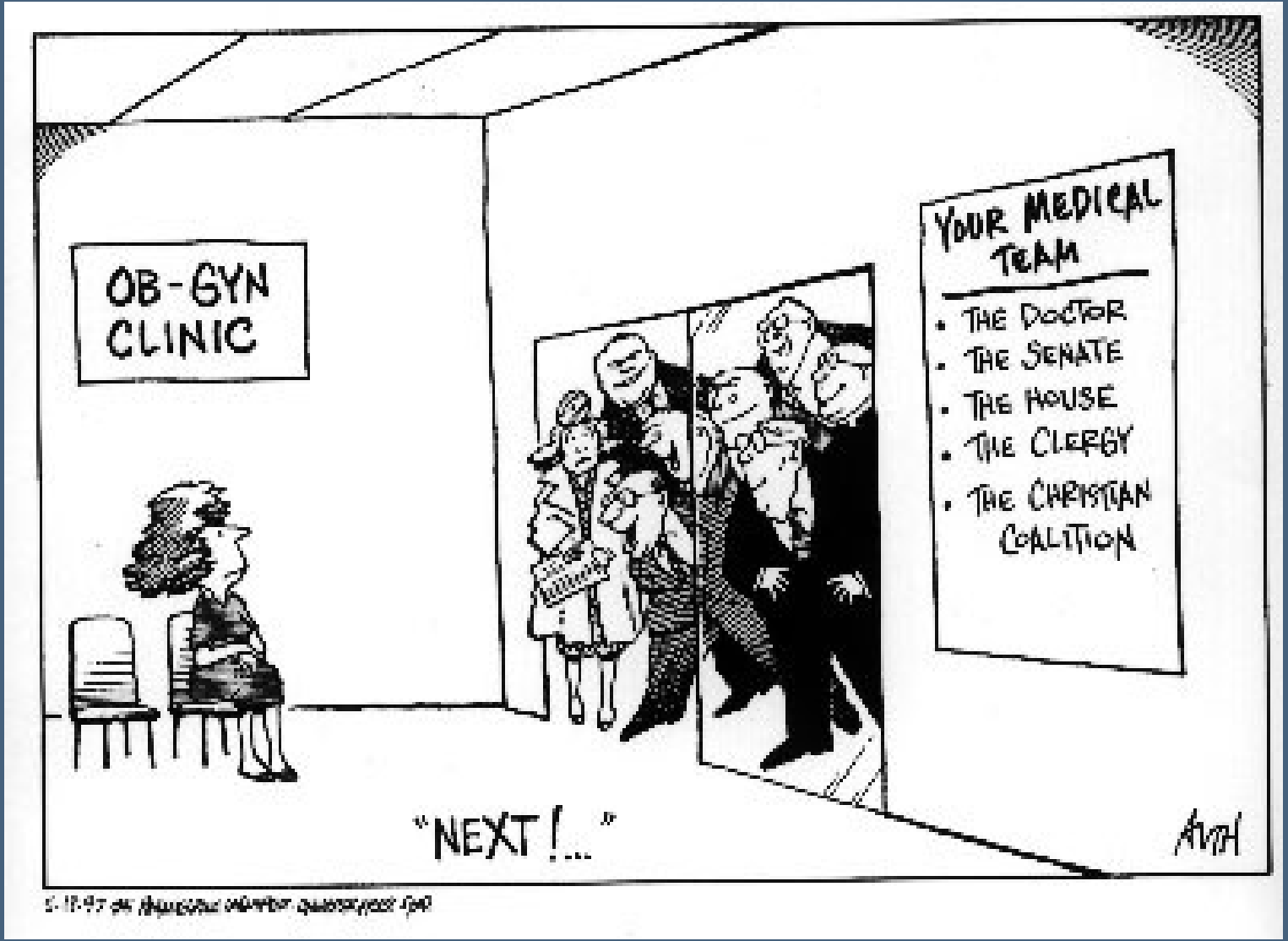
Response of the Government

- Task Force on Women's Health 1985
  - Nothing was known about the unique needs
- 1990 NIH Review of proposals
  - 50% included only men
  - 30% both sexes included (? Proportions)
  - 20% never mentioned gender

NIH Revitalization Act

- Protocols include women
- Phase-3 Clinical Trials study both sexes

Where are we now?

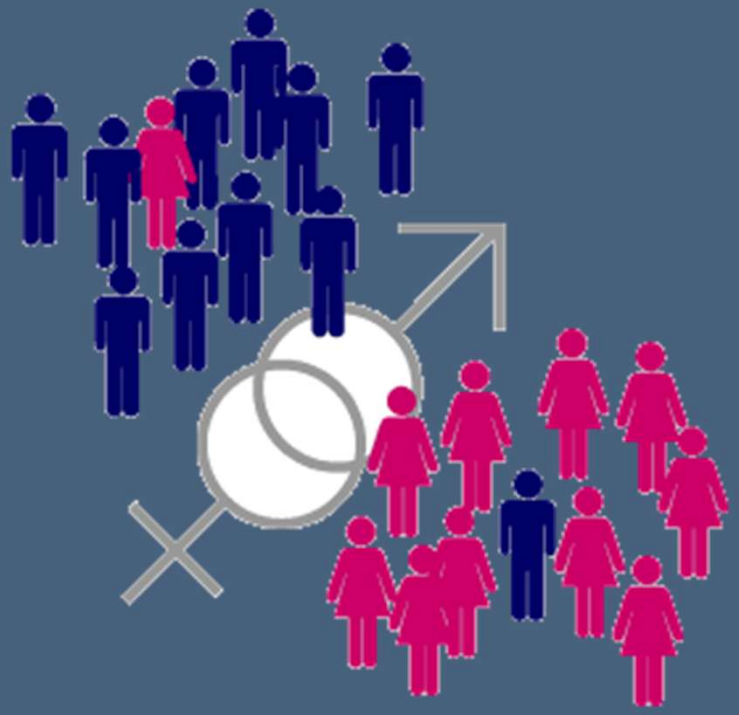


Women as Patients

Gender-Specific Medicine

- The science of the differences in the normal physiology of men and women and the way they experience disease.

Current Research



- Bone
- Brain
- Pain
- Immune System
- Lung
- Cytochrome P-450

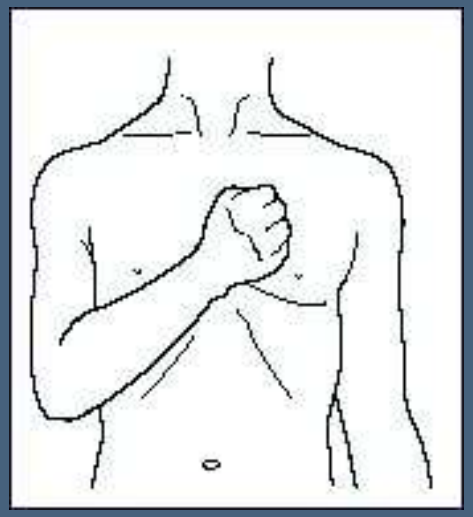
- Cardiovascular System

Cardiovascular

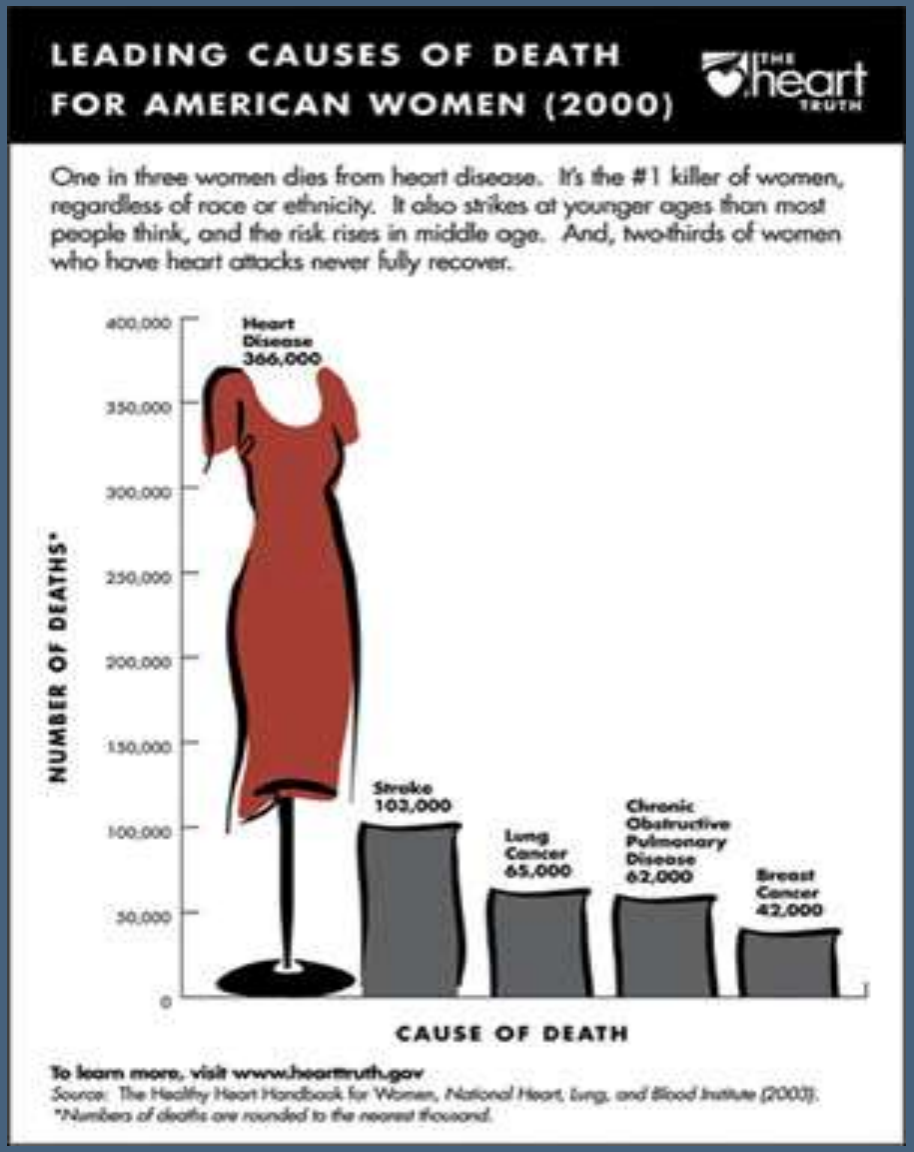
- 20% of articles on CHD provide separate findings on women.

- 2004 Hannover Cardiovascular Grp Project
  - Review all key papers in CVD
  - 489 studies
  - 1% of the studies included women

Myth: Heart Disease is a Man's Disease

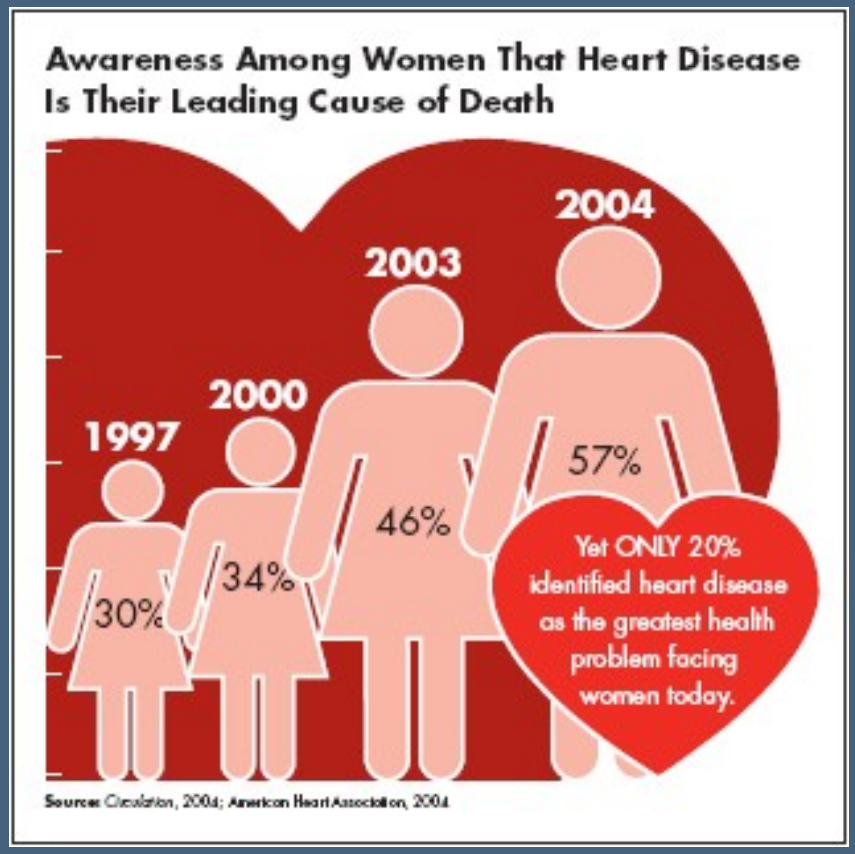


Fact: Heart Disease #1 killer of US women



www.hearttruth.gov

Who Knew?



- 80% American women did not
- 32% of 300 PCPs did not

AMWA Gallop Survey 1995

Prevalence

- Men
  - 6.7% 45-54 yr
  - 13.1% 55-64 yr
  - 17.7% 65-74 yr
  - 18.6% >75
- Women
  - 5.5% 45-54 yr
  - 8.4% 55-64 yr
  - 11.1% 65-74 yr
  - 16.1% >75

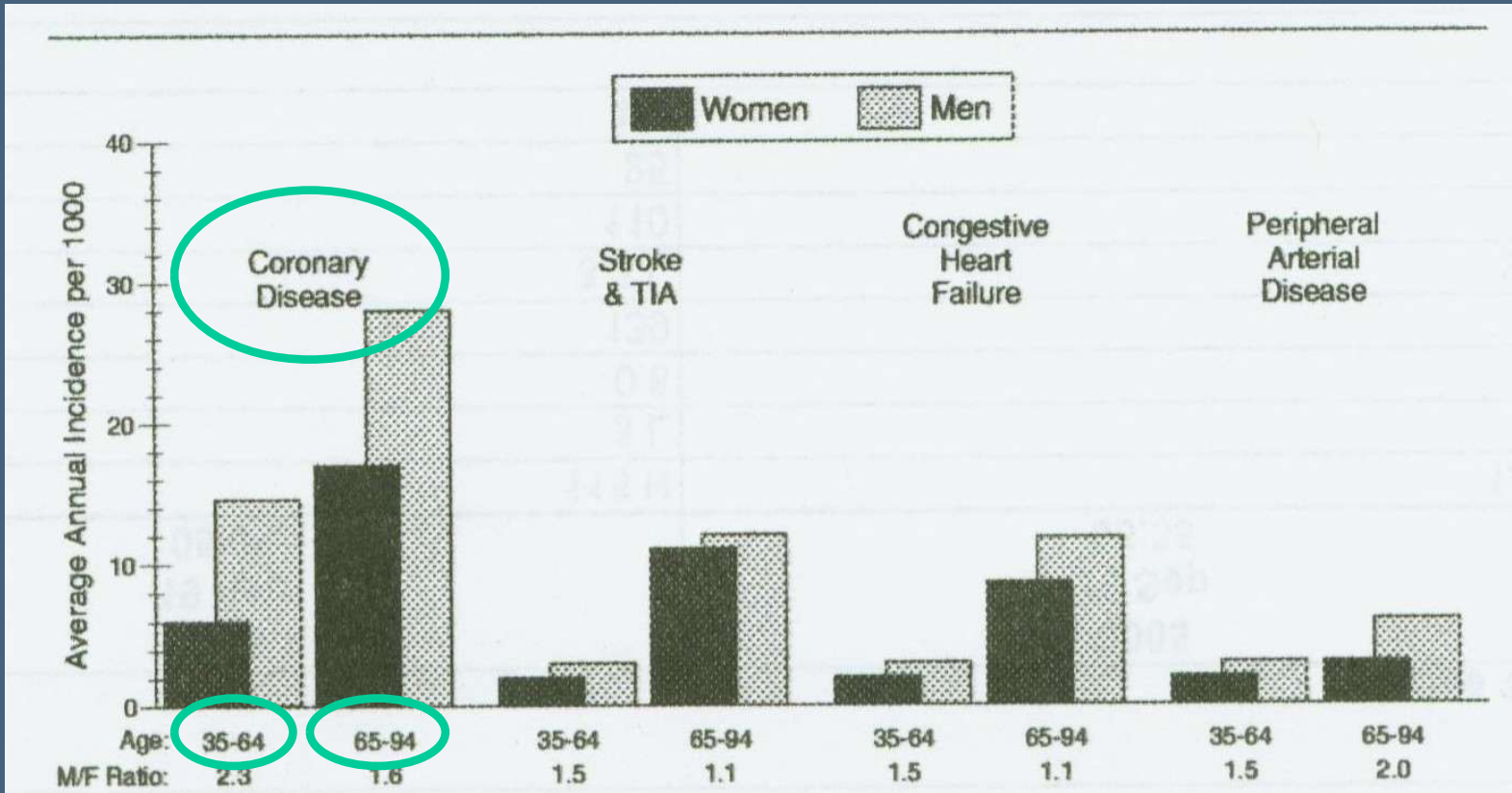
Incidence

- Men age 40-49 are 7x more likely CHD
- Women lag behind men
  - 10yrs at time of presentation
  - 20yrs at time of first AMI
- Women >65 have 3x increase
- Women >75 are 40x more likely than premenopausal women.

The Framingham Heart Study

- Leading longitudinal cohort study of cardiovascular disease
- Includes Men (2,336) and Women(2,873)

Incidence of Cardiovascular Events



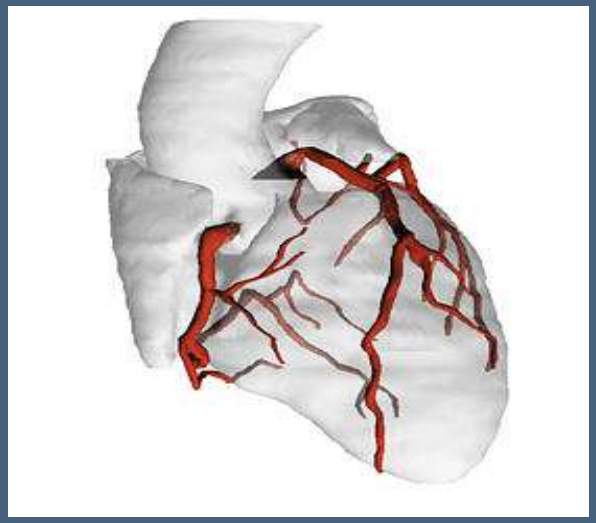
Incidence of Cardiovascular Events, Framingham Study.[7]

JAMWA 1995;50:35


Difference between
men and women

Anatomy

- Size, Shape, and Conducting System
  - Faster resting heart rate
  - Longer QTc for a given rate
  - Concentric hypertrophy
- Coronary Arteries 2-3x smaller



Presentation

- "Typical"
  White middle-aged men chest pain
- "Atypical"
  Anything else

Women's Early Warning Symptoms of AMI

Symptom	Prodomal (%)	Acute (%)
Pain-General	13.0	19.8
Left Arm Numb	7.2	8.7
Sleep Disturb	47.8	---
Fatigue	70.7	42.9
SOB	42.1	57.9
Anxious	35.5	---
Indigestion	39.4	30.5

Circulation 2003;108:2619-2623

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Comparison of Chief Complaint

TABLE 2 Comparison of Chief Complaint Between Women and Men According to Age

Characteristic	<65 Yrs			65–74 Yrs			≥75 Yrs		
	Women (n = 160)	Men (n = 500)	p Value	Women (n = 185)	Men (n = 257)	p Value	Women (n = 499)	Men (n = 382)	p Value
Chest	73.1%	81.0%		61.1%	65.0%		45.5%	56.3%	
Respiratory	14.4%	7.0%	0.01	20.0%	19.8%	0.56	22.0%	24.9%	<0.001
Other	12.1%	11.7%		18.4%	14.8%		31.6%	18.5%	

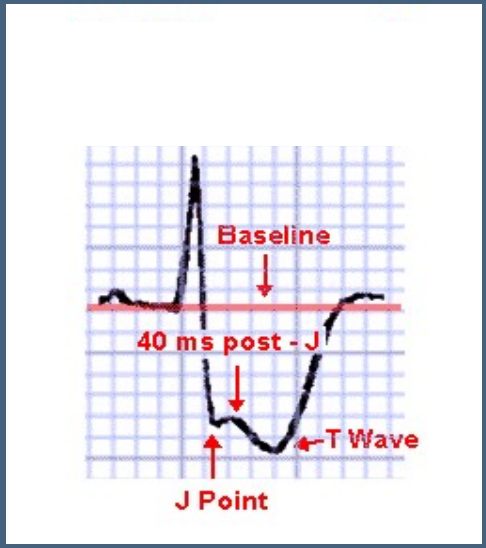
Chest = pain, pressure, tightness, or discomfort in chest; other = one of the following dizziness or lightheadedness; headache; numbness in arm or hand; loss of consciousness; syncope; weakness or fatigue; sweating or diaphoresis; palpitations; pain in arm or shoulder, left or right arm, left shoulder, back, neck, or jaw pain; nausea; vomiting; abdominal pain; or other atypical symptoms; respiratory = dyspnea or cough.

The Am J of Cardiology 2004;93

Acute Coronary Syndromes

- Non-ST elevation MI
  - Women 25%
  - Men 16%

- Troponin equally predicted risk mortality



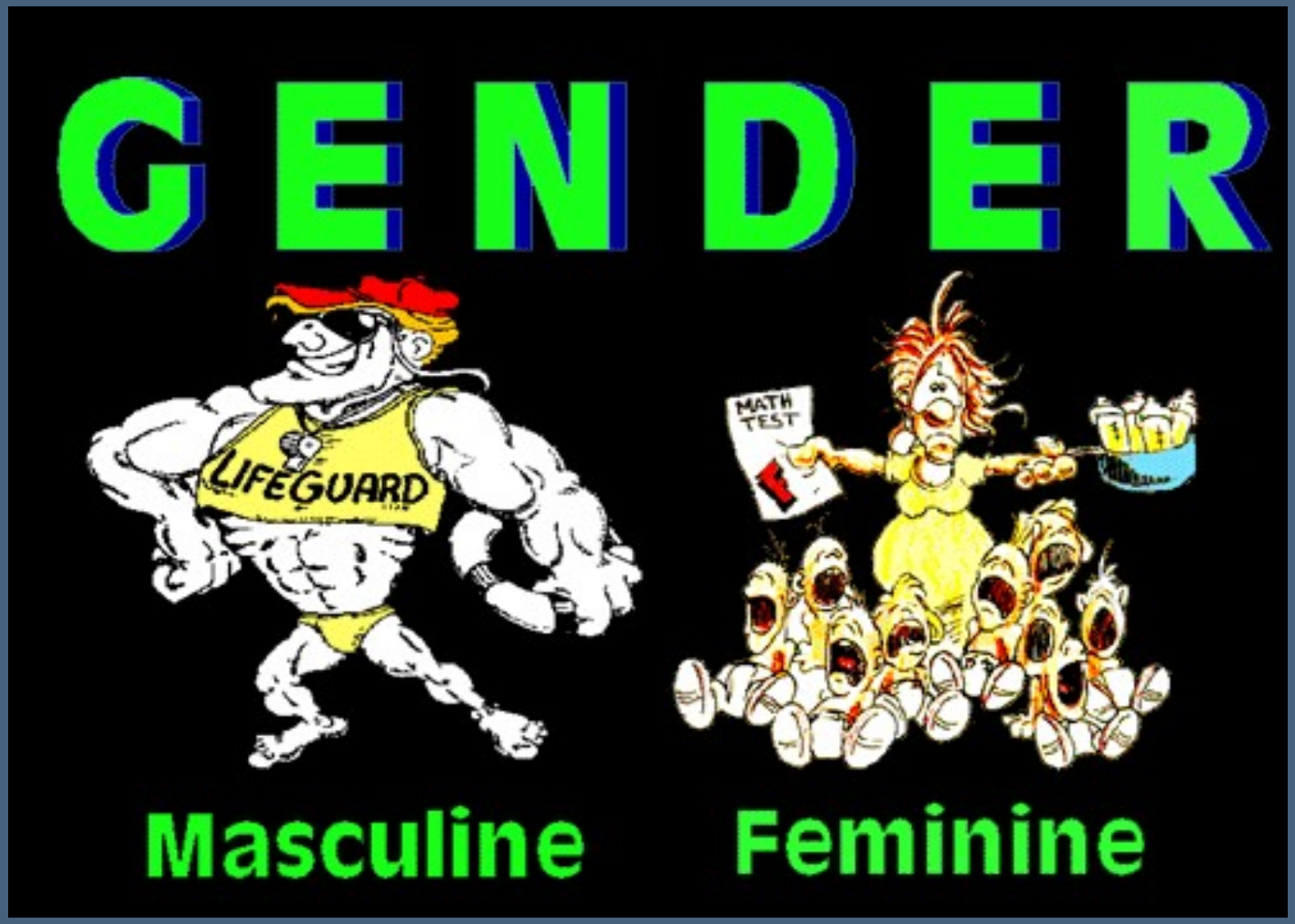
Non-modifiable Risk Factors

- Age
- Sex
- Heredity

Age

- Men more likely to develop CHD earlier
- After menopause that difference lessens
  - Age 20-39 = 1 in 30 women has CHD
  - Age 45-60 = 1 in 9 women has CHD
  - Age >60 = 1 in 3 women has CHD
- Age 75-84 has Incidence 40x premenopausal

Sex



- Independent Risk Factor?

Family History

- Paternal history assoc w/ greater risk for both sexes

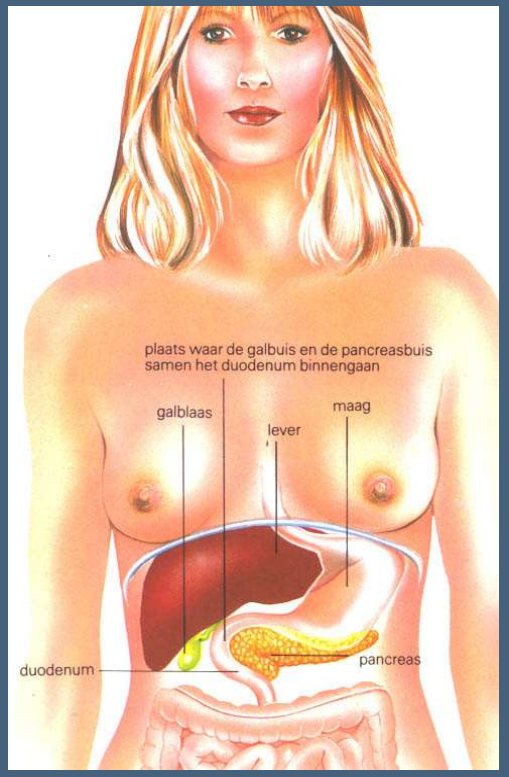
- Women with maternal history are more likely than those with similar paternal history to incur MI

Modifiable Risk Factors

- Diabetes
- Dyslipidemia
- Hypertension
- Hormones
- Obesity
- Cigarettes

Diabetes

- Greater risk for fatal MI
  - Women 7-10x higher than nondiabetic
  - Men 2-3x higher than nondiabetic
- Poorer prognosis after MI



How it differs for men and women?

- Obesity more prevalent
- Experience more Sx of Hyperglycemia
- Increased risk of depression
- More likely to have Hypertension
- Coagulation system in Prothrombotic state

Gender Med 2006;3: 131

Dyslipidemia

- Diabetic Women have more severe lipid abnormalities than Diabetic Men
  - Low HDL-C
  - High Triglycerides
  - Small LDL-C particle size

Different Optimal Levels

- Women have higher HDL levels

- Less "Elbow Room"
  - HDL women >45-50 mg/dL ; men >35 mg/dL
  - TG women <150-200 mg/dL ; men <400 mg/dL

Drug Treatment in Women

Review 13 trials (6 included women)

- Women w/o CHD
  - Did not prolong life
  - Did not reduce odds of dying from heart disease
- Women with CHD
  - Reduced nonfatal cardiac events
  - No affect on mortality

JAMA 2004; 291:18

Hypertension

- Postmenopausal women
- Women are on greater # drugs
- Women have higher levels
  - Salt Sensitivity
  - Hormonal variation
  - Vascular reactivity

Am Heart J 2005;150:1260

Modifiable Risk Factors

- Diabetes
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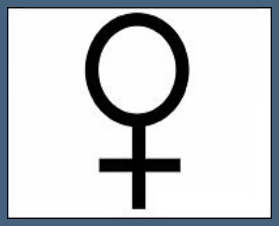
Summary Points



- DM is a bad risk factor
- Different optimum lipid profiles
- Statins haven't been proven as 1°prevention

Modifiable Risk Factors

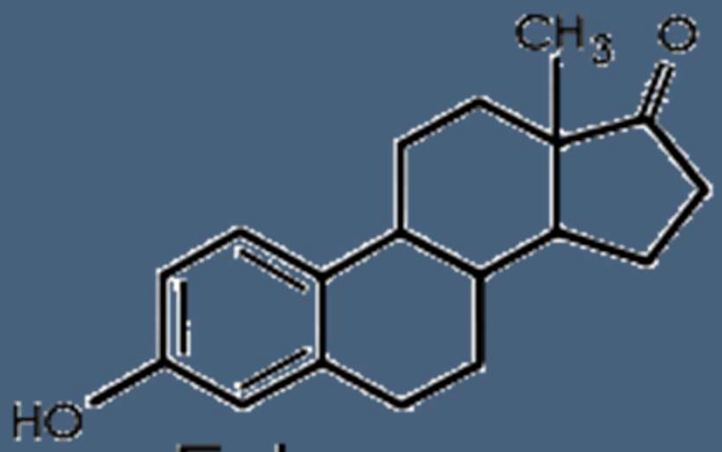
- Diabetes
- Dyslipidemia
- Hypertension
- Hormones
- Obesity
- Cigarettes

Menopause

- Estrogen dilates blood vessels
- Estrogen favorably affects lipid profile

Mechanisms underlying gender differences

- Estrogen
  - Affects endothelium-dependent vasodilatation
  - Ach $\rightarrow$ NO



Estrogen

Mechanisms underlying gender differences

- Increase in bp after puberty in boys
- Testosterone
  - Pressure-Natriuresis
  - Na reabsorption in proximal tubules

- Decrease on CHD outcomes among women receiving HRT

"The Mother of all Trials"

Hypothesis: Hormone therapy decreases risk of Stroke, CAD, and Osteoporotic fx

- 16,608 CEE + MPA vs Placebo
- 10,739 CEE vs Placebo

Unexpected Results

- CEE / MPA
  - Increased risk PE (113%), CAD (29%), CVA (41%)
  - Increased risk invasive Breast CA (26%)
  - Reduction Colorectal CA (37%), Hip Fx (34%)
- CEE
  - Elevated risk of CVA
  - Minimally elevated risk venous thrombosis
  - No cardioprotection

DCMS 2006;57:42

- Clinical Practice Changes
  - HT prescription decreased by 38%
  - CEE / MPA decreased by 74%
- WHI findings in youngest subgroup 50-59
  - Suggested no inc risk in CEE / MPA
  - Suggested cardioprotection in CEE
- Risk vs Benefits

DCMS 2006;57:42

Modifiable Risk Factors

- Diabetes
- Dyslipidemia
- Hypertension
- Hormones
- Obesity
- Cigarettes

Obesity

- Distribution of Body Fat

- Men smoke more than women
- Women have greater incidence of MI
  - Women Smokers 6x : Women Nonsmokers
  - Men Smokers 3x : Men Nonsmokers

Jmhg 2004; 1: 32-37

Mortality

- A women is at a greater risk of dying of a heart attack than a man <u>at any age</u>
  - 2x as likely to die within 60d
  - 2x as likely to have a second MI

Sex related differences in outcomes of AMI

- Why higher mortality among women?
  - Sex is independent risk
  - Older
  - Higher rates unfavorable prognostic factors
  - Delayed presentation to hospital
  - Less typical symptoms
  - Less aggressive treatment

Circ J 2006;70: 222-226

Revascularization

- Clear gender differences
- Higher Mortality in women
  - Same reasons as overall mortality?
  - Coronary vessels smaller

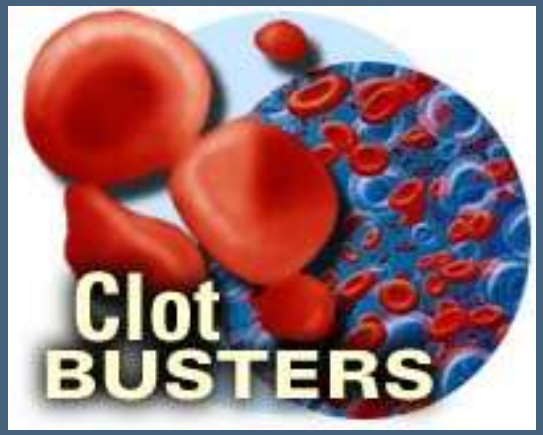
Heart 2006;92:19

PCI

- Registries 1980s – 1990s
  - Higher in-hospital mortality
  - Lower procedural success rate
  - Higher complication rate
- NHLBI 2002
  - Improvement success rate in women
  - Era drug eluting stents / glycoprotein IIb/IIIa inhib

Am J of Card 2006;97:1722

Thrombolytics

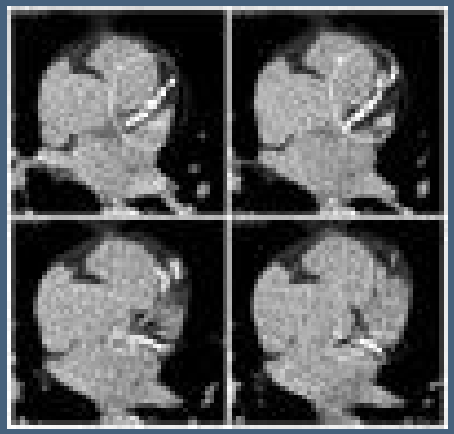


- GUSTO
  - Women 2x risk stroke
- PAMI-I
  - Women 5.3%
  - Men 0.7%
  - No gender differences in outcome of primary angioplasty group in all ages

Heart 2006;92:19

Coronary Imaging

- Coronary artery calcification in women with DM is less strongly correlated with CAD than it is in men with DM.
  - Sensitivity in men 83%
  - Sensitivity in women 46%

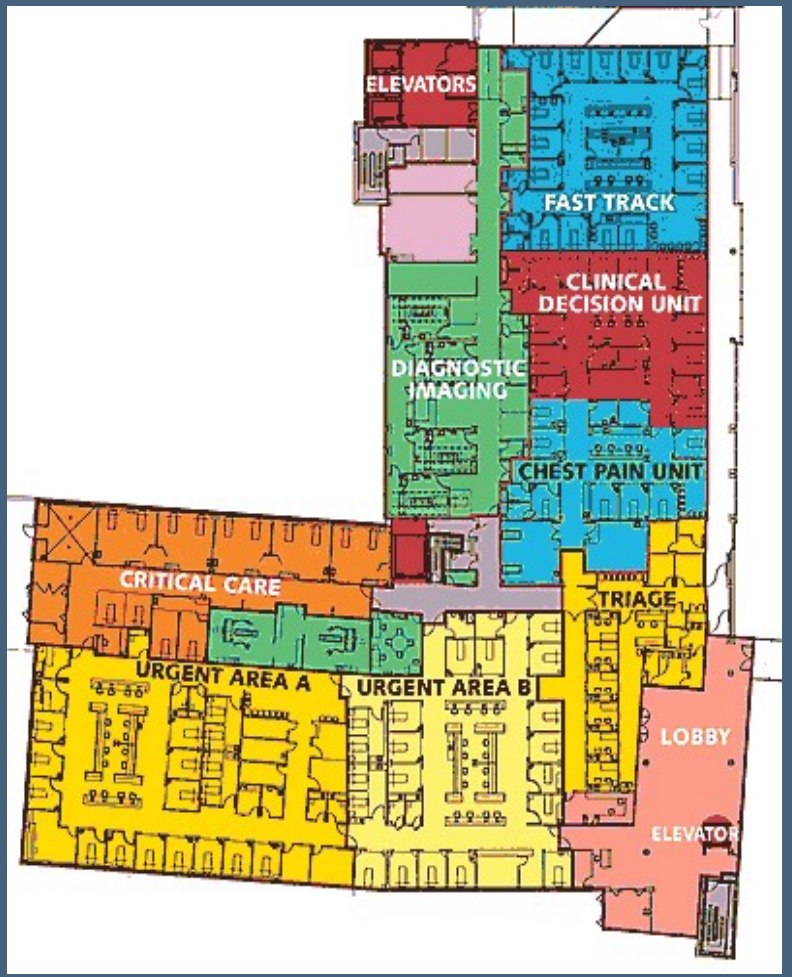


Pittsburgh Epidemiology of Diabetes Complications Study

Questions in the Emergency Department

- Triage decisions
- OU vs. 10A

- TCA / HyperK



"Sex Does Matter"

" It matters in ways that we did not expect. Undoubtedly, it also matters in ways that we have not begun to imagine."

Institute of Medicine1995

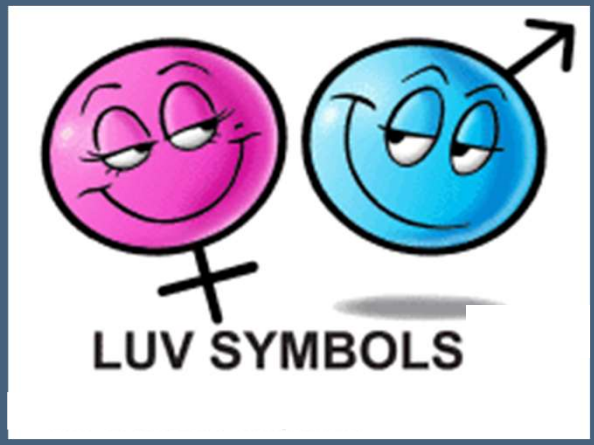
Being a Women or Man is a Health Determinant

- As significant as social origin, economic situation and ethnic origin.

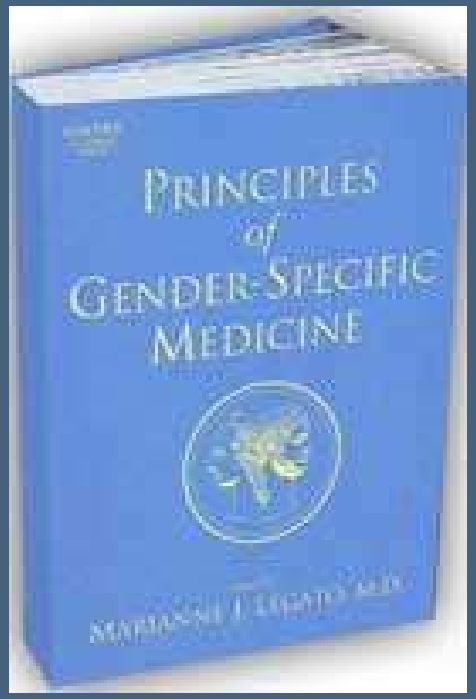
"Old Habits Die Hard"

- Vital that clinical research, medical education and practical application take a gender-based approach.


The 2nd Annual
Conference on
Gender-Specific
Medicine
2000


LUV SYMBOLS


Gender
Medicine


PRINCIPLES
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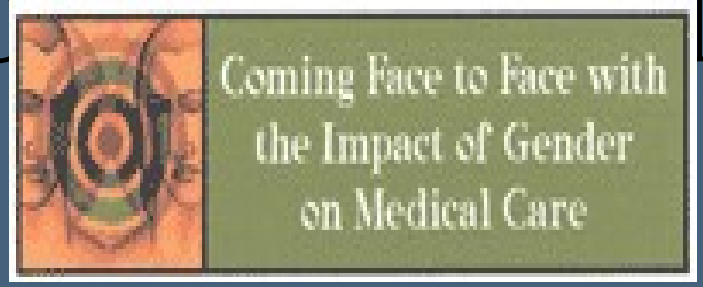
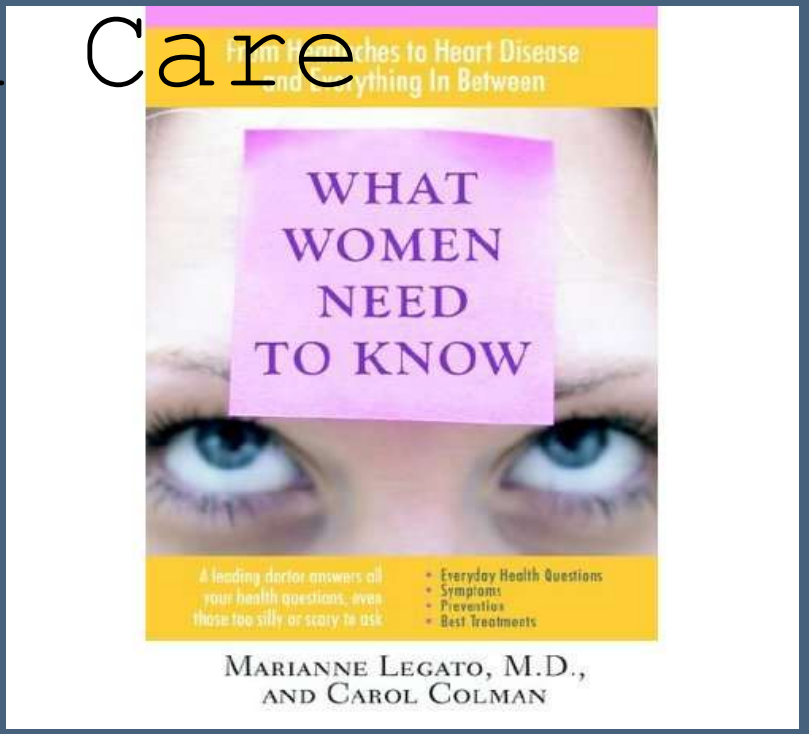
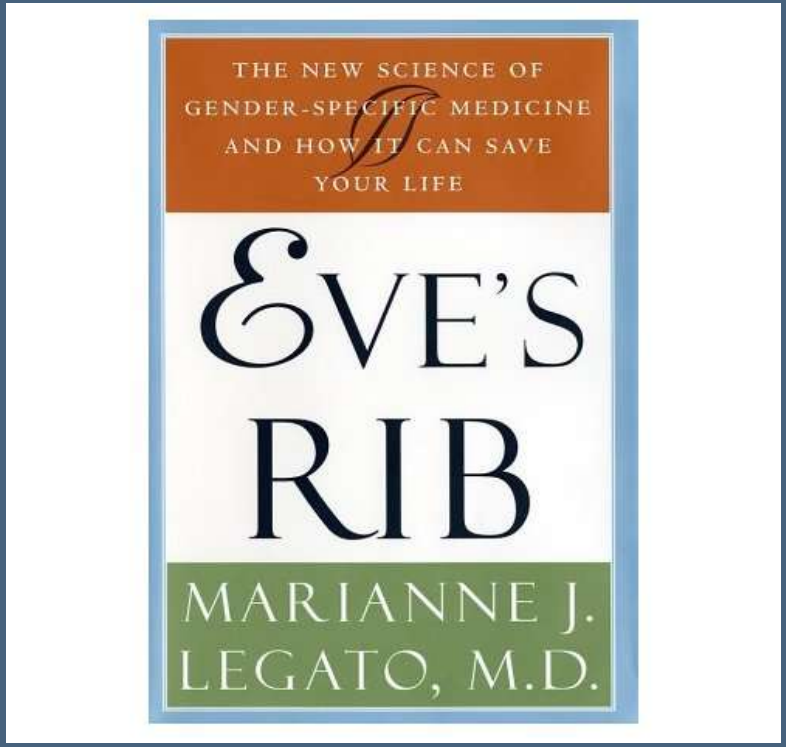
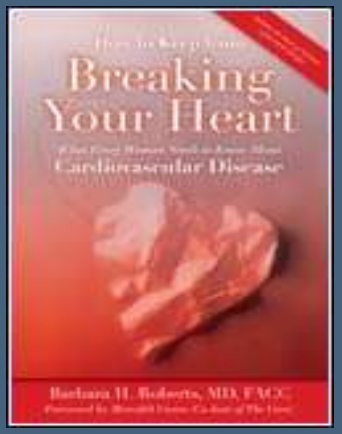
JGSM
The Journal of Gender-Specific Medicine

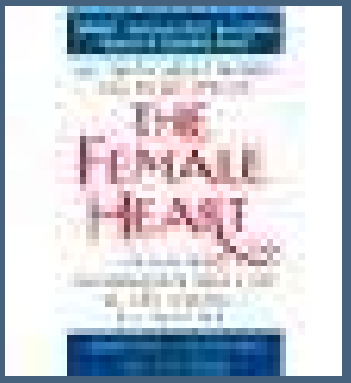
How Gender-Specific Medicine Could Change Health Care











The End