

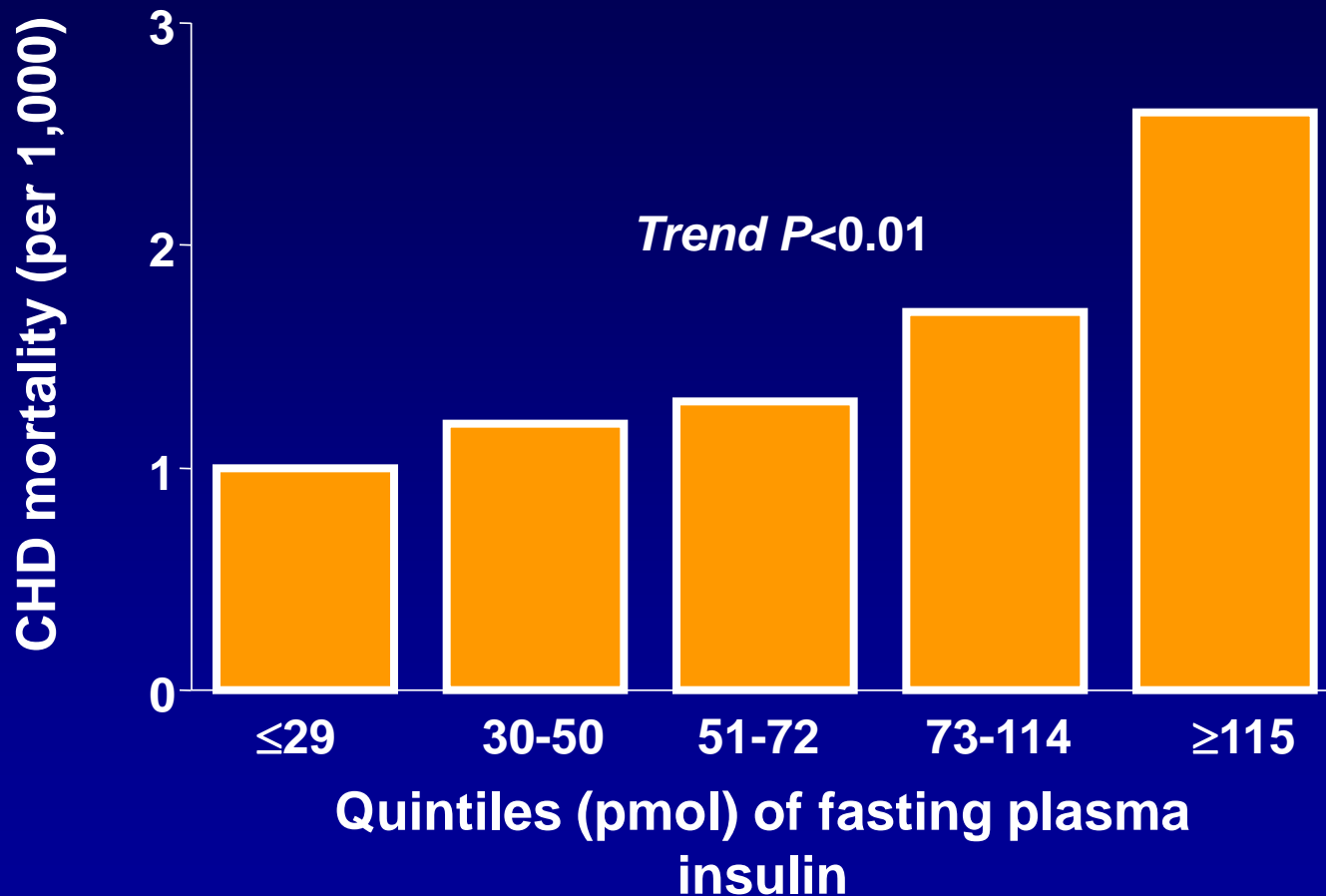
# **Diabetes Mellitus, Insulin Resistance and ACS**

**Peter W. F. Wilson, M.D.  
Emory University, Atlanta, GA**

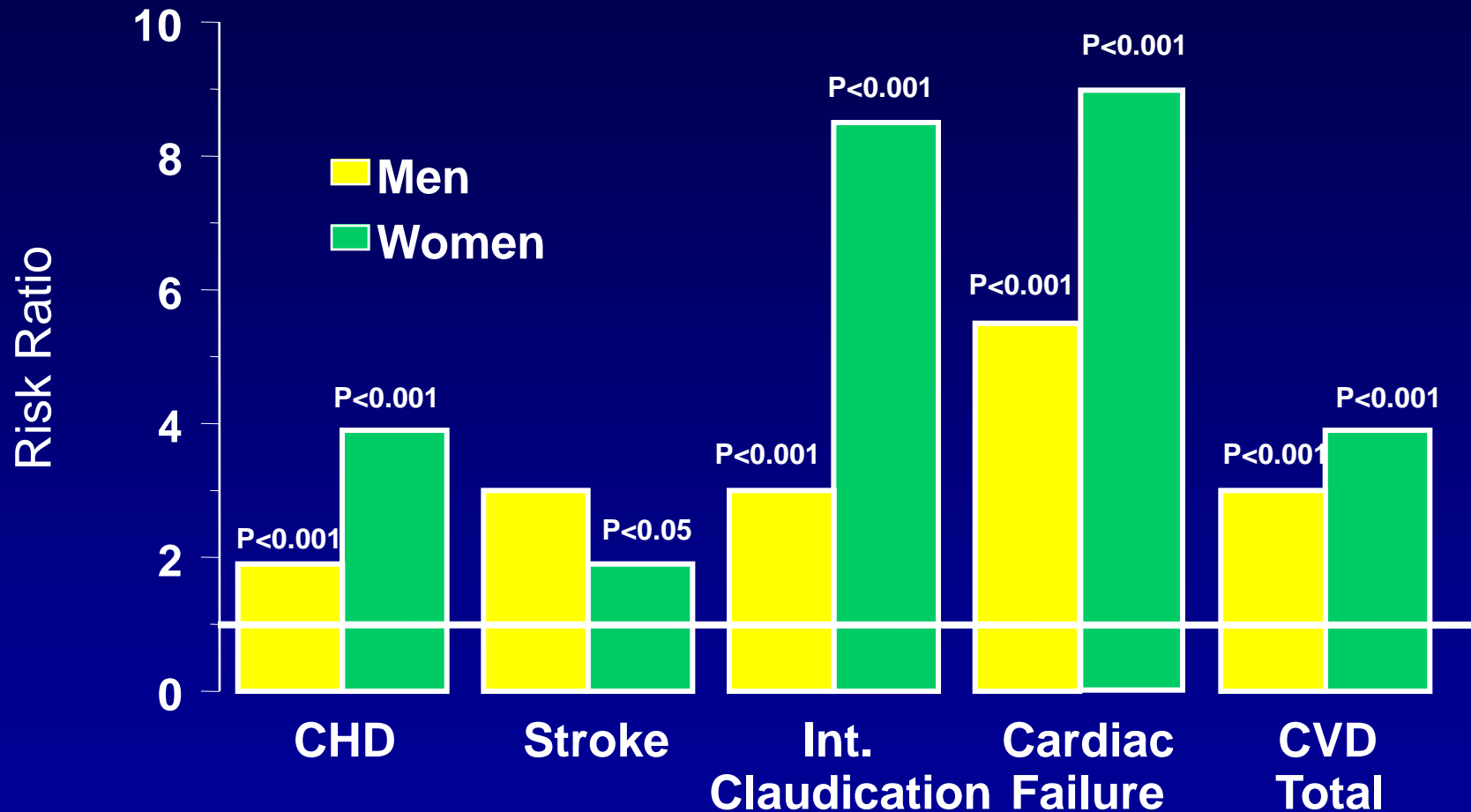
# Outline

- **Diabetes and CVD Risk**
- **CVD Risk Factor Differences**
  - **Blood Pressure**
  - **Lipids**
  - **Longer Term Glycemic Control (HbA1c)**
  - **Short Term Glycemic Control**
- **ACS Patients**
  - **Intravenous insulin protocols**
  - **Transition to subcutaneous insulin**
  - **Plans at Discharge**
  - **Follow-up post discharge**

## CHD Mortality and Hyperinsulinemia: Paris Prospective Study (n=943)

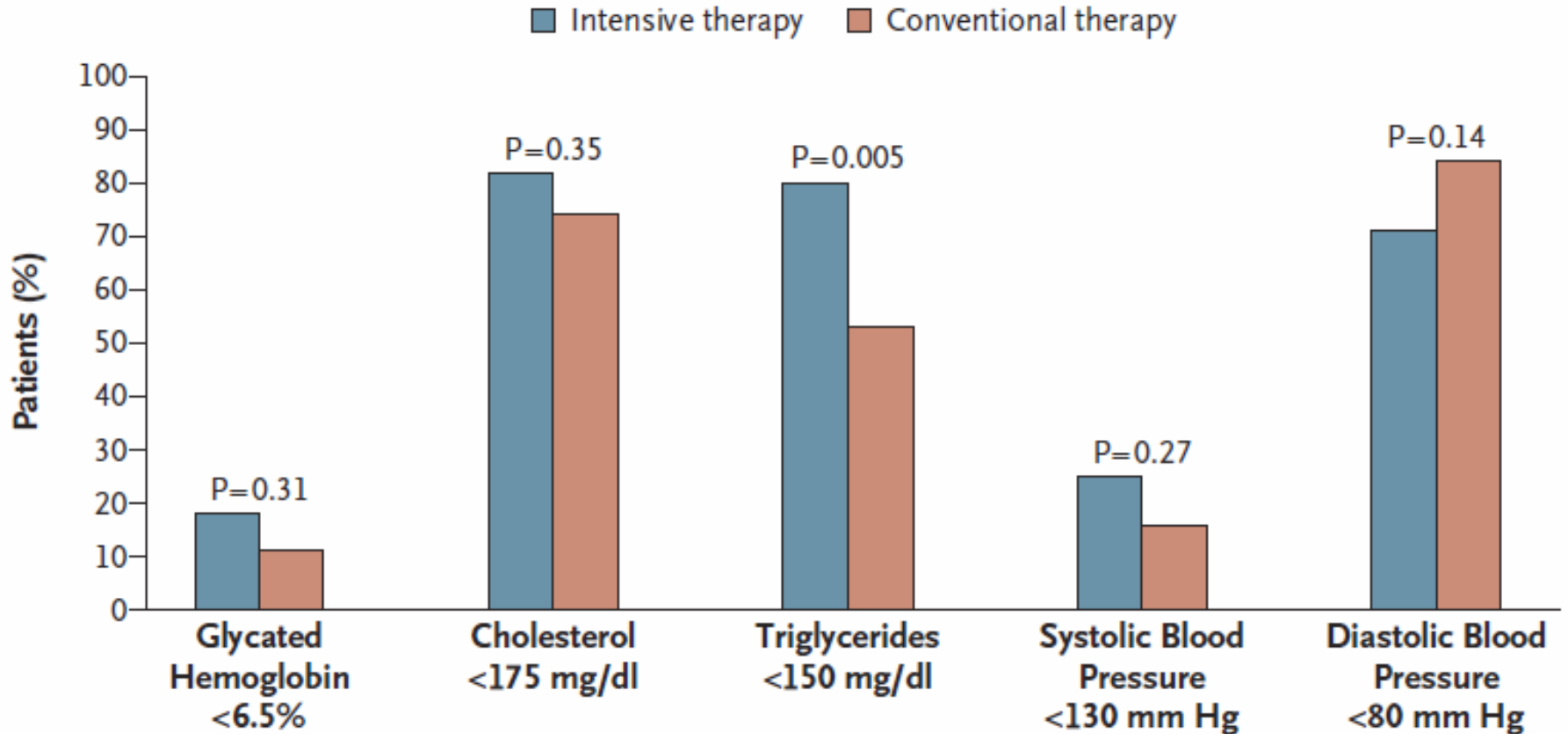


# Diabetes and CVD Risk in Framingham Cohort Age 35-64 Years--30 Year Follow-up



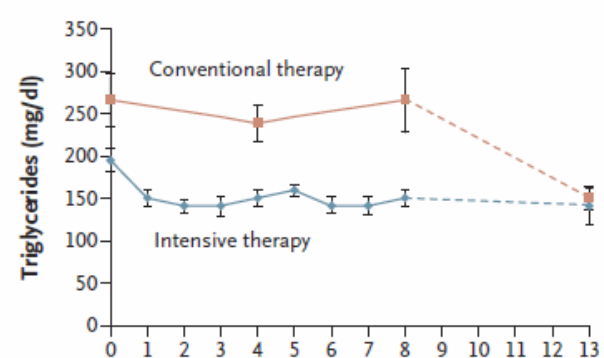
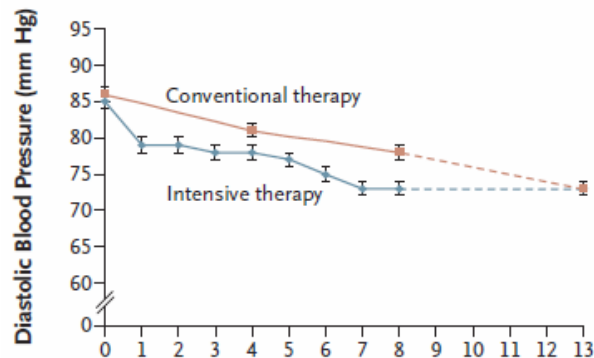
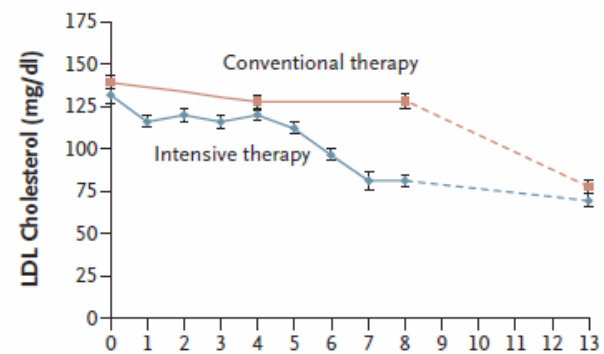
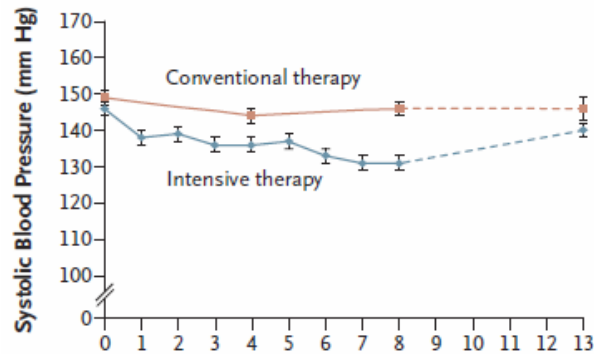
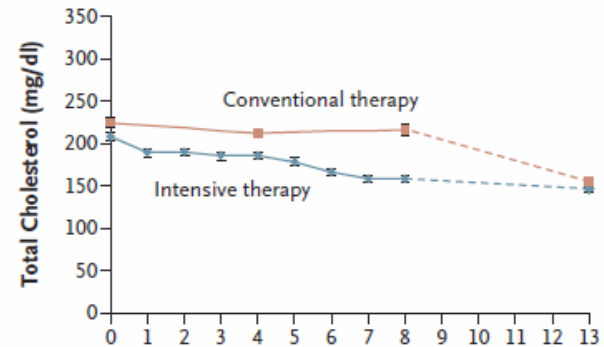
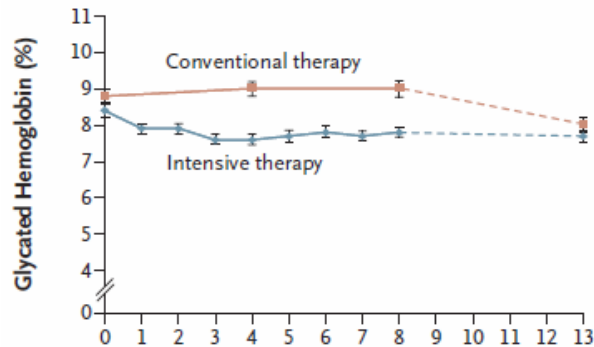
# Steno-2 Trial Results

## Risk Factor Control in T2DM



# Steno-2 Trial

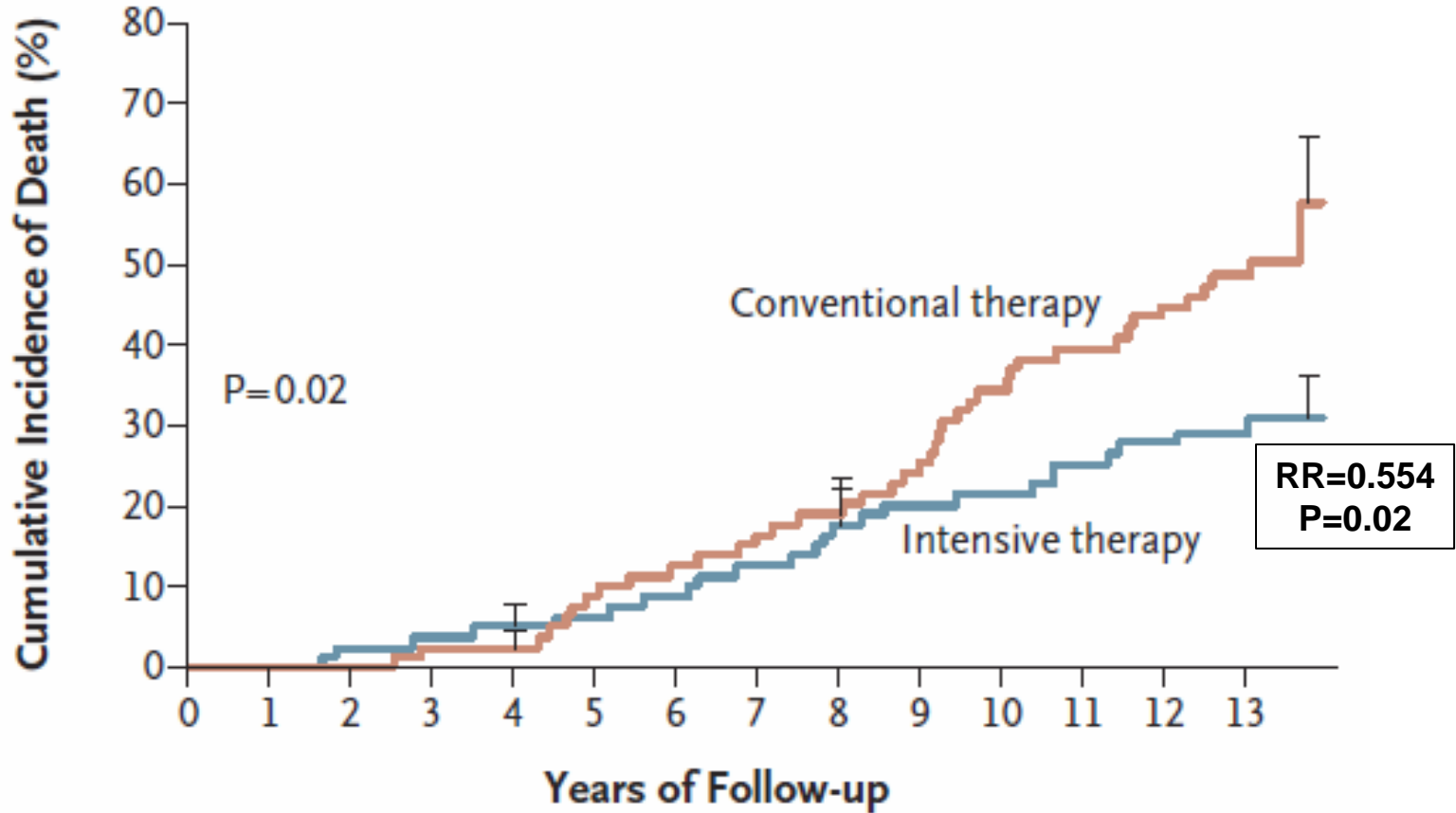
## Risk Factor Levels During Trial



# Steno-2 Trial Results

## All Cause Mortality in T2DM

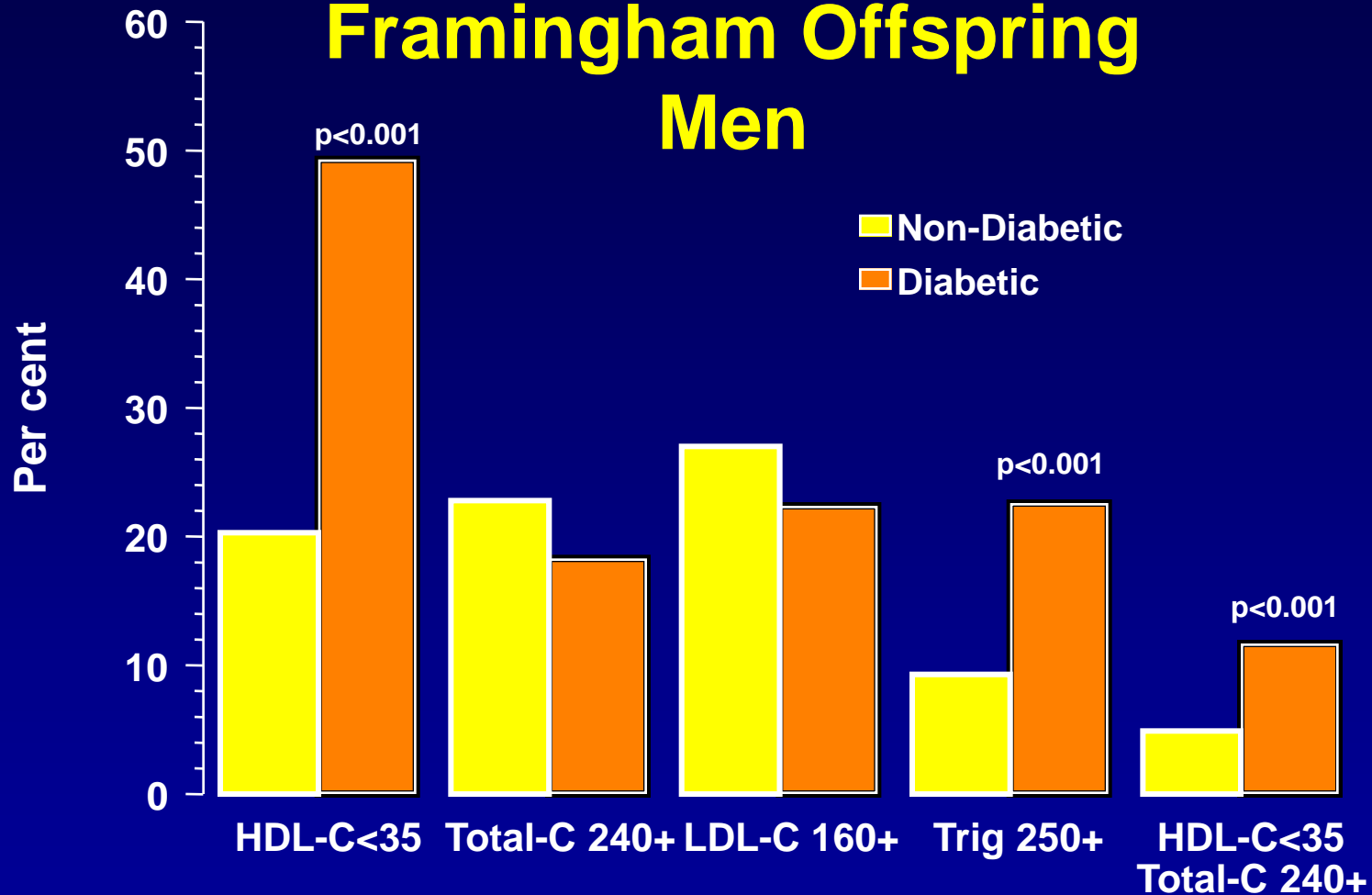
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### No. at Risk

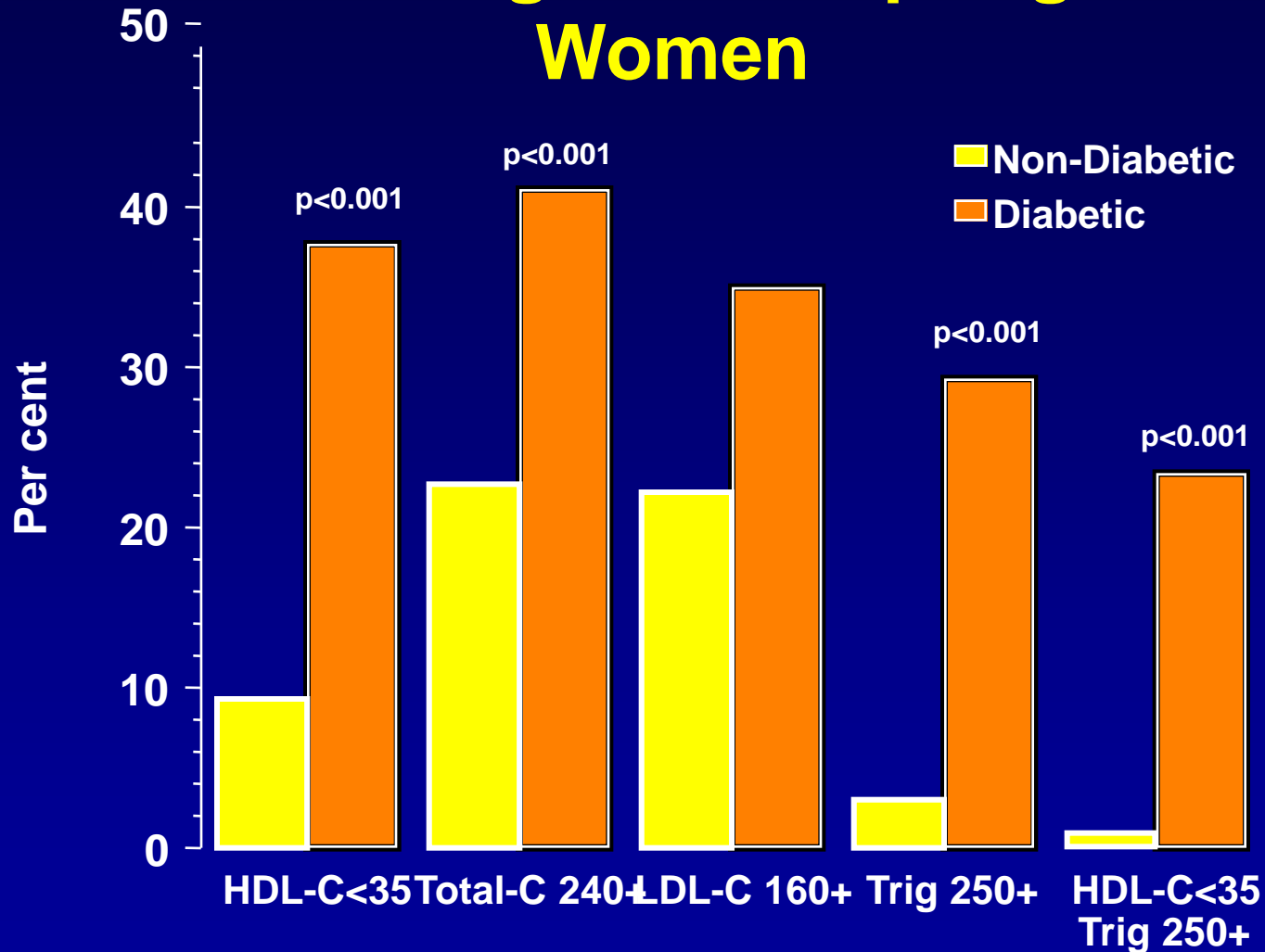
Intensive therapy	80	78	75	72	65	62	57	39
Conventional therapy	80	80	77	69	63	51	43	30

# Diabetes and Lipid Extremes Framingham Offspring Men

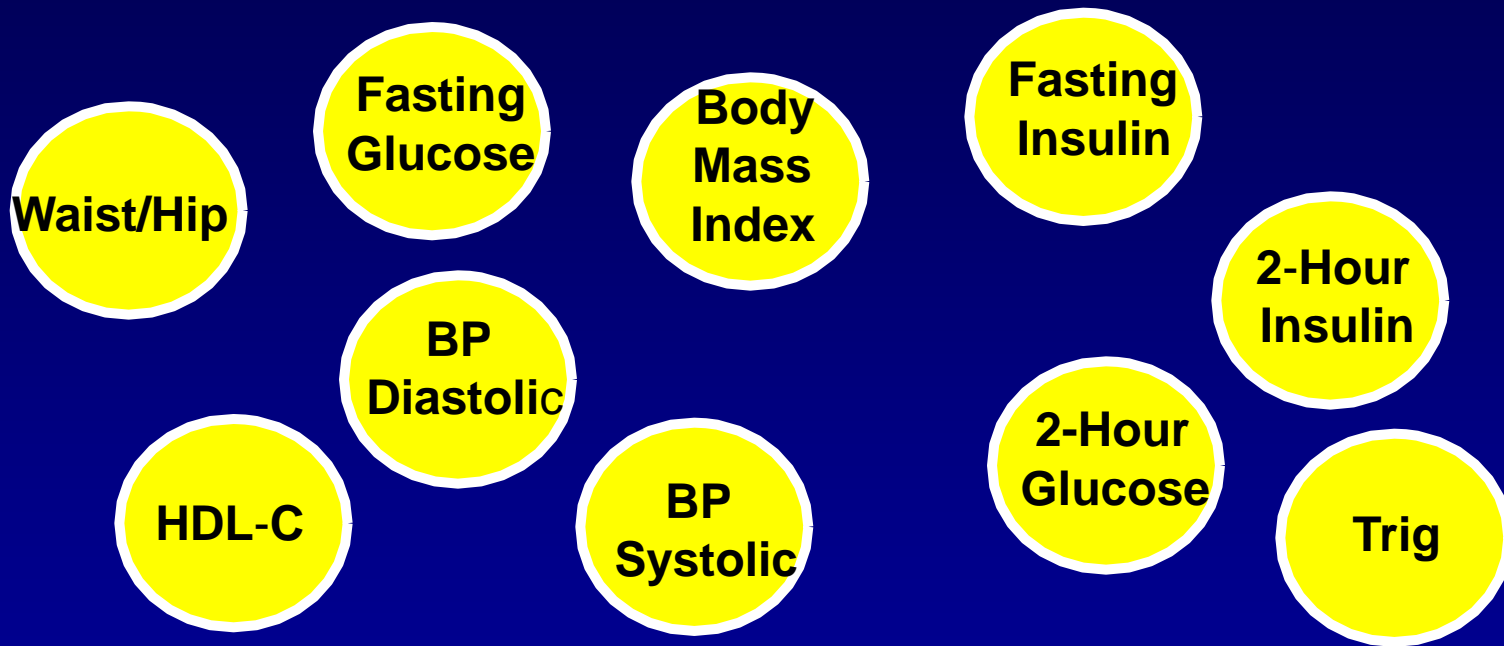




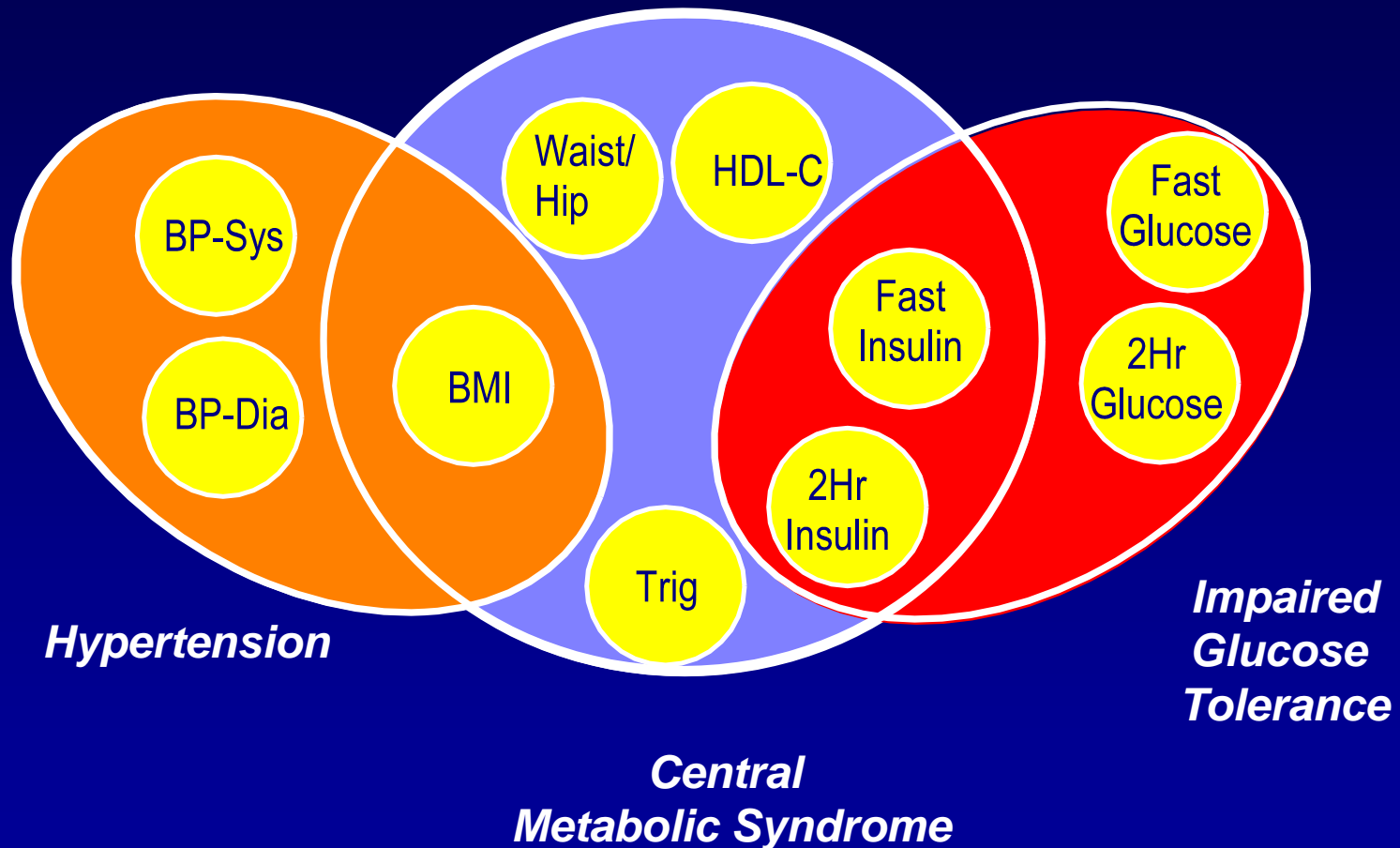
# Diabetes and Lipid Extremes Framingham Offspring Women



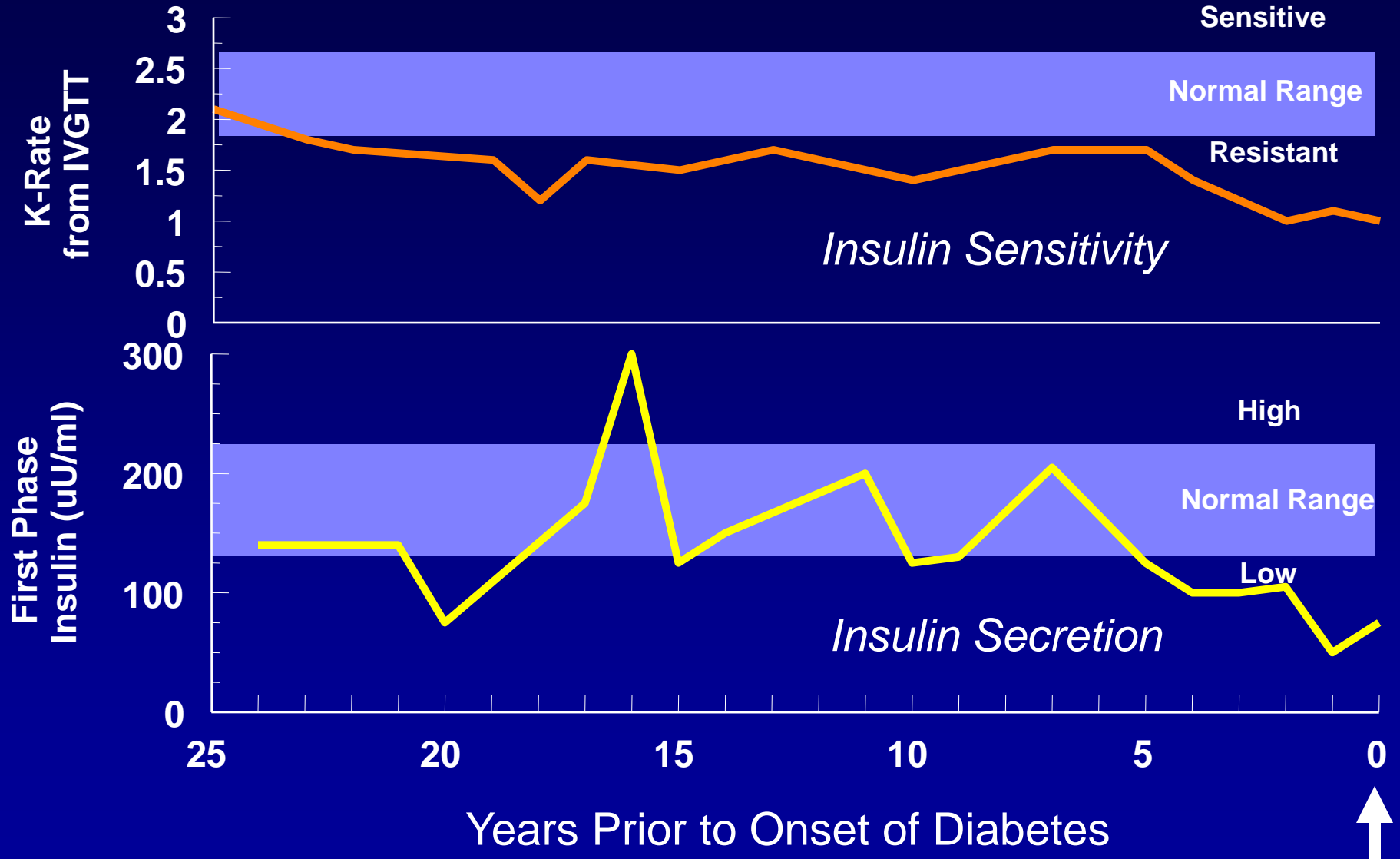
# Risk Variables for a Metabolic Syndrome



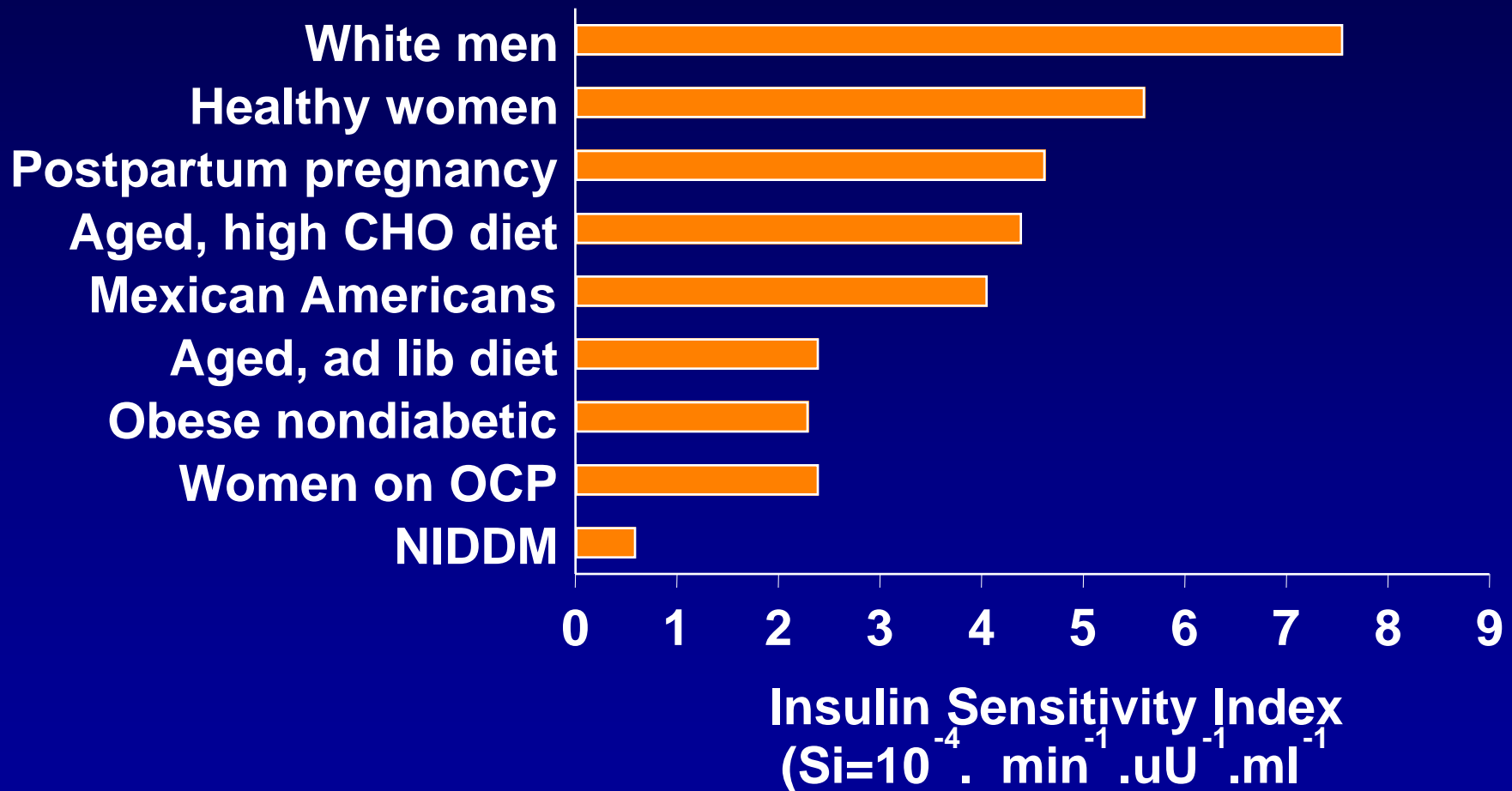
# Risk Variables for a Metabolic Syndrome



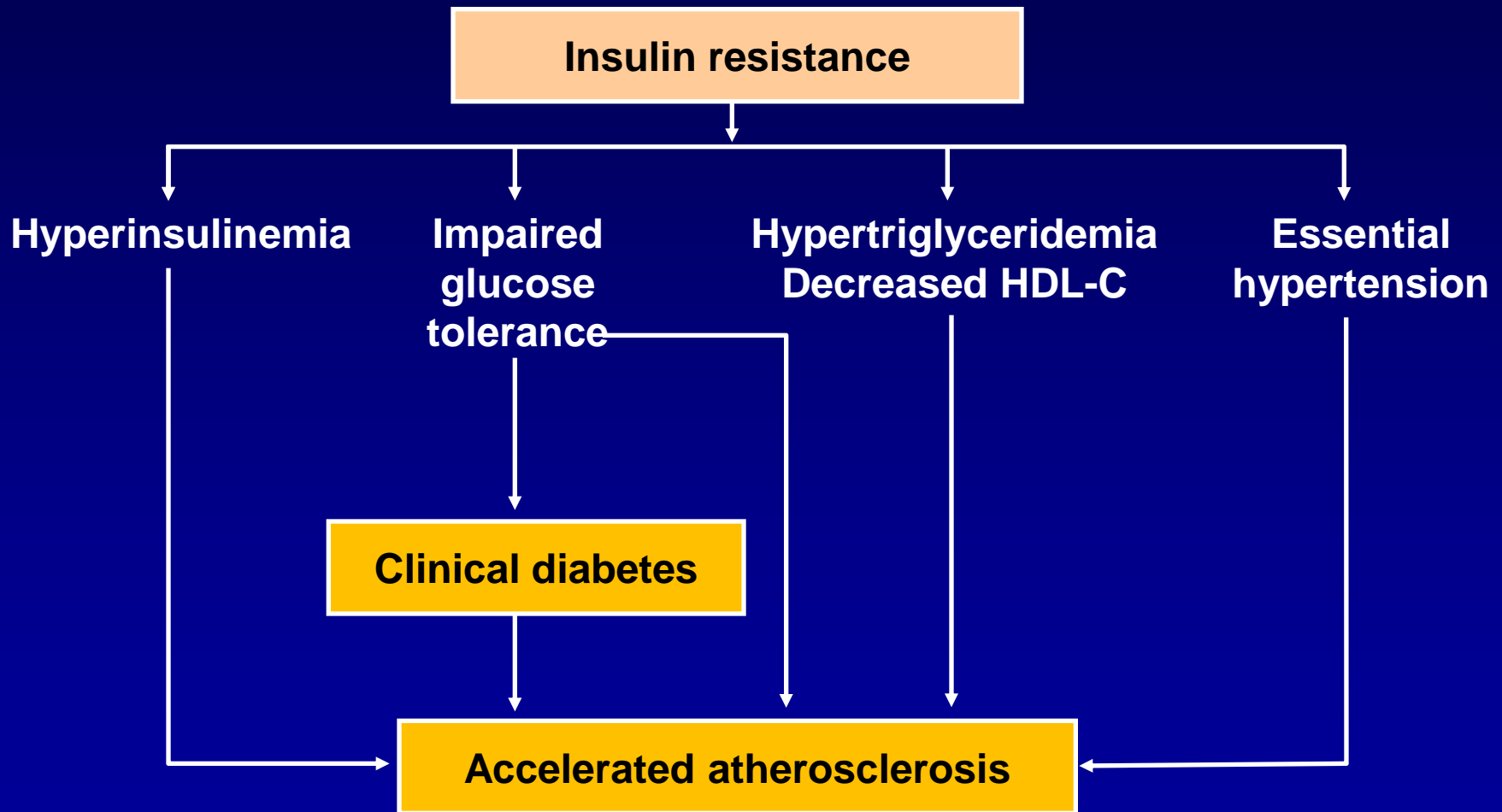
# Natural History of Type 2 Diabetes



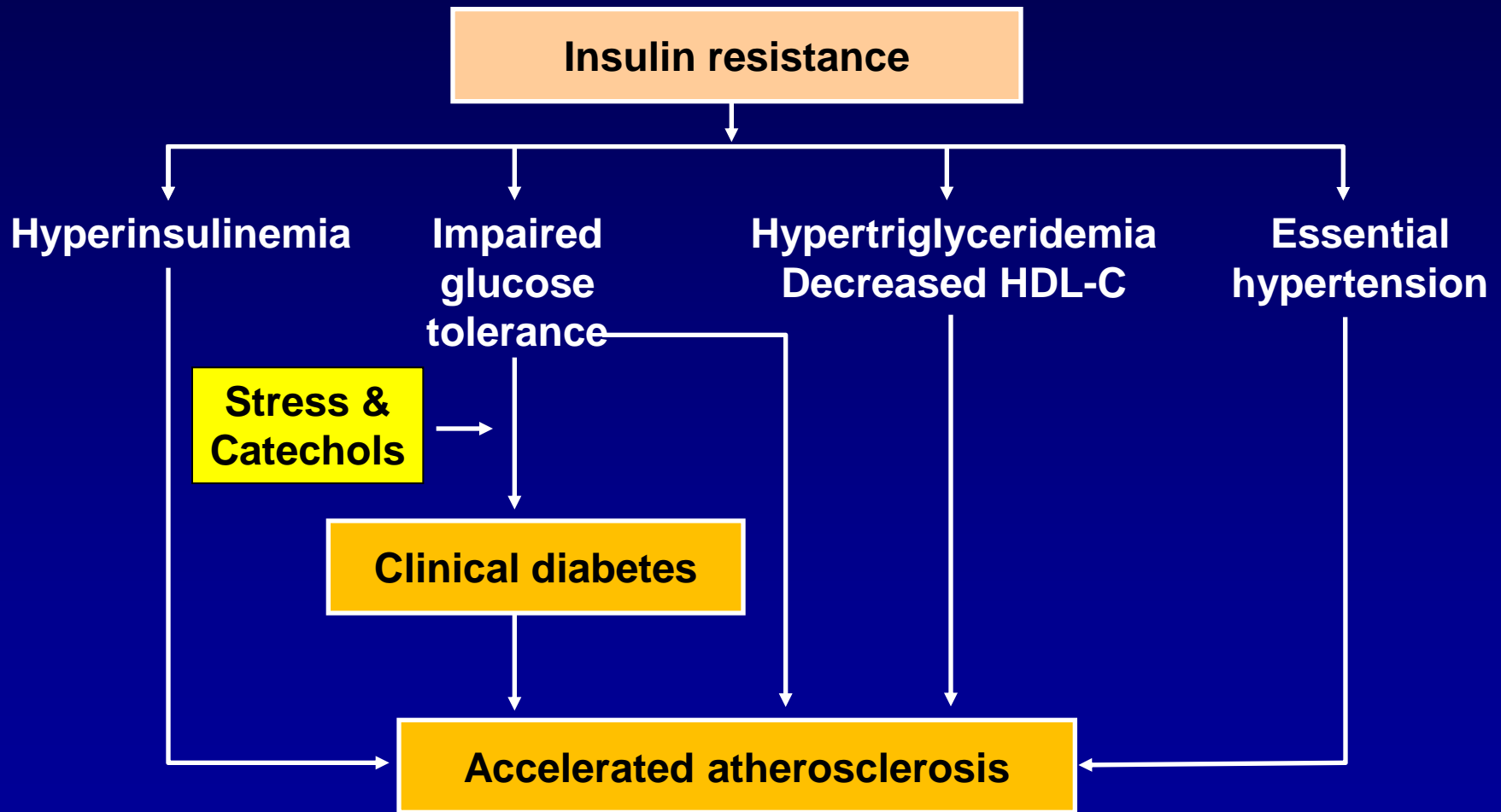
# Typical Levels of Insulin Sensitivity



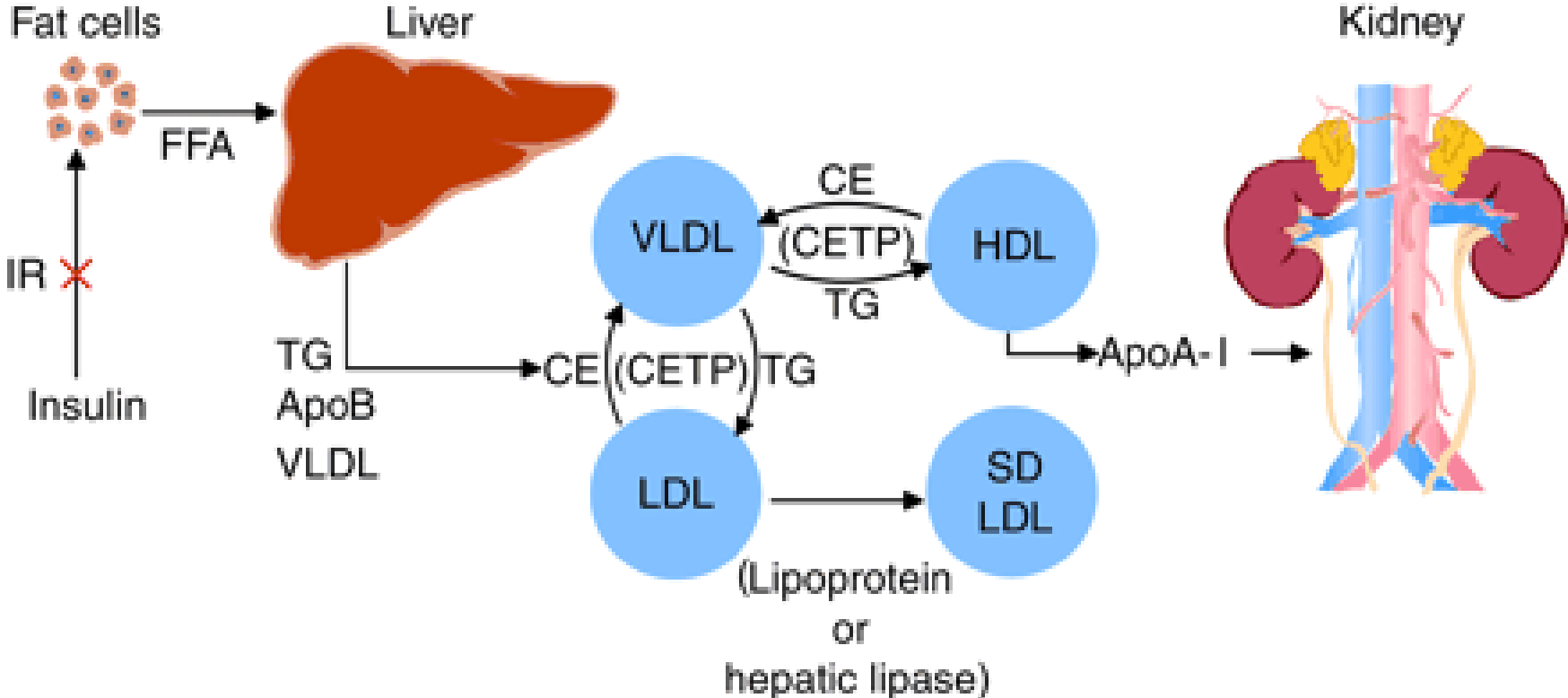
# Insulin Resistance and Atherosclerosis: Proposed Relationships



# Insulin Resistance and Atherosclerosis: Proposed Relationships

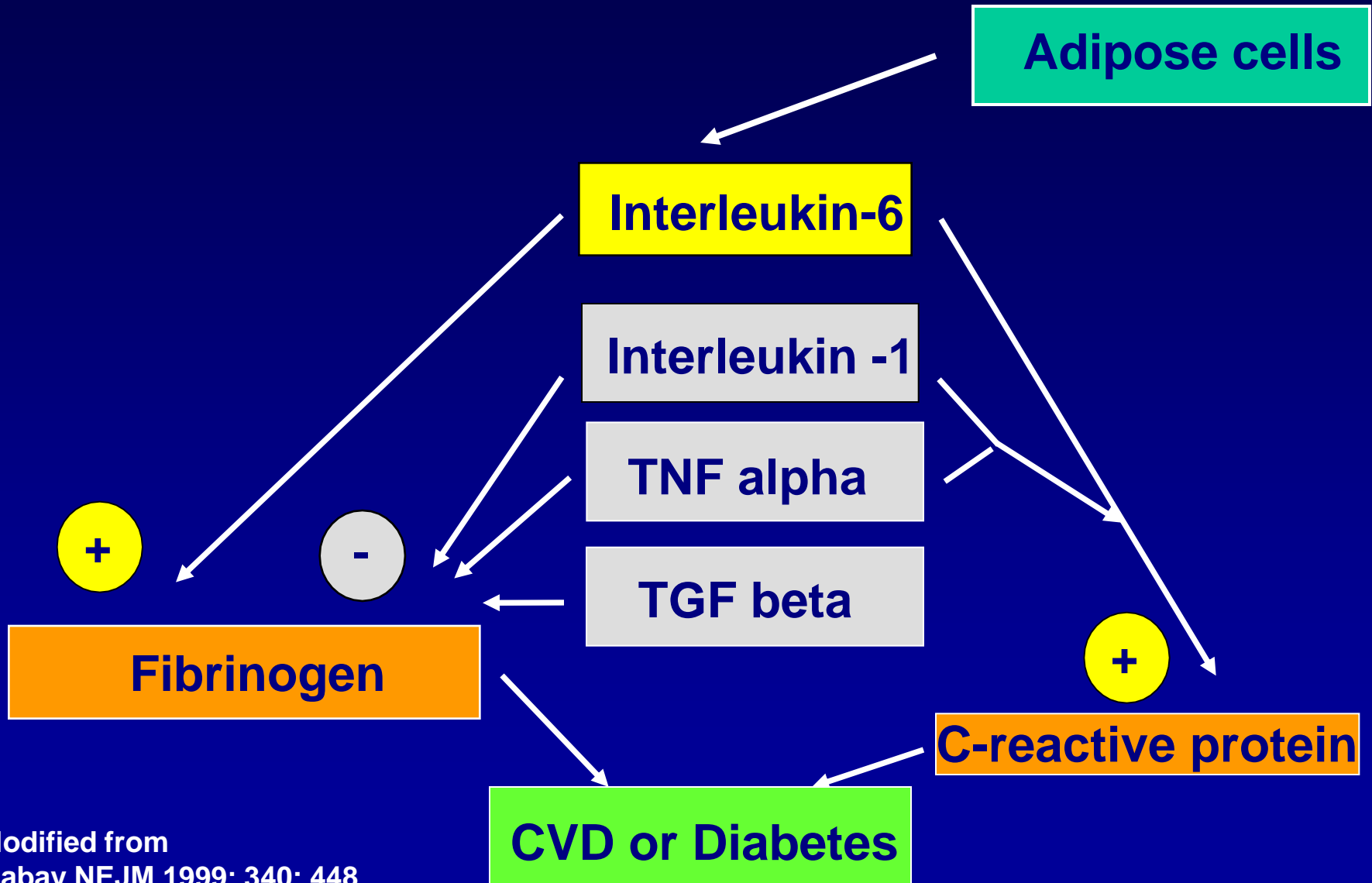


# Lipid Metabolism and Insulin Resistance

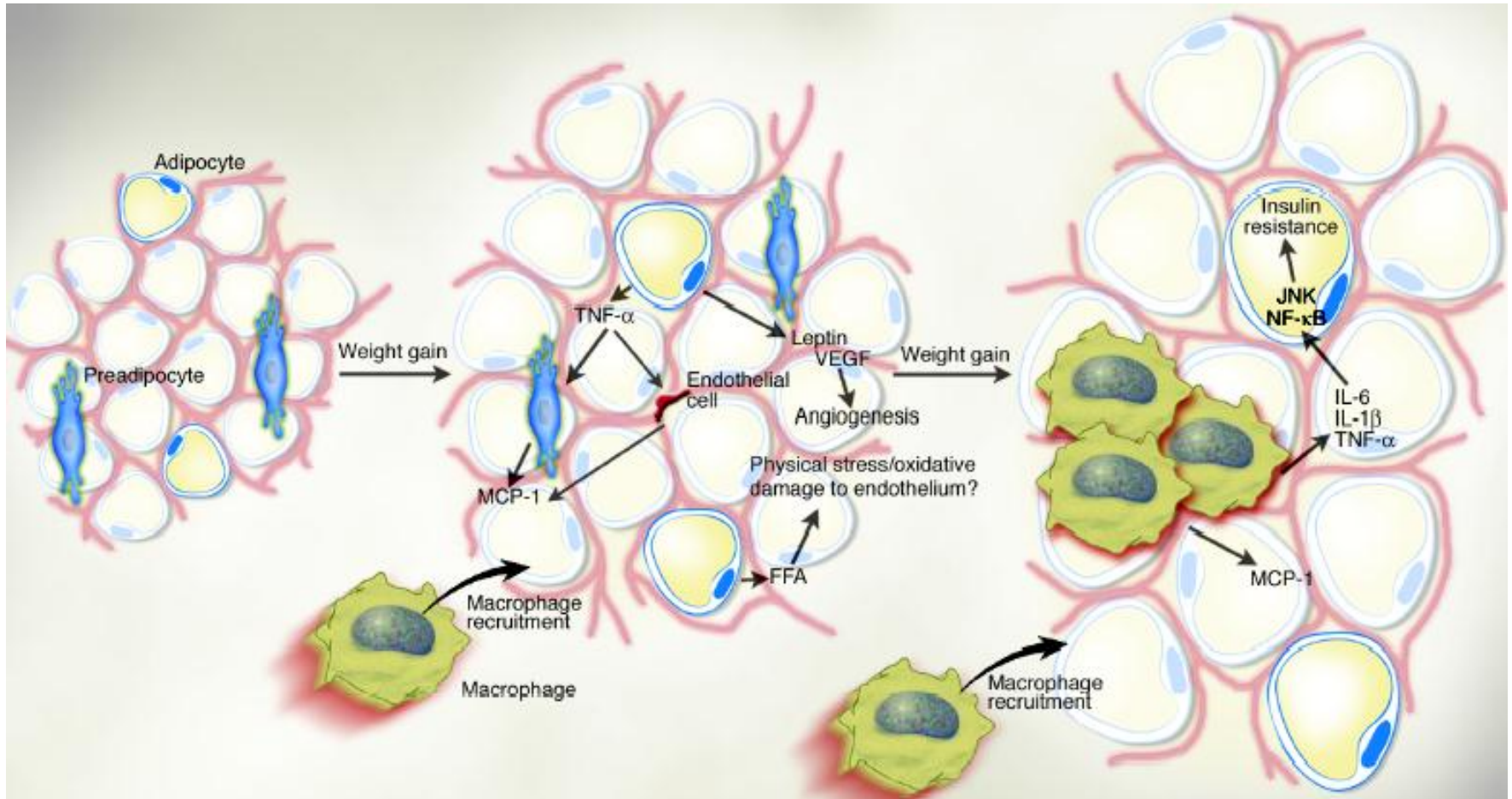




# Adiposity and Vascular Inflammation



# Adipocyte, Weight Gain and Insulin Resistance



# SICU Intensive Insulin Rx Leuven Trial (N=1548)

Mortality Experience	Conventional Therapy	Intensive Insulin Therapy	Stat Significance
Overall 12 month	8%	4.6%	P=0.04
Overall 12 month (>5 days SICU)	20.2%	10.6%	P=0.005
In-Hospital		↓ 34%	

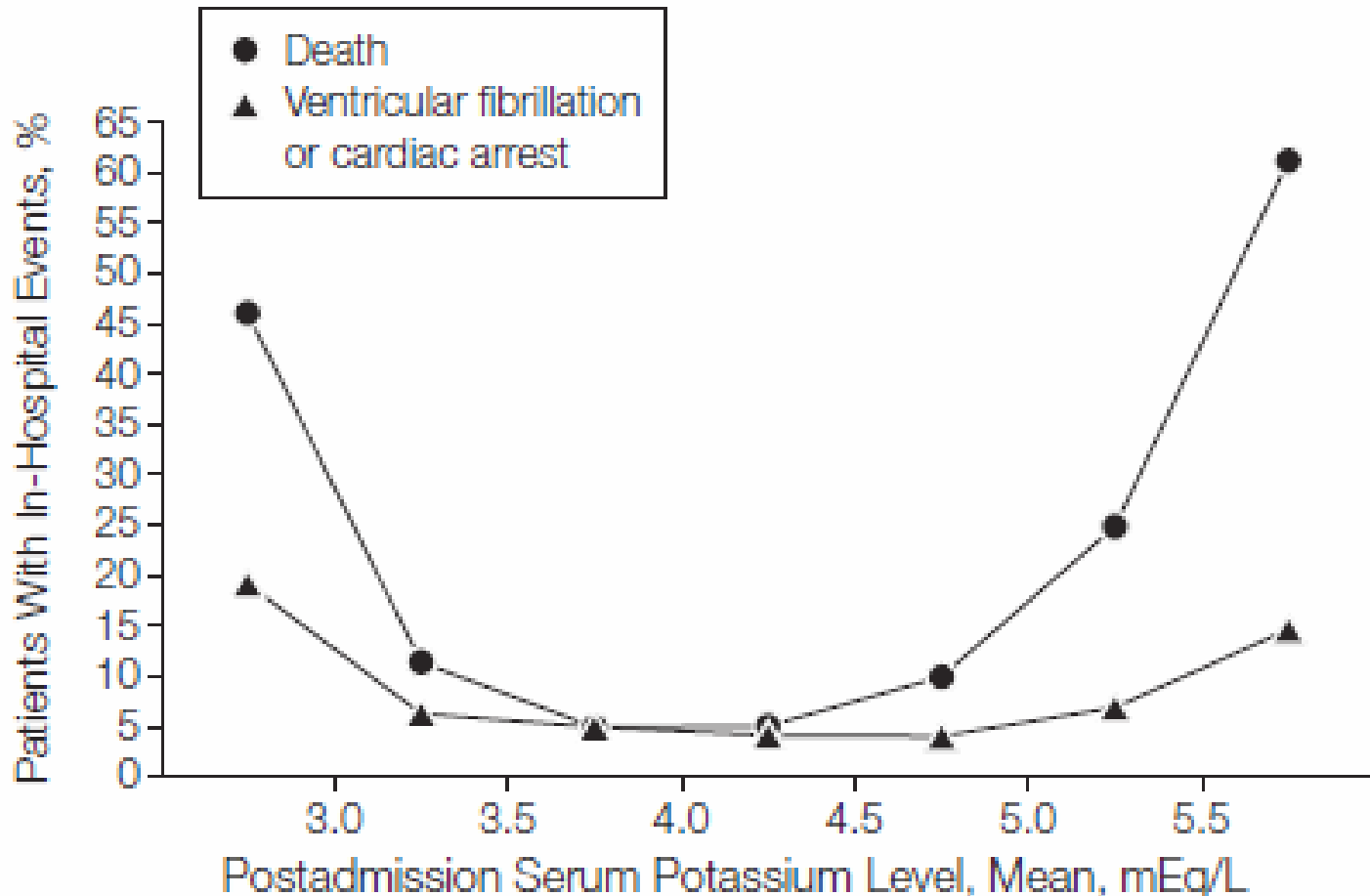
## **Insulin Therapy in ACS**

- **Diabetic patient proportion varies**
- **Infusions (usual care typical comparator)**
  - Insulin**
    - Glucose/Insulin/Potassium= (GIK)**
- **Varying lengths of intensive therapy**
- **Varying targets for glucose control**

# Death at 3 Days with Glucose-Insulin-Potassium Therapy in ST-Segment Elevation MI (OASIS-6 GIK and CREATE-ECLA)

Factor	Levels	Relative Risk	Stat Significance
Glucose (mg/dL)	<126	1.00	P<0.001
	126-144	1.09	
	>144	2.47	
Potassium (mEq/L)	<4	1.00	P<0.001
	4-5	0.93	
	>5	2.02	
Fluid Balance	Negative	1.00	P<0.001
	Neutral	1.14	
	Positive	2.42	

# Serum Potassium and Mortality in Acute MI (Cerner Database, n=38,689)



No. of patients 26 778 11 153 16 536 4 442 840 251

# **Inpatient Insulin for ACS in CCU**

## **Intravenous regular insulin**

**Hourly glucose levels**

**Re-adjust insulin dose hourly**

**Higher doses of insulin**

**Sepsis**

**Catechols Rx**

**Extreme obesity**

## **Subcutaneous insulin**

**Less acutely ill**

**When oral feedings or meals**

# Inpatient Insulin for ACS on the ward

## Traditional Subcutaneous insulin

Sliding Scale Insulin (SSI)

Regular or rapid acting Insulin before meals

## Basal-Bolus Subcutaneous insulin

Glargine

0.4 mg/kg if glucose 140-200 mg/dl

0.5 mg/kg if glucose 200-400 mg/dl

Very rapid acting insulin before meals

Total rapid-acting dose =total glargine

Supplemental rapid-acting insulin before meals

For glucose levels 150-200, 200-250, >250 mg/dl



# **Post Hospital Discharge ACS Patient with Hyperglycemia**

**Is Insulin Needed?**

**Goal is HbA1c less than 7**

**Is Diabetes Education Needed?**

**Diet and Exercise**

**Oral Hypoglycemic Agents**

**Metformin**

**2-4 weeks to work**

**only if Creat<1.3)**

**Glipizide or other sulfonylureas**

**Incretins (probably Rx by endocrinologist)**

**DPP-4**

**GLP drugs**

**Insulin regimens**

**Glargine + before meal rapid acting**

**Glargine + metformin**

**70/30 insulin twice a day (2/3 dose in AM, 1/3 in PM)**

# GRACE Registry

## Predicting 6-Month Mortality after ACS Discharge

Factor	Effect	Hazard Ratio (95% Confidence Interval)
Age (10 yr)	10 yr	1.7 (1.63-1.84)
History of MI	yes/no	1.4 (1.20-1.59)
History of Cardiac Failure	yes/no	2.1 (1.80-2.47)
Pulse	30/min	1.3 (1.23-1.47)
BP systolic	20 mm	1.1 (1.06-1.17)
Creatinine serum	1 mg/dL	1.1 (1.12-1.23)
Cardiac enzyme elevation initially (y/n)	yes/no	1.5 (1.33-1.79)
ST segment depression	yes/no	1.5 (1.29-1.69)
No in-hospital PCI	yes/no	1.9 (1.30-1.88)

# Reducing CVD Risk At ACS Discharge

- **Blood Pressure**

  - US Goal in DM is  $< 130/80$  mm/Hg

  - European guidelines consider albuminuria, eGFR

  - Use of 3 or more BP meds is common

  - In non-hyperglycemic pts

    - Beta blocker and thiazides may worsen glycemia

- **Lipids**

  - US Goal has been LDL-C  $< 100$  (possibly  $<70$ ) mg/dl)

    - Statin --moderate potency or high-potency

  - Triglycerides often elevated ( $> 200$  mg/dl)

    - Diet and alcohol

    - Fibrates

    - Omega-3

- **Anti-platelet therapy**

# PCI vs CABG in Diabetic Patients with Advanced CAD FREEDOM Trial (n=1900)

Outcome	2 Years after Randomization		5 Years after Randomization		Patients with Event		P Value*
	PCI	CABG	PCI	CABG	PCI	CABG	
	<i>number (percent)</i>				<i>number</i>		
Primary composite†	121 (13.0)	108 (11.9)	200 (26.6)	146 (18.7)	205	147	0.005‡
Death from any cause	62 (6.7)	57 (6.3)	114 (16.3)	83 (10.9)	118	86	0.049
Myocardial infarction	62 (6.7)	42 (4.7)	98 (13.9)	48 (6.0)	99	48	<0.001
Stroke	14 (1.5)	24 (2.7)	20 (2.4)	37 (5.2)	22	37	0.03§
Cardiovascular death	9 (0.9)	12 (1.3)	73 (10.9)	52 (6.8)	75	55	0.12

# Summary

## ACS with Insulin Resistance/Diabetes

- **Inpatient**
  - Insulin— target often 140 to 180 mg/dl
  - Potassium in normal range
  - Usual ACS care
  - Revascularization decision
- **Outpatient**
  - BP goal in USA <130/80 mm Hg
  - LDL-C goal in USA  
<100 mg/dl (or <70 mg/dl)  
moderate or high potency statin
  - HbA1c <7 with oral agents or insulins
  - Antiplatelet therapy
  - Revascularization decision

