Henry S, 42 yo male

- BMI 28
- BP 135/88
- Waist circumference 38 inches

- hgbA1C 5.9
- FBG 110
- HDL 38
- LDL 128
- TG 167

Placeholder

- This was a placeholder slide for a polleverywhere poll on What is Henry's Diagnosis?

Placeholder

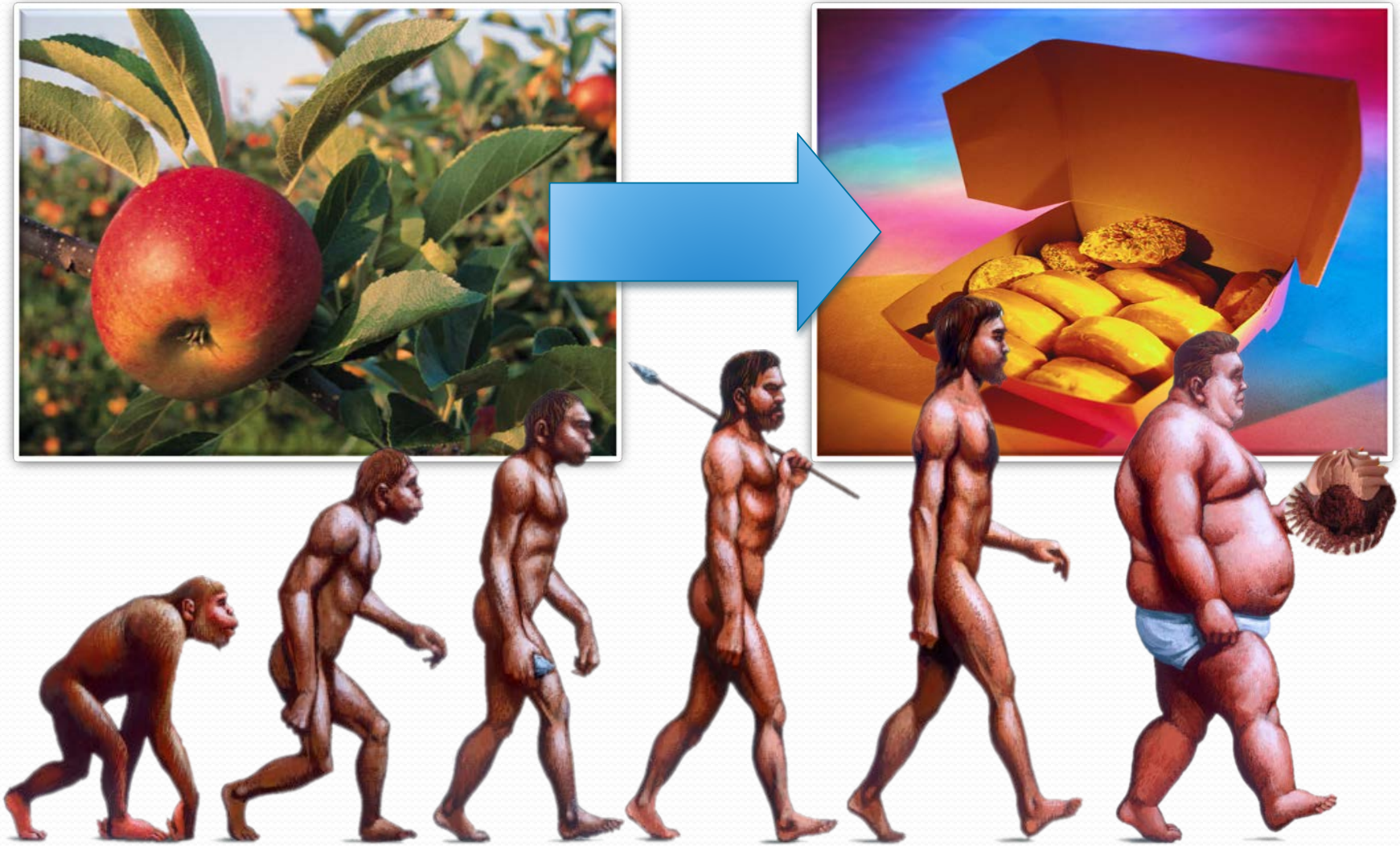
- This was a placeholder slide for a polleverywhere poll on What Treatment Do you Offer?

CardioMetabolic Syndrome, Insulin Resistance, and Diabetes

A Functional Approach

Connie Basch, MD August 2012

Borrowing liberally from the 2012 IFM Symposium, particularly from Mark Hyman and Shilpa Saxena as well as myhealthywaist.org



Today:

- Definitions
- Assessment
- Risk factors: standard and additional
- Treatment Recommendations
- Monitoring

ASSOCIATIONS OF METABOLIC SYNDROME COMPONENTS WITH CRITERIA FOR THE CLINICAL DIAGNOSIS OF THE METABOLIC SYNDROME AS PROPOSED BY THE NCEP-ATP III

Metabolic Syndrome Components	Clinical Criteria
Abdominal Obesity	Waist circumference ≥102 cm (40 in) for men or ≥88 cm (34.6 in) for women
Insulin Resistance	Fasting glucose ≥5.6 mmol/l (100 mg/dL) or on drug treatment for elevated glucose
Atherogenic Dyslipidemia	Triglycerides ≥1.69 mmol/l (150 mg/dL) or on drug tx for elevated triglycerides HDL cholesterol <1.03 mmol/l (40) for men or <1.29 mmol/l (50) for women or on drug tx for reduced HDL cholesterol
Elevated Blood Pressure	Blood pressure ≥130 or ≥85 mmHg or on antihypertensive drug treatment in a patient with history of hypertension
Pro-inflammatory State	none
Pro-thrombotic State	none

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

CRITERIA FOR THE CLINICAL DIAGNOSIS OF THE METABOLIC SYNDROME ACCORDING TO THE IDF

Central Obesity

Waist circumference* - ethnicity specific

Raised Triglycerides

>1.7 mmol/l (150 mg/dl)
Specific treatment for this lipid abnormality

Reduced HDL Cholesterol

<1.03 mmol/l (40 mg/dl) in men
<1.29 mmol/l (50 mg/dl) in women
Specific treatment for this lipid abnormality

Raised Blood Pressure

Systolic ≥130 mmHg
Diastolic ≥85 mmHg
Treatment of previously diagnosed hypertension

*Raised Fasting Plasma Glucose***

Fasting plasma glucose ≥5.6 mmol/l (100 mg/dl)
Previously diagnosed type 2 diabetes
If above 5.6 mmol/l or 100 mg/dl, oral glucose tolerance test is strongly recommended, but is not necessary to define presence of syndrome

*If BMI is over 30 kg/m², central obesity can be assumed and waist circumference does not need to be measured.

**In clinical practice, impaired glucose tolerance is also acceptable, but all reports of prevalence of metabolic syndrome should use only fasting plasma glucose and presence of previously diagnosed diabetes to define hyperglycemia. Prevalences also incorporating 2-h glucose results can be added as supplementary findings.

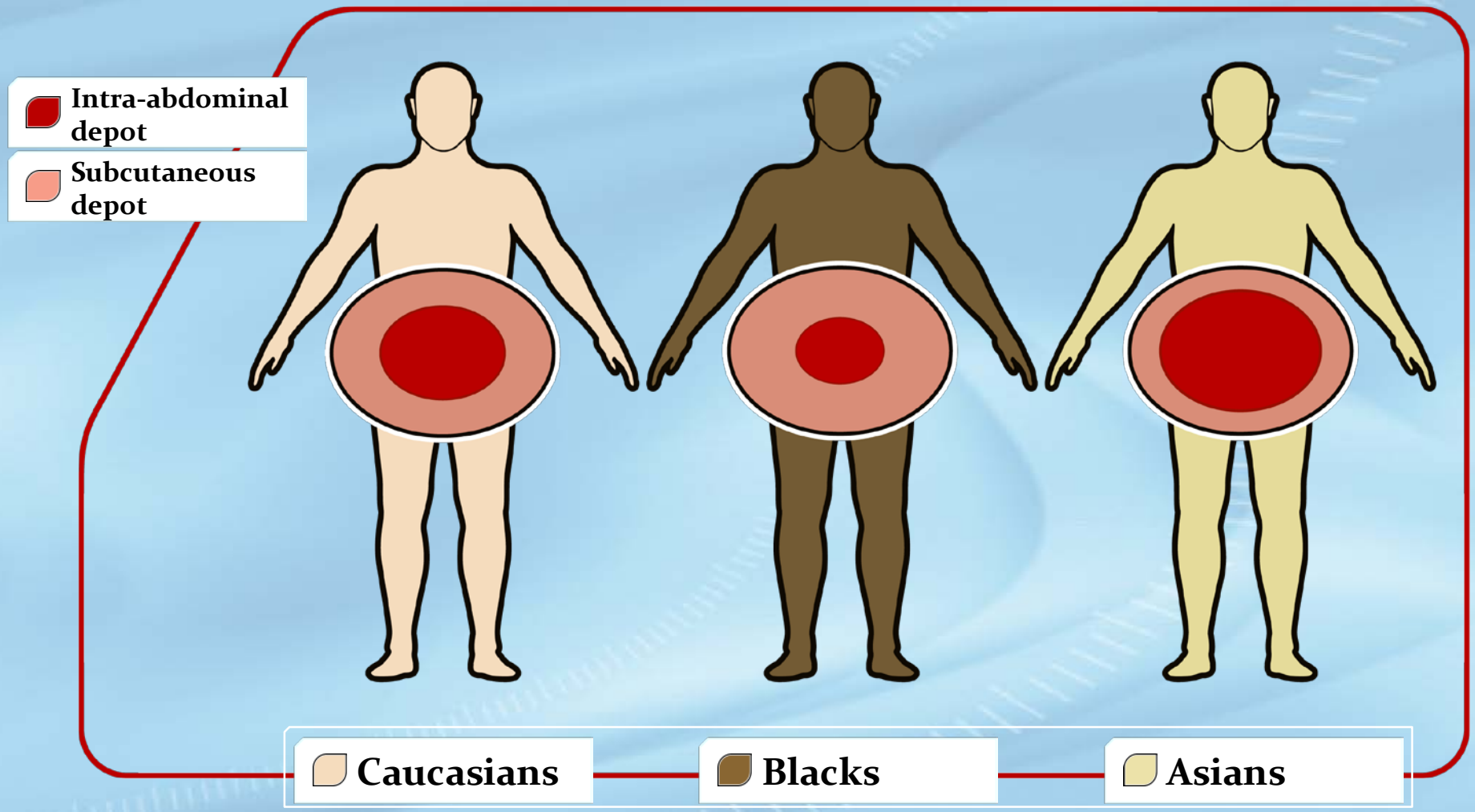
Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Alberti KG et al. Lancet 2005; 366: 1059-62

Placeholder slide

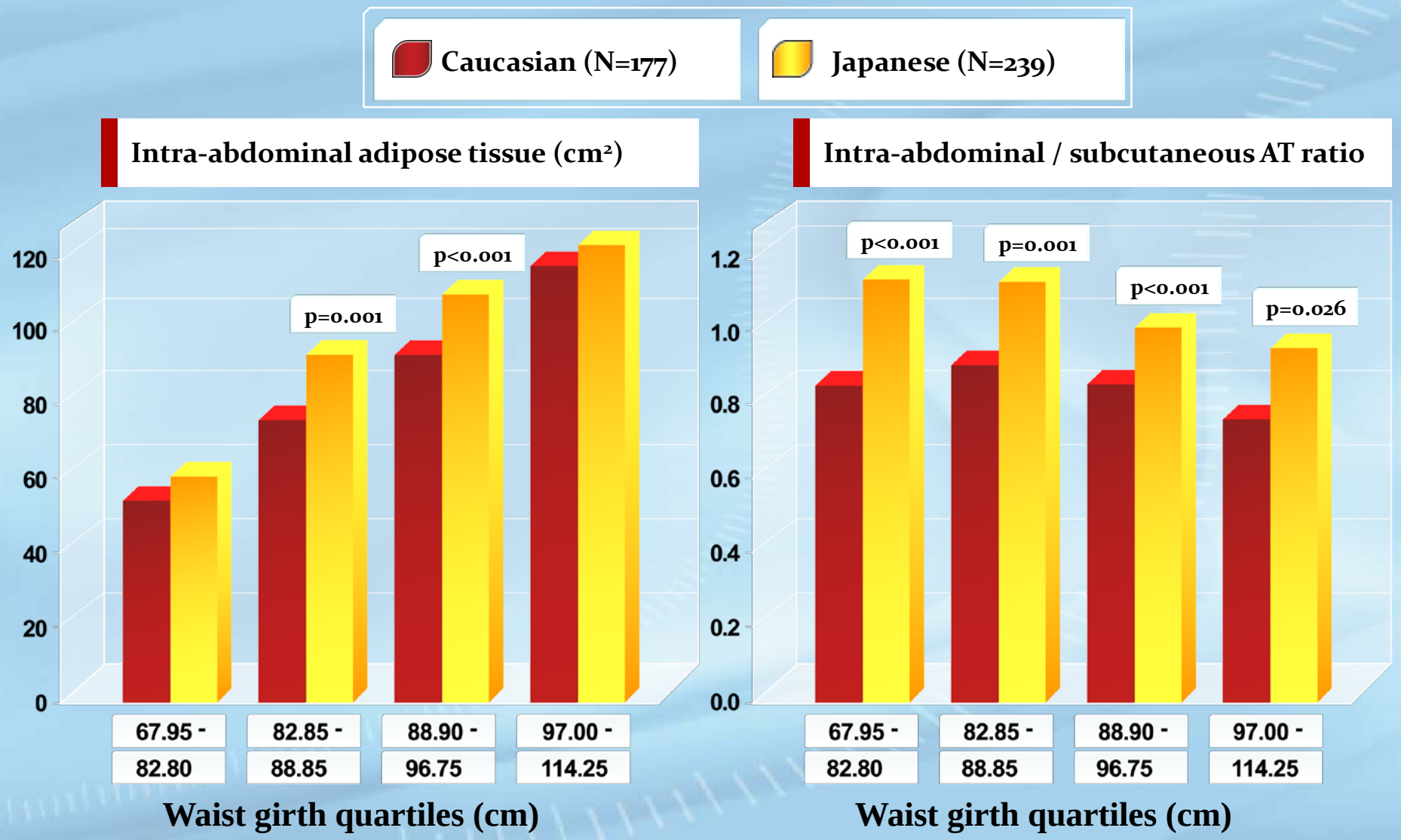
- Polleverywhere slide on which ethnicity is most likely to have insulin resistance

RELATIVE ACCUMULATION OF INTRA-ABDOMINAL VS. SUBCUTANEOUS DEPOT ACCORDING TO ETHNICITY



Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

EVIDENCE FOR A GREATER RELATIVE ACCUMULATION OF INTRA-ABDOMINAL ADIPOSE TISSUE (AT) IN JAPANESE THAN IN CAUCASIAN AMERICANS



Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Kadowaki T et al. Int J Obes 2006; 30: 1163-5

ETHNIC-SPECIFIC VALUES FOR WAIST CIRCUMFERENCE FOR THE CLINICAL DIAGNOSIS OF THE METABOLIC SYNDROME AS PROPOSED BY THE IDF

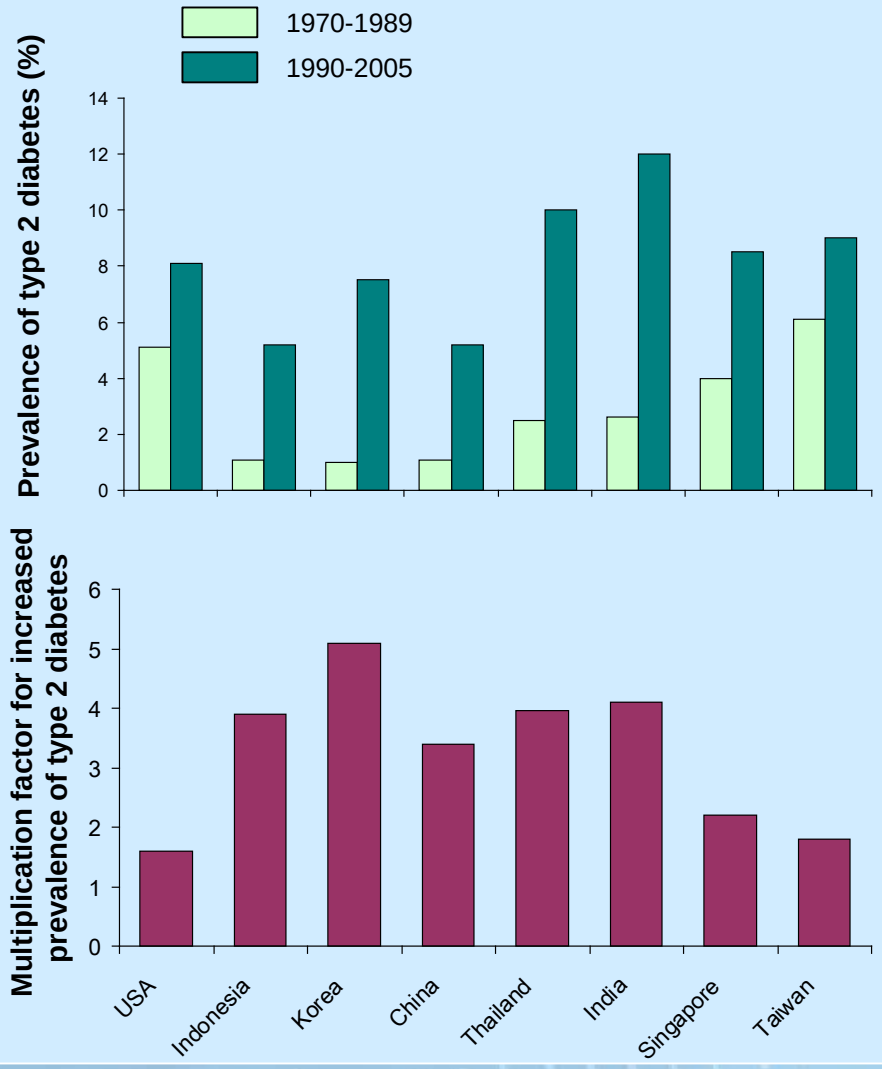
Europids*	
Men	≥94 cm
Women	≥80 cm
South Asians	
Men	≥90 cm
Women	≥80 cm
Chinese	
Men	≥90 cm
Women	≥80 cm
Japanese	
Men	≥90 cm
Women	≥80 cm
Ethnic south and central Americans	
Men	Use south Asian recommendations until more specific data are available
Women	
Sub-Saharan Africans	
Men	Use European data until more specific data are available
Women	
Eastern Mediterranean and middle east (Arab) population	
Men	Use European data until more specific data are available
Women	

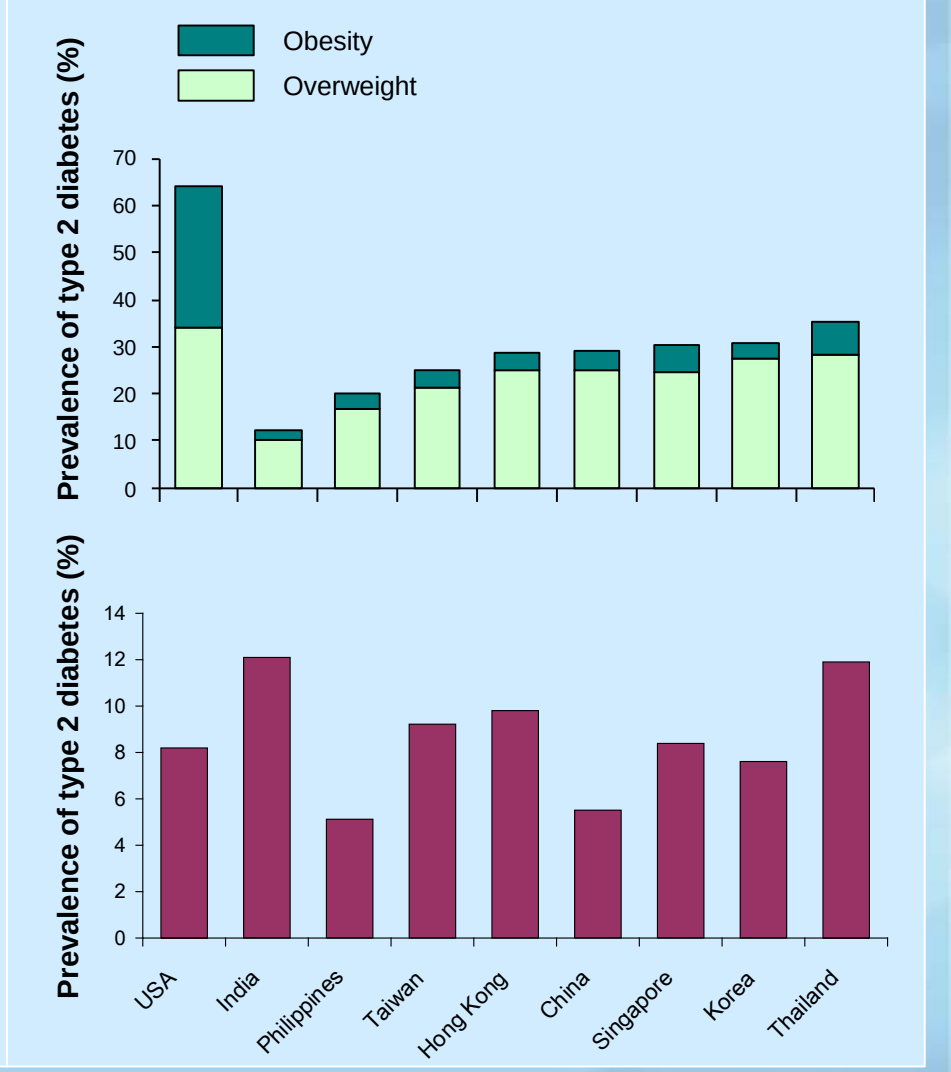
Data are pragmatic cut-offs and better data are required to link them to risk. Ethnicity should be basis for classification, not country of residence. *In USA, Adult Treatment Panel III values (102 cm male, 88 cm female) are likely to continue to be used for clinical purposes. In future epidemiological studies of populations of Europid origin (white people of European origin, regardless of where they live in the world), prevalence should be given, with both European and North American cut-offs to allow better comparisons.

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Alberti KG et al. Lancet 2005; 366: 1059-62

Same Body Mass Index, Higher Risk for Diabetes in Asians





Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Yoon KH et al. Lancet 2006; 368: 1681-8
Reproduced with permission

CRITERIA PROPOSED FOR CLINICAL DIAGNOSIS OF THE METABOLIC SYNDROME

Clinical Measure	WHO (1998)	EGIR	NCEP-ATP III (2005)	AACE (2003)	IDF (2005)
Insulin Resistance	IGT, IFG, T2D, or lowered insulin sensitivity* plus any 2 of the following	Plasma insulin >75th percentile plus any 2 of the following	None, but any 3 of the following 5 features	IGT or IFG plus any of the following based on clinical judgment	None
Adiposity Index	Men: WHR >0.90; Women: WHR >0.85 and/or BMI >30 kg/m²	WC ≥94 cm in men or ≥80 cm in women	WC ≥102 cm in men or ≥88 cm in women	BMI ≥25 kg/m²	Increased WC (population specific) plus any 2 of the following
Lipid	TG ≥1.69 mmol/l and/or HDL-C <0.90 mmol/l in men or <1.01 mmol/l in women	TG ≥2.0 mmol/l and/or HDL-C <1.0 mmol/l in men or women	TG ≥1.69 mmol/l or on TG Rx; HDL-C <1.03 mmol/l in men or <1.29 mmol/l in women or on HDL-C Rx	TG ≥1.69 mmol/l and HDL-C <1.03 mmol/l in men or <1.29 mmol/l in women	TG ≥1.69 mmol/l or on TG Rx; HDL-C <1.03 mmol/l in men or <1.29 mmol/l in women or on HDL-C Rx
Blood Pressure	≥140/90 mmHg	≥140/90 mmHg or on hypertension Rx	≥130 mmHg systolic or ≥85 mmHg diastolic or on hypertension Rx	≥130/85 mmHg	≥130 mmHg systolic or ≥85 mmHg diastolic or on hypertension Rx
Glucose	IGT, IFG, or T2D	IGT or IFG (but not diabetes)	≥5.6 mmol/l (includes diabetes)	IGT or lFG (but not diabetes)	≥5.6 mmol/l (includes diabetes)
Other	Microalbuminuria			Other features of insulin resistance	

Legend:
WHO, World Health Organization; EGIR, European Group for the Study of Insulin Resistance; NCEP-ATP III, National Cholesterol Education Program-Adult Treatment Panel III; AACE, American Association of Clinical Endocrinologists; IDF, International Diabetes Federation; T2D, type 2 diabetes; WHR, waist-to-hip ratio; WC, waist circumference; BMI, body mass index; and TG, triglycerides.

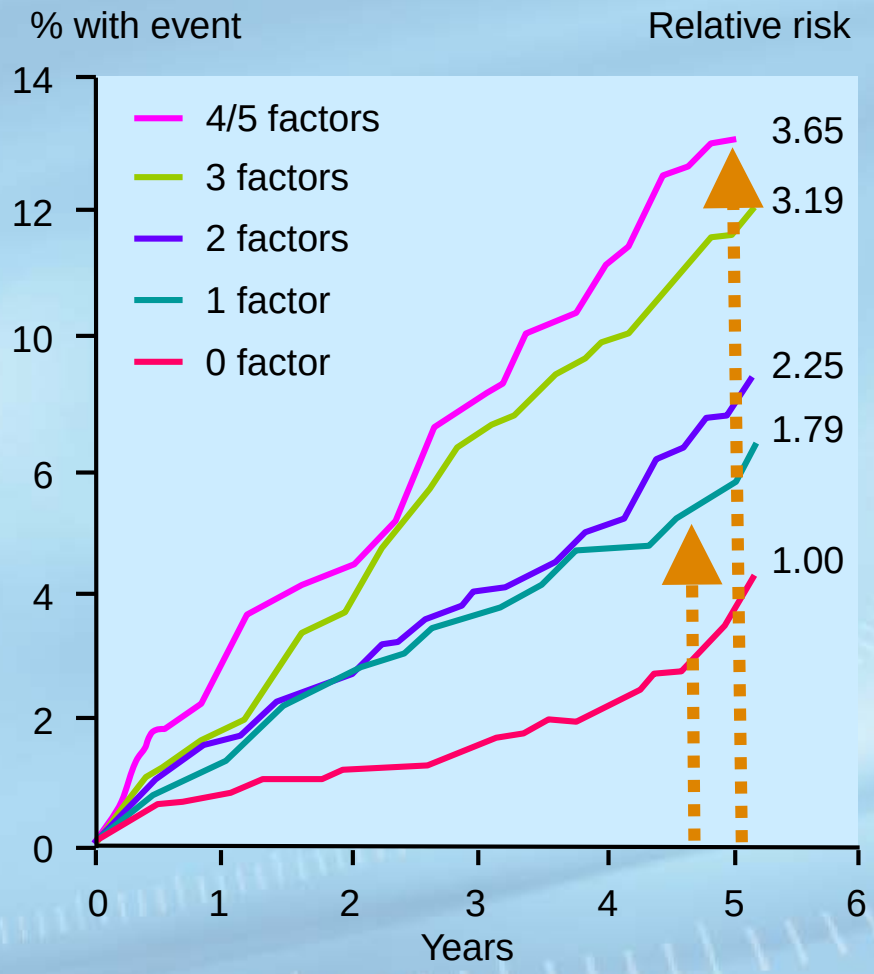
*Insulin sensitivity measured under hyperinsulinemic-euglycemic conditions.

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

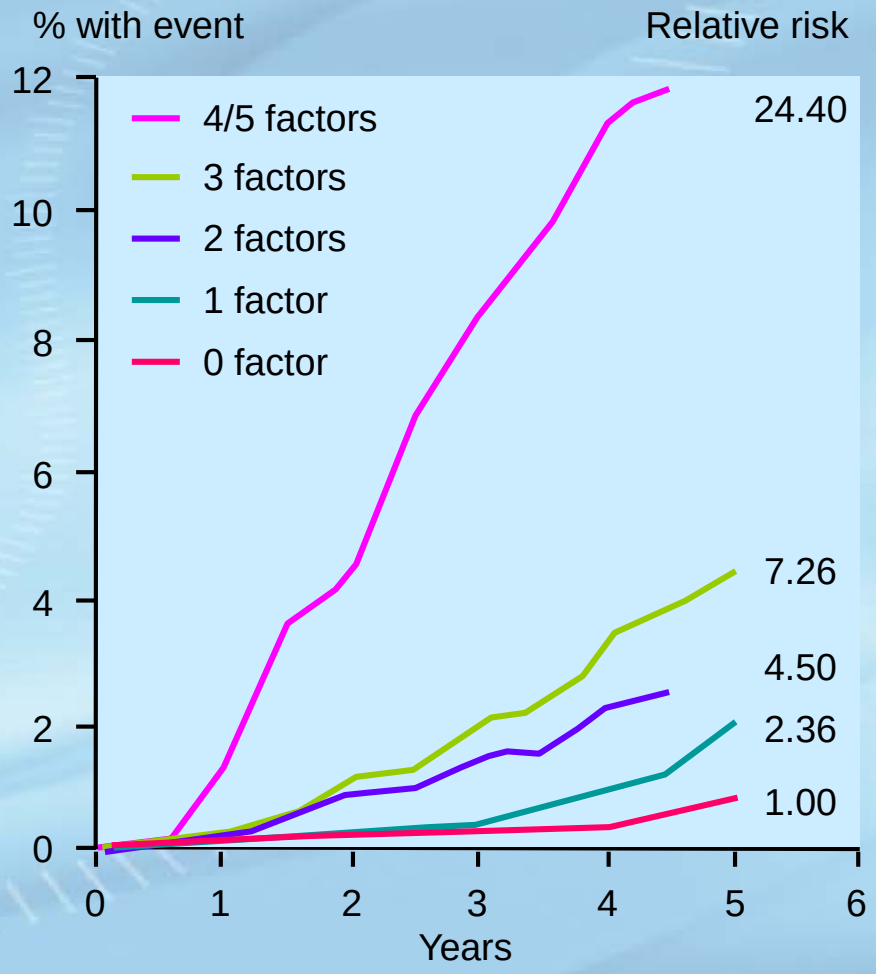
And why we care about MetSyn:

Metabolic Syndrome as a Predictor of Coronary Heart Disease (CHD) and Diabetes in WOSCOPS

CHD death/nonfatal myocardial infarction



Onset of new type 2 diabetes



Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Sattar N et al. Circulation 2003; 108: 414-9

Metabolic Syndrome and Acute Myocardial Infarction (MI) in the Young (<45 years)

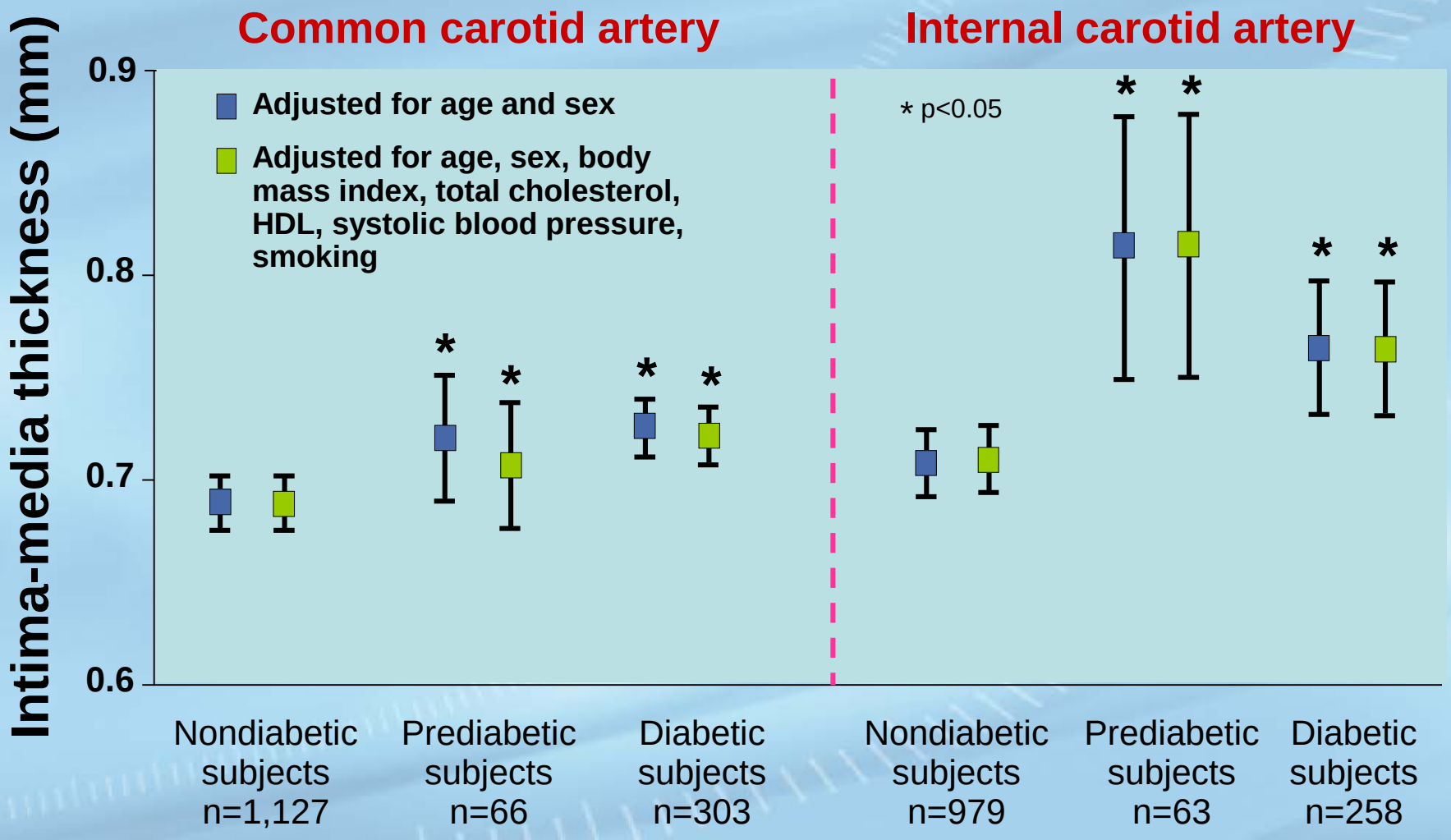
AT LAHEY CLINIC:

- 165 consecutive patients <45 years of age with acute MI and transferred for emergency percutaneous coronary intervention
- 59% met NCEP clinical criteria for metabolic syndrome
  - 8 had prior type 2 diabetes
  - 16 had new diagnoses of type 2 diabetes at MI or within 3 months
  - Mean Framingham 10-year risk score = 5% in metabolic syndrome (in absence of diabetes)

60% had metabolic syndrome and the most common feature was obesity

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

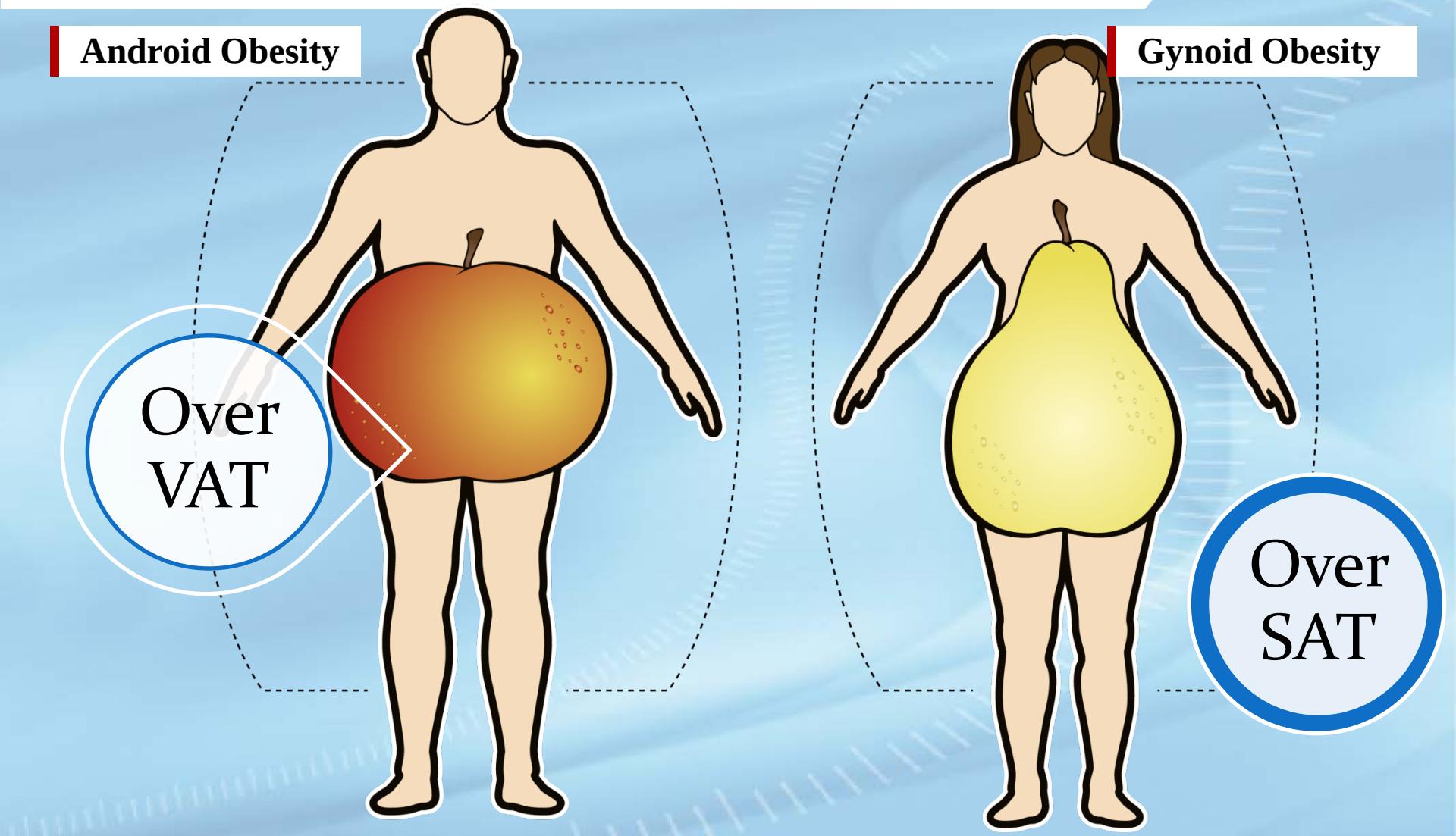
Prediabetes is Associated with Accelerated Atherosclerosis: Mexico City Diabetes Study



Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Hunt KJ et al. Arterioscler Thromb Vasc Biol 2003; 23: 1845-50

ADIPOSE TISSUE DISTRIBUTION IN MEN AND WOMEN



Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

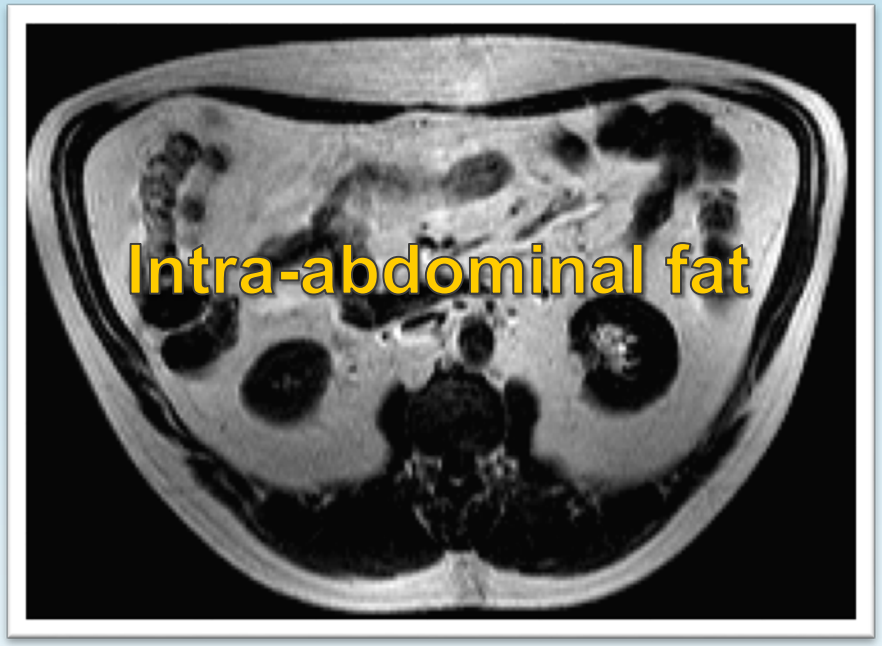
Adapted from Vague J Presse Med 1947; 30: 339-40

Abdominal Obesity and Cardiometabolic Risk

OUTSIDE

INSIDE

Intra-abdominal or visceral fat

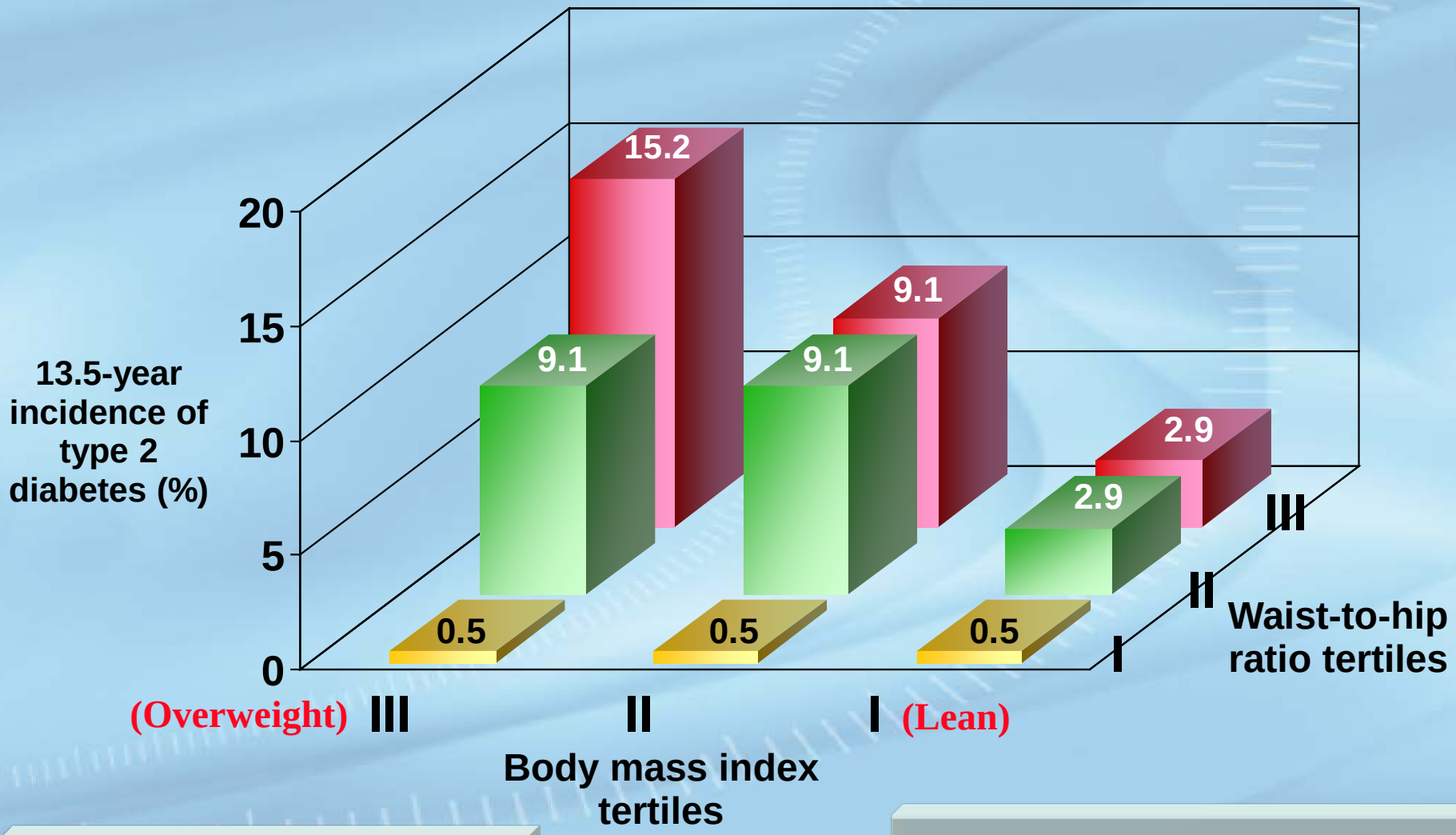


Intra-abdominal fat is a strong correlate of cardiometabolic risk

Produced by the International Chair on Cardiometabolic Risk

Source: www.myhealthywaist.org

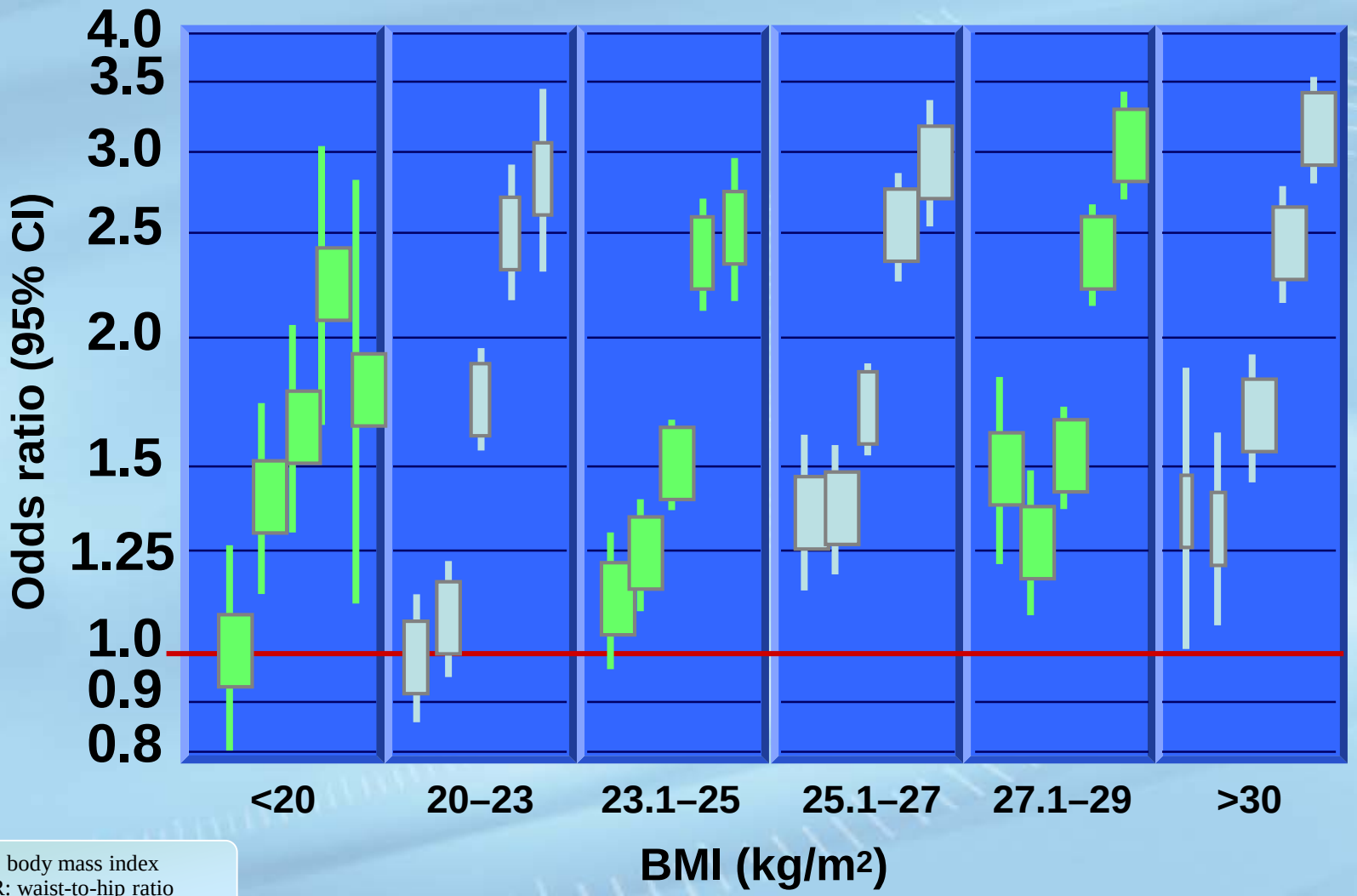
Obesity as a Risk Factor for Type 2 Diabetes: Importance of Abdominal Fat Accumulation



Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Ohlson LO et al. Diabetes 1985; 34: 1055-8

Risk of Myocardial Infarction Across Quintiles of BMI and WHR: INTERHEART

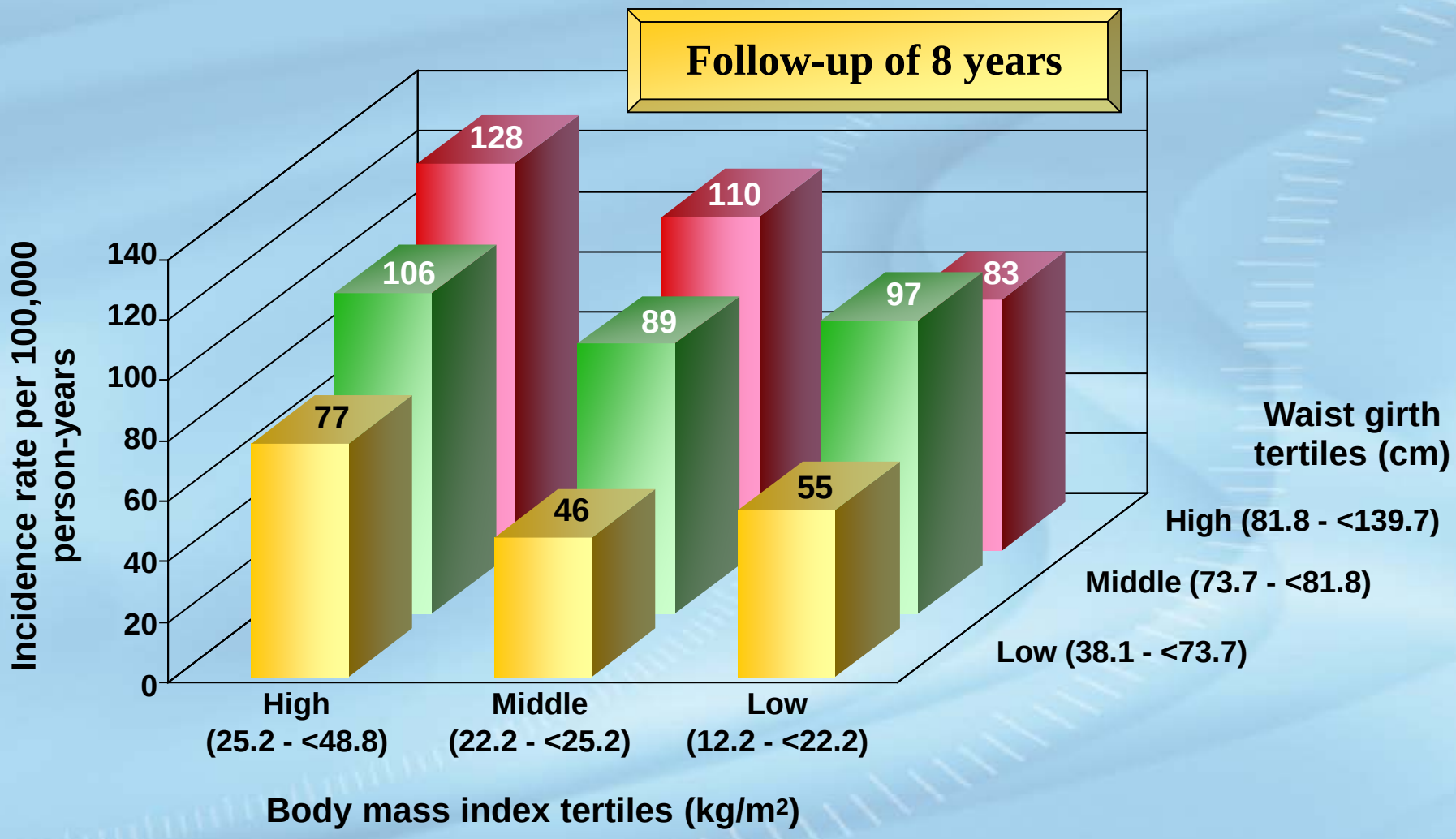


BMI: body mass index
WHR: waist-to-hip ratio

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Yusuf S et al. Lancet 2005; 366: 1640-9

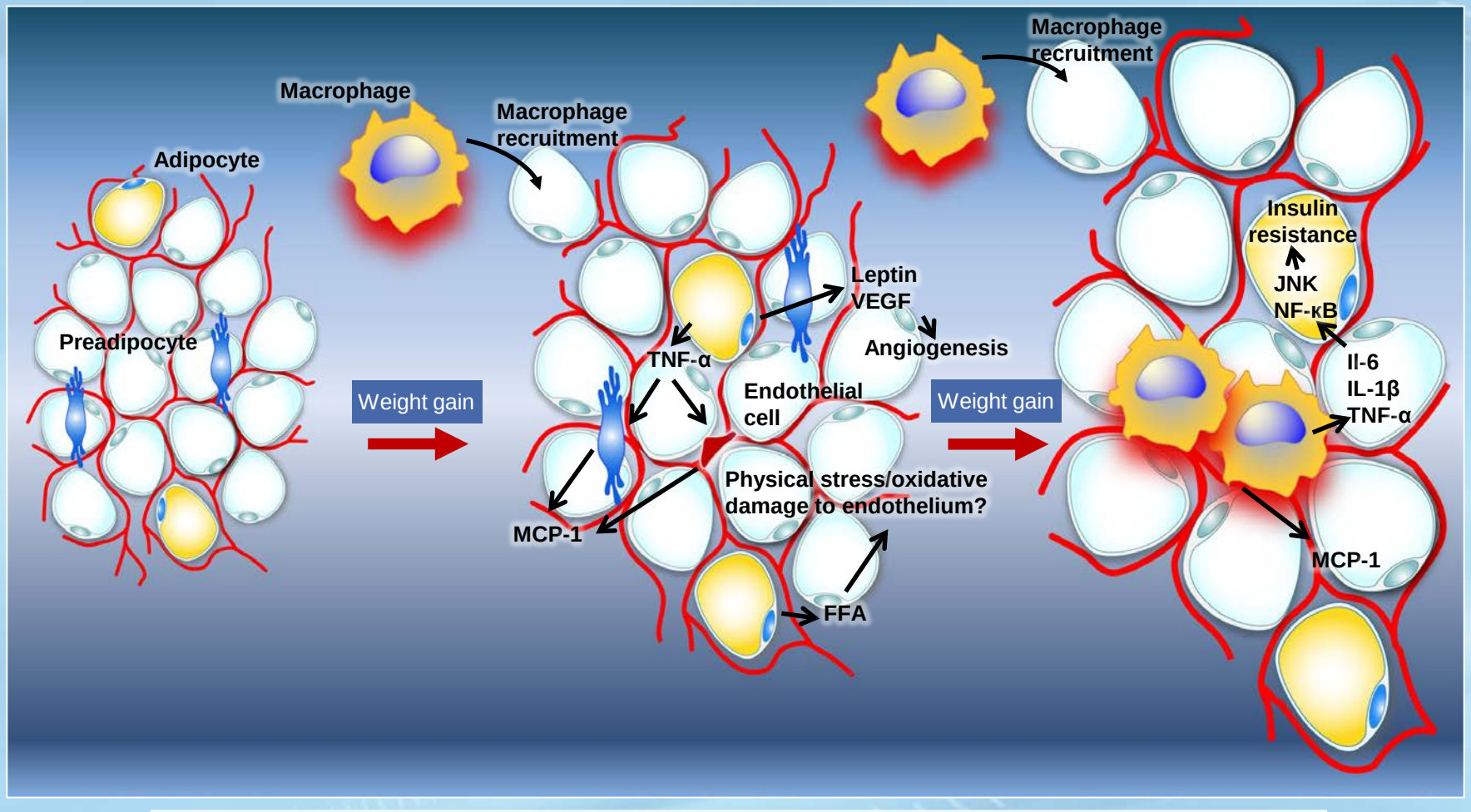
Abdominal Obesity and Coronary Heart Disease in Women: The Nurses' Health Study



Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Rexrode KM et al. JAMA 1998; 280: 1843-8

Intra-abdominal (Visceral) Fat is a Metabolically Active Organ Infiltrated by Inflammatory Cells



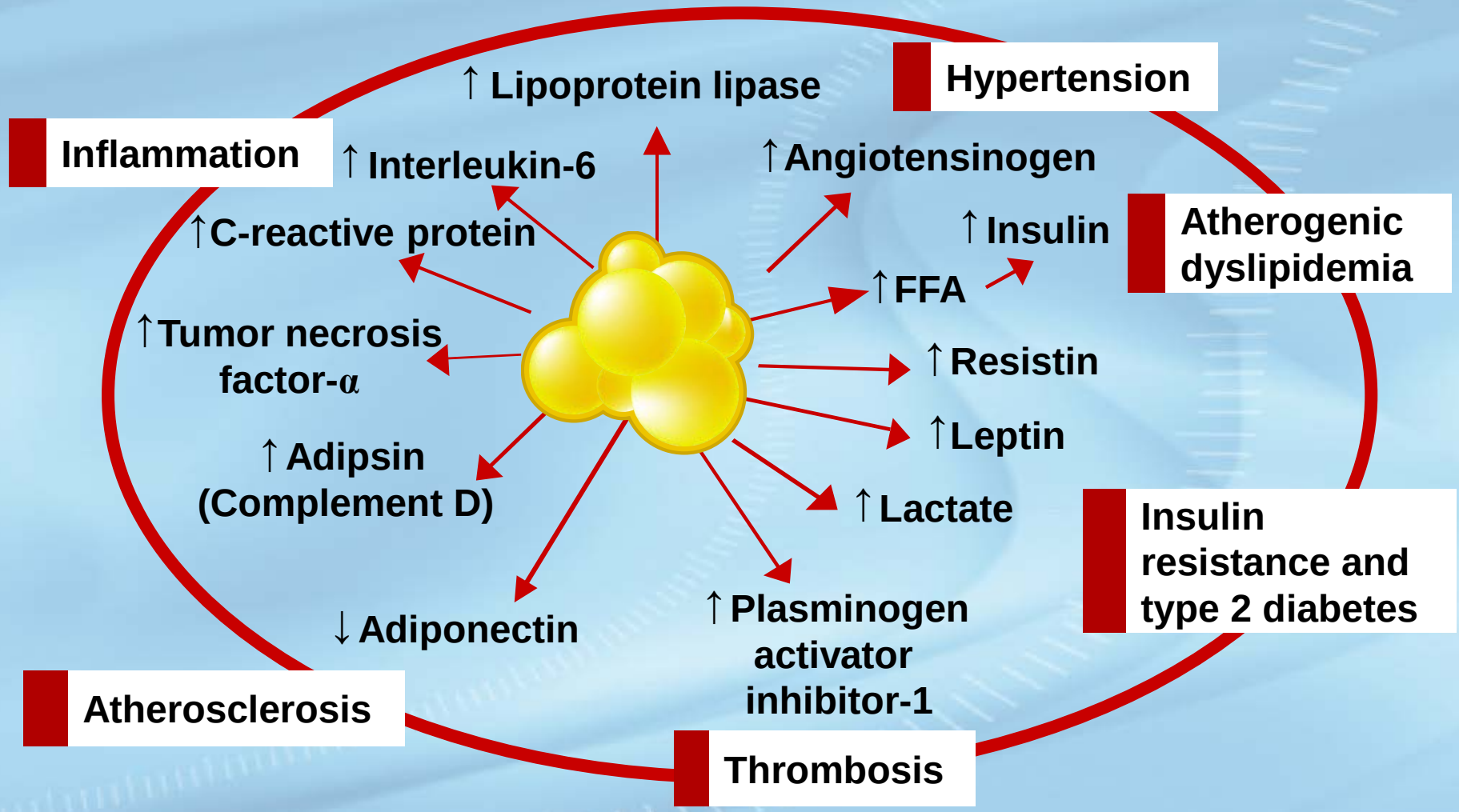
FFA: free fatty acids
IL-1β: interleukin-1β
IL-6: interleukin-6
JNK: jun N-terminal kinase

MCP-1: monocyte chemotactic protein-1
NF-κB: nuclear factor-κB
TNF-α: tumor necrosis factor-α
VEGF: vascular endothelial growth factor

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Tilg H and Moschen AR Nat Rev Immunol 2006; 6: 772-3
and Wellen KE and Hotamisligil GS J Clin Invest 2003; 112: 1785-8

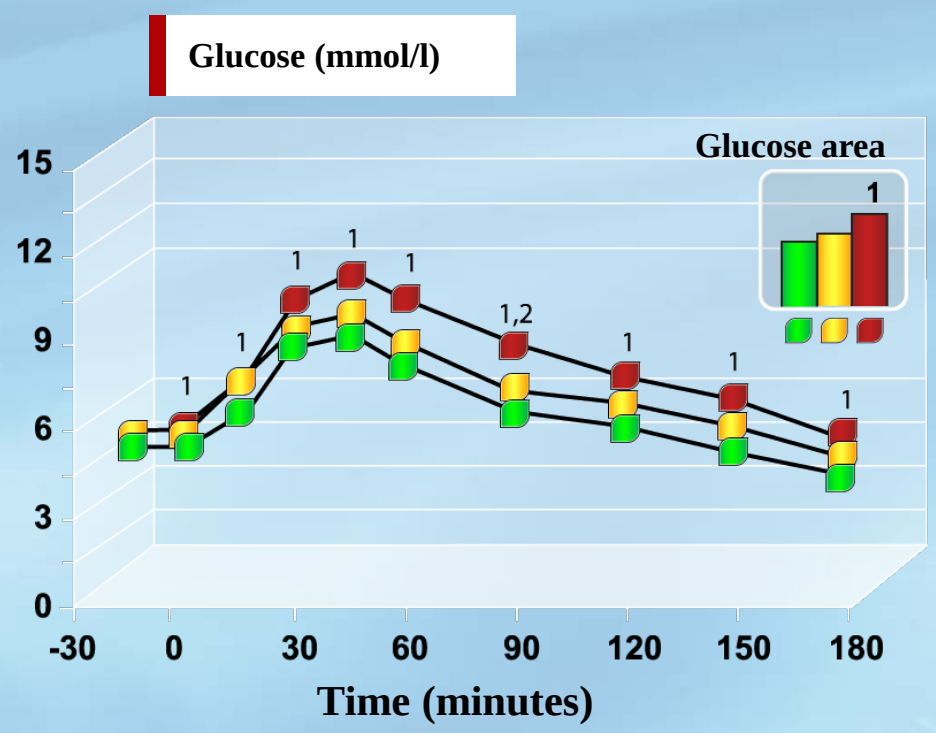
Adverse Cardiometabolic Effects of Intra-abdominal (Visceral) Adipocytes

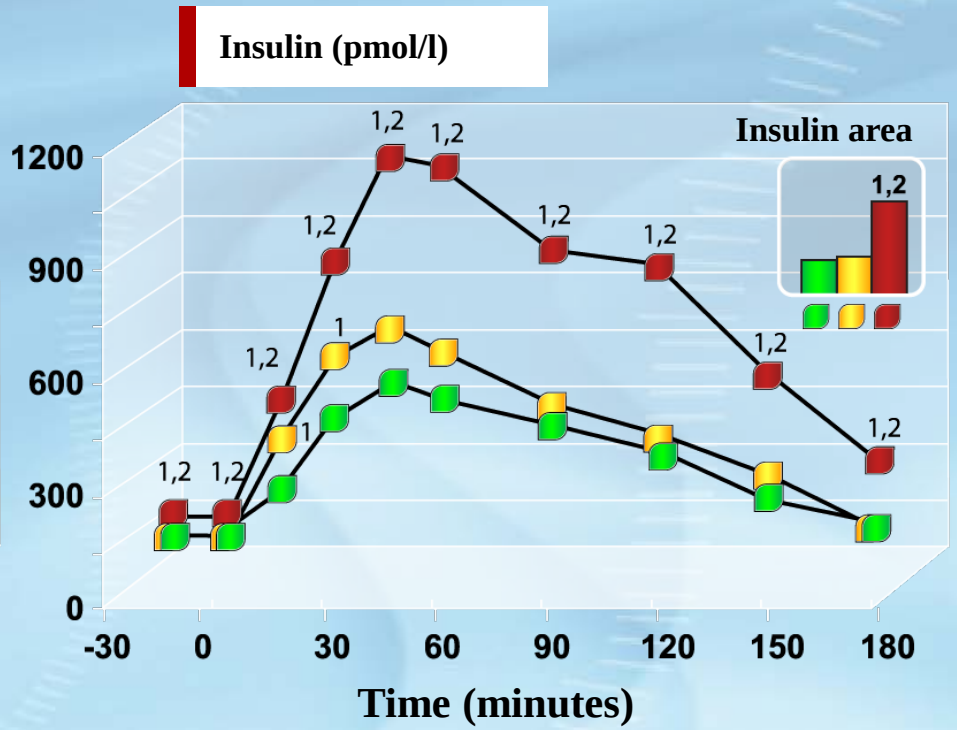


Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Lyon CJ et al. Endocrinology 2003; 144: 2195-200 |
Trayhurn P and Wood IS Br J Nutr 2004; 92: 347-55 |
Eckel RH et al. The Lancet 2005; 365: 1415-28

IMPACT OF INTRA-ABDOMINAL FAT ON PLASMA GLUCOSE-INSULIN HOMEOSTASIS





Non-obese

Obese with low intra-abdominal fat accumulation

Obese with high intra-abdominal fat accumulation

Legend

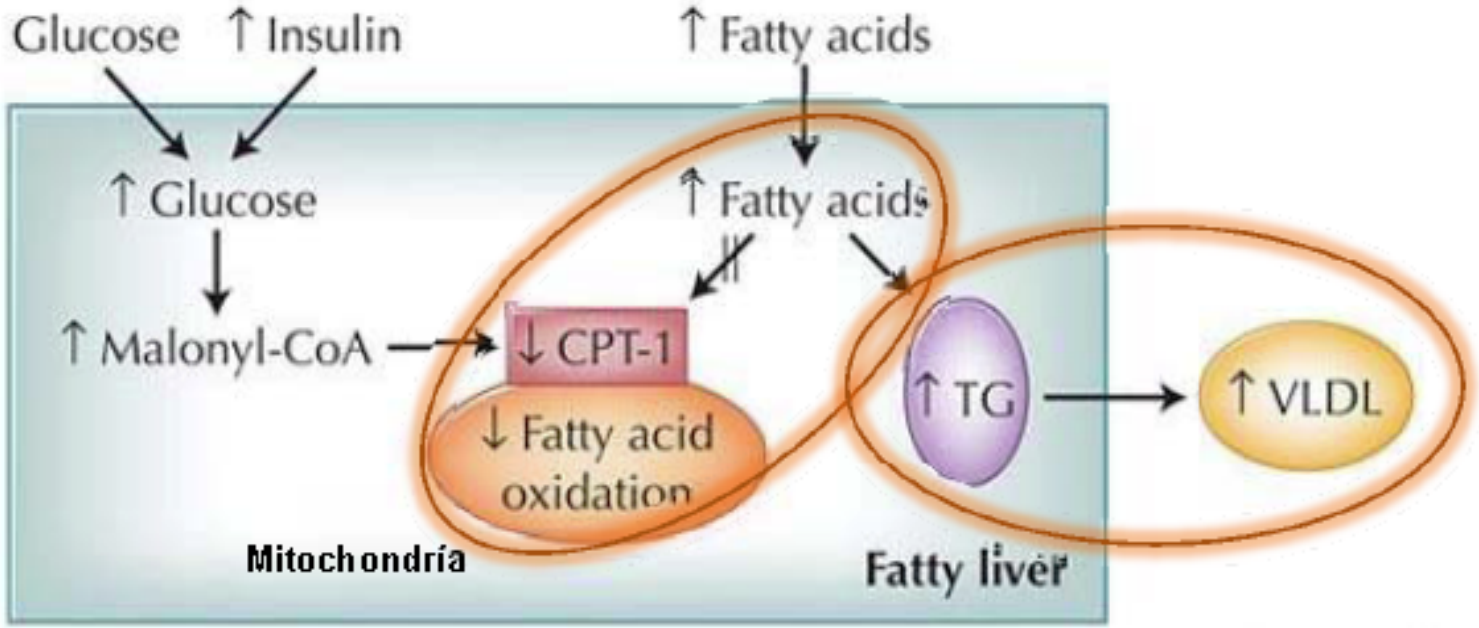
1 different from non-obese subjects (p<0.05)
2 different from obese subjects with low intra-abdominal fat (p<0.05)

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Hyperinsulinemia is toxic, even with normal glucose

- Drives appetite and further weight gain
- Atherogenic
  - Inhibition of Fatty Acid Oxidation
  - Growth factor properties, stimulating cell hypertrophy
- Carcinogenic

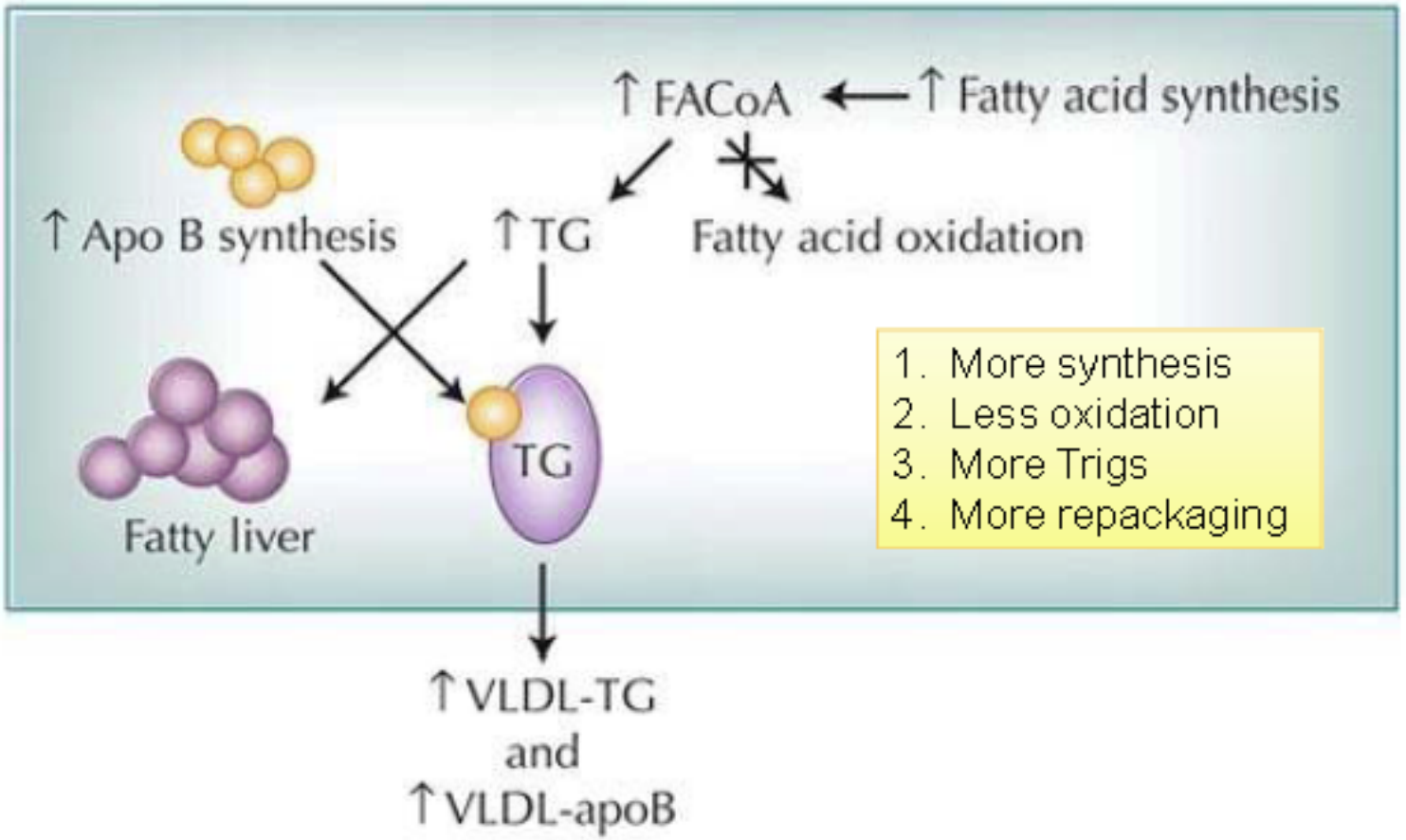
Mechanism of Inhibition of Fatty Acid Oxidation by Hyperinsulinemia



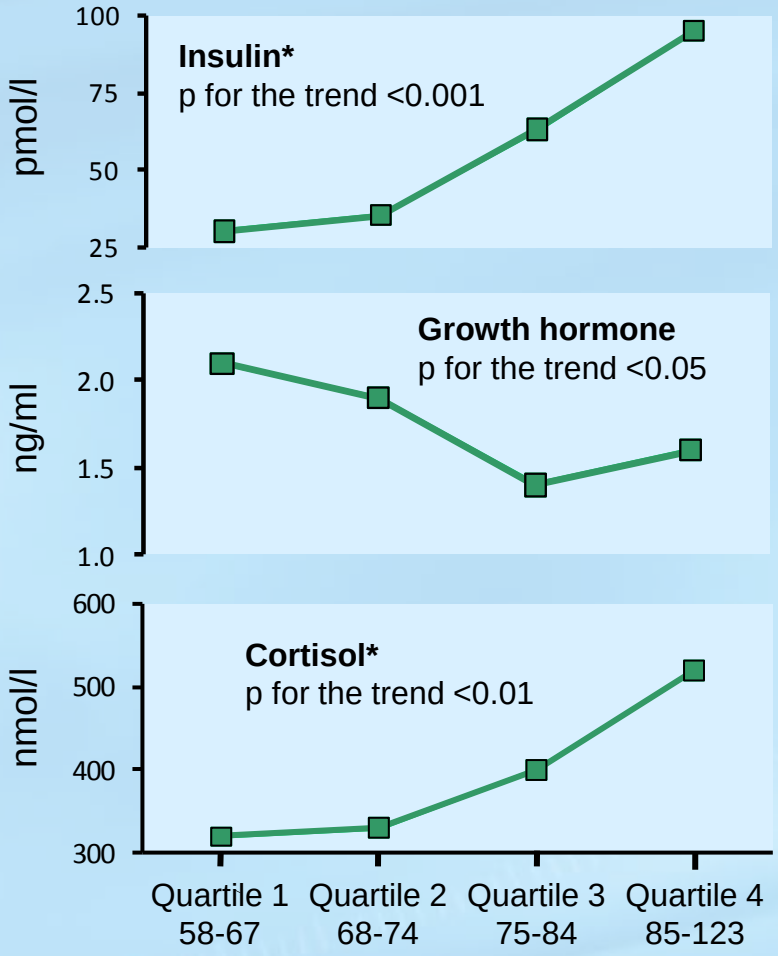
HIGH TRIG SHIFT BEFORE IMPAIRED FASTING GLUCOSE

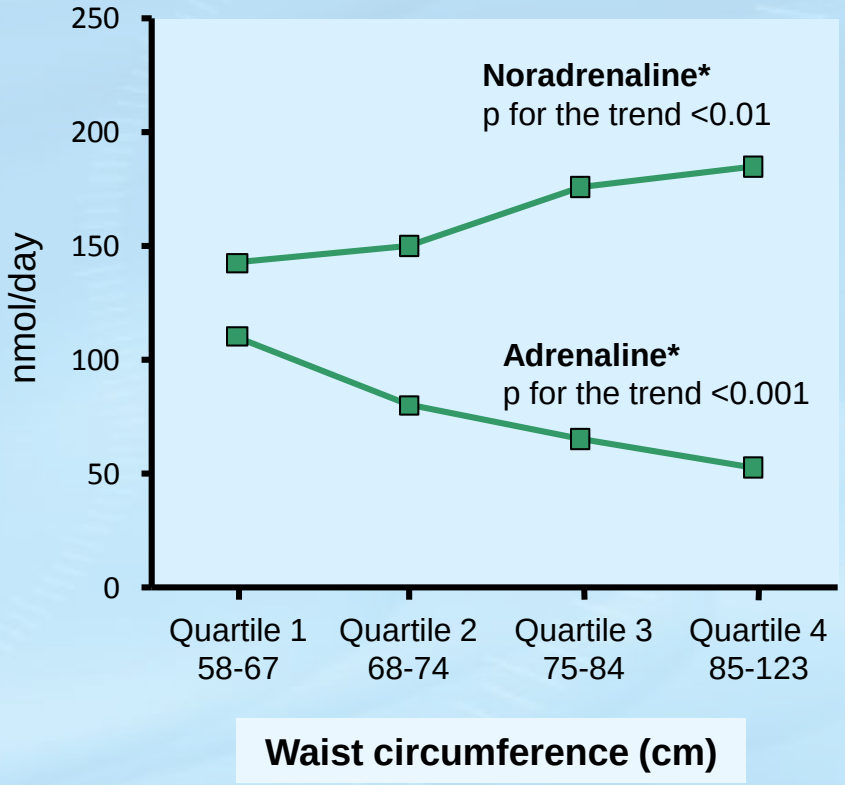
Carnitine palmitoyltransferase I

Fatty acid synthesis is stimulated by excess insulin



Central Obesity, Insulin Cortisol, Growth Hormone and 24-hour Urinary Catecholamines in 100 Young Type 2 Diabetic Patients and 90 Control Subjects



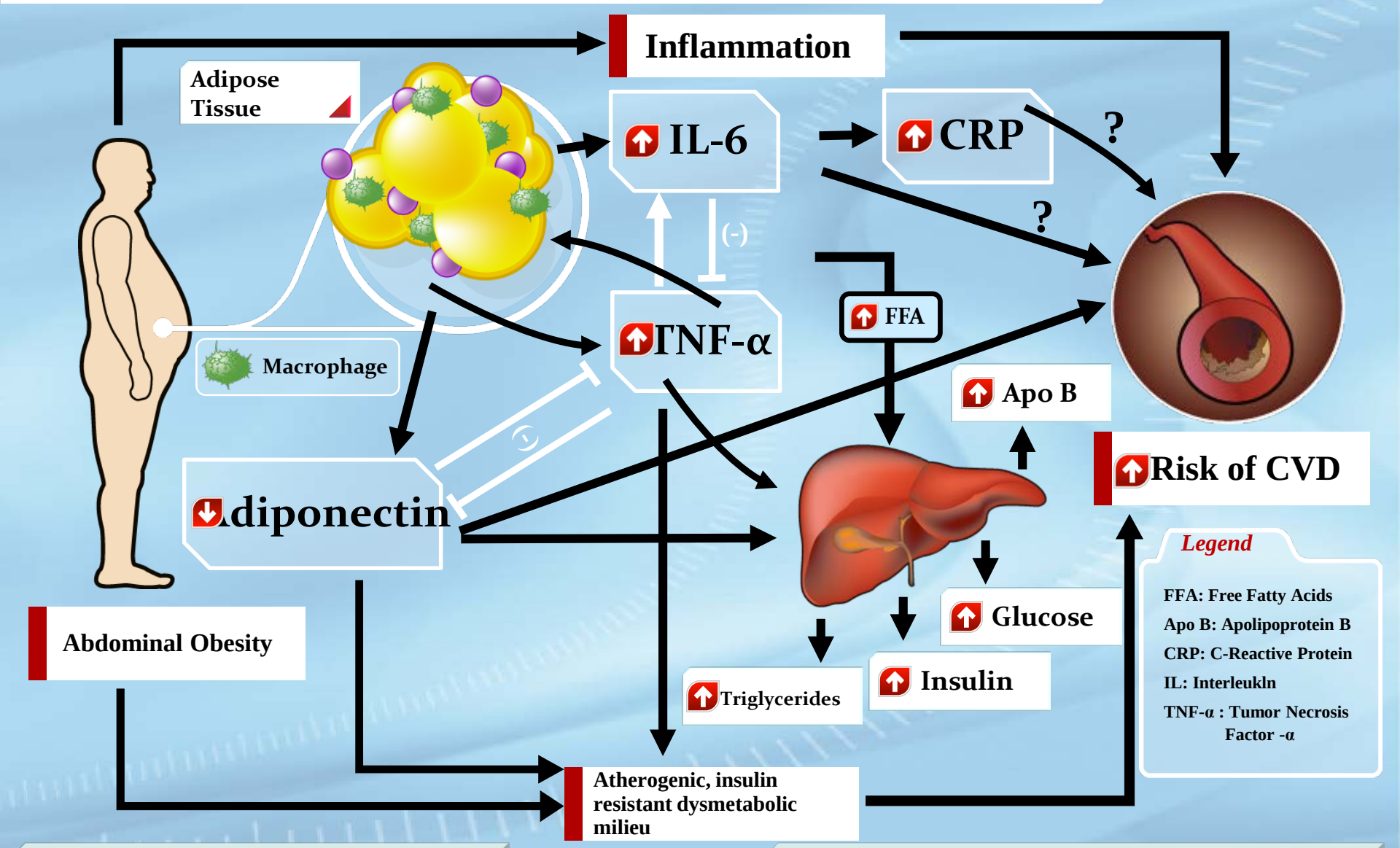


*Dates are expressed as * geometric means and ** means*

Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Lee ZSK et al. Diabetes Care 1999; 22: 1450-7
and Lee ZSK et al. Metabolism 2001; 50: 135-43

INFLAMMATION: THE LINK BETWEEN ABDOMINAL OBESITY AND GLOBAL CARDIOMETABOLIC RISK (CVD RISK)



Source: International Chair on Cardiometabolic Risk
www.cardiometabolic-risk.org

Adapted from Després JP Int J Obes Metab Disord 2003; 27: 5224

Today:

- Definitions
- Assessment
- Risk factors: standard and additional
- Treatment Recommendations
- Monitoring

Assessment

- Anthropometrics
  - Body Mass Index
  - BIA(Bioelectrical Impedance Analysis)
  - **Waist Circumference**
  - Waist to Hip Ratio

1

- **Over Weight**
- Scale and BMI

2

- **Over FAT**
- BioImpedance Analysis

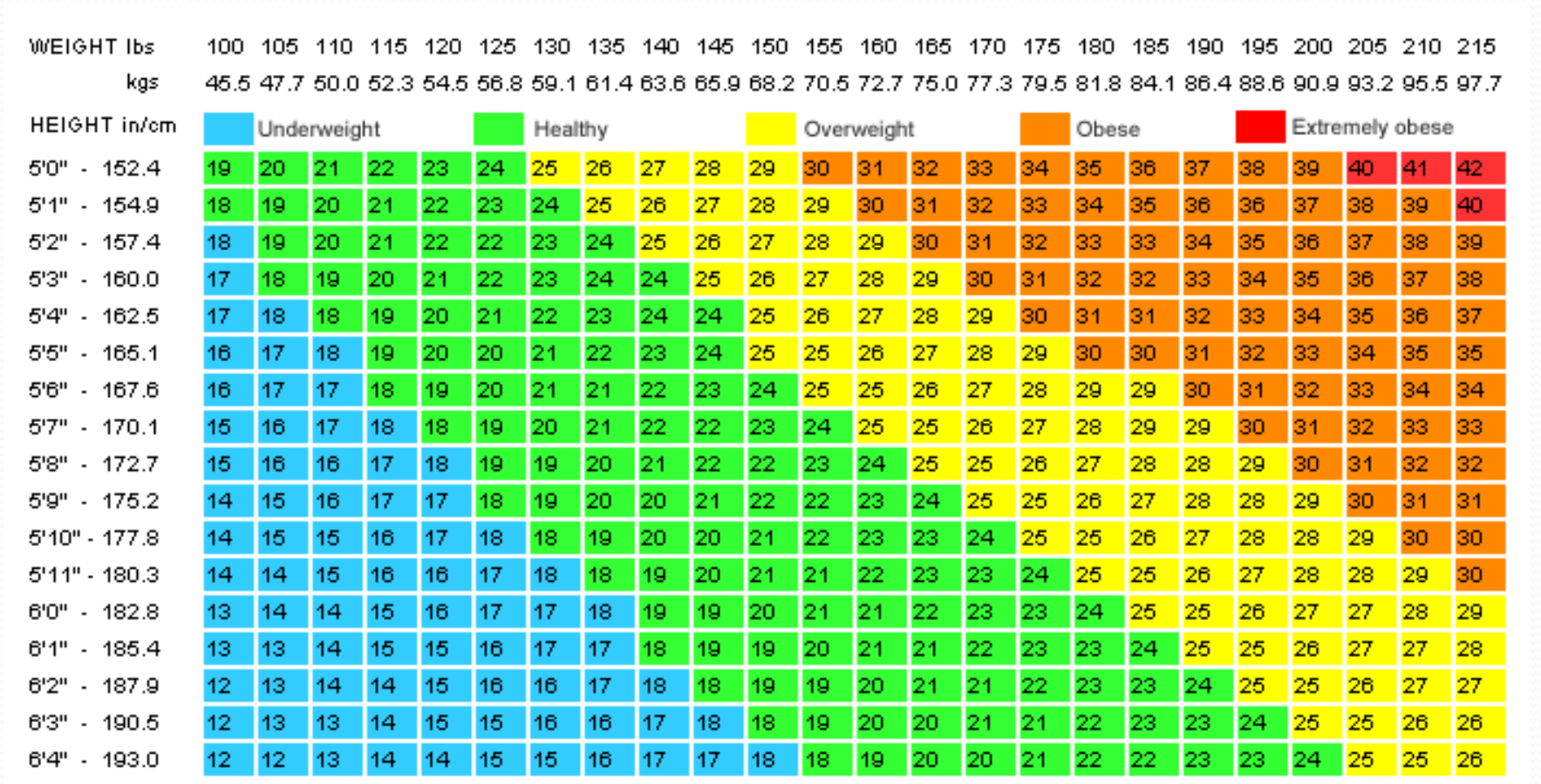
3

- **Over VAT**
- Waist circumference, Waist Hip Ratio

Overweight


"It's a genetic thing. My parents are too short for their weight, too."

BMI



WEIGHT lbs	100	105	110	115	120	125	130	135	140	145	150	155	160	165	170	175	180	185	190	195	200	205	210	215
kgs	45.5	47.7	50.0	52.3	54.5	56.8	59.1	61.4	63.6	65.9	68.2	70.5	72.7	75.0	77.3	79.5	81.8	84.1	86.4	88.6	90.9	93.2	95.5	97.7
HEIGHT in/cm	Underweight					Healthy					Overweight					Obese				Extremely obese				
5'0" - 152.4	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42
5'1" - 154.9	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	36	37	38	39	40
5'2" - 157.4	18	19	20	21	22	22	23	24	25	26	27	28	29	30	31	32	33	33	34	35	36	37	38	39
5'3" - 160.0	17	18	19	20	21	22	23	24	24	25	26	27	28	29	30	31	32	32	33	34	35	36	37	38
5'4" - 162.5	17	18	18	19	20	21	22	23	24	24	25	26	27	28	29	30	31	31	32	33	34	35	36	37
5'5" - 165.1	16	17	18	19	20	20	21	22	23	24	25	25	26	27	28	29	30	30	31	32	33	34	35	35
5'6" - 167.6	16	17	17	18	19	20	21	21	22	23	24	25	25	26	27	28	29	29	30	31	32	33	34	34
5'7" - 170.1	15	16	17	18	18	19	20	21	22	22	23	24	25	25	26	27	28	29	29	30	31	32	33	33
5'8" - 172.7	15	16	16	17	18	19	19	20	21	22	22	23	24	25	25	26	27	28	28	29	30	31	32	32
5'9" - 175.2	14	15	16	17	17	18	19	20	20	21	22	22	23	24	25	25	26	27	28	28	29	30	31	31
5'10" - 177.8	14	15	15	16	17	18	18	19	20	20	21	22	23	23	24	25	25	26	27	28	28	29	30	30
5'11" - 180.3	14	14	15	16	16	17	18	18	19	20	21	21	22	23	23	24	25	25	26	27	28	28	29	30
6'0" - 182.8	13	14	14	15	16	17	17	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27	28	29
6'1" - 185.4	13	13	14	15	15	16	17	17	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27	28
6'2" - 187.9	12	13	14	14	15	16	16	17	18	18	19	19	20	21	21	22	23	23	24	25	25	26	27	27
6'3" - 190.5	12	13	13	14	15	15	16	16	17	18	18	19	20	20	21	21	22	23	23	24	25	25	26	26
6'4" - 193.0	12	12	13	14	14	15	15	16	17	17	18	18	19	20	20	21	22	22	23	23	24	25	25	26

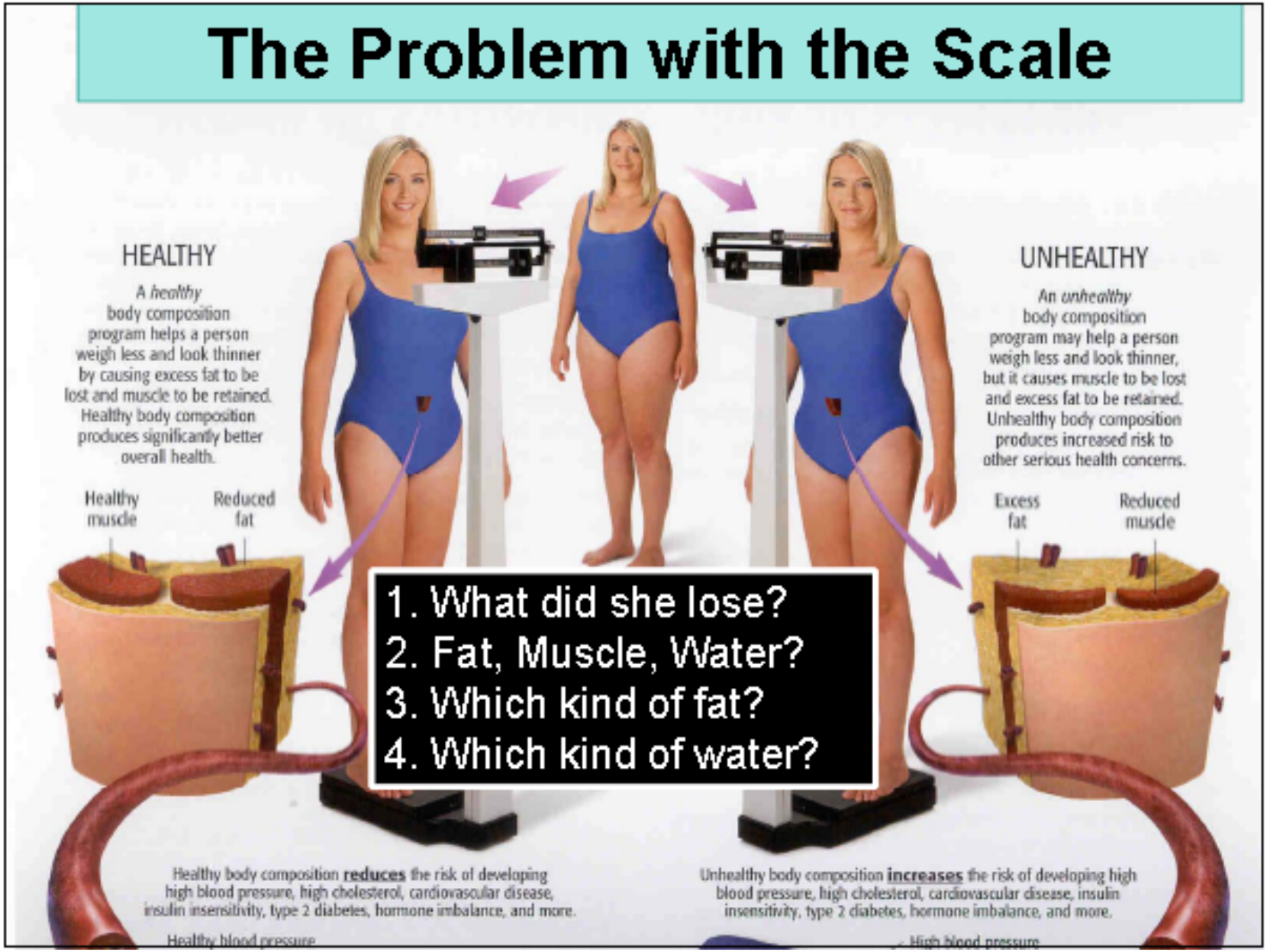
Generation XL

- BMI percentile in kids

The Problem with BMI

'Skinny fat'

The Problem with the Scale



BioImpedance Analysis

- Hydration status
- Fluid Distribution:
  - Intracellular water ☺
  - Extracellular water 😐/☹
- Fat Mass
- Lean Body Mass
- Basal Metabolic Rate

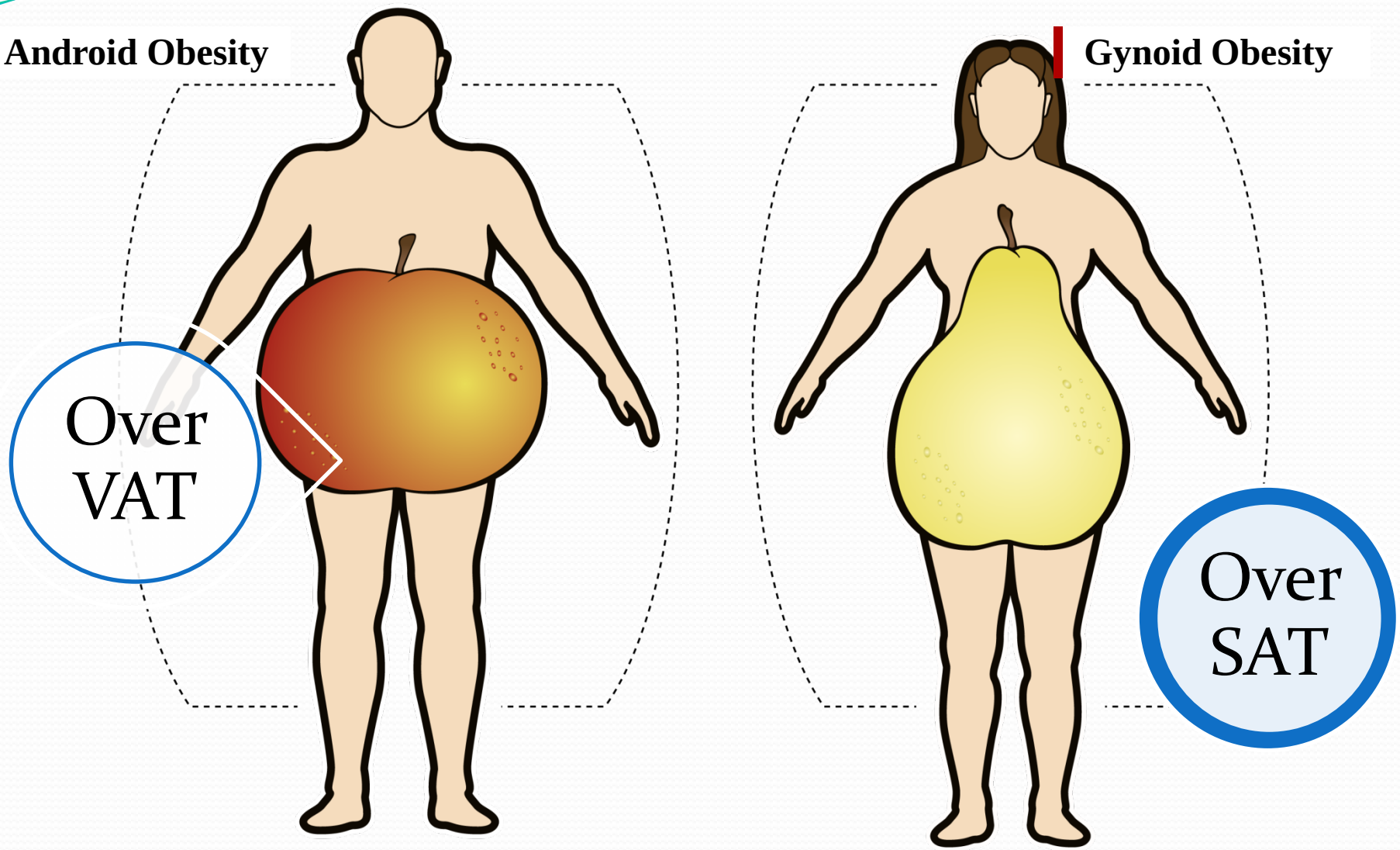
Over FAT

Reference Ranges		
Body Fat %		
Age	**Men**	**Women**
20	11-14%	17-20%
30	12-15%	18-21%
40	14-17%	19-22%
50	15-18%	20-23%
60	16-19%	21-24%
70	17-20%	22-25%
80	17-20%	22-25%

Track Leanness, Not Lightness

- Goals
  - Gain Muscle Mass
  - Lose Excess Fat Mass

ADIPOSE TISSUE DISTRIBUTION IN MEN AND WOMEN



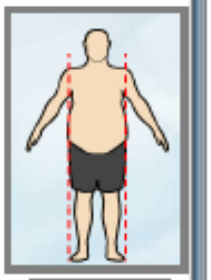
Adapted from Vague J Presse Med 1947; 30: 339-40

Waist Circumference Measurement Guidelines - Healthcare Professional

Step 1

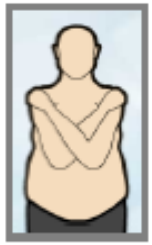
Ask the patient to place himself in the following manner:

- Clear the abdominal region
- Feet shoulder-width apart
- Arms crossed over the chest



Man

Woman



Step 2

It is suggested to kneel down to the right of the patient in order to measure waist girth.

- Palpate the patient's hips to locate the top of the iliac crest.
- Draw a horizontal line halfway between the patient's back and abdomen.

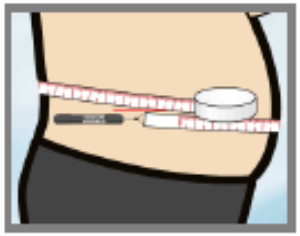
Step 3

- Place the measuring tape horizontally around the patient's abdomen.

- To work comfortably, it is suggested to wrap the tape around the patient's legs and then move it up.

Step 4

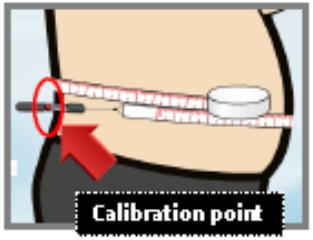
- Align the bottom edge of the tape with your marked point.



Step 5

It is recommended to use a measuring tape with a spring handle, such as the Gulick measuring tape, in order to control the pressure exerted on the patient's abdomen.

- Gently tighten the tape around the patient's abdomen without depressing the skin.

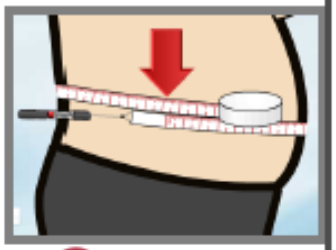


- When using a measuring tape with a spring handle, pull the end of the tensioning mechanism until the calibration point is just visible.

Step 6

It is suggested to request the patient to relax and breathe NORMALLY (abdominal muscles should not be contracted).

- Ask the patient to take 2 or 3 NORMAL breaths.
- Measure from the zero line of the tape (to the nearest millimetre) at the end of a NORMAL expiration.



International Chair on Cardiometabolic Risk

myhealthywaist.org

WC

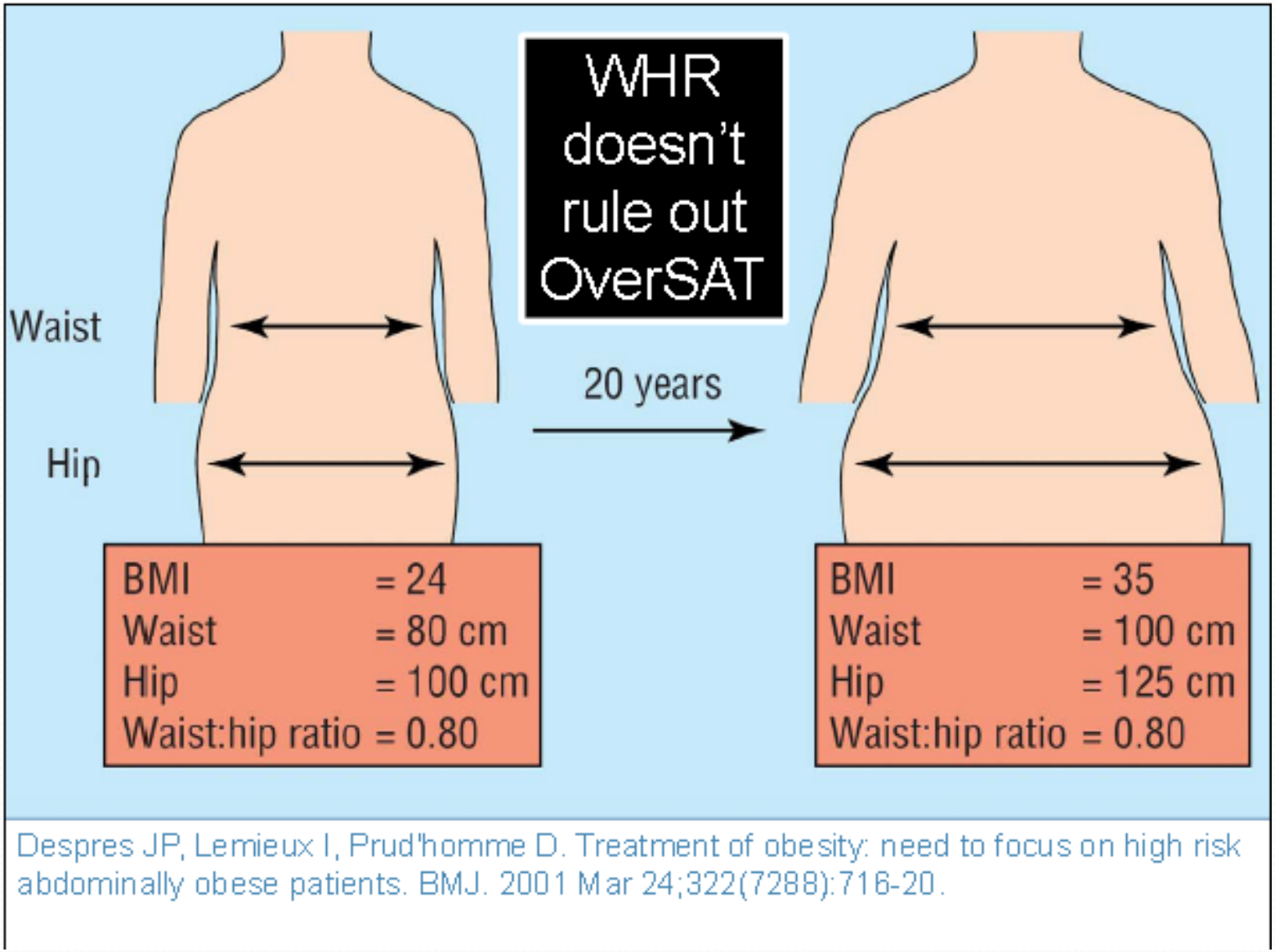
	Europids	South Asians, Chinese, Japanese	Americans (per NCEP-ATP III)
Men	≥94 cm 37 in	≥90 cm 35 in	102 cm 40 in
Women	≥80 cm 31 in	≥80 cm 31 in	88 cm 35 in

Health Risk Based on Waist to Hip Ratio

Male	Female	Health Risk Based Solely on WHR
= or < 0.90	= or < 0.80	Low Risk
0.90 to 1.0	0.81 to 0.85	Moderate Risk
>1.0	>0.85	High Risk

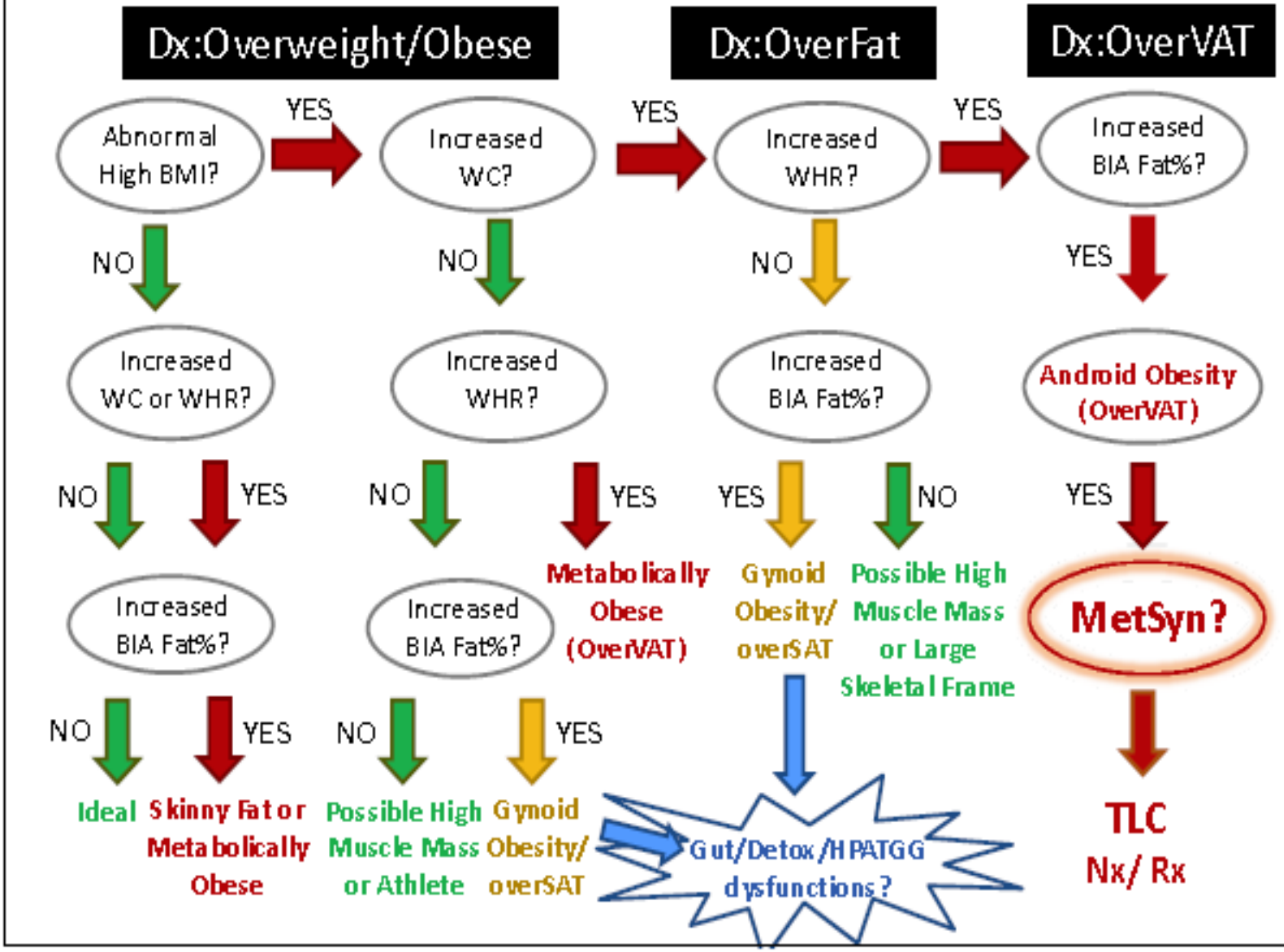
Ford ES, Giles WH, Dietz WH (2002). Prevalence of metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. *JAMA* 287(3):356-359

"WHR, rather than or waist circumference], appears to be the more appropriate yardstick for obesity-related risk stratification of high-functioning older adults, and possibly all older adults."
~*Ann Epidemiol*. 2009;19:724-731.



Despres JP, Lemieux I, Prud'homme D. Treatment of obesity: need to focus on high risk abdominally obese patients. BMJ. 2001 Mar 24;322(7288):716-20.

Assessing Body Composition



Physical exam

- **Blood Pressure**, pulses
- Heart exam
- Peripheral edema
- Eye exam
- Neuro exam
- Hormonal: gynecomastia, hirsutism, striae
- Skin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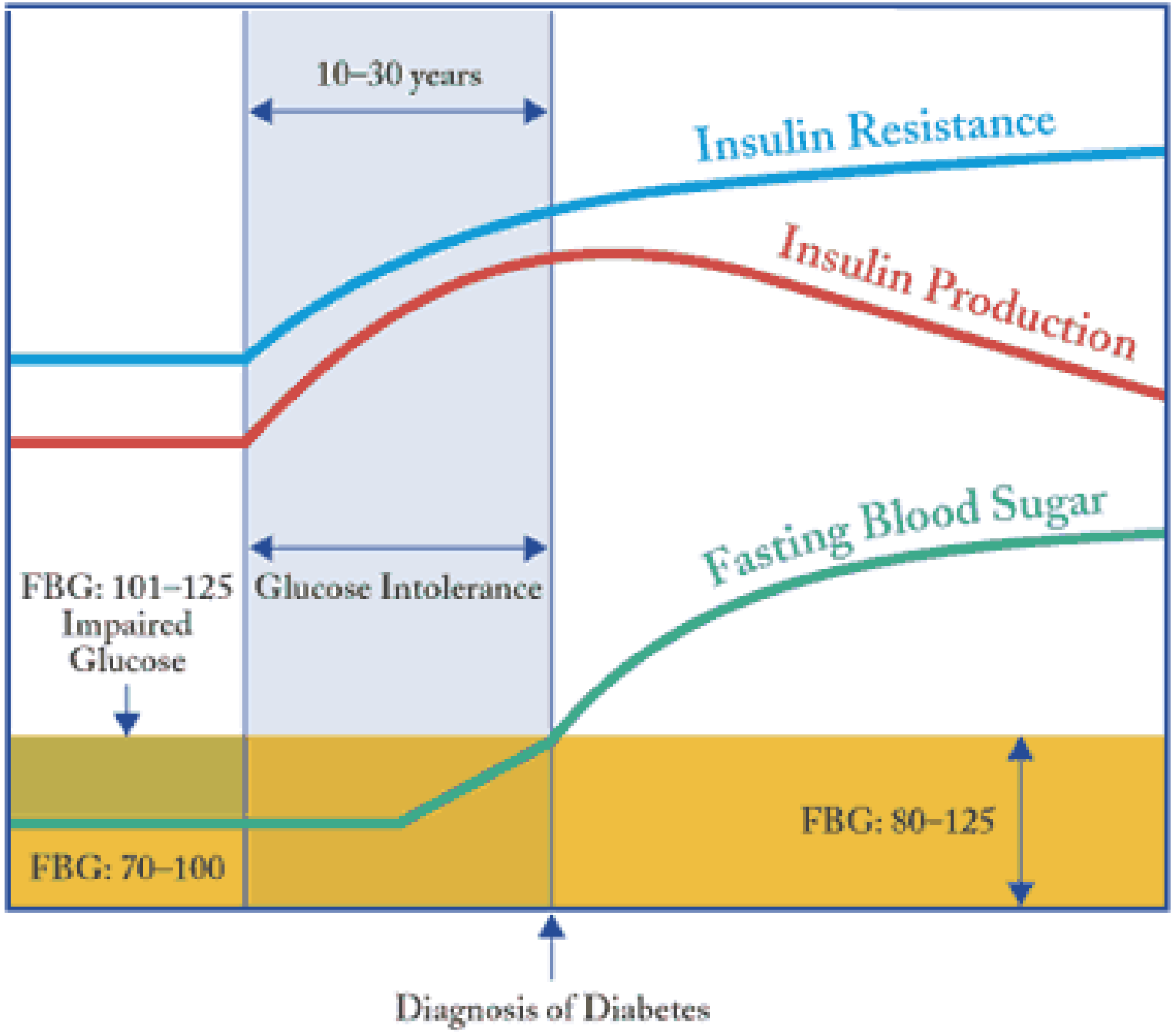
A.D.A.M.

Laboratory

- Glucose
  - HgbA1C
  - FBG
  - GTT
- Lipid
  - LDL
  - HDL
  - TG
    - TG/HDL ratio ≥ 3.0 suggests insulin resistance
- Insulin – will rise before the glucose does



Adapted from Type 2 Diabetes BASICS, ©2000 International Diabetes Center, Minneapolis, MN.

Additional Laboratory

- • **Inflammation:** CBC, hs-CRP, homocysteine, fibrinogen
- • **Oxidative Stress/Toxicity:** GGT
- • **Endocrine:** TSH, Free T4, Free T3
- • **Nutrition:** 25 OH Vitamin D3

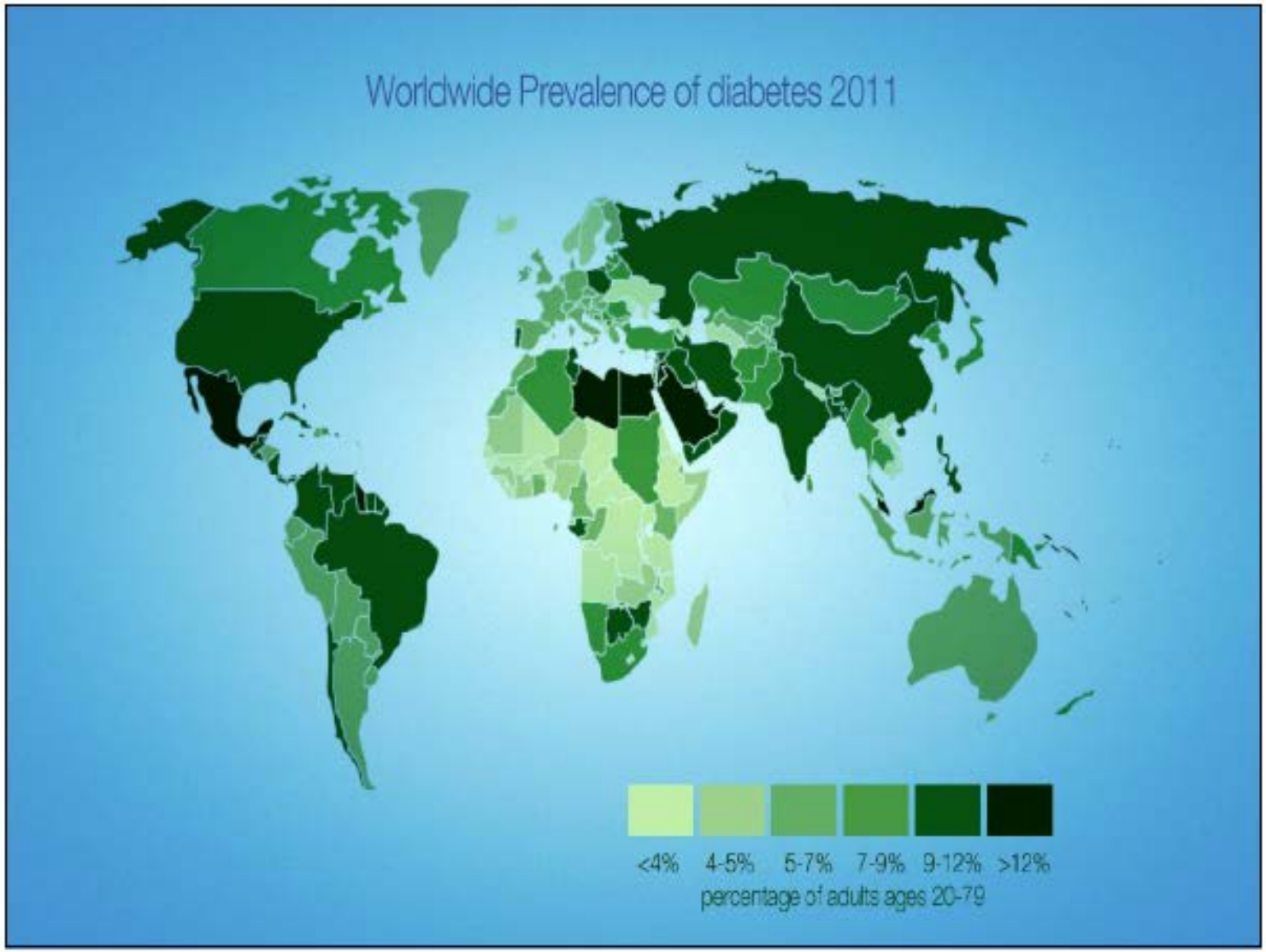
- VAP Cholesterol test per our lab:
  - LDL Cholesterol , LDL size
  - Lp(a) Cholesterol
  - Total HDL Cholesterol, HDL 2, HDL 3 (Small, Dense, Least Protective)
  - VLDL Cholesterol
  - Total APO B100, APO A1

Today:

- Definitions
- Assessment
- Risk factors: standard and additional
- Treatment Recommendations
- Monitoring

Risk Factors

- Family history
  - Disease
  - Ethnic background(s)



By 2020, >50% of the US adult population will have diabetes or prediabetes, with annual costs approaching $500 billion Heidenreich. Circulation 2011, Jan 24