Defining Insulin Resistance and Metabolic Syndrome

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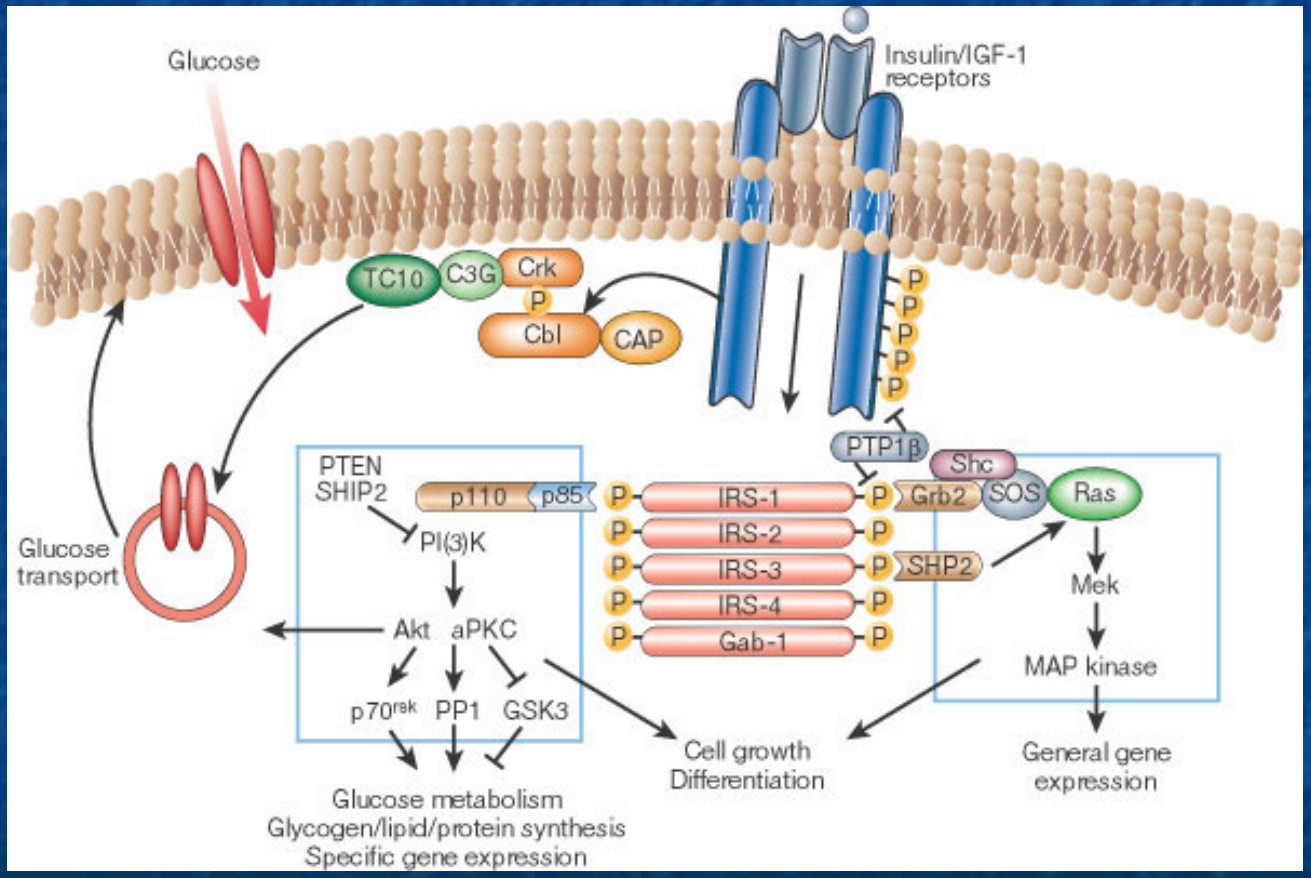
Insulin Resistance is a physiological, adaptative and selective phenomenon



Alan R. Saltiel and C. Ronald Kahn Insulin signalling and the regulation of glucose and lipid metabolism. Nature 414, 799-806(13 December 2001)

ADIPOTOXICITY
is the main cause of pathological IR

Genes
Environment

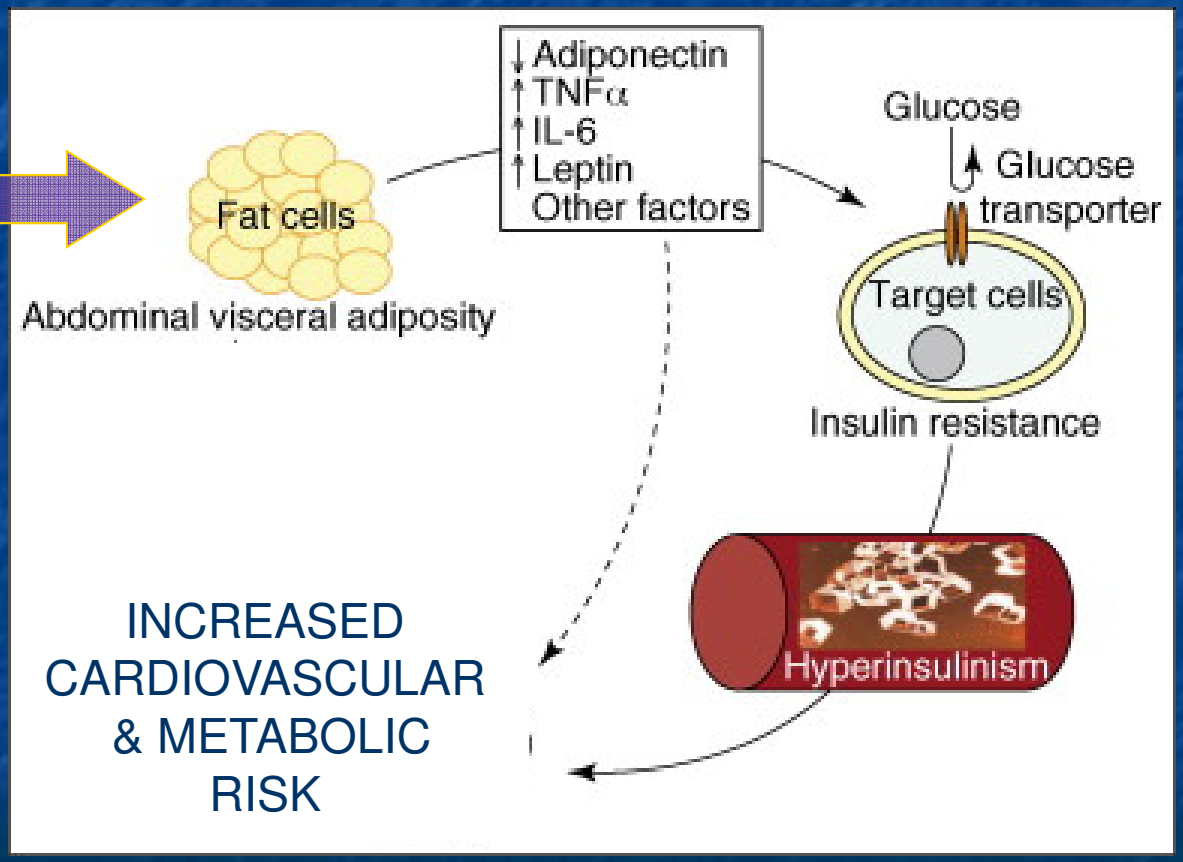


Table 1. *Current approaches for assessing insulin sensitivity and resistance in vivo*

Method	Measurement of Insulin Sensitivity
	Direct measurements
Hyperinsulinemic euglycemic glucose clamp	Steady-state GIR = M. SI_{Clamp} = M/(G × ΔI), where M is normalized for G (steady-state blood glucose concentration) and ΔI (difference between fasting and steady-state plasma insulin concentrations)
IST	SSPG concentration during constant infusions of insulin and glucose with suppressed endogenous insulin secretion
	Indirect measurements
Minimal model analysis – FSIVGTT	Minimal model uniquely identifies model parameters that determine a best fit to glucose disappearance during the modified FSIVGTT. S_I: fractional glucose disappearance per insulin concentration unit; S_G: ability of glucose per se to promote its own disposal and inhibit HGP in the absence of an incremental insulin effect (i.e., when insulin is at basal levels)
	Simple surrogate indexes
Surrogates derived from fasting steady-state conditions	
1/(Fasting insulin)	Reciprocal of fasting plasma insulin concentration, μU/ml
G/I ratio	Ratio of fasting plasma glucose (mg/dl) and insulin (μU/ml) concentration
HOMA	HOMA-IR = {[fasting insulin (μU/ml)] × [fasting glucose (mmol/l)]}/22.5
QUICKI	QUICKI = 1/[Log (fasting insulin, μU/ml) + Log (fasting glucose, mg/dl)]
Surrogates derived from dynamic tests (OGTT)	
Matsuda index	$ISI(Matsuda) = 10{,}000/\sqrt{[(G_{fasting\ (mg/dl)} \times I_{fasting\ (mU/l)}) \times (G_{mean} \times I_{mean})]}$
Gutt index: $ISI_{(0,\ 120)}$, $mg \cdot l^2 \cdot mmol^{-1} \cdot mIU^{-1} \cdot min^{-1}$	$ISI_{(0,\ 120)} = 75{,}000 + (G_0 - G_{120})_{(mg/dl)} \times 0.19 \times BW/120 \times G_{mean(0,\ 120)\ (mmol/l)} \times \mathrm{Log}\ (I_{mean\ (0,\ 120)})_{(mU/l)}$
Avignon index, SiM	SiM = [(0.137 × Sib) + Si2 h]/2, where $Sib = 10^8/(I_{0\ (mU/l)} \times G_{0\ (mmol/l)} \times VD)$ and $Si2\ h = 10^8/(I_{120\ (mU/l)} \times G_{120\ (mmol/l)} \times VD)$
Stumvoll index	$ISI_{Stumvoll} = 0.156 - 0.0000459 \times I_{120\ (pmol/l)} - 0.000321 \times I_{0\ (pmol/l)} - 0.00541 \times G_{120\ (mmol/l)}$

GIR, glucose infusion rate; M, glucose disposal rate; IST, insulin suppression test; SSPG, steady-state plasma glucose; FSIVGTT, frequently sampled intravenous glucose tolerance test; S_I, insulin sensitivity index; S_G, glucose effectiveness index; HGP, hepatic glucose production; G/I ratio, glucose/insulin ratio; HOMA, homeostasis model assessment; HOMA-IR, homeostasis model assessment of insulin resistance; QUICKI, quantitative insulin sensitivity check index; OGTT, oral glucose tolerance test; G_{mean}, mean plasma glucose concentration during OGTT; I_{mean}, mean insulin concentration during OGTT; G_o, plasma glucose concentration during fasting; G_{120}, plasma glucose concentration at 120 min; BW, body weight; I_o, plasma insulin concentration during fasting; I_{120}, plasma insulin concentration at 120 min; VD, glucose distribution volume (150 ml/kg BW).

RESEARCH

Muniyappa R et al., Am J Physiol Endocrinol Metab. 2008;294:E15-26.

Surrogate indexes of insulin sensitivity

using fasting basal determinations of G and I

- HOMA-IR:

  I (mIU/L) x G (mmol/L)/22.5

- QUICKI:

  1/ log I (mIU/L) + log G (mg/dl)

- G/I:

  G (mg/dl) / I (mIU/L)

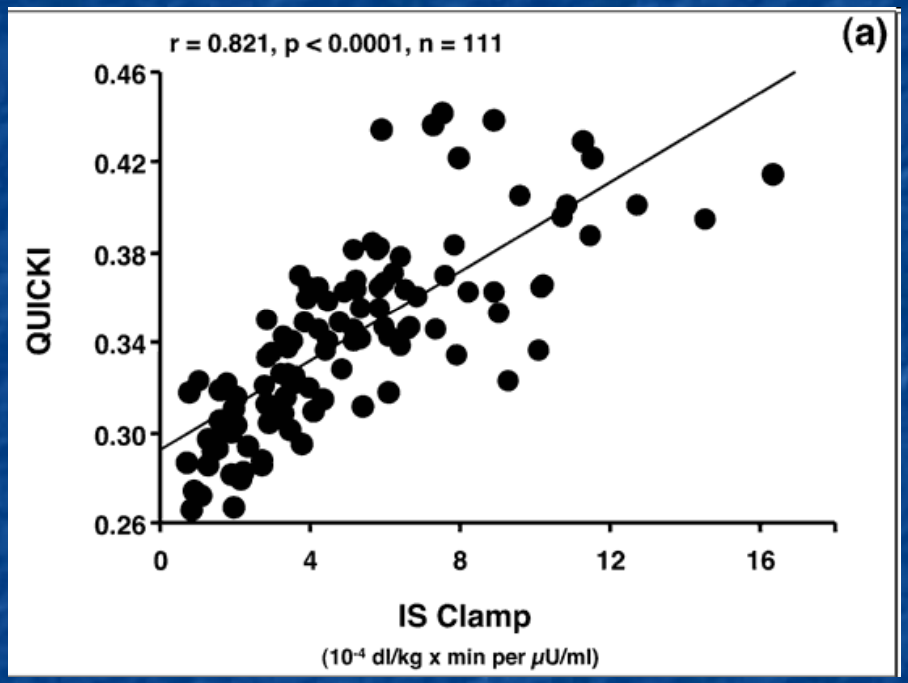
Table II

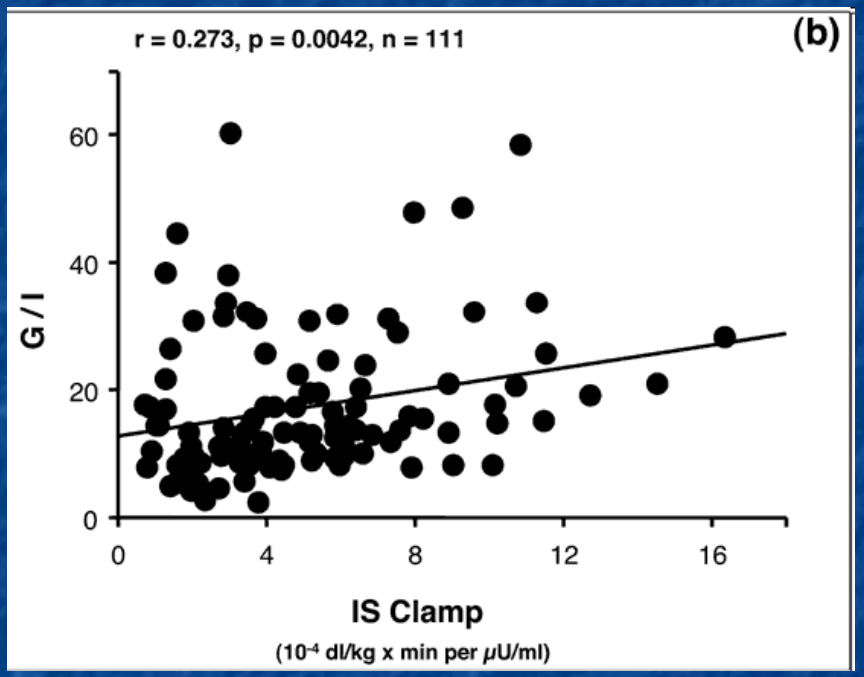
Univariate Spearman's correlation between simple measures of insulin resistance and directly-measured insulin sensitivity by hyperinsulinemic euglycemic clamp (n = 111).

Simple measures	Spearman's *r*	*p*
HOMA	– 0.820	< 0.0001
FIRI	– 0.820	< 0.0001
QUICKI	0.821	< 0.0001
G/I	– 0.273	= 0.0042
I/G	– 0.272	= 0.0043
40/I	– 0.701	< 0.0001

Bastard JP et al., Diabetes Metab 2003, 29:285-8

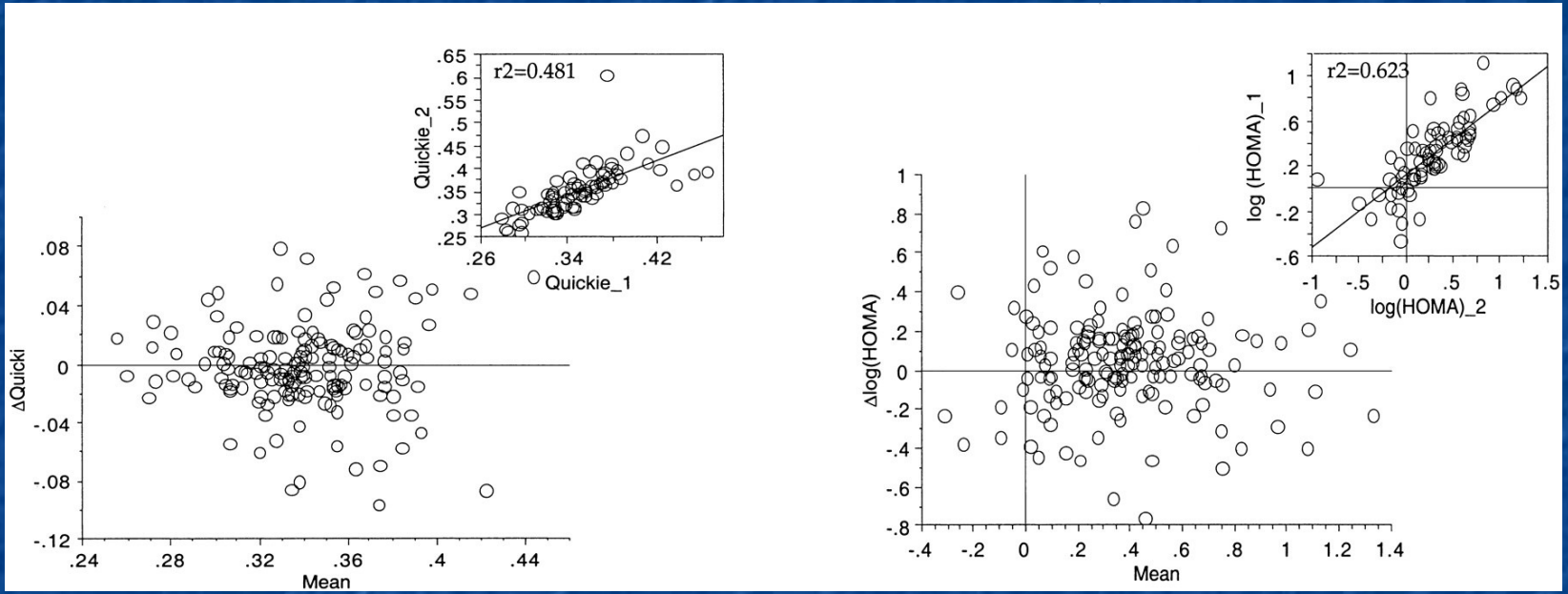
QUICKI is better than G/I





Bastard JP et al., Diabetes Metab 2003, 29:285-8

QUICKI and Log(HOMA) are similar



Mather, K. J. et al. J Clin Endocrinol Metab 2001;86:5457-5464

Surrogate indexes of insulin sensitivity

Caveats

- Depend on I assay that is not standardized
- Skewed distribution of I values (improved by log transformation)
- Not optimal in diabetic subjects (G/I)
- Not optimal in healthy insulin-sensitive subjects

Usefulness

- Epidemiological studies
- Research clinical studies (correlations)
- Follow up after therapeutic interventions

Detecting IR in clinical practice

Table 3. Familial, clinical and physical features as risks factors for IR in children and adolescents

Family history	Patient's history	Physical examination
Glucose intolerance or T2DM	Birth weight (small or large for gestational age)	Acanthosis nigricans
Overweight or obesity	Precocious pubarche	Striae
Hypertension	Evolution of obesity	Centripetal obesity
Metabolic syndrome	Dietary habits	Adipomastia
Hyperuricemia or gout	Physical activity	Hypertension
Coronary heart disease	Medication/drugs which affect appetite, glucose or lipid metabolism	Acne
Stroke		Hirsutism
Chronic pancreatitis		Tall stature
Gestational diabetes		Precocious puberty
Polycystic-ovary syndrome or hirsutism		Genu valgum
Nonalcoholic fatty liver disease		

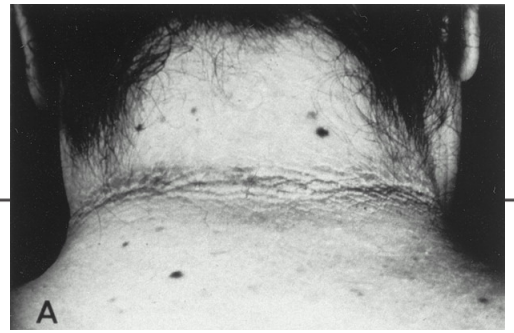


Table 4. Medications associated with IR

Hormones	HIV therapy	Antipsychotic drugs	Immune suppressants	Others
Glucocorticoids	HIV nucleoside reverse-transcriptase inhibitors	Clozapine	Tacrolimus	Tiazides
Growth hormone	HIV protease inhibitors	Olanzapine	Cyclosporine A	Valproate
		Risperidone	Sirolimus	Glucosamine

Eyzaguirre F, Mericq V. Insulin resistance markers in children. Horm Res. 2009;71:65-74

The Metabolic Syndrome (MetS)

Requiescat in pace?

G. Reaven

2005

The « old » definitions of MetS

Table 1. WHO, EGIR and ATPIII definitions of the metabolic syndrome.

WHO 1999	EGIR 1999	ATPIII 2001
Diabetes or impaired glucose tolerance or insulin resistance*	Insulin resistance* or hyperinsulinaemia (only non-diabetic subjects)	
Plus two or more of the following:	Plus two or more of the following:	Three or more of the following:
1. Obesity: BMI > 30 kg/m² or WHR > 0.9 (M) > 0.85 (F)	1. Central obesity: Waist circumference ≥ 94 cm (M), ≥ 80 cm (F)	1. Central obesity: Waist circumference >102 cm (M), > 88 cm (F)
2. Dyslipidaemia: Triglycerides ≥ 150 mg/dl (1.7 mmol/l) or HDL-C < 35 mg/dl (0.9 mmol/l) (M) < 39 mg/dl (F) (1.0 mmol/l)	2. Dyslipidaemia: Triglycerides > 177 mg/dl (2.0 mmol/l) or HDL-C < 39 mg/dl (1.0 mmol/L)	2. Hypertriglyceridaemia: Triglycerides ≥ 150 mg/dl (1.7 mmol/l)
3. Hypertension: Blood pressure ≥ 140/90 mmHg or medication	3. Hypertension: Blood pressure ≥ 140/90 mmHg or medication	3. Low HDL -C: < 40 mg/dl (1.03 mmol/l) (M), < 1.29 mmol/l (50 mg/dl) (F)
4. Microalbuminuria: Albumin excretion ≥ 20 μg/min or albumin:creatinine ratio ≥ 30 mg/g	4. Fasting plasma glucose ≥ 110 mg/dl (6.1 mmol/l)	4. Hypertension: Blood pressure ≥ 130/85 mmHg or medication
		5. Fasting plasma glucose ≥ 110 mg/dl (6.1 mmol/l)

* defined as the top quartile of fasting insulin in the non-diabetic population.

Table 2. IDF Metabolic Syndrome World-wide Definition.

CENTRAL OBESITY
Waist circumference*– ethnicity specific (Table 2)

Plus any two of the following:

- RAISED TRIGLYCERIDES:
  ≥ 150mg/dl (1.7 mmol/l)
  or specific treatment for this lipid abnormality

- REDUCED HDL-CHOLESTEROL
  < 40 mg/dl (1.03 mmol/l) in males
  < 50 mg/dl (1.29 mmol/l) in females
  or specific treatment for this lipid abnormality

- RAISED BLOOD PRESSURE
  Systolic : ≥ 130 mmHg
  or Diastolic: ≥ 85 mmHg
  or treatment of previously diagnosed hypertension

- RAISED FASTING PLASMA GLUCOSE**
  Fasting plasma glucose ≥ 100 mg/dl (5.6 mmol/l)
  or previously diagnosed type 2 diabetes
  If above 5.6 mmol/l or 100 mg/dl, OGTT is strongly recommended but is not necessary to define presence of the syndrome.

* If BMI is > 30 kg/m^2 then central obesity can be assumed, and waist circumference does not need to be measured. Ethnic specific waist circumference are listed in table 2.

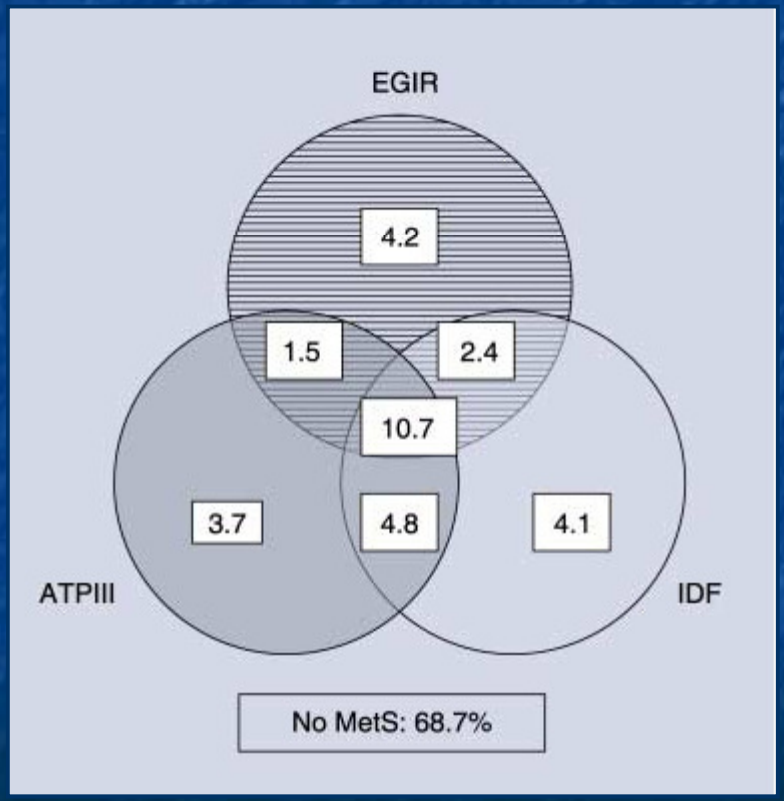
For women in western countries: 80 cm !

The metabolic syndrome and incidence of cardiovascular disease in non-diabetic subjects

a population-based study comparing three different definitions

Nilsson PM et al., Diabetic Medicine, 2007, **24**, 464– 472

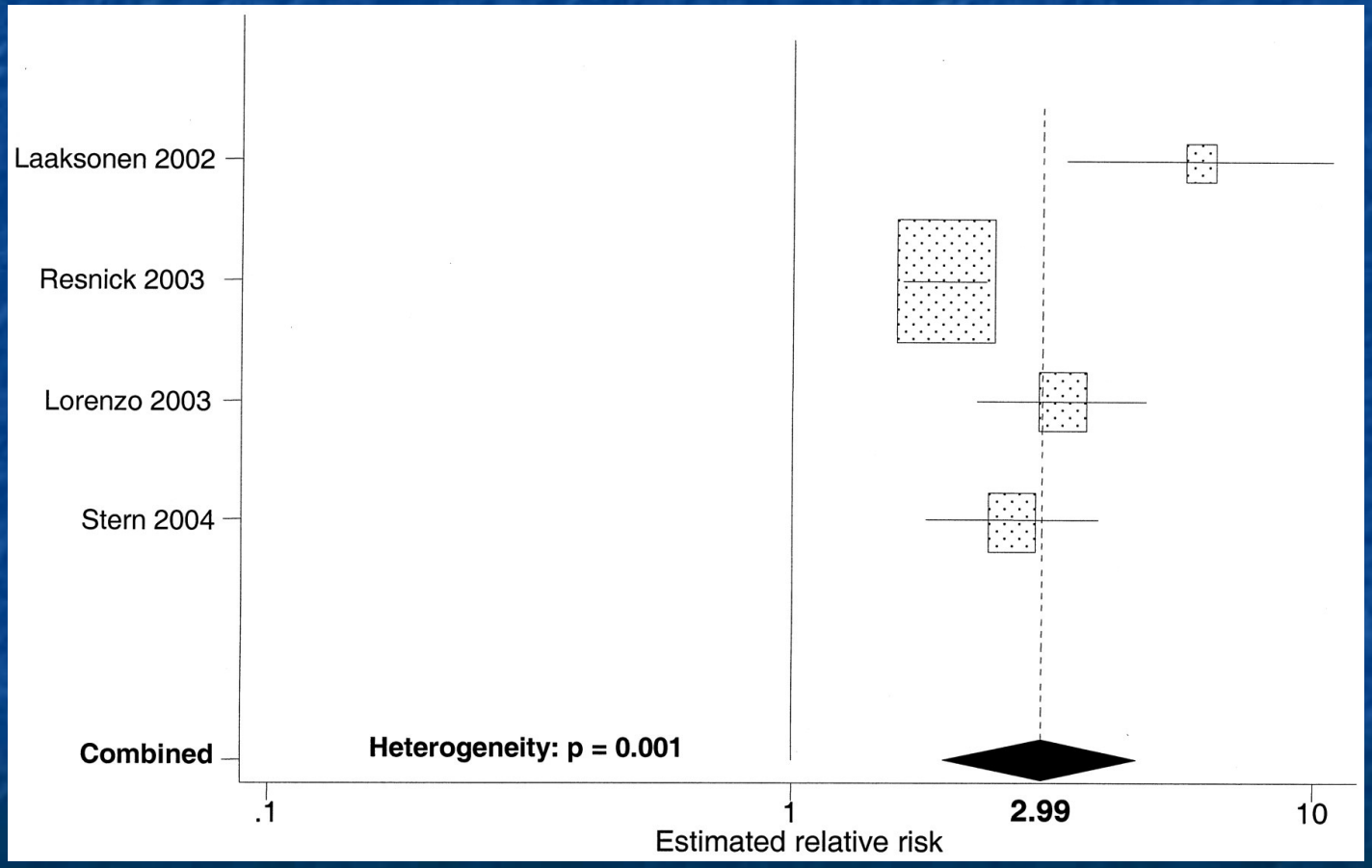
5,047 non-diabetic subjects (66% women), 11 years of follow-up.



	Prevalence (%)	HR* (95% CI)
MetS NCEP-ATPIII	21	1.95 (1.56–2.43)
MetS EGIR	19	1.55 (1.23–1.95)
MetS IDF	22	1.37 (1.09–1.72)
Hypertension (A, I)	79	2.97 (1.90–4.63)
Hypertension (E)	63	2.22 (1.67–2.95)
Obesity (A)	15	1.81 (1.42–2.31)
Obesity (E, I)	37	1.20 (0.97–1.48)
Low high-density lipoprotein (A, I)	30	2.01 (1.63–2.49)
Dyslipidemia (E)	21	1.65 (1.31–2.07)
Hypertriglyceridaemia (A, I)	22	1.37 (1.09–1.73)
Hyperglycemia (A, E, I)	14	1.39 (1.07–1.81)
Insulin resistance (E)	25	1.45 (1.16–1.81)
Current smoking	23	1.95 (1.55–2.45)

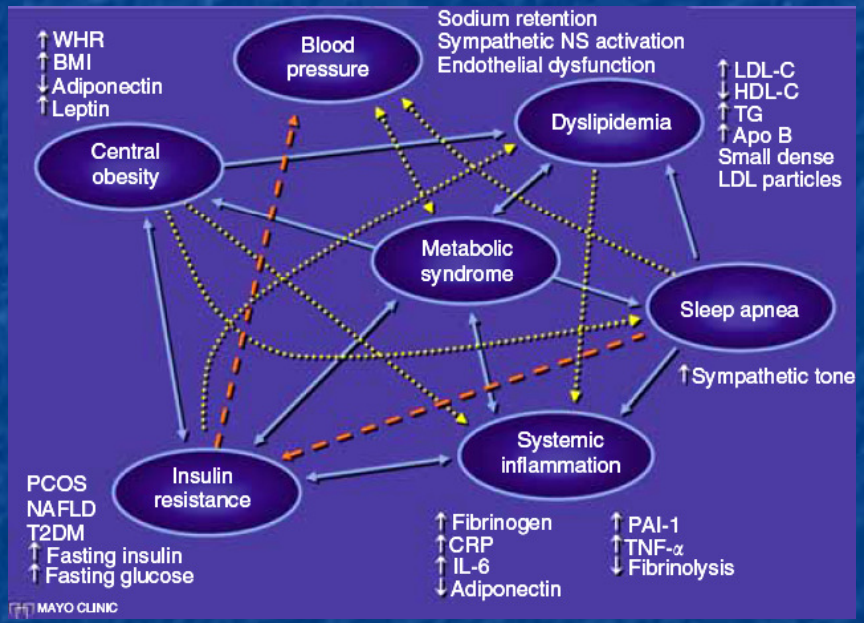
*RR adjusted for age and sex compared with those without the risk factor.
Variables included in the definition of metabolic syndrome (MetS): A, Adult Treatment Panel III (ATPIII); E, European Group for the study of Insulin Resistance (EGIR); I, International Diabetes Federation (IDF); based on criteria.

MetS as a predictor of T2DM

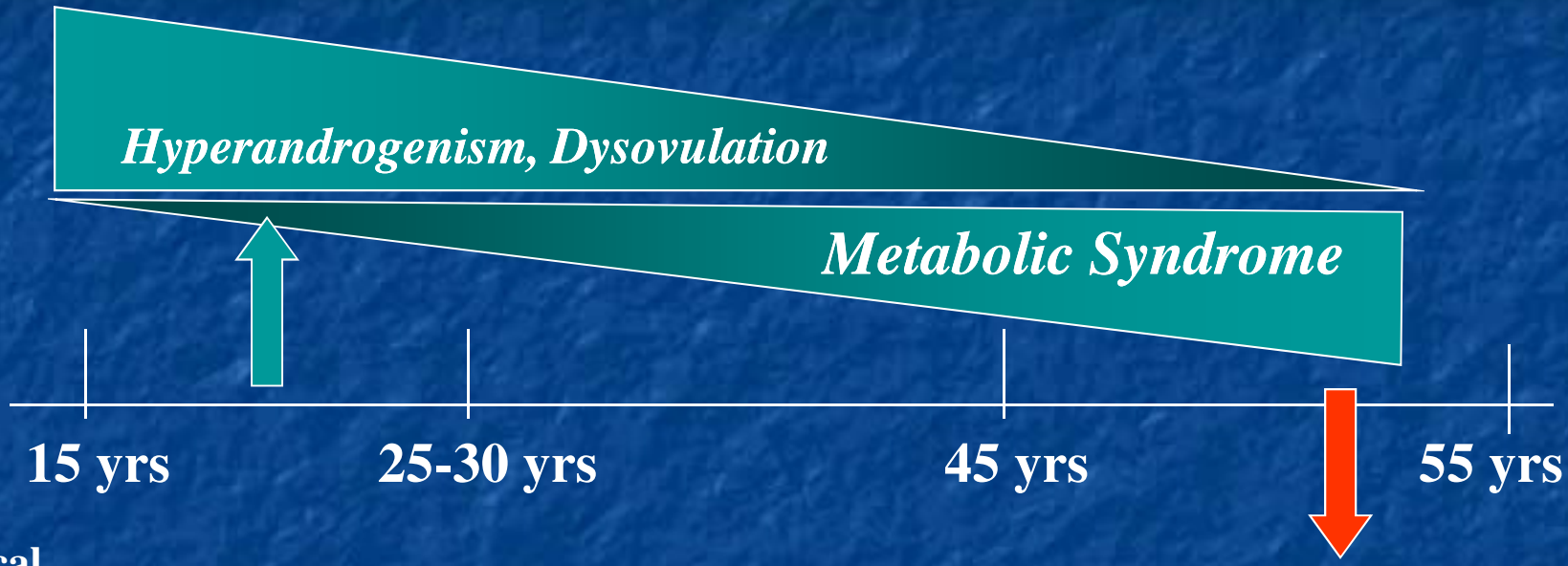


MetS: caveats

- Extremely abnormal values for any particular criterion receive the same weight as values that are barely abnormal
- Some patients may be misclassified as "normal" when indeed they have values that are close to the upper limit of normal.
- The selection of cutoff points has been arbitrary, in the most part, and not guided by biological and epidemiological principles of normality
- Not appropriate for early detection of IR in the young



Detecting IR and MetS in PCOS



- Clinical hyperandrogenism
- Menstrual irregularities

- Infertility
- Hyperandrogenism

- Hyperandrogenism
- Glucose intolerance

- Cardiovascular events
- Type 2 diabetes

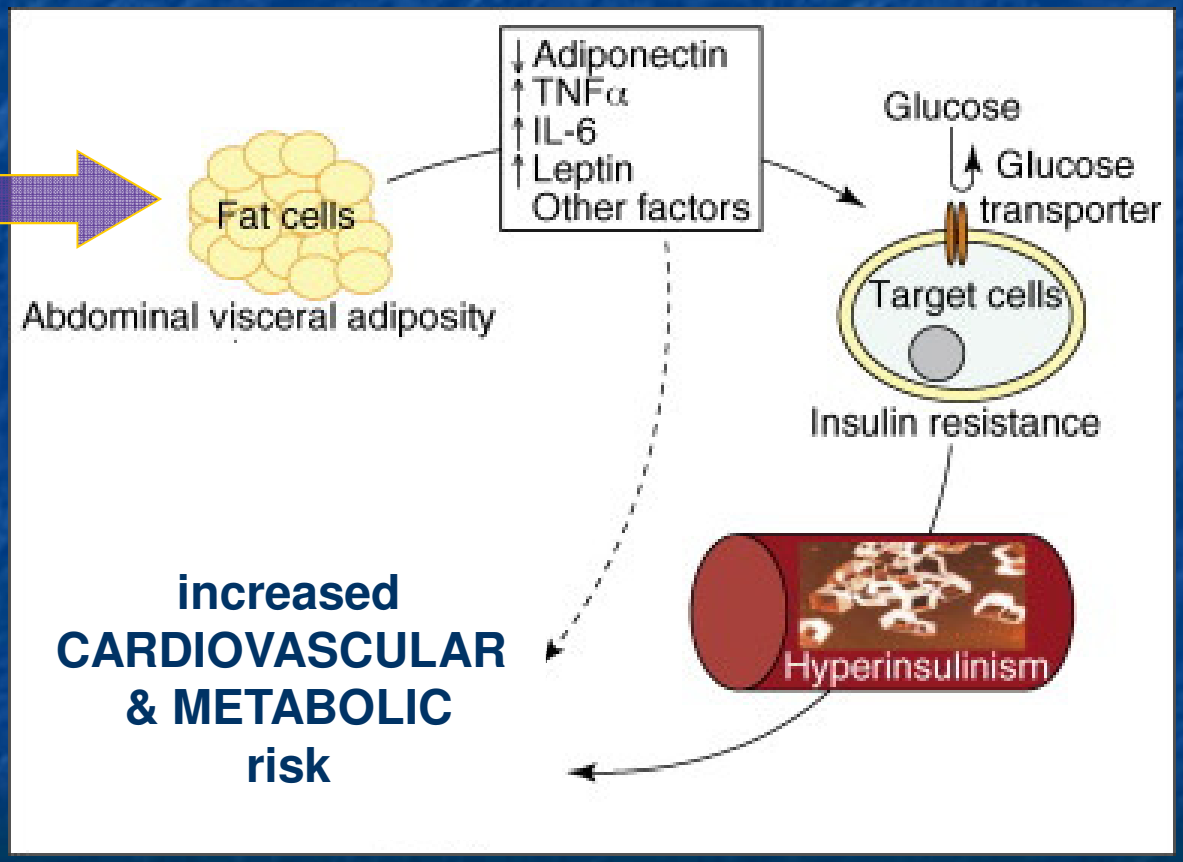
ENDOCRINOLOGIST
GYNAECOLOGIST

CARDIOLOGIST
DIABETOLOGIST

PCOS:

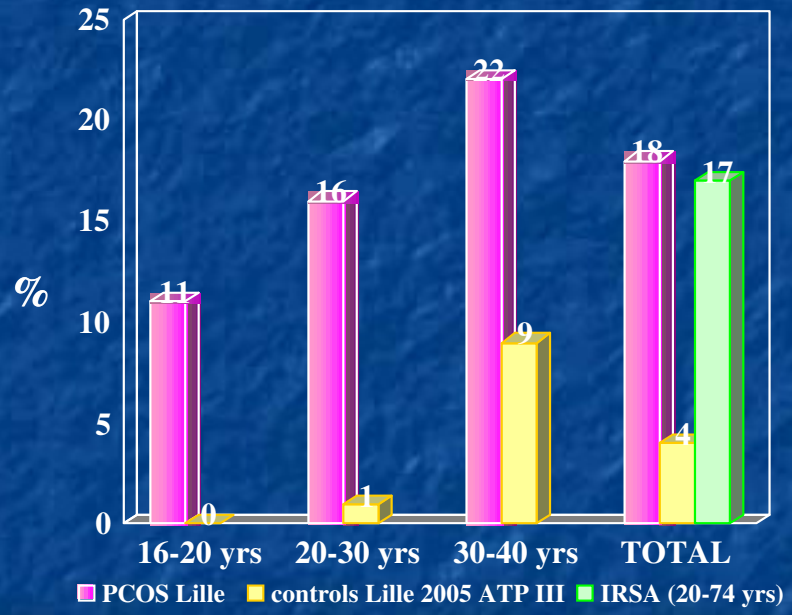
the « chance » of women at risk

Genes
Environment

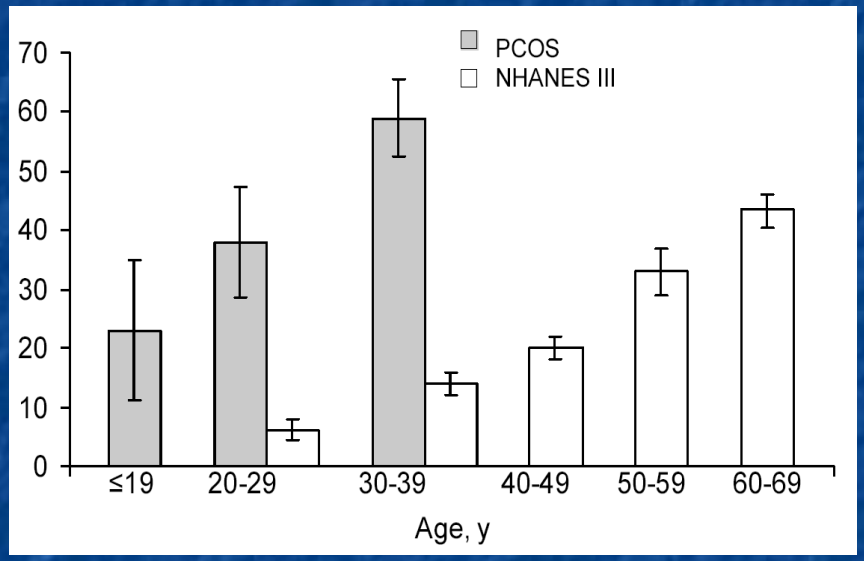


Early
detection

% of Metabolic Syndrome in PCOS *according to age*



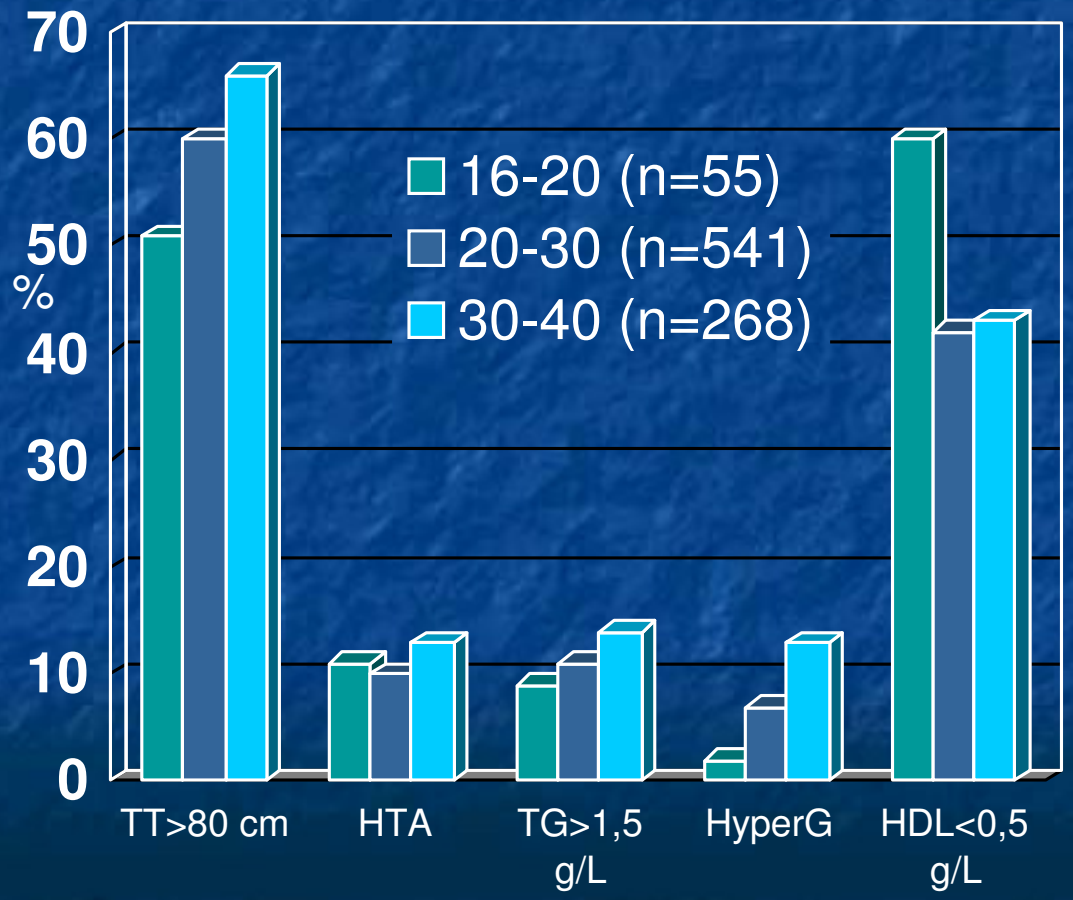
Lille Population (n=864)
IDF classification
Dewailly D et al. BJOG. 2009 Oct 13



North-American Population (n=160)
ATP III Classification
Apridonidze T et al, J Clin Endocrinol Metab. 2005; 90: 1929 - 1935

% of each item included in MetS classification according to age in PCOS *(IDF thresholds)*

Dewailly D, Contestin M, Gallo C, Catteau-Jonard S.
BJOG. 2009 Oct 13



Wrong thresholds?

Definition of MetS in children and adolescents

Age 6 to <10 years	Age 10 to <16 years	Age ≥16 years
Obesity ≥90th percentile, as assessed by waist circumference	Obesity ≥90th percentile (or adult cutoff if lower), as assessed by waist circumference	Use existing IDF criteria for adults
Metabolic syndrome cannot be diagnosed, but further measurements should be made if the patient has a family history of metabolic syndrome, T2DM, dyslipidemia, cardiovascular disease, hypertension or obesity	Triglycerides ≥1.7 mmol/l; HDL cholesterol <1.03 mmol/l; blood pressure ≥130 mm Hg systolic or ≥85 mm Hg diastolic; glucose ≥5.6 mmol/l (oral glucose tolerance test recommended) or known T2DM	

Eyzaguirre F, Mericq V. Insulin resistance markers in children. Horm Res. 2009;71(2):65-74

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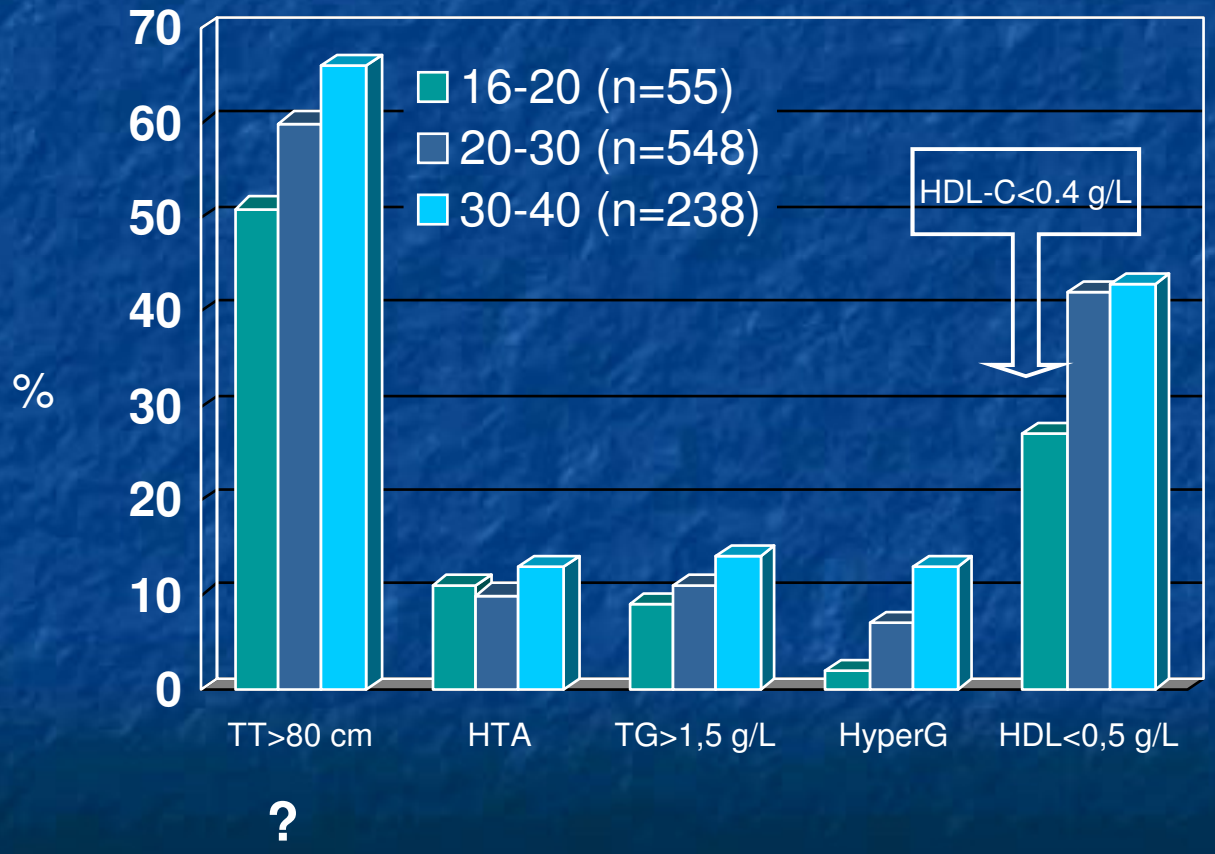
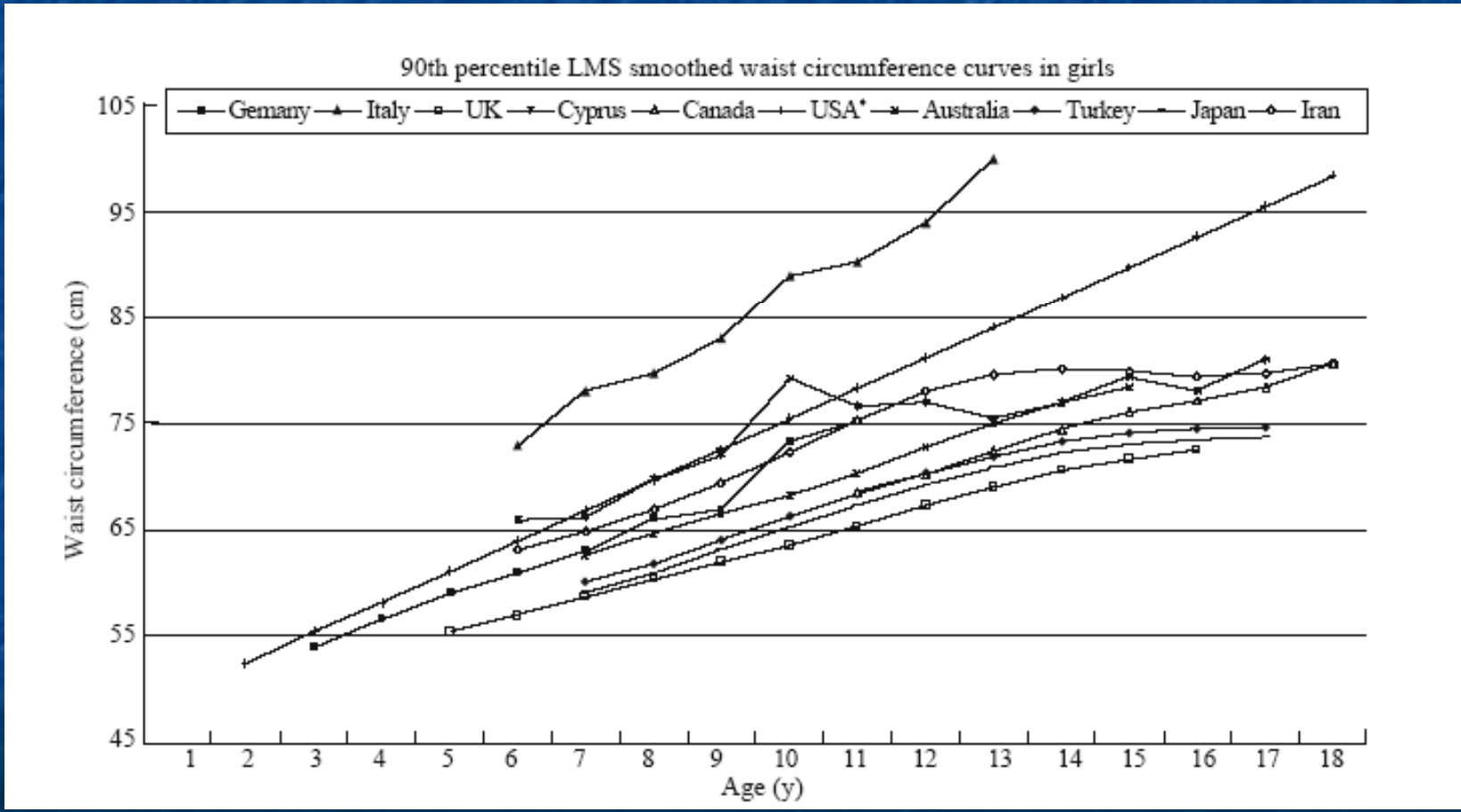
Dewailly D, Contestin M, Gallo C, Catteau-Jonard S.
BJOG. 2009 Oct 13



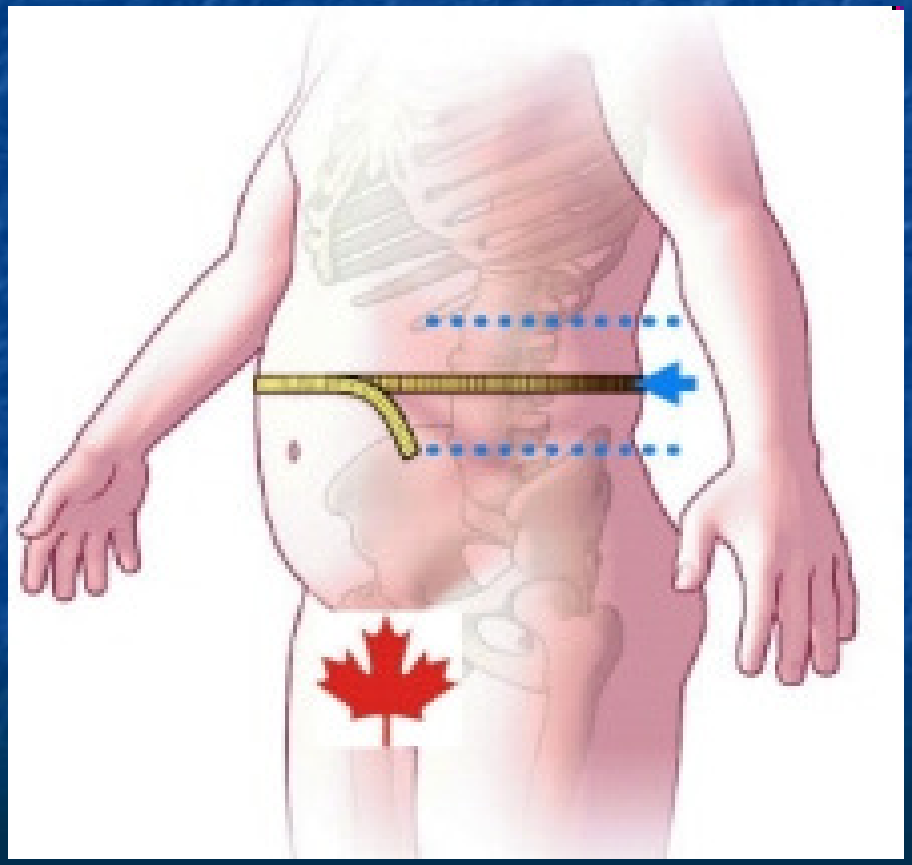
?

Upper normal limit for WC in adolescent girls: *similar to adults*



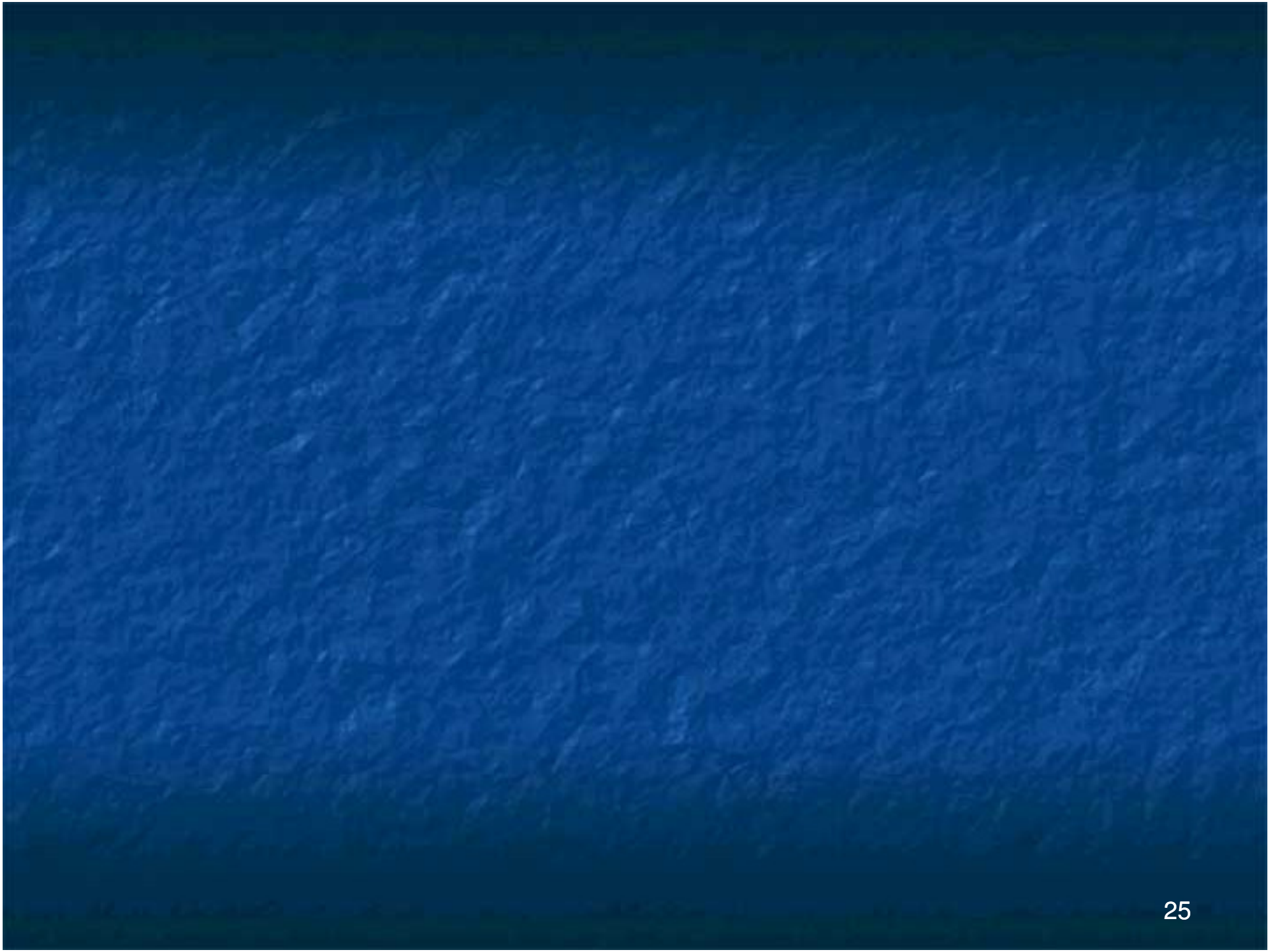
Waist circumference:

the most cost-effective predictor for insulin resistance and CV risk

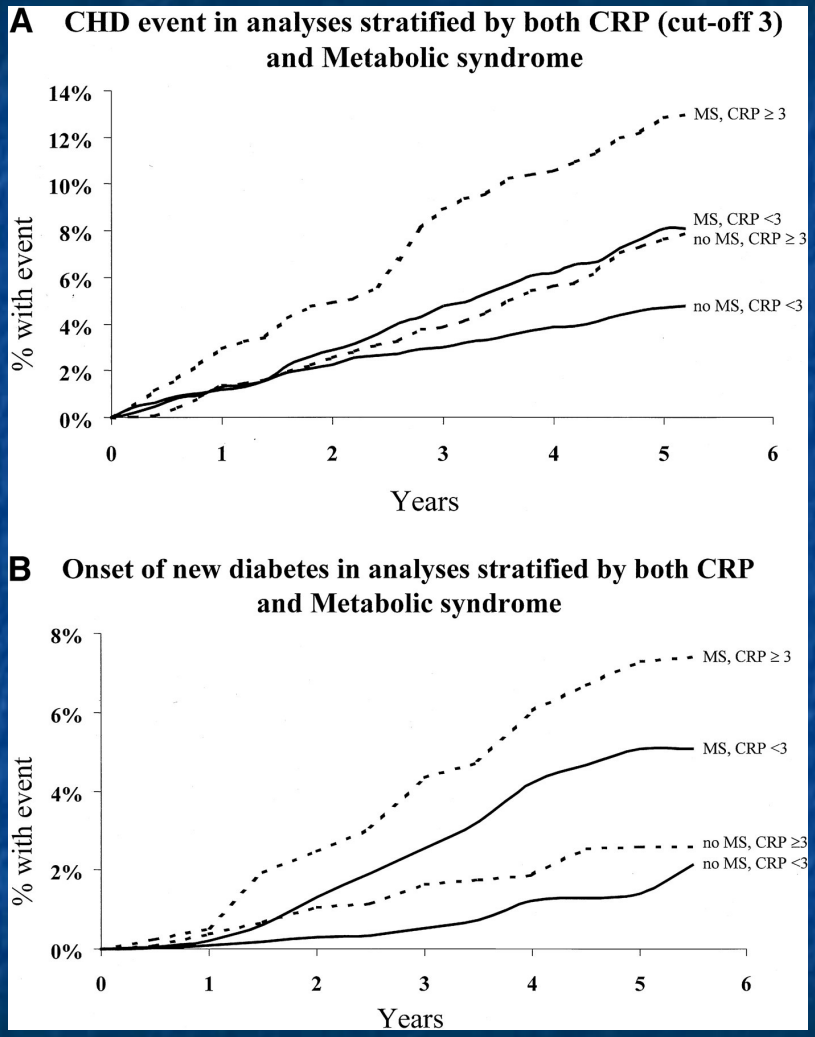


CONCLUSIONS

- Detecting IR in clinical practice should rely on clinical data (WC+++);
- Defining IR in clinical research can rely on simple surrogate indexes;
- Stratifying patients according to the MetS yields an incomplete estimation of the CV&M risk.



CHD events and new-onset diabetes stratified by both CRP (</>=3 mg/L) and presence of absence of metabolic syndrome (MS)

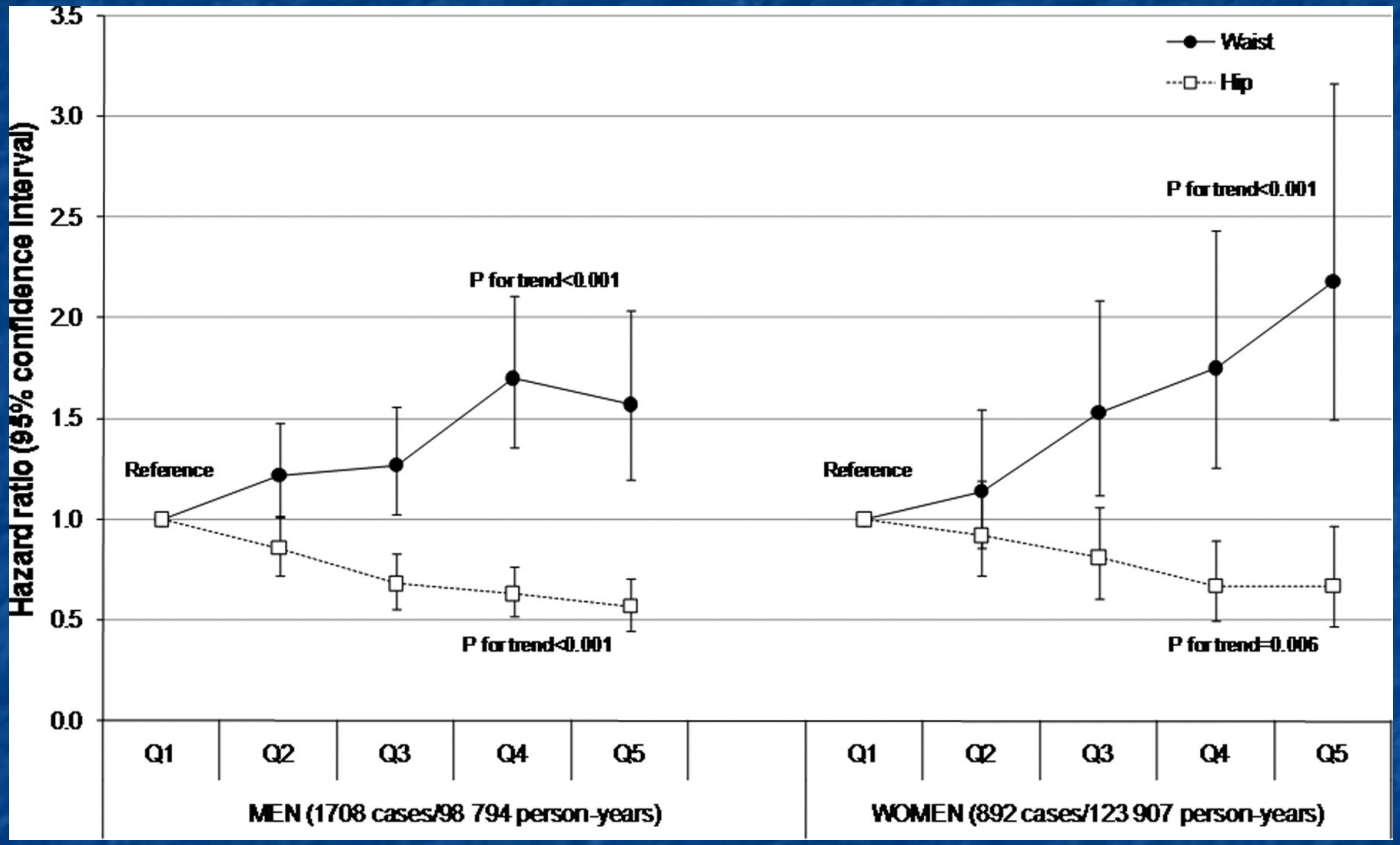


Sattar, N. et al. Circulation 2003;108:414-419

American Heart Association
Learn and Live

Hazard ratios for coronary heart disease by waist and hip circumference quintiles in men and women 45 to 79 years of age

with adjustment for body mass index, age, systolic blood pressure, total cholesterol, cigarette smoking, physical activity, and alcohol intake.



Canoy, D. et al. Circulation 2007;116:2933-2943

American Heart Association
Learn and Live

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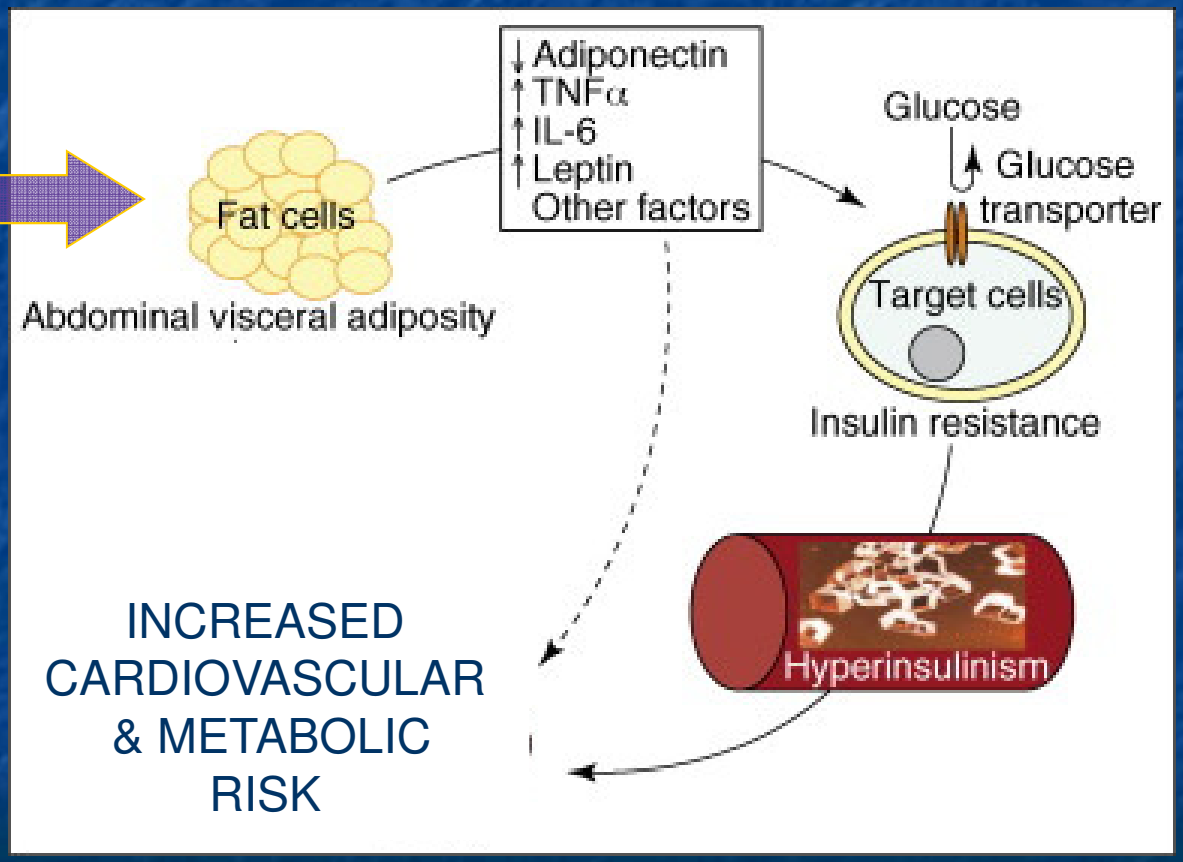
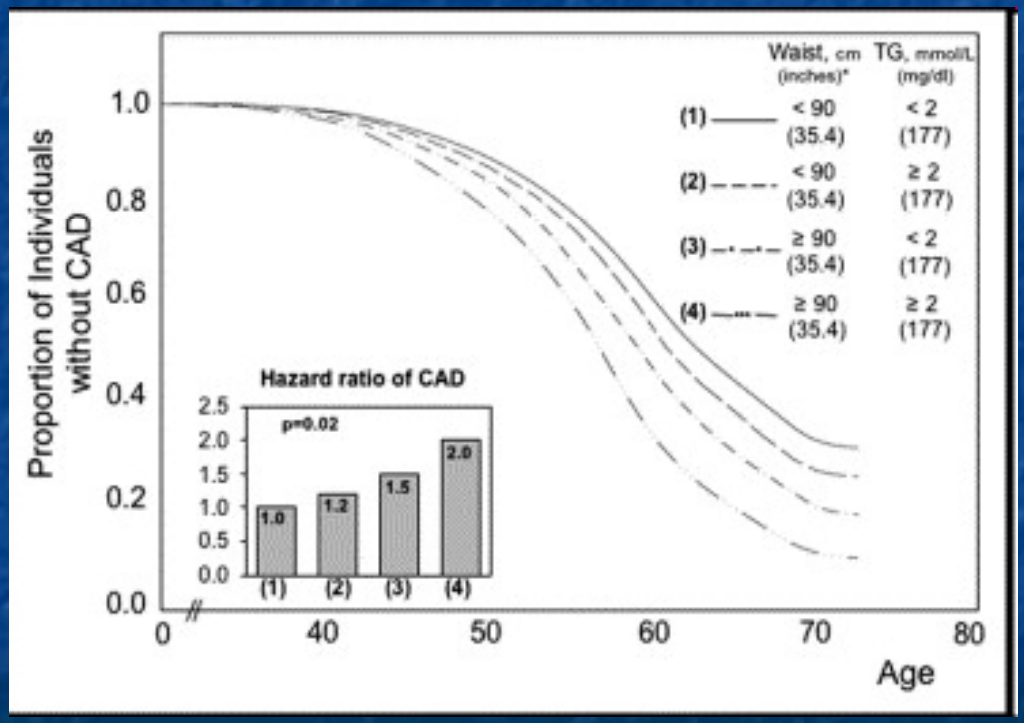
Eyzaguirre F, Mericq V. Insulin resistance markers in children. Horm Res. 2009;71(2):65-74

ADIPOTOXICITY

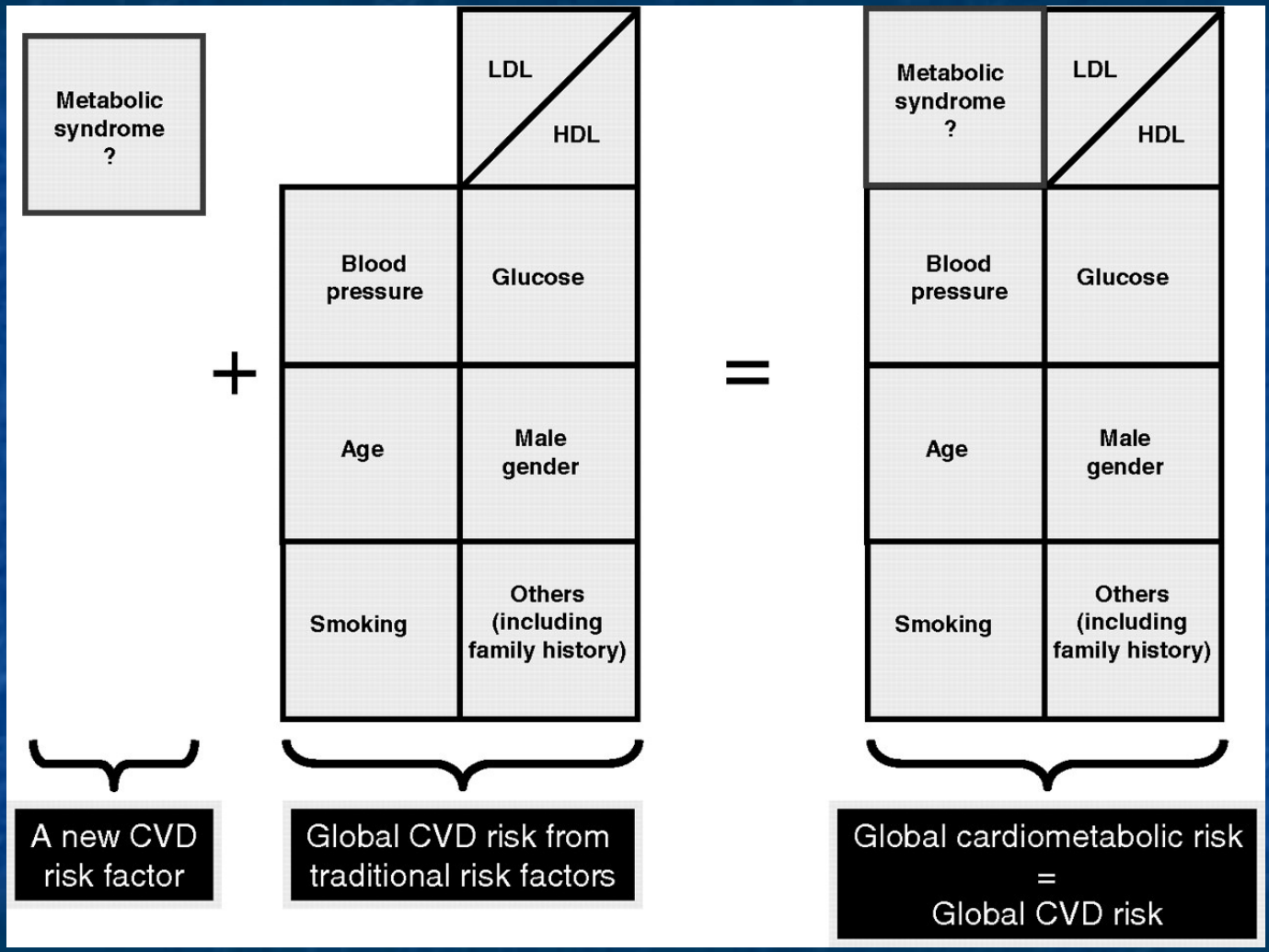
Genes
Environment



The hypertriglyceridemic waist phenotype



The "building blocks" of global cardiometabolic risk

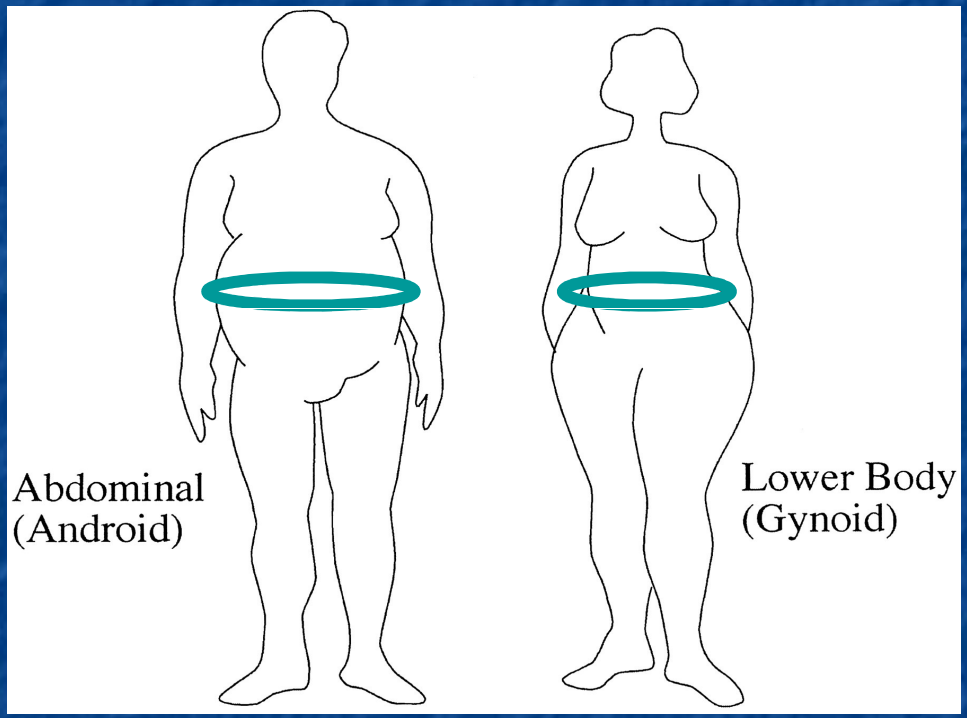


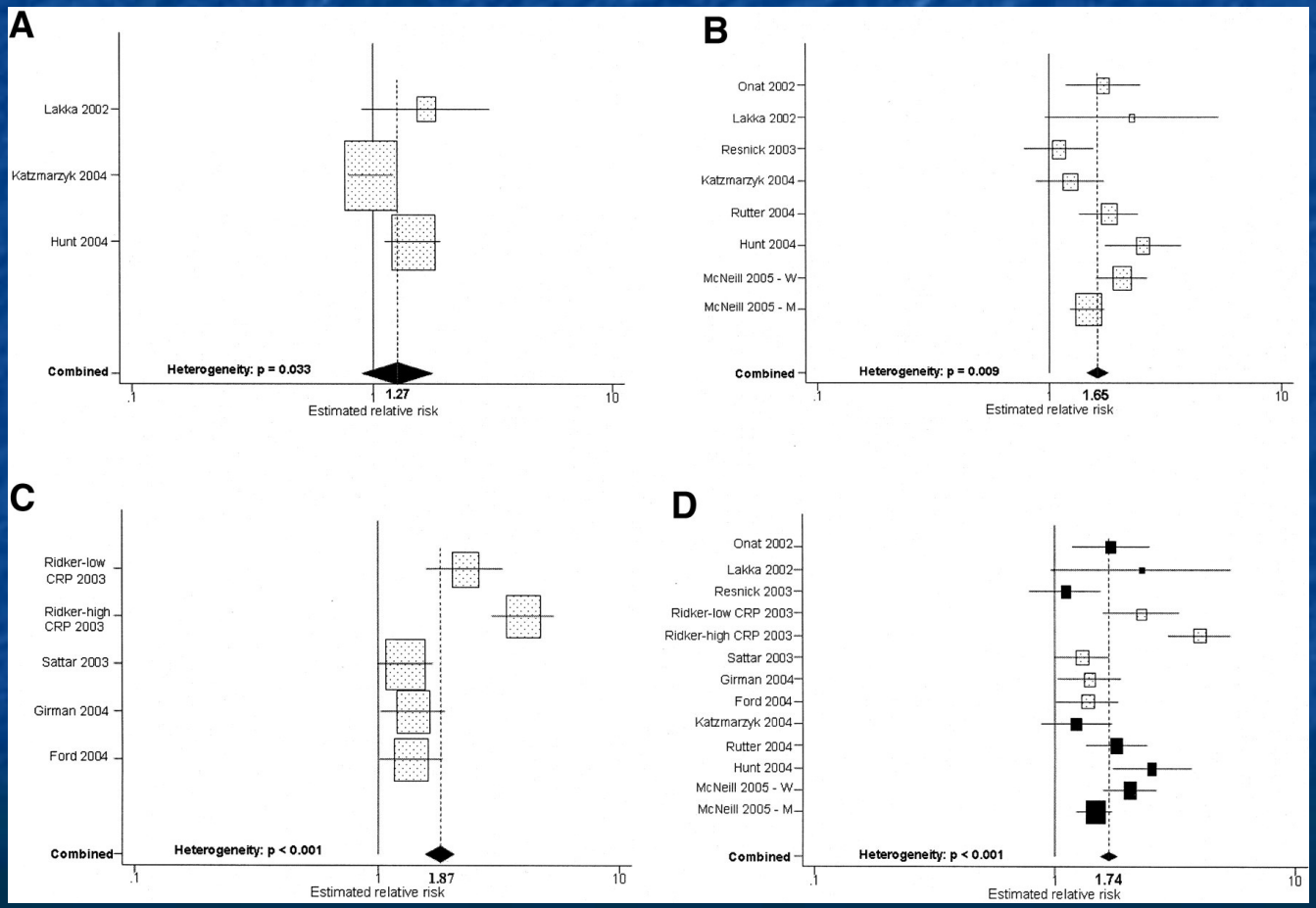
Despres, J.-P. et al. Arterioscler Thromb Vasc Biol 2008;28:1039-1049

- MIRACLE score included: family history (early cardiovascular disease, type 2 diabetes, and hypertension), individual history (small for gestational age and ethnic origin), clinical features (BMI, waist circumference > 90th percentile and blood pressure > 95th percentile) and metabolic abnormalities (glucose intolerance or type 2 diabetes). It was assigned a value of 1 to "presence" and 0 to" absence" in every patient. The children were considered as having metabolic risk when at least 5 items were present. Triglycerides, HDL-cholesterol, apolipoprotein B, apolipoprotein A1, glucose and HOMA index, were measured too. The most frequent clinical features of MIRACLE score were: excess waist circumference (95.4%) and hypertension (41.8%). Family history criteria were frequent (55.3% for type 2 diabetes, 39.1% for hypertension and 31.3% for early cardiovascular disease). Individual risk factors were not frequent. Glucose intolerance was detected in 22.2% of the obese patients. A MIRACLE score > or = 5 was found in 37.4% of the children studied, being associated with a significant risk of dyslipidemia (triglycerides, p = 0.040; HDL-cholesterol, p = 0.006; LDL-cholesterol p = 0.038; apolipoprotein B, p = 0.008) only in females.
- J Physiol Biochem. 2007 Dec;63(4):347-55.
- **Metabolic risk-factor clustering estimation in obese children.**
- Bueno G,

En pratique, chez l'adolescente…

- Mesurez le tour de taille
- Dosez le HDL-C…
  - Si vous avez une norme adaptée à l'âge!
- Oubliez le score métabolique!

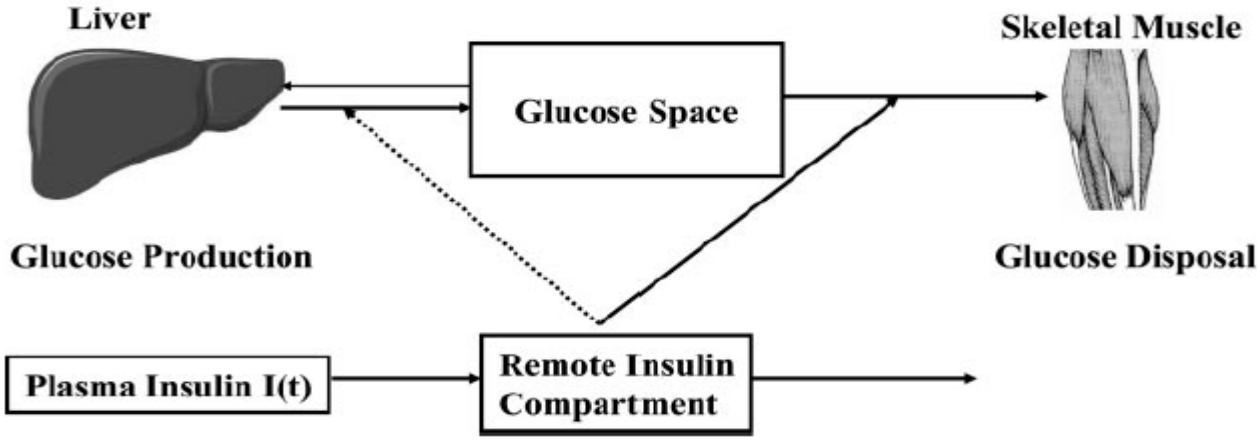




Ford ES Diabetes Care. 2005;28:1769-78.

$$dG(t)/dt = -[p_1 + X(t)]\, G(t) + p_1 G_b$$

$$dX(t)/dt = -p_2 X(t) + p_3 [I(t) - I_b]$$



	méthodologie	difficultés	avantages	résultats
clamp euglycémique hyperinsulinique	infusion d'insuline calcul quantité de glucose à perfuser pour maintenir glycémie constante	2 abords veineux glycémie/ 5-10 min durée test et dose insuline non standardisé	méthode de référence	moyenne de la quantité de glucose infusée pdt les 30 dernières minutes, en tenant compte du delta de l'insulinémie
clamp hyperglycémique	infusion de glucose pour élever la glycémie 5 à 7 mmol/l au dessus de la glycémie basale	2 abords veineux glycémie/ 5-10 min possibilité de suppression incomplète de la production hépatique de glucose, non réalisable si la GAJ est significativement élevée	mesure concomitante de la sensibilité et de la sécrétion insulinique	moyenne de la quantité de glucose infusée pendant les 30 dernières minutes du test
minimal model	infusion d'un bolus de glucose, étude de la cinétique de disparition du glucose	2 abords veineux dosage très fréquents de la glycémie souvent difficile à calculer en cas de diabète nécessité d'un programme informatique spécifique	mesure concomitante de la sensibilité et de la sécrétion insulinique	vitesse de disparition du glucose calculée à l'aide d'un programme informatique spécifique
test de suppression insulinique	infusion de glucose et d'insuline+/-agents pharmacologiques inhibant la sécrétion endogène d'insuline	2 abords veineux perfusion d'agents pharmacologiques	facile à réaliser	estimation de la sensibilité à l'insuline

Table I

Insulin sensitivity measured by hyperinsulinemic normoglycemic clamp and by simple indexes of insulin sensitivity.

	Controls N = 28	PCOS N = 16	Obese non-diabetics N = 10	Glucose-intolerant subjects N = 28	Type 2 diabetics N = 29
BMI (kg/m^2)	22.7 ± 0.4	23.6 ± 0.8	34.5 ± 1.3	31.9 ± 0.9	30.6 ± 0.7
Glucose (mmol/l)	4.7 ± 0.1	4.6 ± 0.1	5.1 ± 0.2	6.5 ± 0.1	11.8 ± 0.6
Insulin (μU/ml)	5.5 ± 0.5	9.5 ± 1.5	13.1 ± 2.2	9.7 ± 1.0	11.8 ± 1.1
HOMA	1.16 ± 0.10	1.98 ± 0.34	2.96 ± 0.50	2.89 ± 0.36	6.06 ± 0.62
FIRI	1.04 ± 0.09	1.78 ± 0.30	2.66 ± 0.45	2.60 ± 0.32	5.45 ± 0.56
QUICKI	0.384 ± 0.006	0.353 ± 0.006	0.331 ± 0.006	0.338 ± 0.006	0.302 ± 0.004
G/I ($mg/10^{-4}U$)	18.4 ± 1.5	10.7 ± 0.9	8.3 ± 0.9	17.0±2.3	23.1±2.6
I/G (pmol/mmol)	7.07 ± 0.58	12.24 ± 1.90	15.63 ± 2.90	8.79 ± 0.87	6.61 ± 0.76
40/I (ml/μU)	8.88 ± 0.78	5.18 ± 0.46	3.64 ± 0.40	5.87 ± 0.78	4.27 ± 0.37
IS clamp	8.44 ± 0.55	5.45 ± 0.62	3.92 ± 0.050	3.98 ± 0.41	2.78 ± 0.36

PCOS: polycystic ovary syndrome; BMI: body mass index; HOMA: homeostasis model assessment (fasting plasma insulin [μIU/ml] X fasting plasma glucose mmol/L])/22.5; FIRI: fasting insulin resistance index (fasting plasma insulin [μIU/ml] X fasting plasma glucose [mmol/L])/25; QUICKI: quantitative insulin sensitivity check index (1/(log fasting plasma insulin [μIU/ml] + log fasting plasma glucose [mg/dl]; G/I: glucose to insulin ratio; I/G: insulin to glucose ratio; 40/I: Raynaud index; IS clamp: insulin sensitivity during euglycemic hyperinsulinemic clamp ($GIR_{ss}/G_{ss} \times \Delta I_{ss}$ expressed in 10^{-4} dl/kg x min per μU/ml) where GIR_{ss} is the glucose infusion rate during steady state of the clamp (mg/kg x min), G_{ss} is the steady state blood glucose concentration (mg/dl) and ΔI_{ss} is the difference between the steady state and basal insulin concentration (μU/ml).

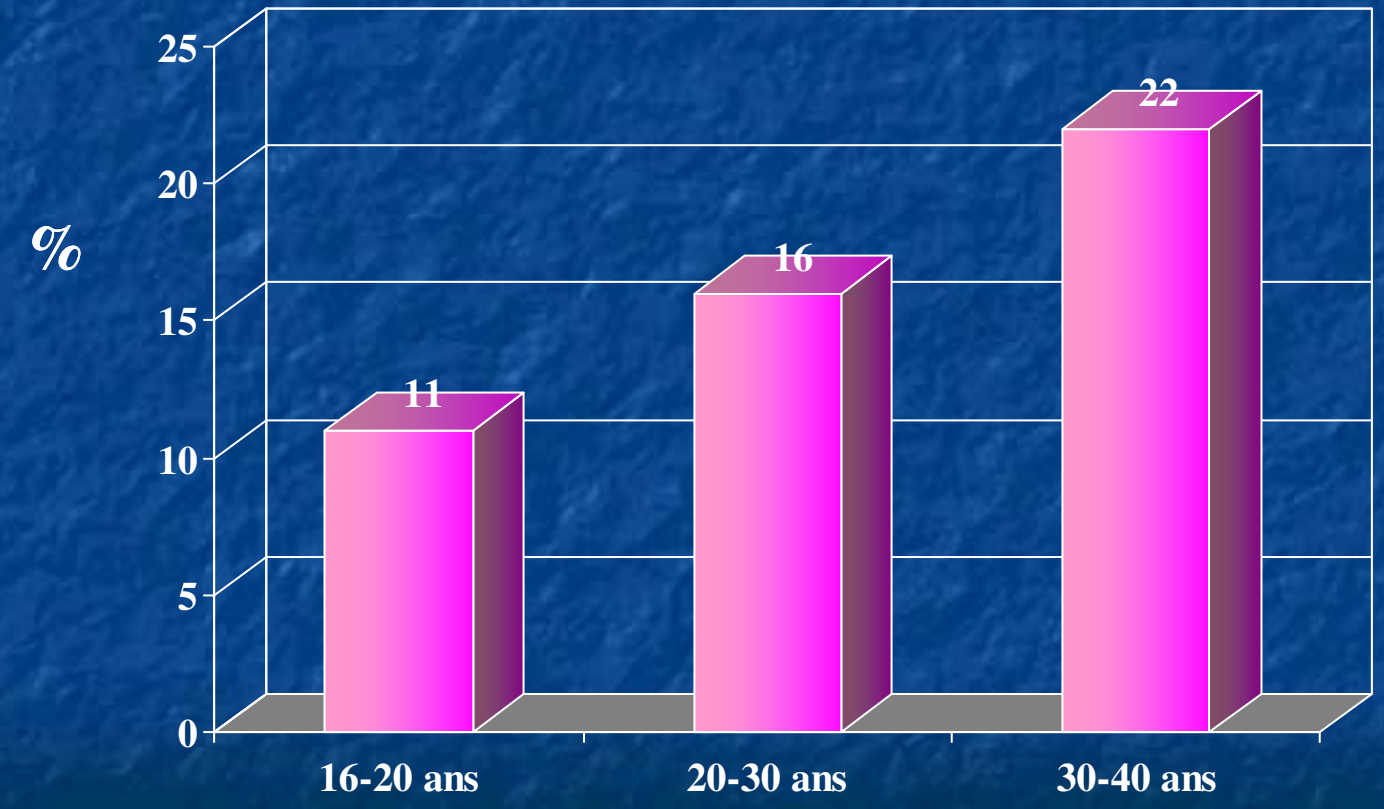
Table 1 Evolving definitions of the MetS 1998–2005

	Definition					
	WHO[6]	EGIR[8]	ATPIII[9]	AACE[5]	IDF[7]	AHA/NHLBI[10]
Criterion	1998	1999	2001	2003	2005	2005
Measure of obesity	WHR Men: >0.90 Women: >0.85 and/or BMI >30 kg/m^2	Waist circumference Men: ⩾94 cm Women: ⩾80 cm Specifically, BMI should not be included	Waist circumference Men: >102 cm Women: >88 cm	—	Waist circumference—ethnicity specific (see Table 2)	Waist circumference Men: ⩾102 cm Women: ⩾88 cm Consider adjusting for race
TGs (mmol/l)	⩾1.7	⩾2.0	⩾1.7	⩾1.7	>1.7 or specific treatment for this abnormality	⩾1.7 or treatment for elevated TGs (fibrates and nicotinic acid)
HDL-C (mmol/l)	Men: ⩽0.9 Women: ⩽1.0	<1.0	Men: <1.03 Women: <1.3	Men: ⩽1.03 Women: ⩽1.3	Men: ⩽1.03 Women: ⩽1.3 or specific treatment for this abnormality	Men: <1.03 Women: <1.3 or treatment for low HDL-C (fibrates and nicotinic acid)
Blood pressure (mm Hg)	⩾160/90	⩾140/90 or treatment for hypertension	⩾130/85	⩾130/85	Systolic: ⩾130 or diastolic: ⩾85 or treatment of previously diagnosed hypertension	Systolic: ⩾135 or diastolic: ⩾85 or antihypertensive treatment in a patient with a history of hypertension
Fasting plasma glucose (mmol/l)	For patients with T2DM: Fasting: ⩾7.0 or 2-h post: ⩾11.1 For patients with impaired glucose tolerance: Fasting: <7.0 and 2-h post: 7.8–11.1 For patients with impaired fasting glycemia: Fasting: 6.1–7.0 2-h post: <7.8	Non-diabetics only and fasting plasma glucose ⩾6.1	⩾6.1	Impaired fasting glucose (6.1–6.9)[a] or ⩾7.7 after 120 min post-glucose challenge (75 g)	⩾5.6 or previously diagnosed T2DM If above 5.6, OGTT recommended but not required	⩾5.6 or on drug treatment for elevated glucose
Insulin resistance	Glucose uptake below lowest quartile for background population under investigation (assessed by clamp study)	Required Fasting hyperinsulinemia	Not required	Patients must have risk factors for insulin resistance[b]	—	Not required
Urinary protein	Microalbuminuria: ⩾20 μg/min Albumin/creatinine ratio ⩾20 mg/g	—	—	—	—	—
No. of criteria required	One of glucose intolerance, impaired glucose tolerance, or diabetes mellitus and two of either: blood pressure, dyslipidemia (TGs or HDL-C), obesity, urinary protein	Insulin resistance and two of: hyperglycemia, hypertension, dyslipidemia (TGs or HDL-C), central obesity	3 of 5 above	At least 2 of 4 metabolic abnormalities of blood pressure, plasma glucose, TGs, and HDL-C in an individual with risk factors constituting the insulin resistance syndrome	Central obesity as assessed by waist circumference and two others above	Any 3 of 5 above

AACE, American Association of Clinical Endocrinologists; AHA/NHLBI, American Heart Association/National, Heart, Lung, and Blood Institute; ATPIII, National Cholesterol Education Program—Adult Treatment Panel III; BMI, body mass index; EGIR, European Group for Insulin Resistance; HDL-C, high-density lipoprotein cholesterol; IDF, International Diabetes Federation; MetS, metabolic syndrome; OGTT, oral glucose tolerance test; T2DM, type 2 diabetes mellitus; TG, triglyceride; WHO, World Health Organization; WHR, waist-hip ratio. [a]This was modified in 2004 and reduced to ⩾5.6 mmol/l. [b]Diagnosis of cardiovascular disease, hypertension, polycystic ovarian syndrome, non-alcoholic fatty liver disease, acanthosis nigricans, family history of gestational diabetes or glucose intolerance, non-Caucasian ethnicity, sedentary lifestyle, BMI >25.0 kg/m^2 (or waist circumference >101.6 cm in men, >88.9 cm in women); age >40 years.

Le Syndrome Métabolique (IDF): effet de l'âge

Population Lilloise (2009): 854 SOPMK



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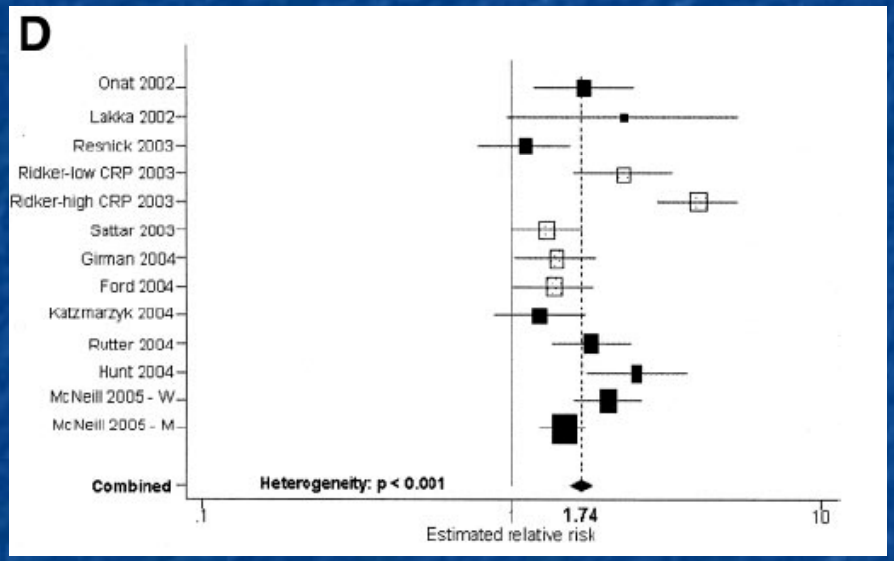
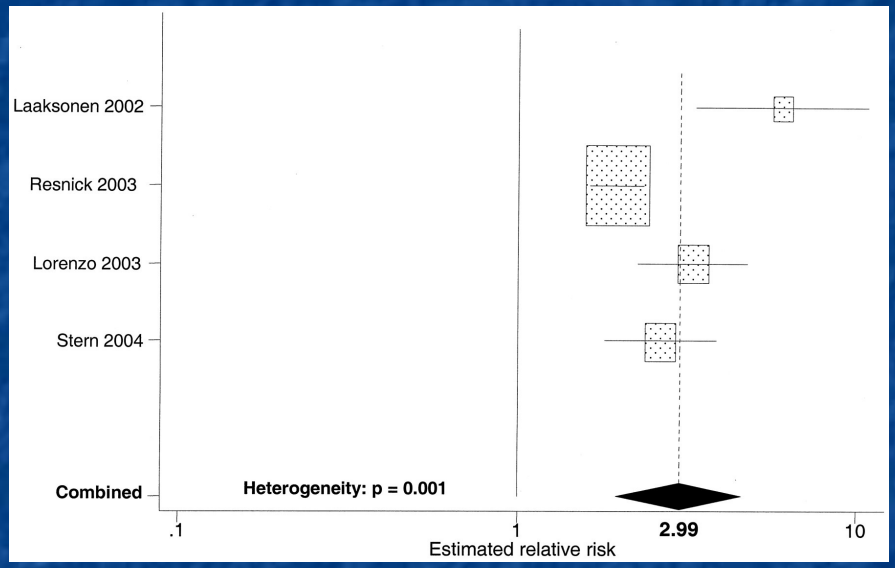
MetS: is it a good predictor of the major risks?



Cardiovascular risk



T2DM risk

Ford ES Diabetes Care. 2005;28:1769-78.

MetS: is it a good predictor of the major risks?

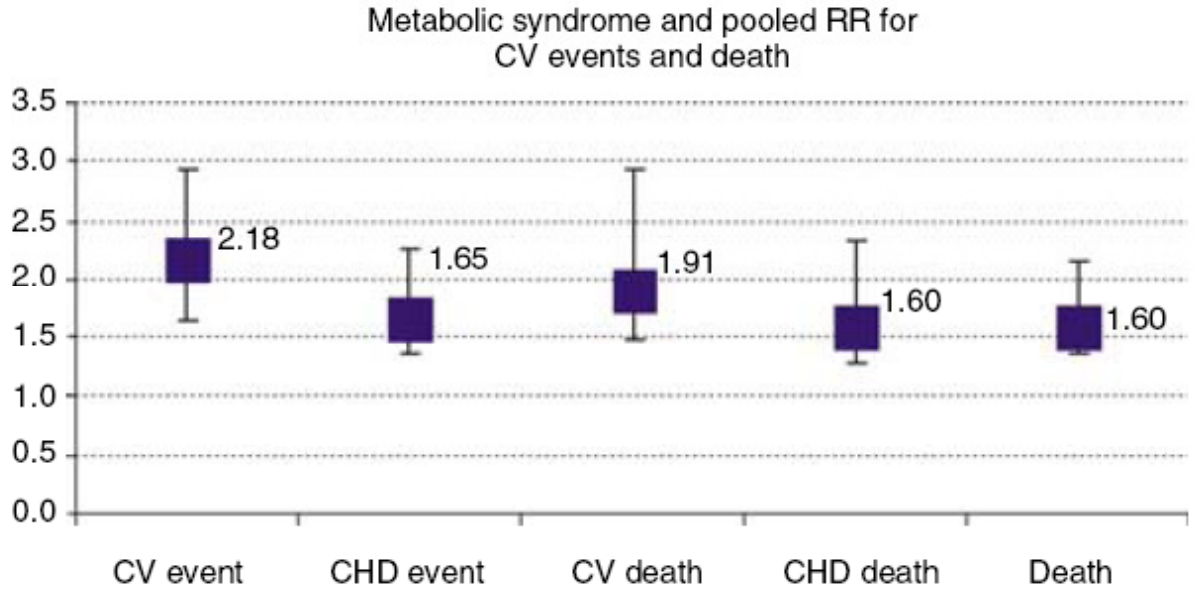
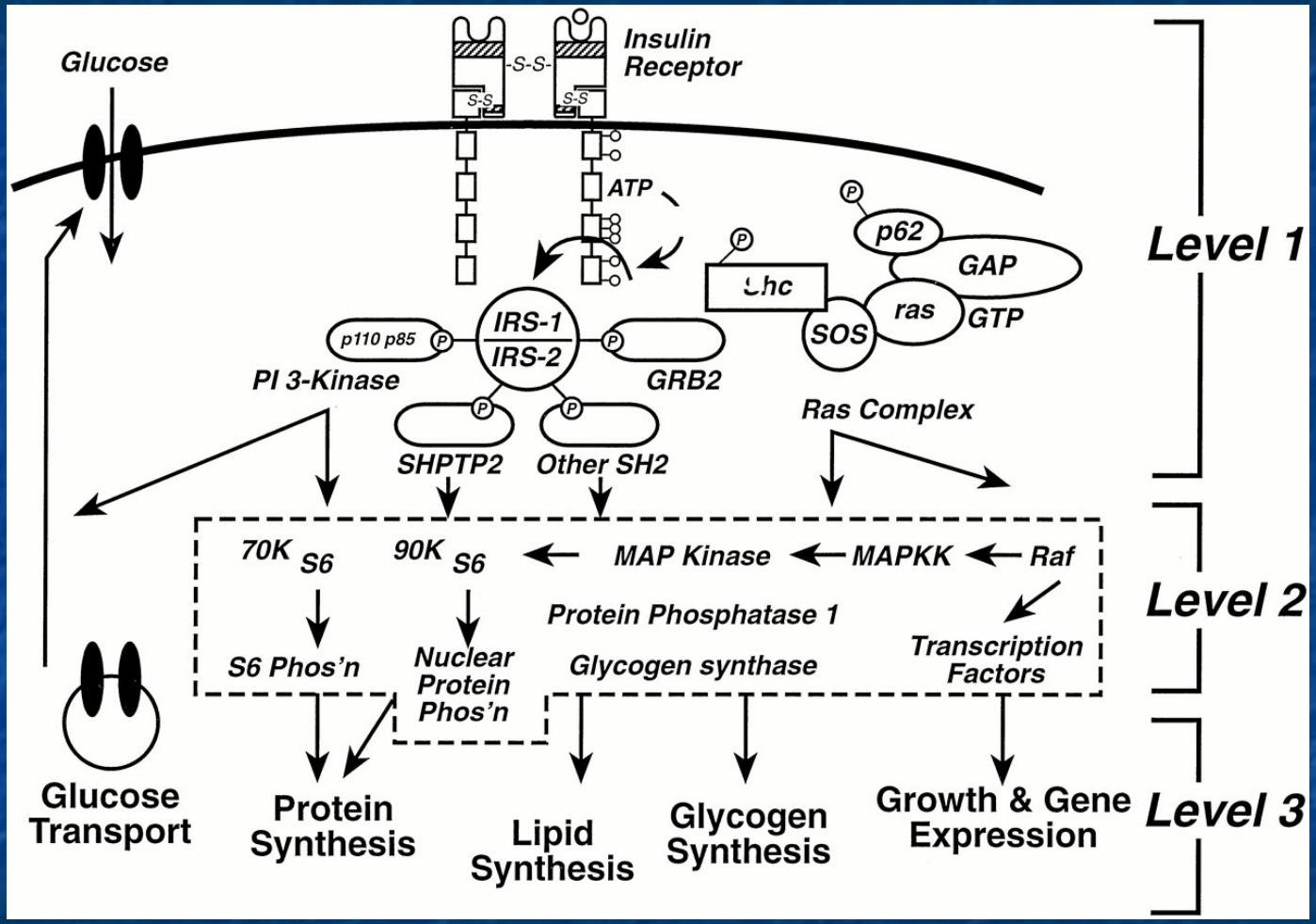


Figure 2 The pooled RR for CV events and death in patients with the metabolic syndrome. There were 11 studies examined for CV events, 18 studies for coronary heart disease (CHD) events, 10 studies for CV death, 7 studies for CHD death, and 12 studies for death. The squares on the graph represent the pooled RRs, and the bars represent the 95% confidence intervals. The data were adapted from Gami *et al.*[13]

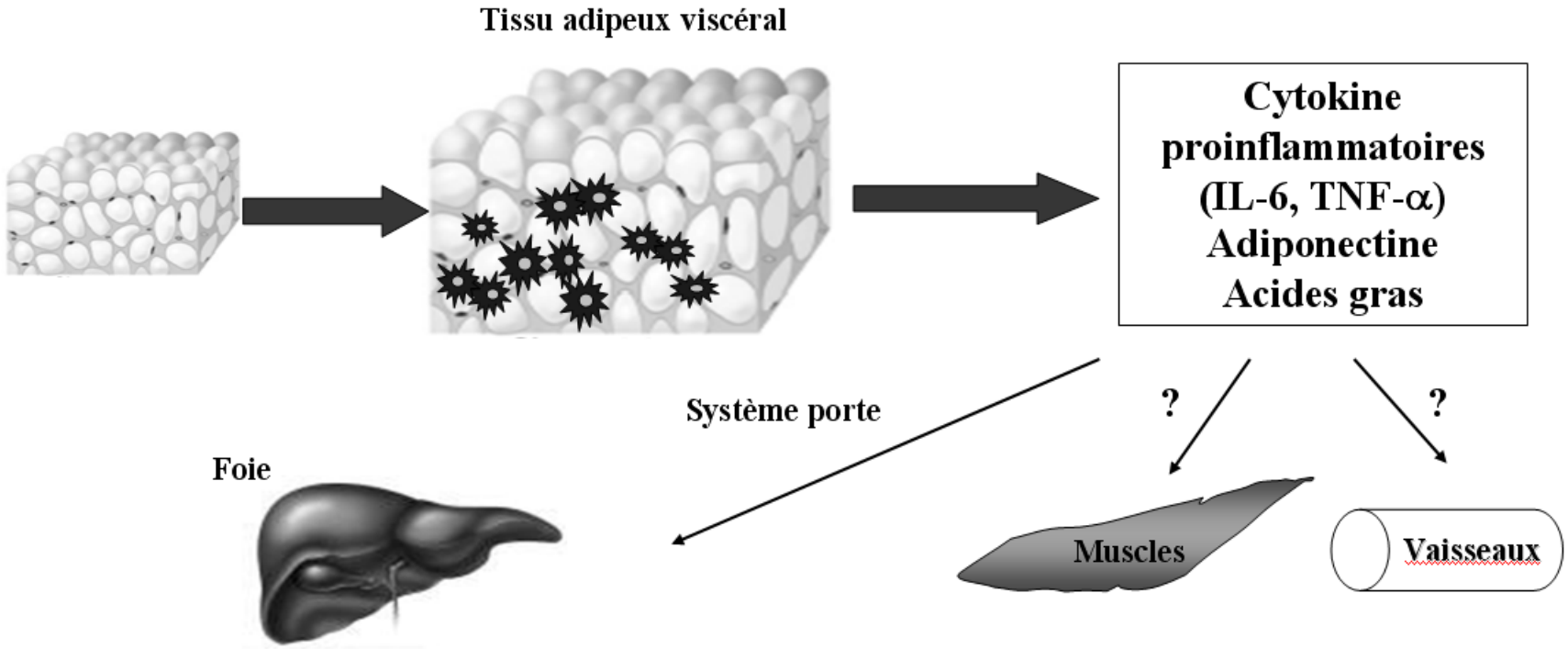
No Caption Found



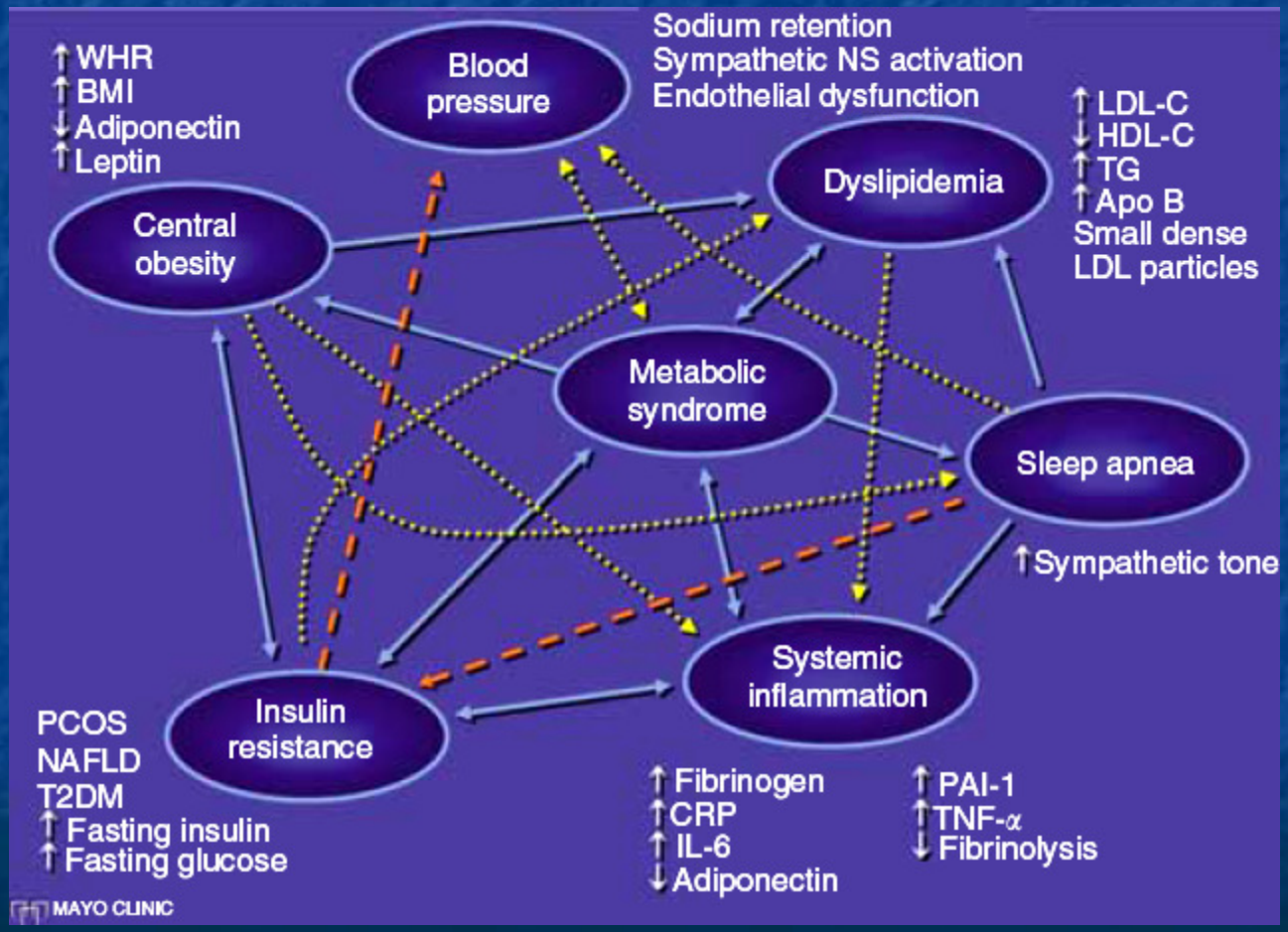
Dunaif, A. Endocr Rev 1997;18:774-800

ENDOCRINE REVIEWS

Constitution de l'obésité et accumulation de macrophages



THE CONSTRAINT and LIMITATIONS OF DEFINITIONS…



The pitfall of arbitrary thresholds:

normal HDL-C in young women with PCOS: >0.4 or 0.5 g/L?

Dewailly D, Contestin M, Gallo C, Catteau-Jonard S.
BJOG. 2009 Oct 13

Table 3. Frequencies of the metabolic items in the three subgroups

	16–20 years (*n* = 55)	20–30 years (*n* = 548)	30–40 years (*n* = 238)	*P* (chi-square test)
WC >80 cm	50.9%	59.7%	65.7%	0.07
SBP >130 mmHg and/or DBP >85 mmHg	10.9%	10.2%	13%	0.61
HDL-C <0.5 g/l (or <0.4 g/l)	60.0% (27.0%)	42.3%	43.3%	0.04 (0.05)
TG >1.5 g/l	9.1%	10.9%	14.2%	0.32
Hyperglycaemia*	1.8%	6.8%	12.7%	0.004

*Hyperglycaemia was defined by the presence of either fasting hyperglycaemia (≥1 g/l) or previously diagnosed diabetes.