How you will vote?

- Paul Zimmet conducted an impromtu electronic poll of delegates at an EASD Satellite: 88% said they still believe in the concept of metabolic syndrome…

MedPage Today, Sept 2006

How you will vote?

- Paul Zimmet conducted an impromtu electronic poll of delegates at an EASD Satellite: 88% said they still believe in the concept of metabolic syndrome…
- Today we are NOT talking about a concept, we are talking about the diagnostic and therapeutic utility of a definition

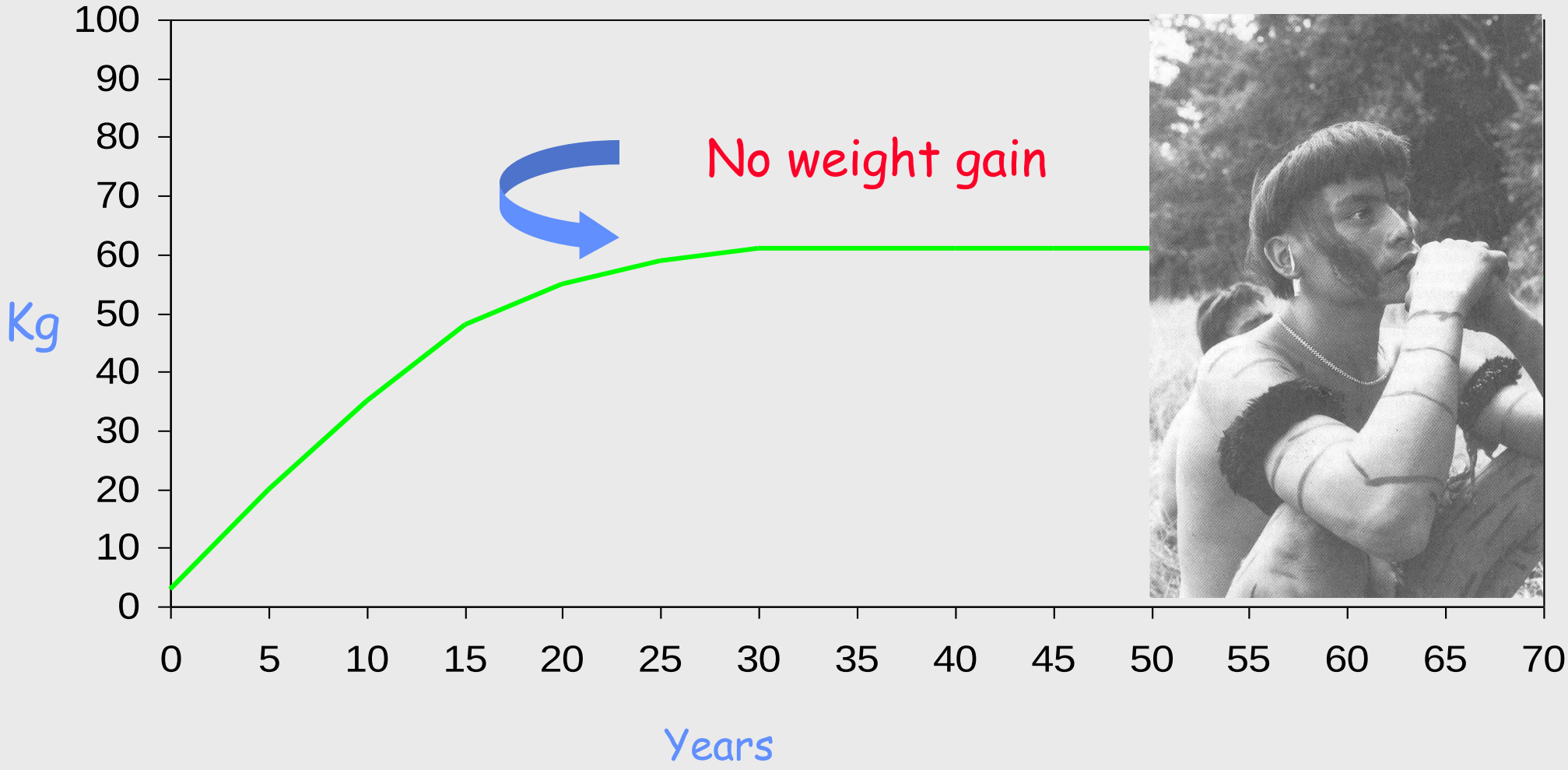
Diagnosis of the metabolic syndrome adds nothing to the care of patients with or at risk of type 2 diabetes or cardiovascular disease

Edwin Gale

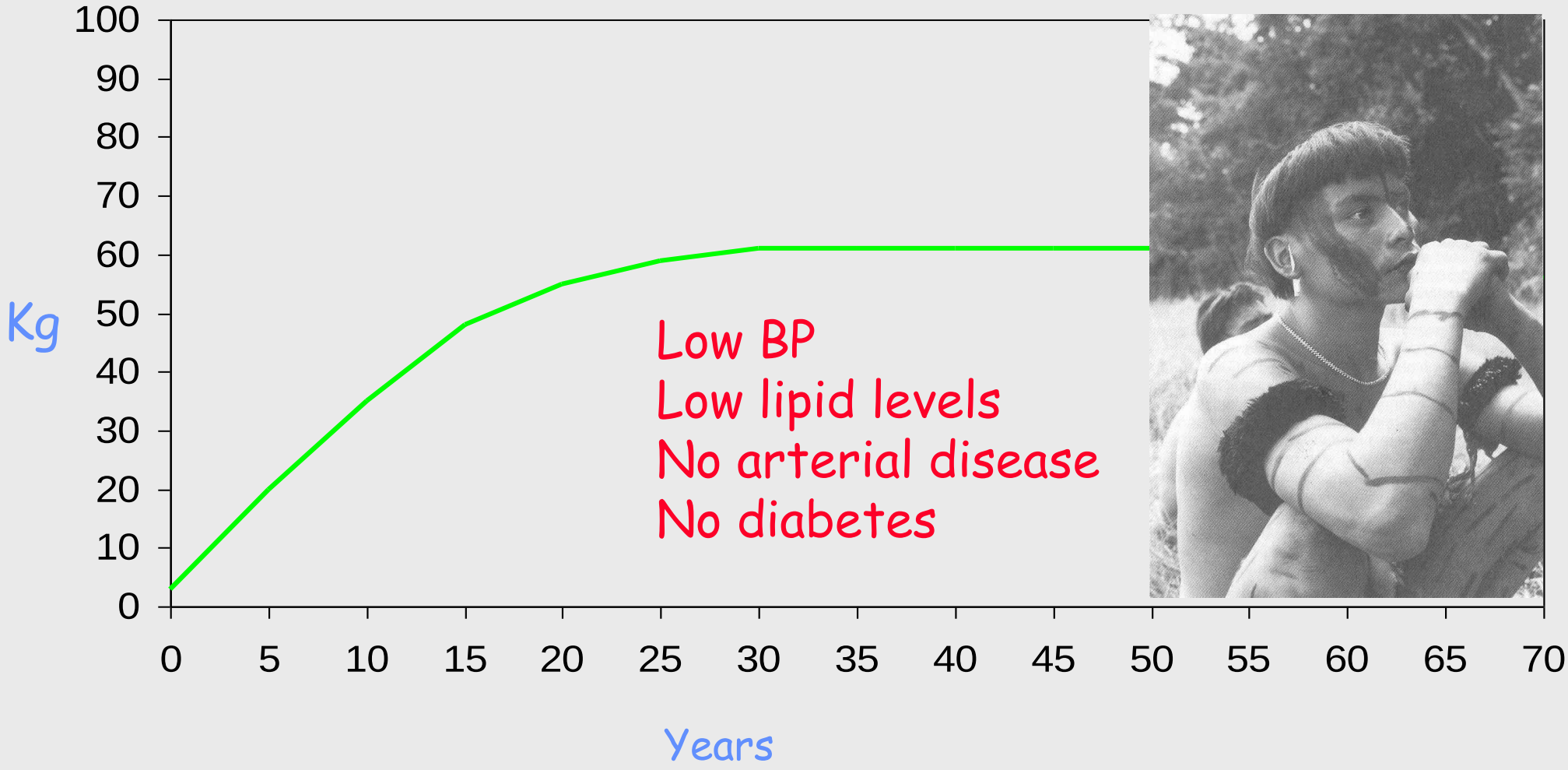
I shall point out that:

- There is no pathophysiological basis for the syndrome, as defined by IDF
- It is a redundant diagnosis in those with type 2 diabetes, and a useless diagnosis in those without
- Its use as an epidemiological tool is suspect
- There are better ways of predicting diabetes and cardiovascular disease
- There is no "added value" in terms of therapy

Weight gain in "wild type" humans

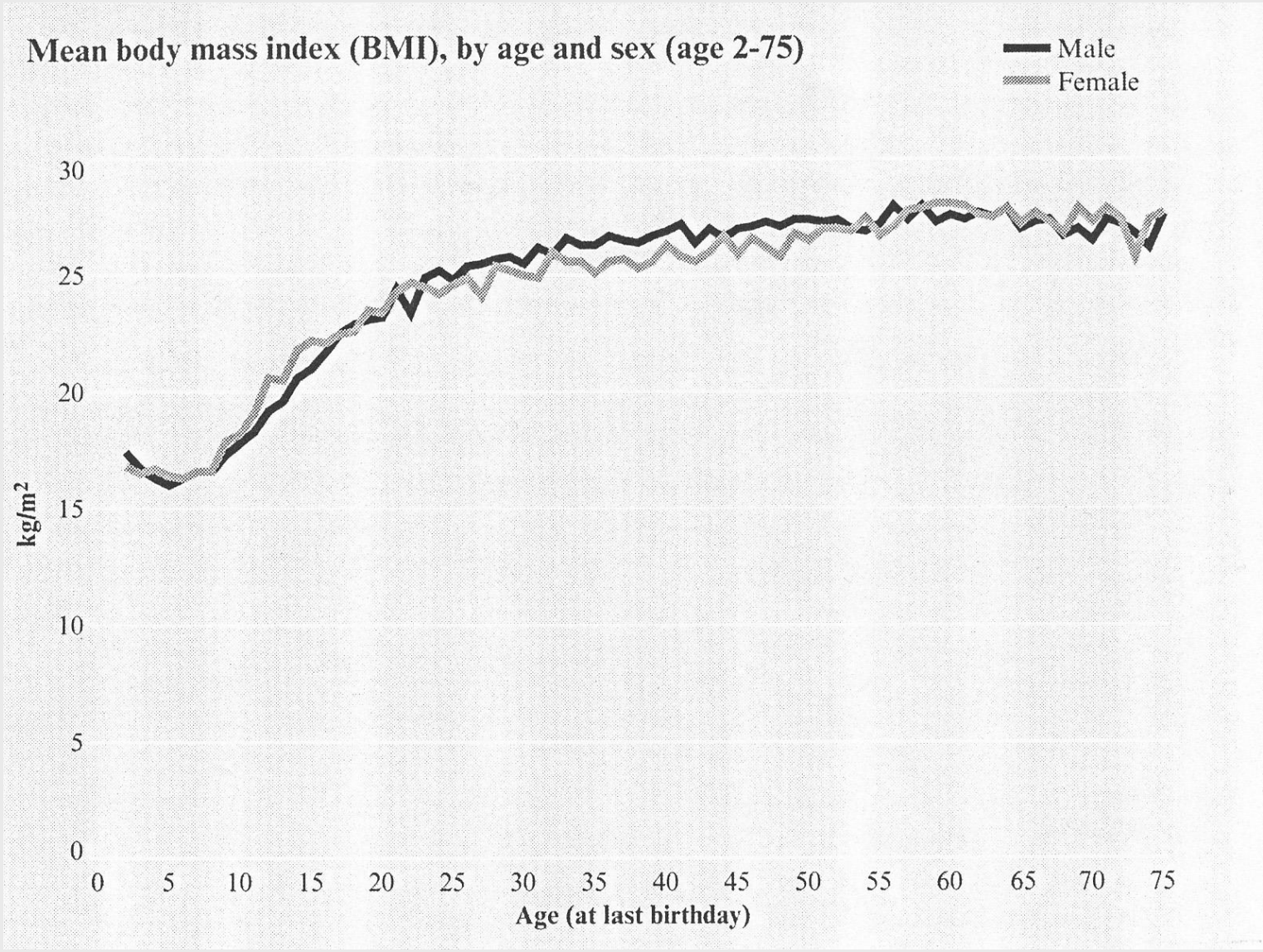


Weight gain in "wild type" humans



PIG NATION

Mass Consumption is EVERYBODY'S DUTY!



Body weight increases by ~ 0.9 gram per day between the ages of 25-55 (UK 1997)

As we get older we get fatter,
Our blood pressure rises
Our lipids go up
And our glucose tolerance deteriorates

As we get older we get fatter,
Our blood pressure rises
Our lipids go up
And our glucose tolerance deteriorates

These processes are associated
They are age-related, and dynamic
And they affect the whole population

What is the metabolic syndrome?

1. Can we identify core elements or mechanisms?
2. What are we trying to achieve by defining the metabolic syndrome?

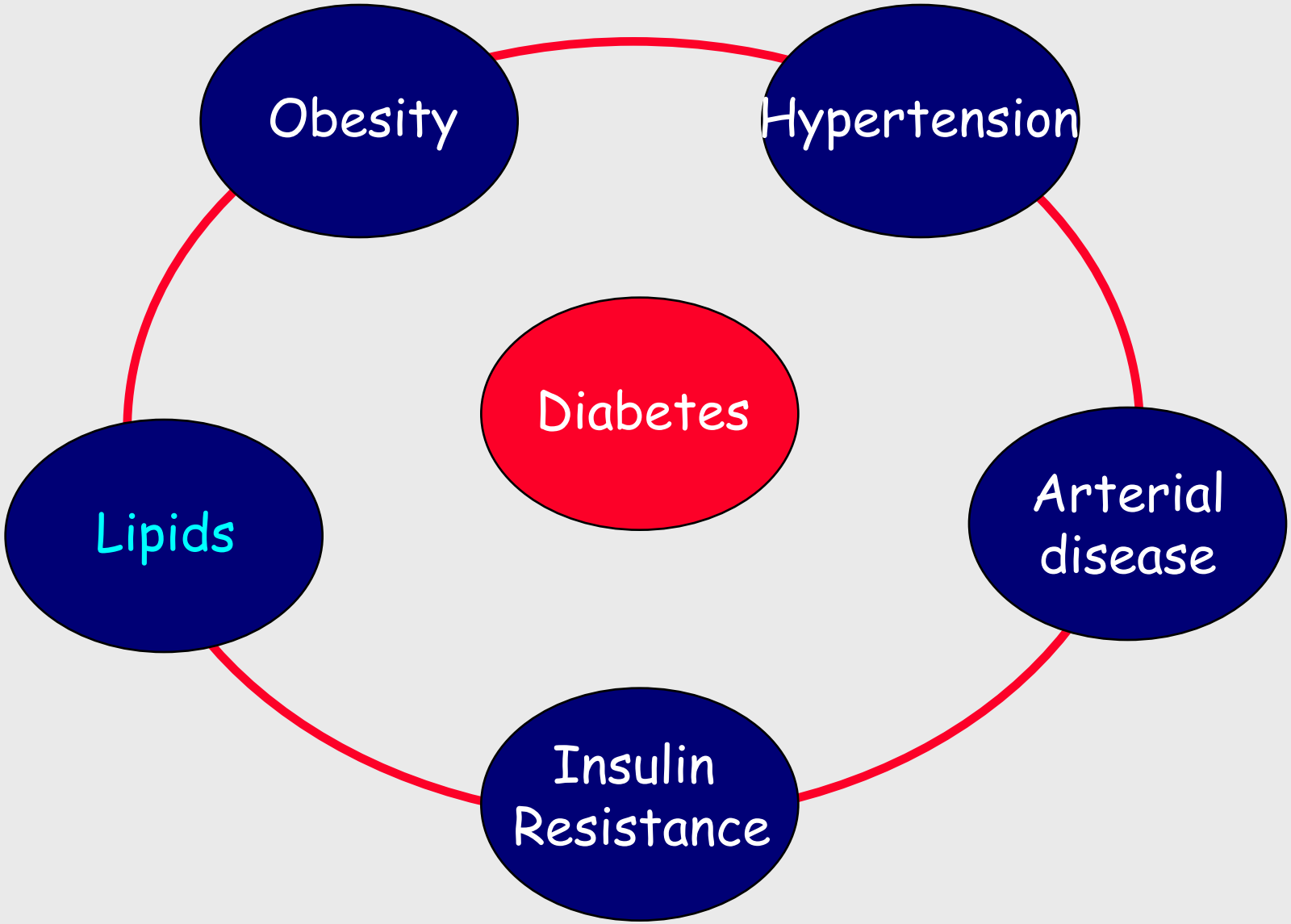
"Most scientific problems are far better understood by studying their history than their logic"

Ernst Mayr

Constitution and insulin sensitivity in diabetes mellitus

John Lister, John Nash and Una Ledingham

British Medical Journal 1951; I: 376-9

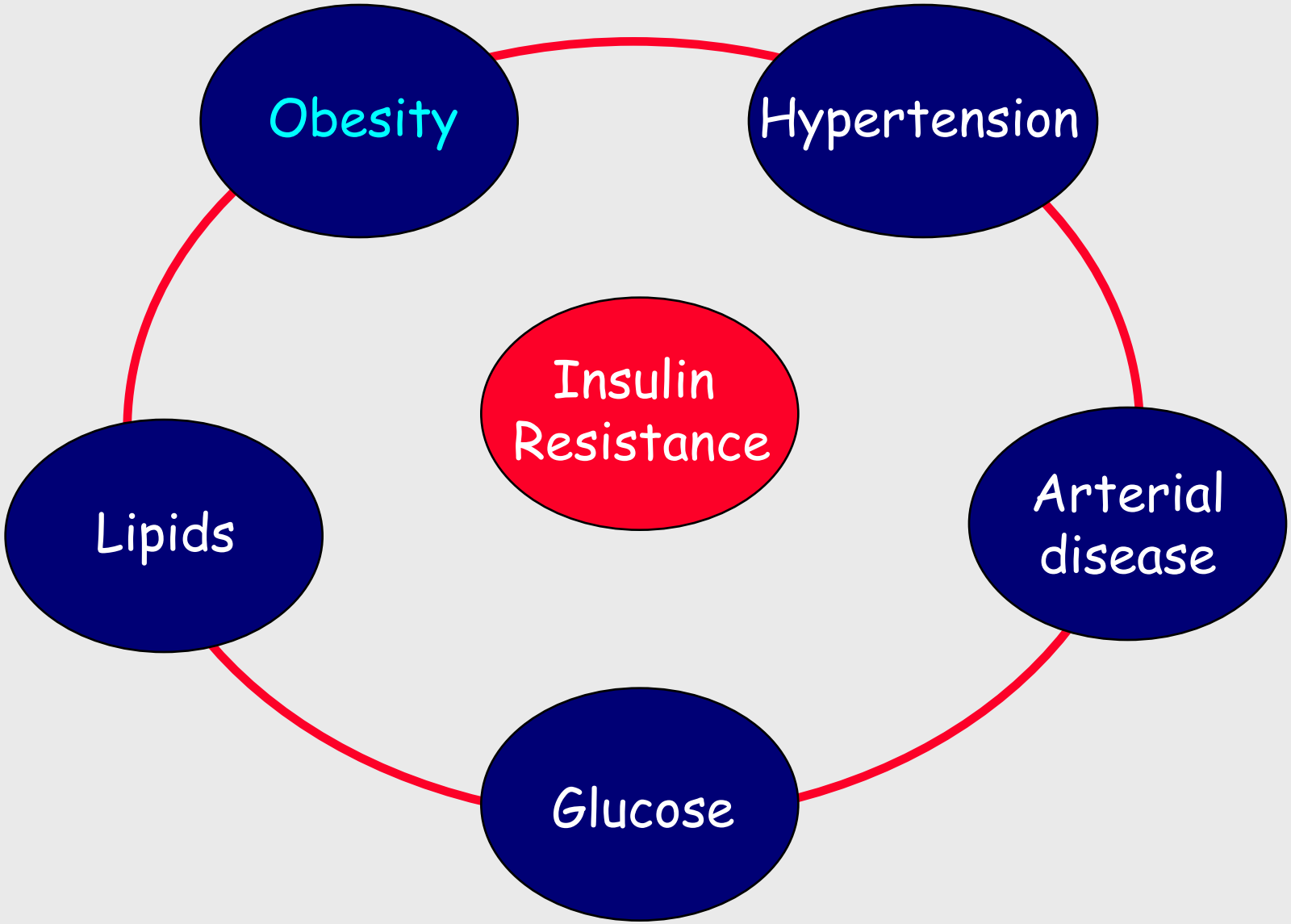

Obesity
Hypertension
Diabetes
Lipids
Arterial disease
Insulin Resistance

- The "metabolic syndrome" is integral to the classic description of type 2 diabetes
- The label adds nothing in terms of understanding or treatment
- Controversy only arises when we extend the definition beyond the context of overt diabetes

Banting Lecture 1988

Role of Insulin Resistance in Human Disease

GERALD M. REAVEN


Obesity
Hypertension
Insulin Resistance
Lipids
Arterial disease
Glucose

Insulin Resistance

- 6-fold variation in insulin-mediated glucose disposal in healthy individuals
- Insulin resistance is hard to measure and variously defined
- One third of those with clinical features of the metabolic syndrome are not insulin resistant
- One third of those with insulin resistance do not have the metabolic syndrome

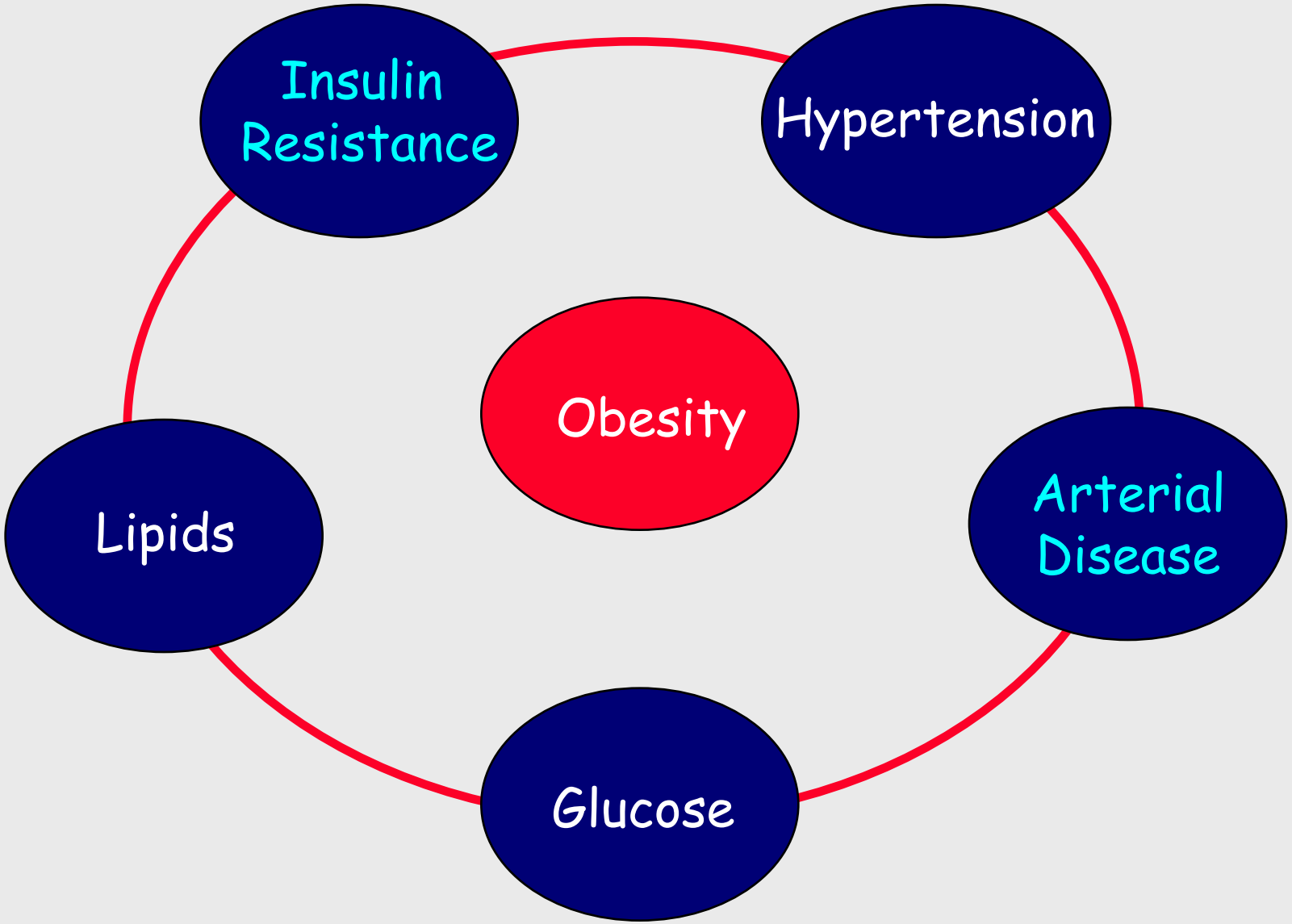
Gerald M Reaven. The metabolic syndrome: *requiescat in pace.* Clinical Chemistry 2005; 51: 931-38

Insulin Resistance

"The primary value of the concept of insulin resistance is that it provides a conceptual framework with which to place a substantial number of apparently unrelated biological events into a pathophysiological construct.

In contrast, the metabolic syndrome was introduced as a diagnostic category…."

Gerald M Reaven. The metabolic syndrome: *requiescat in pace.* Clinical Chemistry 2005; 51: 931-38


Insulin Resistance
Hypertension
Obesity
Lipids
Arterial Disease
Glucose

IDF

- Waist circumference

  - PLUS two of -

- Raised triglycerides
- Low HDL Cholesterol
- Raised BP
- Raised FPG

How fat is fat?

IDF

Europeans

- 94 cm in men
- 80 cm in women

How fat is fat?

IDF

Europeans

- 94 cm in men
- 80 cm in women

AHA

Americans

- 102 cm in men
- 88 cm in women

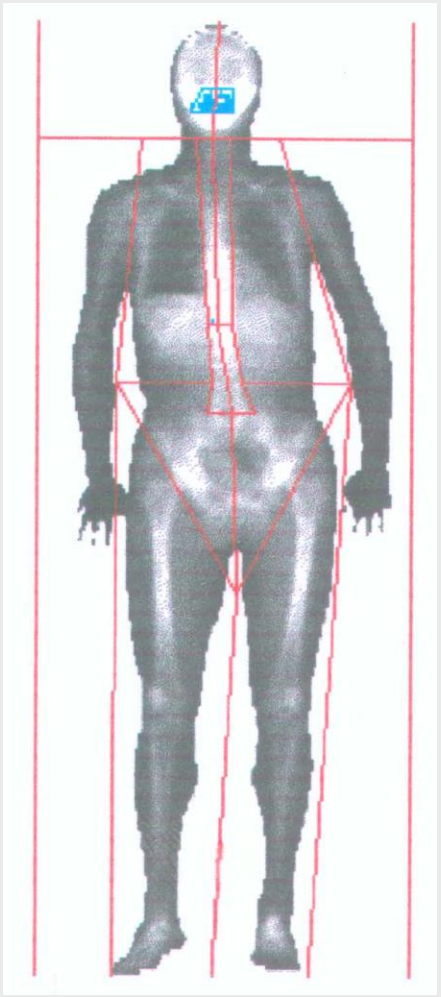
What type of fat, where deposited, and how measured?

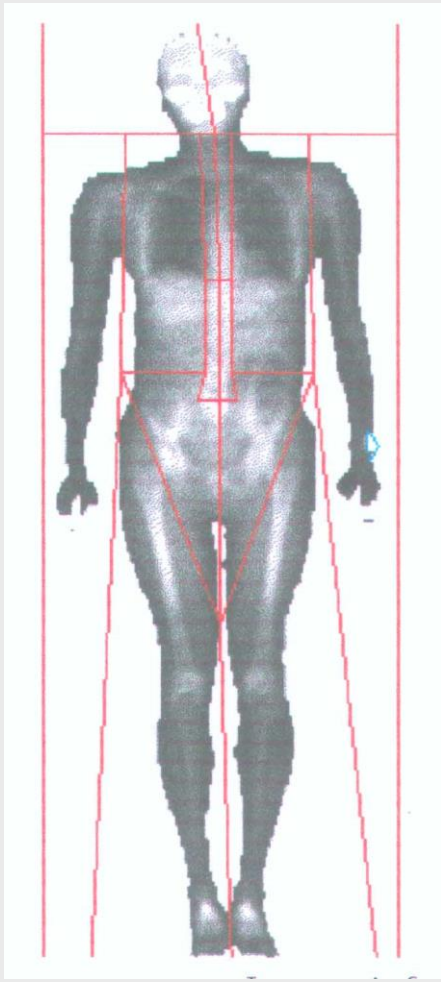
Fat distribution and body composition vary between different populations and ethnic groups

Which means that we have to define both obesity and ethnicity

BMI

22.3 22.3





Body fat

9.1% 21.2%

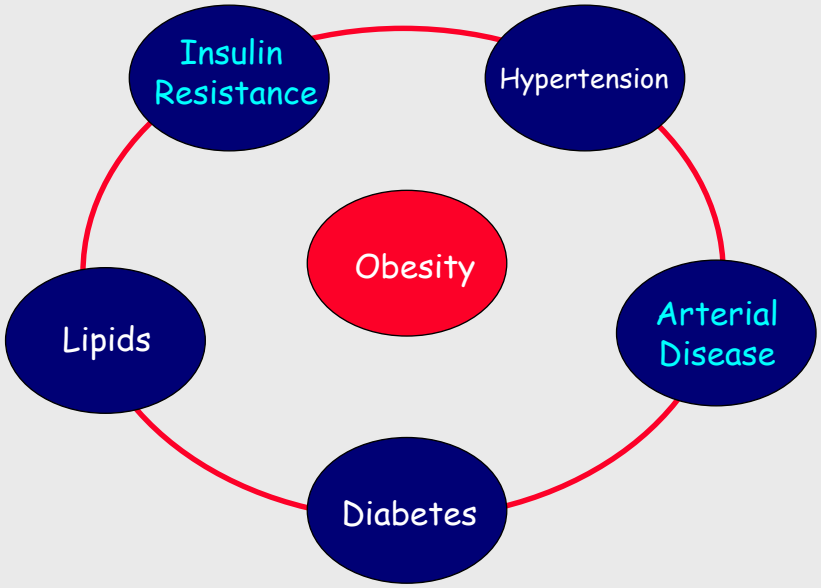
And can we define ethnicity?

"Human populations are not unambiguous, clearly demarcated, biologically distinct groups. Evidence from the analysis of genetics (e.g. DNA) indicates that most physical variation, about 94%, lies *within* so-called racial groups … there is greater variation within 'racial' groups than between them"

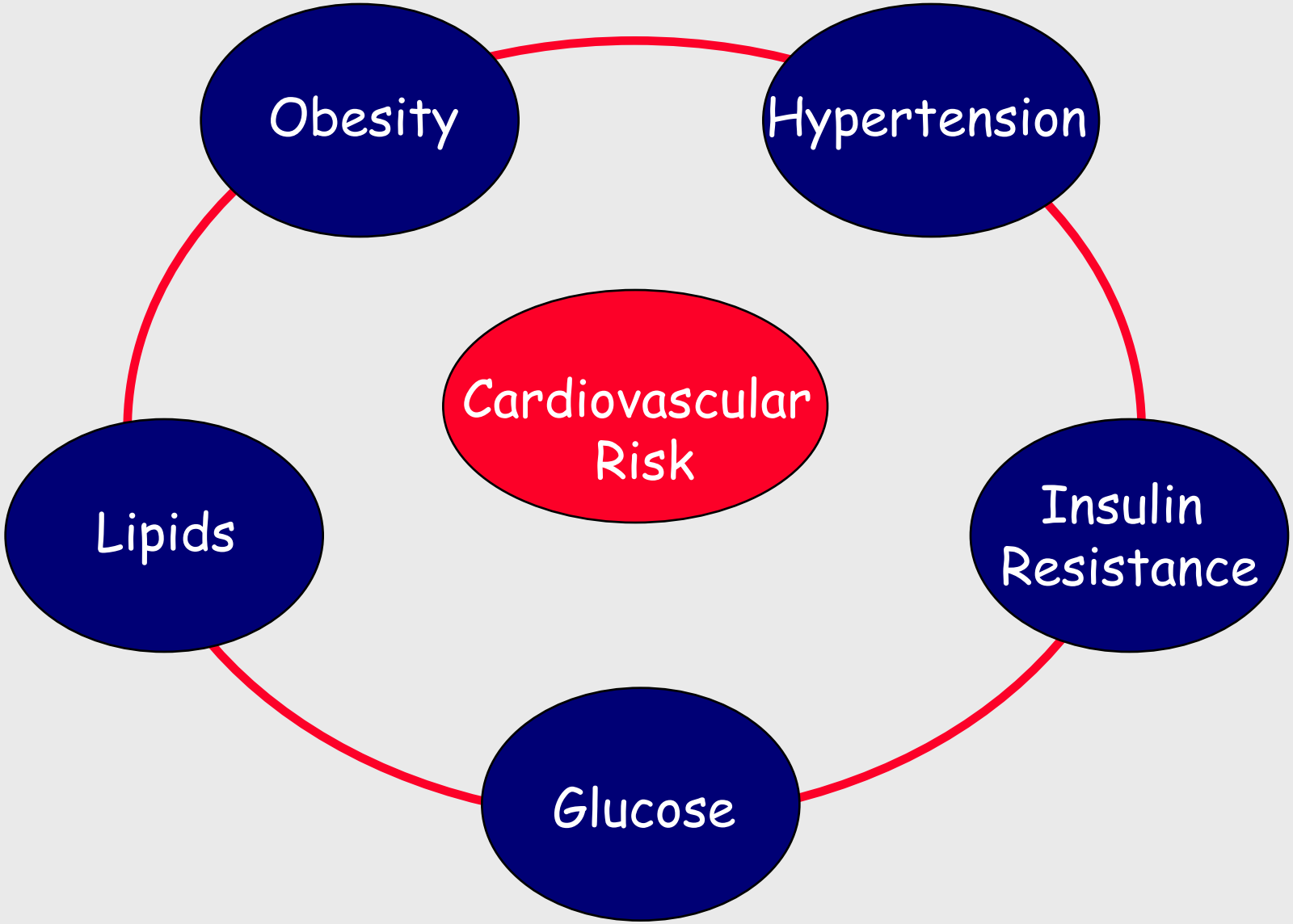
American Anthropological Association

May 17, 1998

If obesity has to be defined differently in different populations …

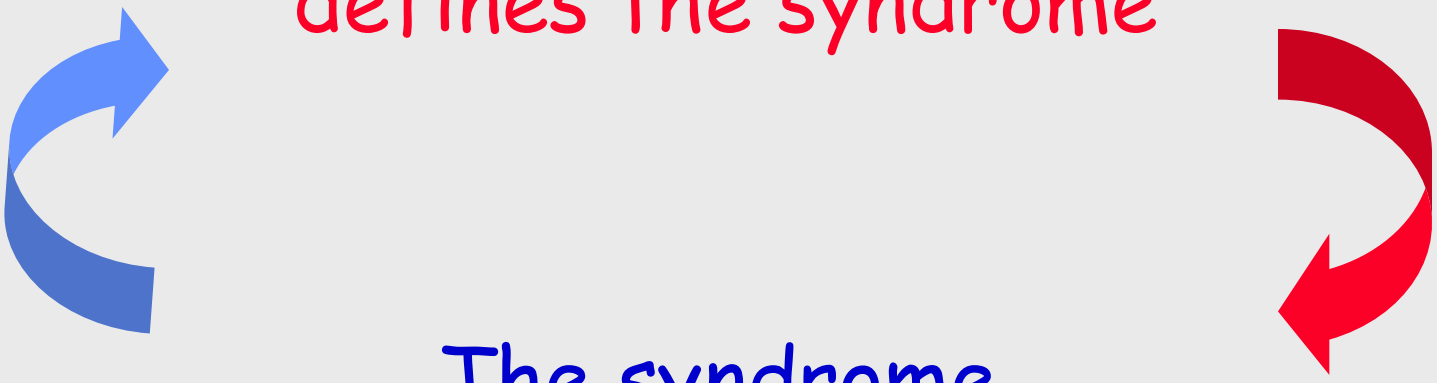


What criterion is used to judge obesity?

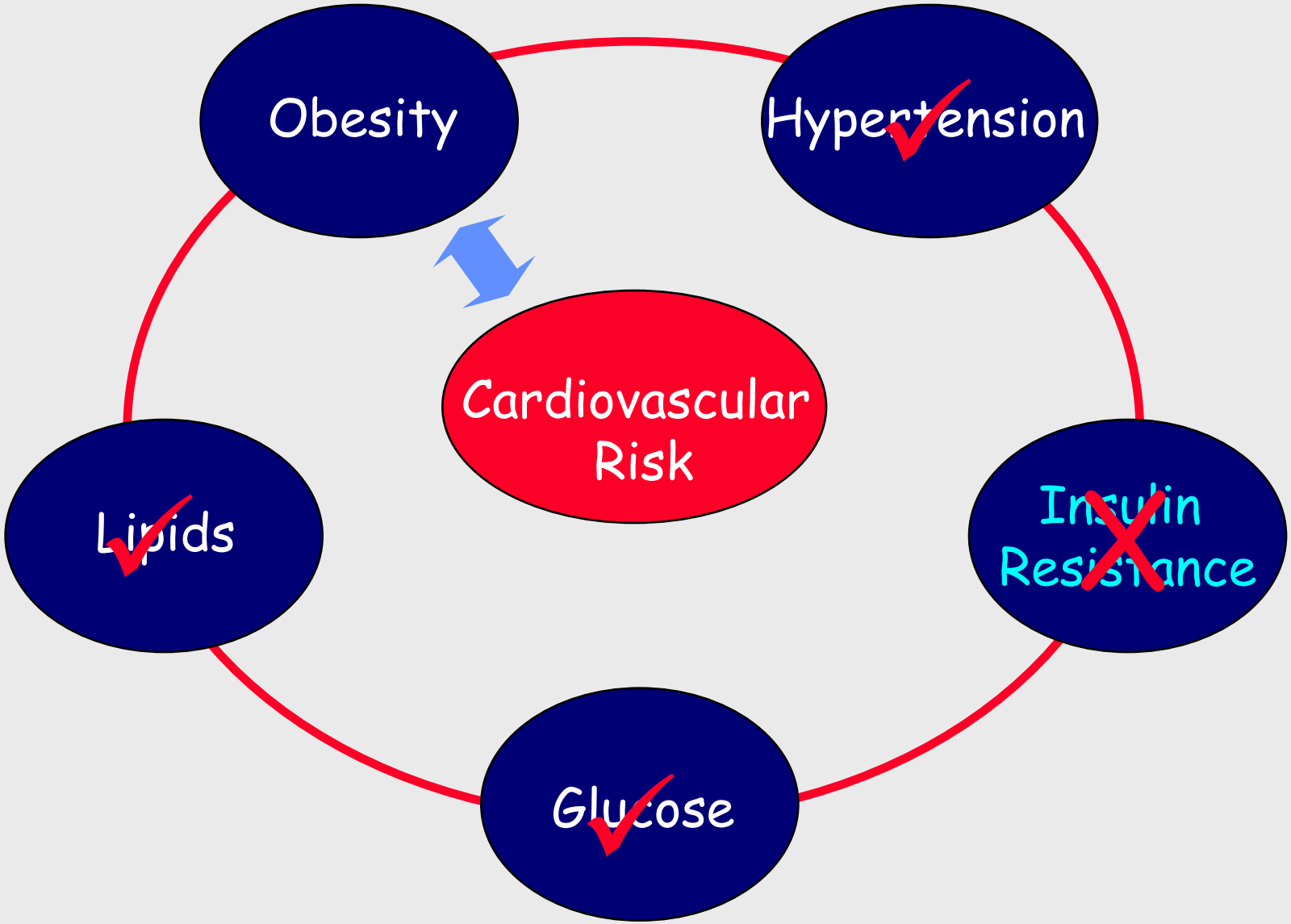

Obesity
Hypertension
Cardiovascular Risk
Lipids
Insulin Resistance
Glucose

Cardiovascular Risk

Vascular risk defines the syndrome



The syndrome defines vascular risk


Obesity
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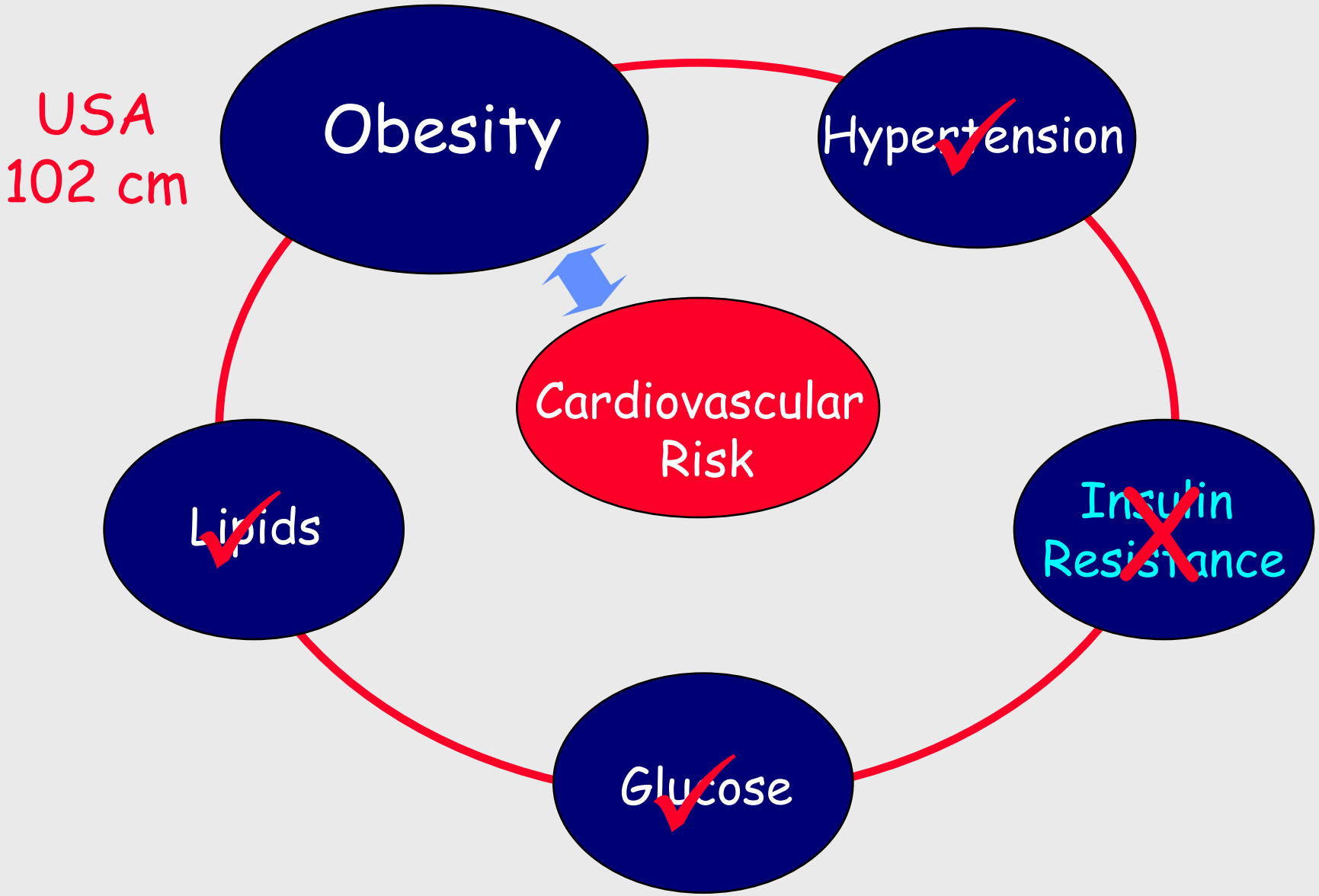
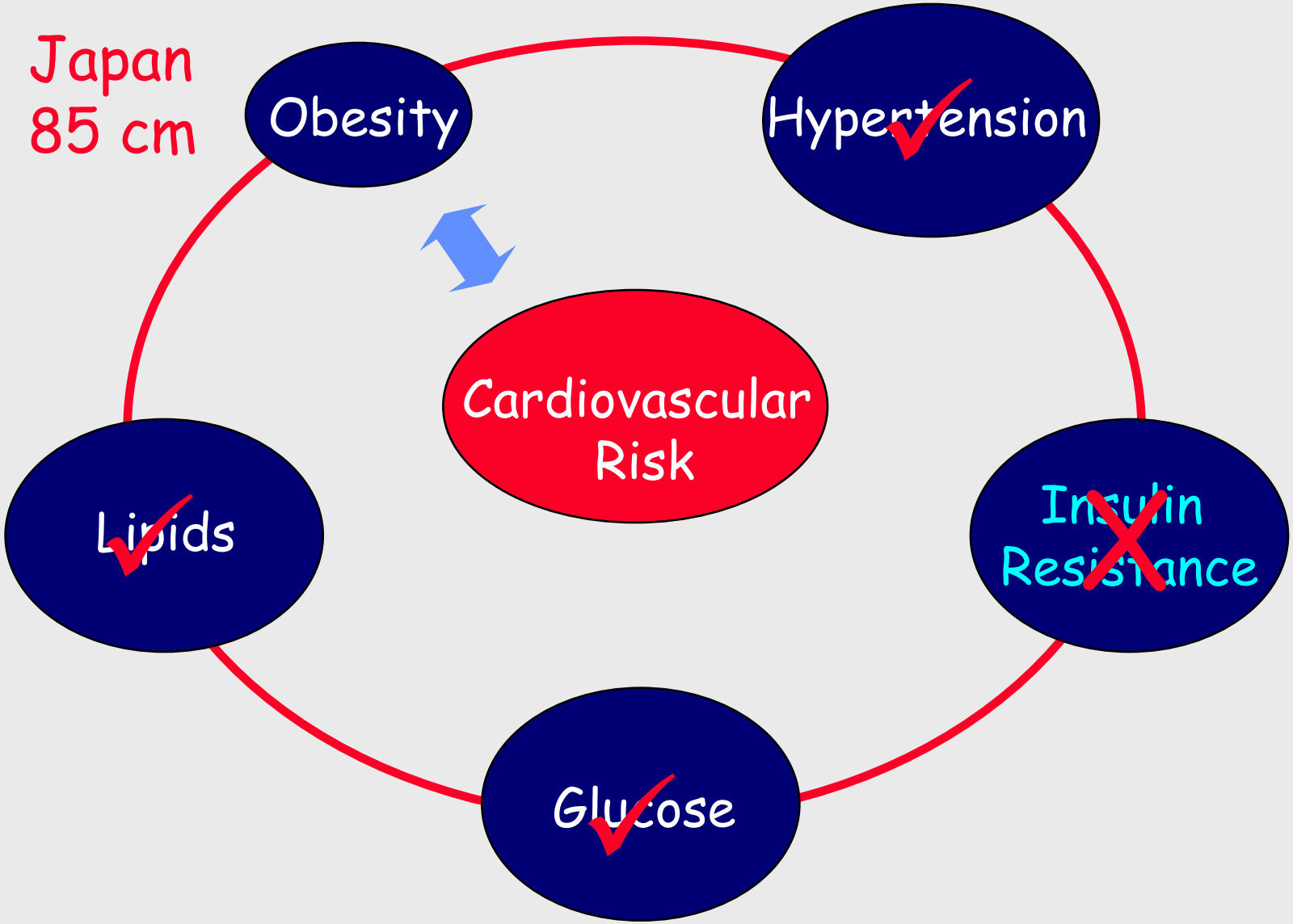

USA
102 cm
Obesity
Hypertension
Cardiovascular Risk
Lipids
Insulin Resistance
Glucose


Japan
85 cm
Obesity
Hypertension
Cardiovascular Risk
Lipids
Insulin Resistance
Glucose

Question:

- Does this mean that a Japanese man with a waistline of 85 cm has the same cardiovascular risk as an American with a waistline of 102 cm?

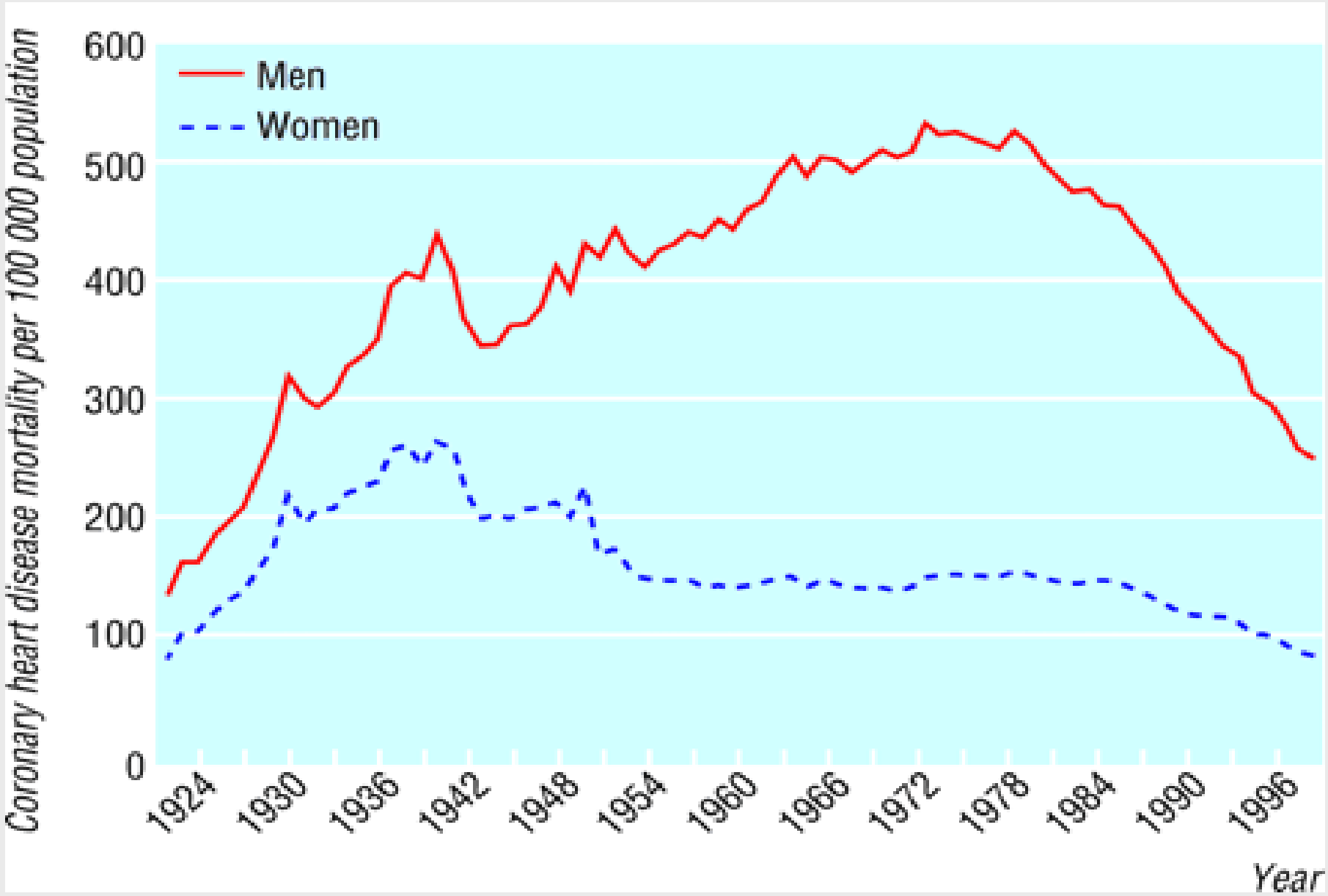
Question:

- Does this mean that a Japanese man with a waistline of 85 cm has the same cardiovascular risk as an American with a waistline of 102 cm?
- Japanese men have a higher risk of stroke and a much lower CHD risk; they have a higher BP and are more likely to smoke
- Japanese stroke mortality has fallen by 70% and CHD mortality by 20% over the past 30 years

Iso et al, Preventive Med 1999; **29**:S102-S105

"IDF believes that metabolic syndrome is driving the twin global epidemics of type 2 diabetes and cardiovascular disease"

IDF website



Lawlor et al, BMJ, 2001

So, who's driving?

So, who's driving?

- Obesity and the metabolic syndrome are NOT driving an epidemic of cardiovascular disease in westernised countries
- The rise of heart disease in the developing world is primarily related to cigarette smoking
- The only people not escaping heart disease in the West are those with IGT/diabetes…

So, who's driving?

Diabetes

Review Point

- The metabolic syndrome is an evolving concept, better understood in historical rather than logical terms
- It began as a diabetes syndrome, evolved into an insulin resistance syndrome, from there into an obesity syndrome, and from there into a cardiovascular risk syndrome…

Review Point

- The metabolic syndrome is an evolving concept, better understood in historical rather than logical terms
- It began as a diabetes syndrome, evolved into an insulin resistance syndrome, from there into an obesity syndrome, and from there into a cardiovascular risk syndrome…
- Before coming back to diabetes again

Why might a diagnosis of the Metabolic Syndrome be useful?

- Because it predicts cardiovascular disease

Why might a diagnosis of the Metabolic Syndrome be useful?

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- BUT, is it surprising that 5 cardiovascular risk factors predict cardiovascular disease?

Why might a definition of the Metabolic Syndrome be useful?

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- What about age, established c.v. disease, smoking and family history?

Why might a definition of the Metabolic Syndrome be useful?

- Because it predicts cardiovascular disease
- BUT, is it surprising that 5 cardiovascular risk factors predict cardiovascular disease?
- What about age, established c.v. disease, smoking and family history?
- Standard models incorporating these out-perform the metabolic syndrome.

Conclusion (1)

- If you want to define cardiovascular risk, there are better ways of doing it

Why might a diagnosis of the Metabolic Syndrome be useful?

- Because it predicts cardiovascular disease
- Because it predicts diabetes

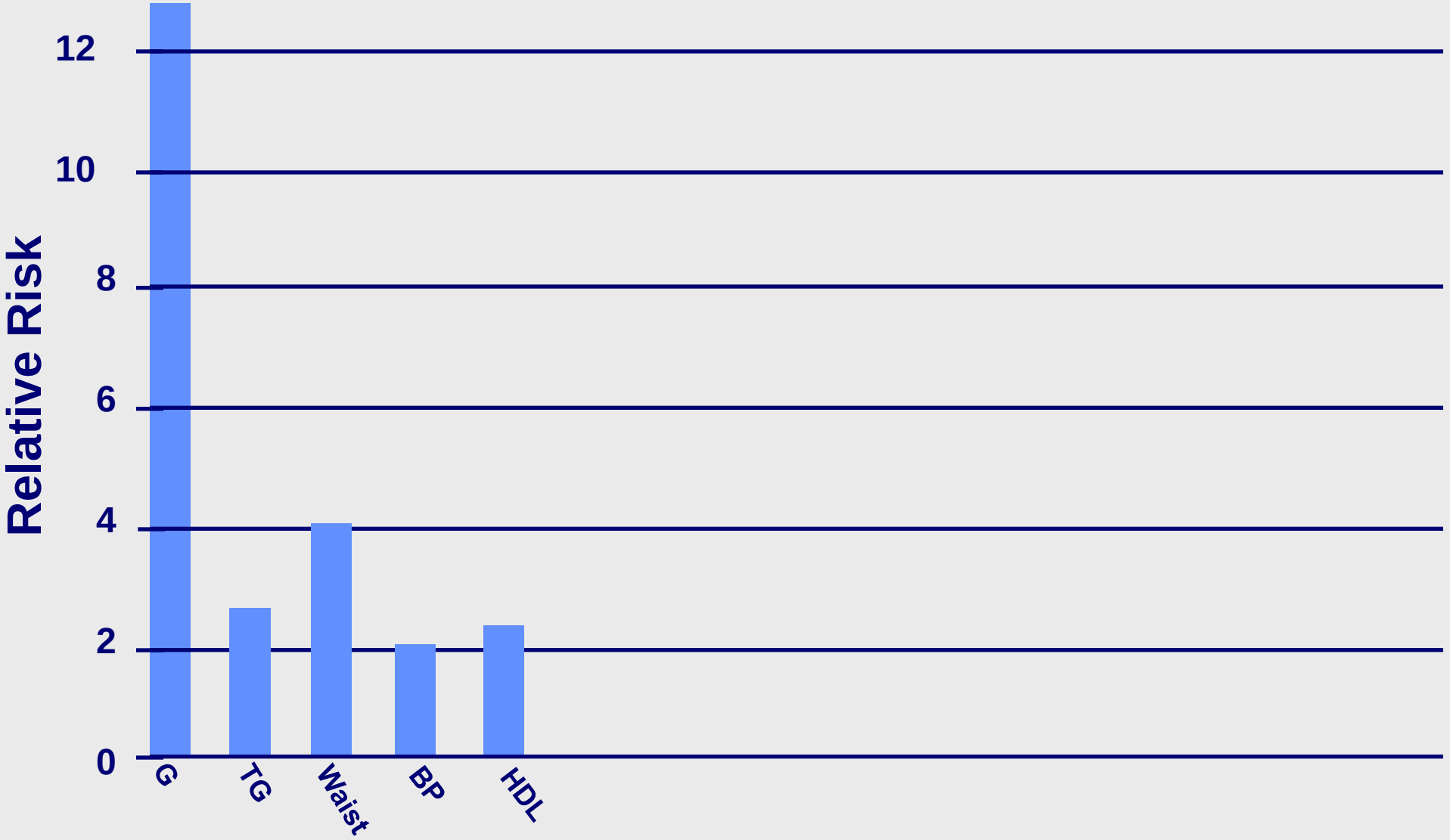
Metabolic Syndrome and risk of diabetes
(Insulin Resistance Atherosclerosis Study)

Variable	OR** (95% CI)
IDF	3.40 (2.28 – 5.06)
IGT alone	5.42 (3.60 – 8.17)

** Adjusted for age, sex and ethnicity

Hanley et al., *Circulation* 112:3713-3721,2005

Metabolic Syndrome and risk of Diabetes



Wilson et al. Circulation 112:3066-3072, 2005

Conclusion (2)

- If you want to define cardiovascular risk, there are better ways of doing it
- If you want to define future risk of diabetes, there are better ways of doing it

Conclusion (3)

- If you want to define cardiovascular risk, there are better ways of doing it
- If you want to define future risk of diabetes, there are better ways of doing it
- If you want to define the health consequences of obesity, there are better ways of doing it

Conclusion (4)

- If you want to define cardiovascular risk, there are better ways of doing it
- If you want to define future risk of diabetes, there are better ways of doing it
- If you want to define the health consequences of obesity, there are better ways of doing it
- If you want to reduce cardiovascular risk, you should treat the individual components

Insulin Resistance

"In conclusion, it appears that making the diagnosis of the metabolic syndrome does not bring with it much in the way of pathophysiologic understanding or clinical utility…"

Gerald M Reaven. The metabolic syndrome: *requiescat in pace.* Clinical Chemistry 2005; 51: 931-38

Who needs a metabolic syndrome?

"It has been suggested in an editorial that recognition of the metabolic syndrome has been largely driven by industry to create new markets"

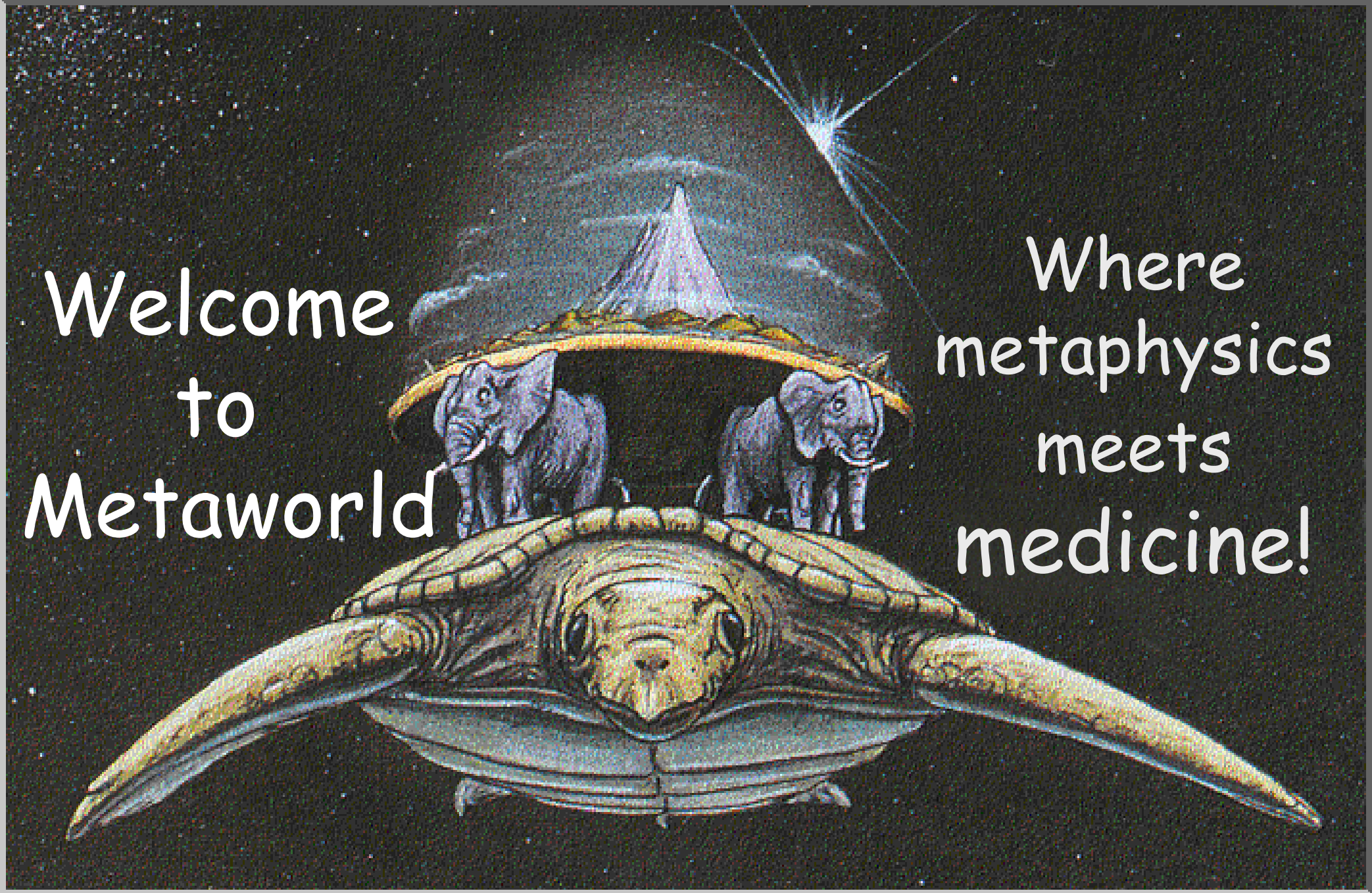
Alberti KGMM, Zimmet P, Shaw J (2005)
The metabolic syndrome, a new worldwide definition.
Lancet 366:1059-62

And my own concerns …

- The metabolic syndrome implies an entity where none exists.
- It uses cut off points rather than continuous variables
- It disregards important risk elements
- It implies an outdated "screen and treat" strategy for a situation that should be tackled at a population level, and early in life.

Questions for George

- Is this a homogeneous disease entity?
- What does it add to understanding?
- What does it add to prediction?
- What does it add to treatment?
- Why is the rise of the metabolic syndrome matched by a fall in cardiovascular disease?
- Isn't it just telling us that dysglycaemia is bad for you?


Welcome
to
Metaworld
Where
metaphysics
meets
medicine!

Competing Interests:

None