
Unravelling the causes of premature heart disease among South Asians

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Excess Coronary Heart Disease in South Asian Migrants



CHD is a Global Epidemic among South Asians

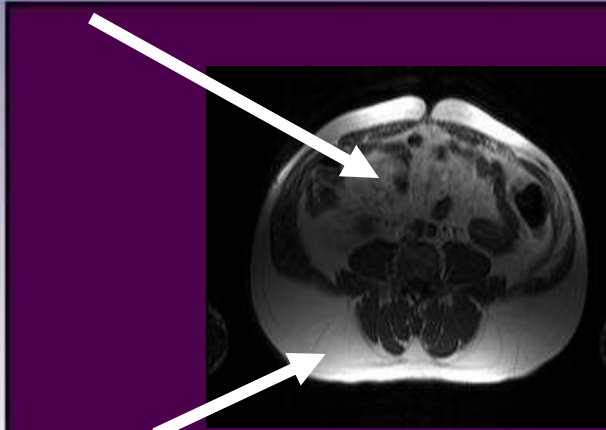
- CHD strikes S. Asians at a four-fold rate compared to the general population
- S. Asians in North America suffer heart attacks at an earlier age, often without prior symptoms or warning
- Half of all heart attacks in this population occur under the age of 50 years
- By 2010, India will bear 60% of the worlds CHD burden

Risk Factors of that are More Common in South Asians

- Dyslipidemia (LDL, HDL, Apo B, Triglycerides)— 44%
- High lipoprotein(a) — 42%
- Metabolic syndrome — 35% men and 50% women
- Diabetes — 17%
- Pre-diabetes — 63%
- Abdominal obesity — 62%
- High CRP — 65%
- High homocysteine — 41% to 75%
- No daily intake of fruits and vegetables —73%
- Physical inactivity — 94%

Metabolic Syndrome Phenotype: A Cluster of Metabolic Abnormalities

Visceral Adipose Tissue



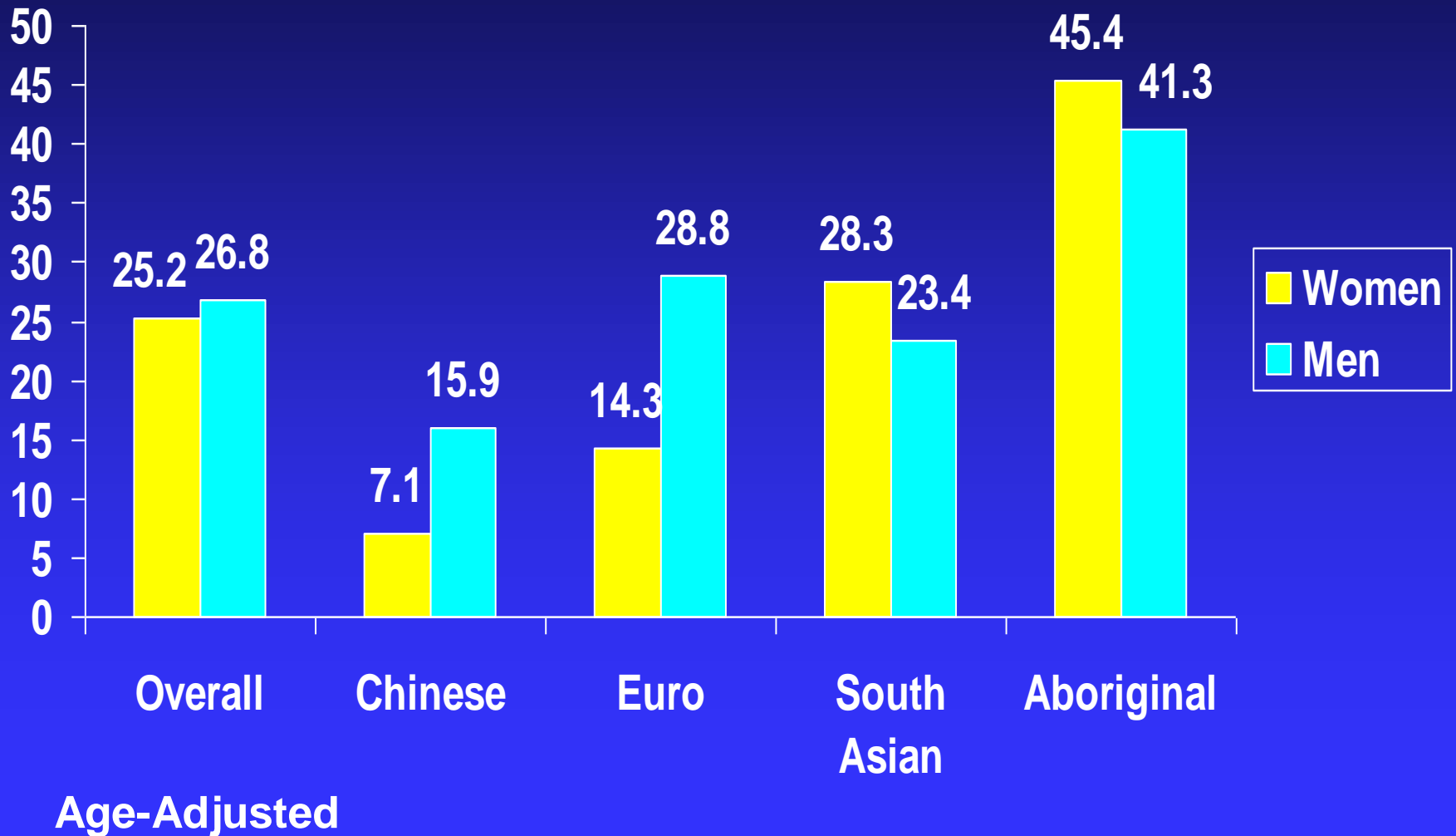
Subcutaneous Adipose
Tissue



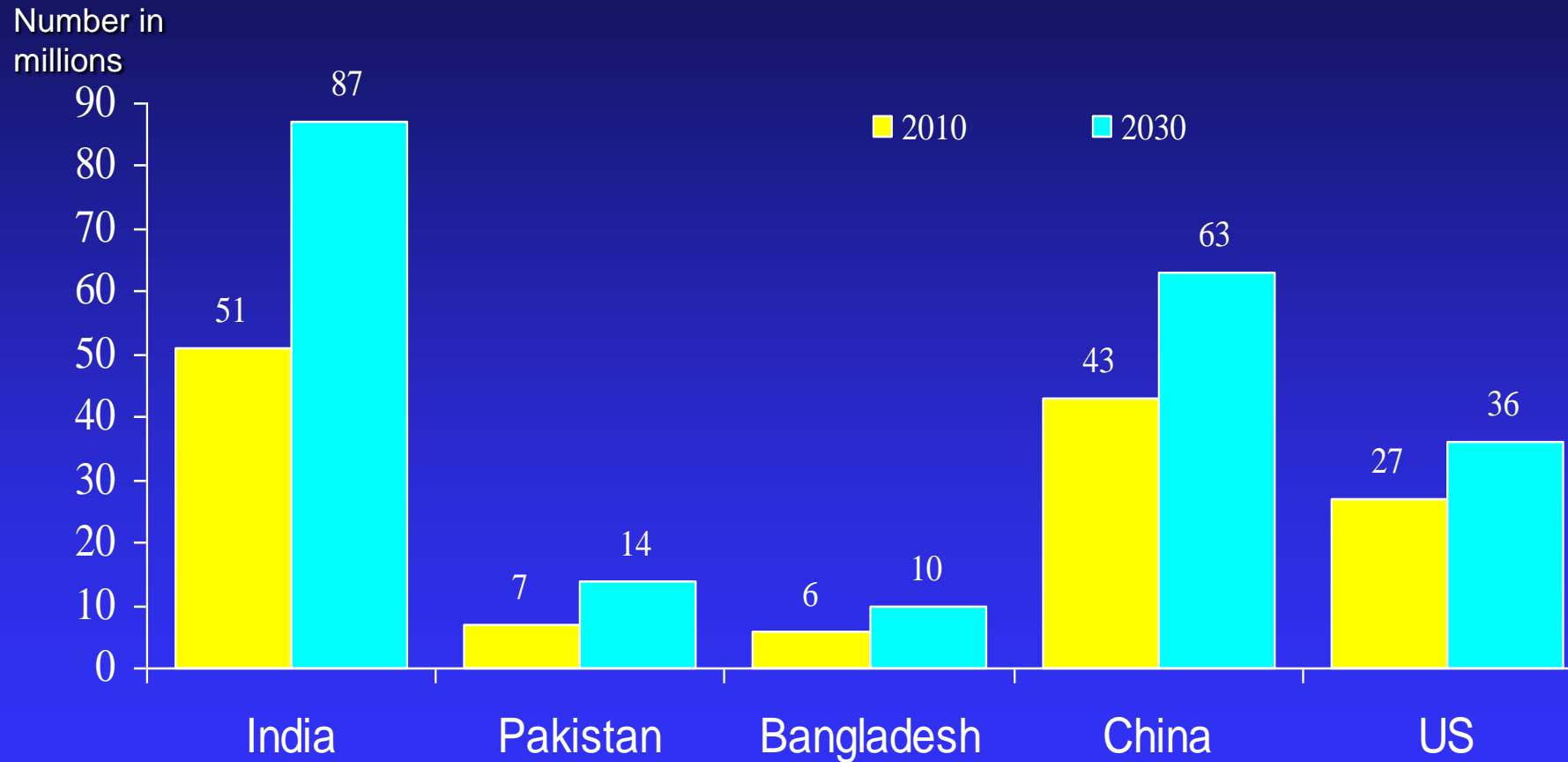
- Abdominal Adiposity
- Dysglycemia
- ↓HDL Cholesterol
- Triglycerides
- +/- Elevated BP

Associated with a significant increase in type 2 diabetes and CHD

Age-Adjusted Prevalence of Metabolic Syndrome in Canada

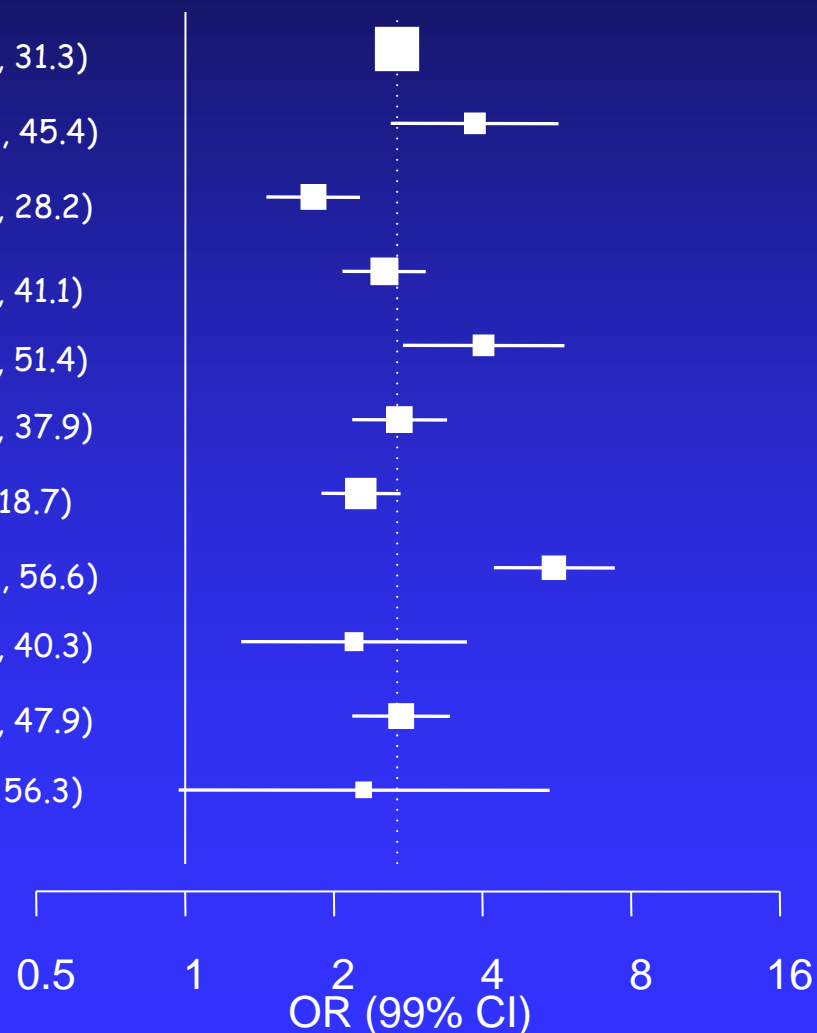


Global Estimates of the burden of Diabetes in Millions for 2010 and 2030:



INTERHEART: MS and MI by Region

Region	% Contr	OR (99% CI)	PAR (99% CI)
Overall	26.1	2.69 (2.48,2.92)	29.2 (27.1, 31.3)
W Europe	16.7	3.86 (2.61,5.70)	36.0 (27.5, 45.4)
C/E Europe	32.0	1.82 (1.46,2.26)	20.4 (14.3, 28.2)
Middle E/Egypt	35.7	2.53 (2.08,3.08)	34.8 (29.1, 41.1)
Africa	24.6	4.02 (2.76,5.86)	41.7 (32.6, 51.4)
South Asia	26.9	2.72 (2.18,3.39)	31.6 (25.9, 37.9)
China /H.K.	13.9	2.27 (1.89,2.73)	15.1 (12.1, 18.7)
S.E. Asia/Japan	22.4	5.59 (4.22,7.41)	50.0 (43.5, 56.6)
Aust/N. Z.	26.4	2.20 (1.30,3.72)	22.0 (10.5, 40.3)
South Am./Mex.	36.3	2.74 (2.18,3.44)	40.3 (33.1, 47.9)
North Am	27.4	2.30 (0.97,5.47)	21.5 (5.5, 56.3)



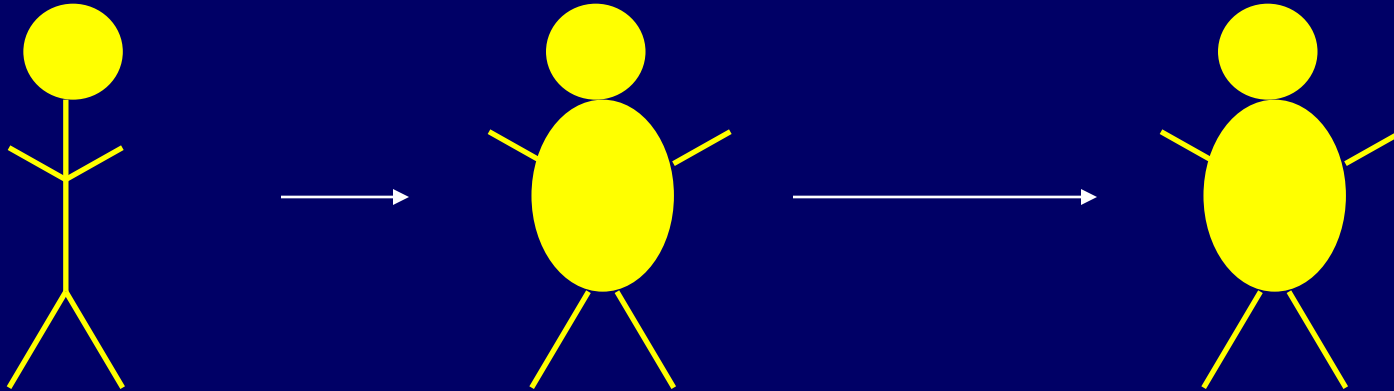
Everyone has a theory....

May be all are partly true....

Theories

- 1) “Stress” of Migration
- 2) S. Asian diet including “ghee” or “coconut oil”
- 3) Genetic Factors
- 4) Early origins: Thrifty Phenotype

Evolution of risk factors in South Asians

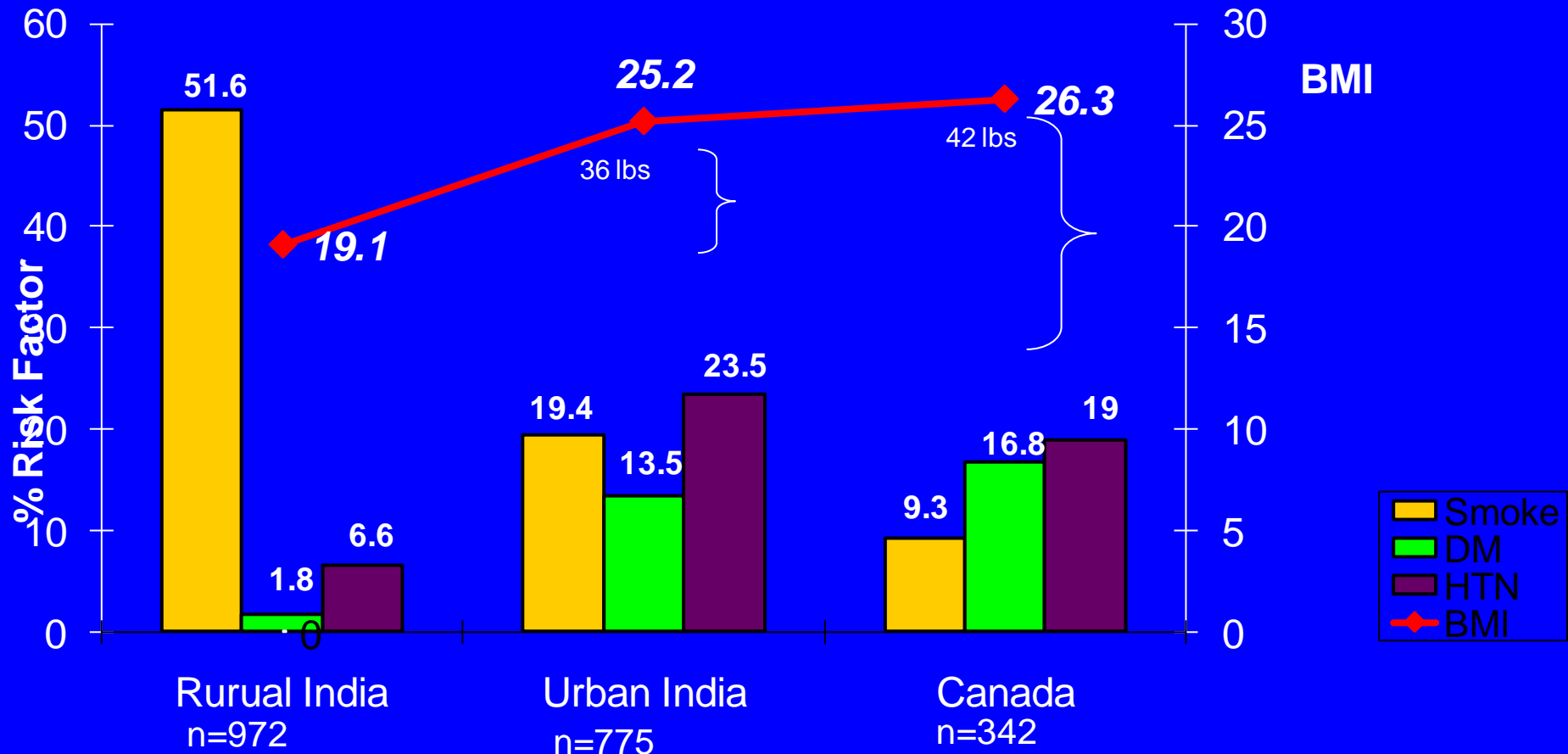


1. Weight gain → 2. pre-Diabetes → 3. Diabetes → 4. Heart Disease

- Lipids
- Blood Pressure

5.? Some Cancers

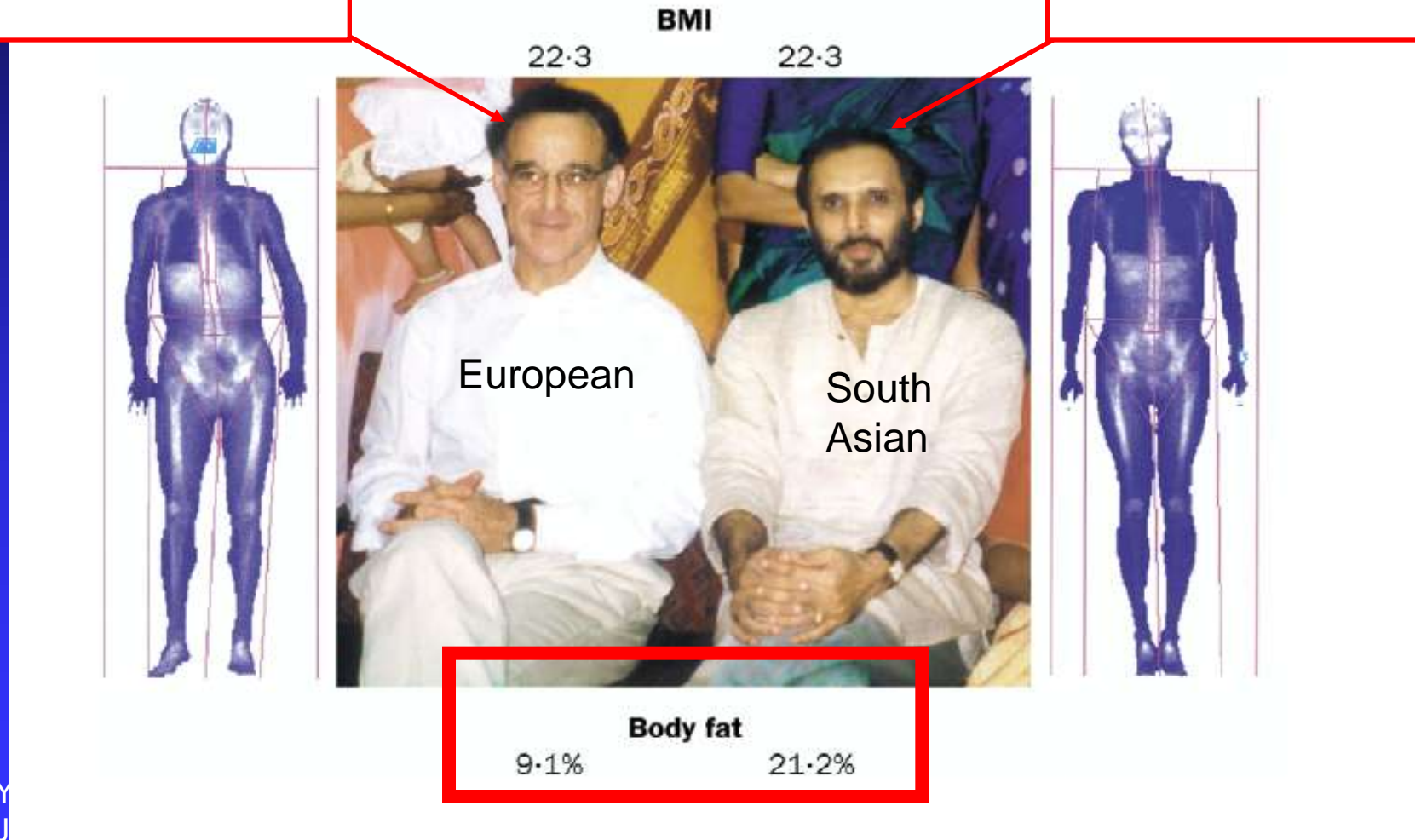
Changes in Risk Factors with Migration



Why Does This Occur?

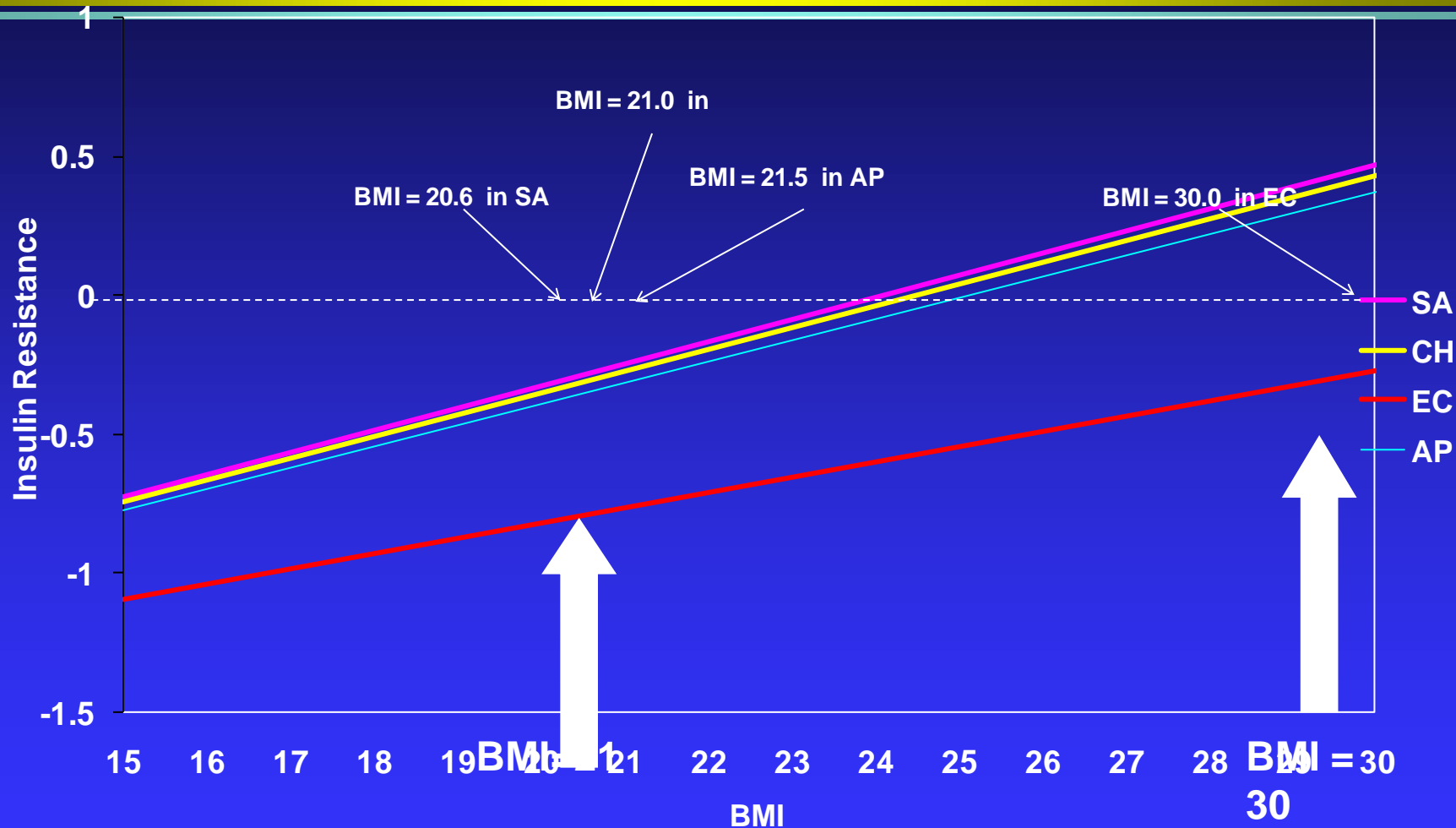
Runs Marathons

Runs to beat the closing Elevator Doors



DXA scan of two individuals with the same BMI but markedly different percent body fat.

Relationship of Insulin Resistance to Body Mass Index Among South Asians, Chinese, Aboriginals and Europeans





Waist Measurements

White Caucasians

: >100 cm or 40 inches

: > 88 cm or 35 inches

South Asians

: > 90 cm or 35 inches

: > 80 cm or 32 inches

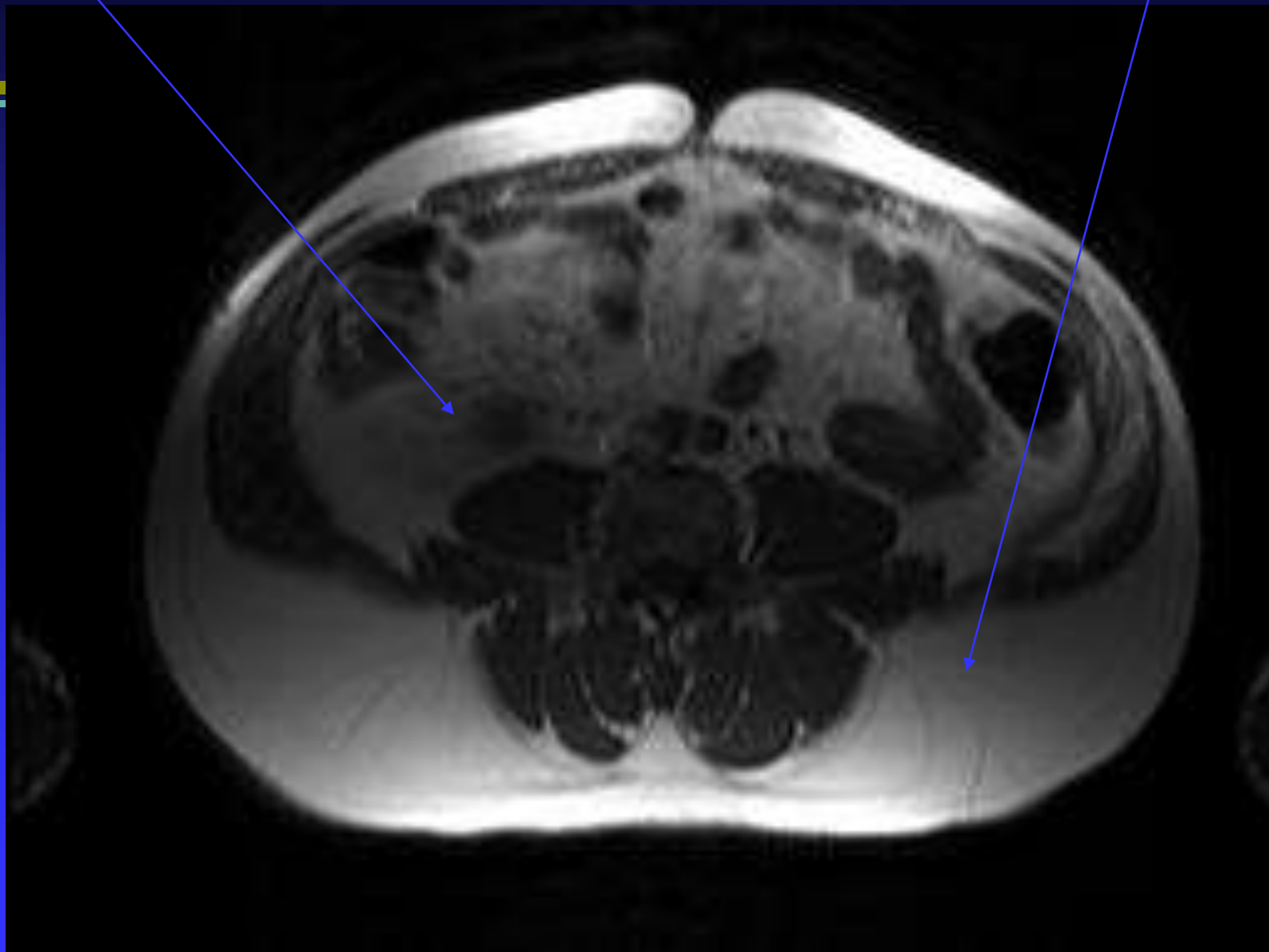
Why do South Asians develop Early Metabolic Changes?



MRI Cross Section of Abdomen

VAT

SAT



Molecular SHARE

- Age and sex-matched individuals of European and South Asian ancestry
- Recruited into 3 strata defined by BMI:
- Stratum 1: BMI ≤ 25 kg/m²
- Stratum 2: BMI = 26-29
- Stratum 3: ≥ 30

- Exclude: Individuals with T2DM or CVD
- 20 individuals per ethnic group in each BMI strata (40/strata = 120 overall) equally divided by sex

Molecular SHARE

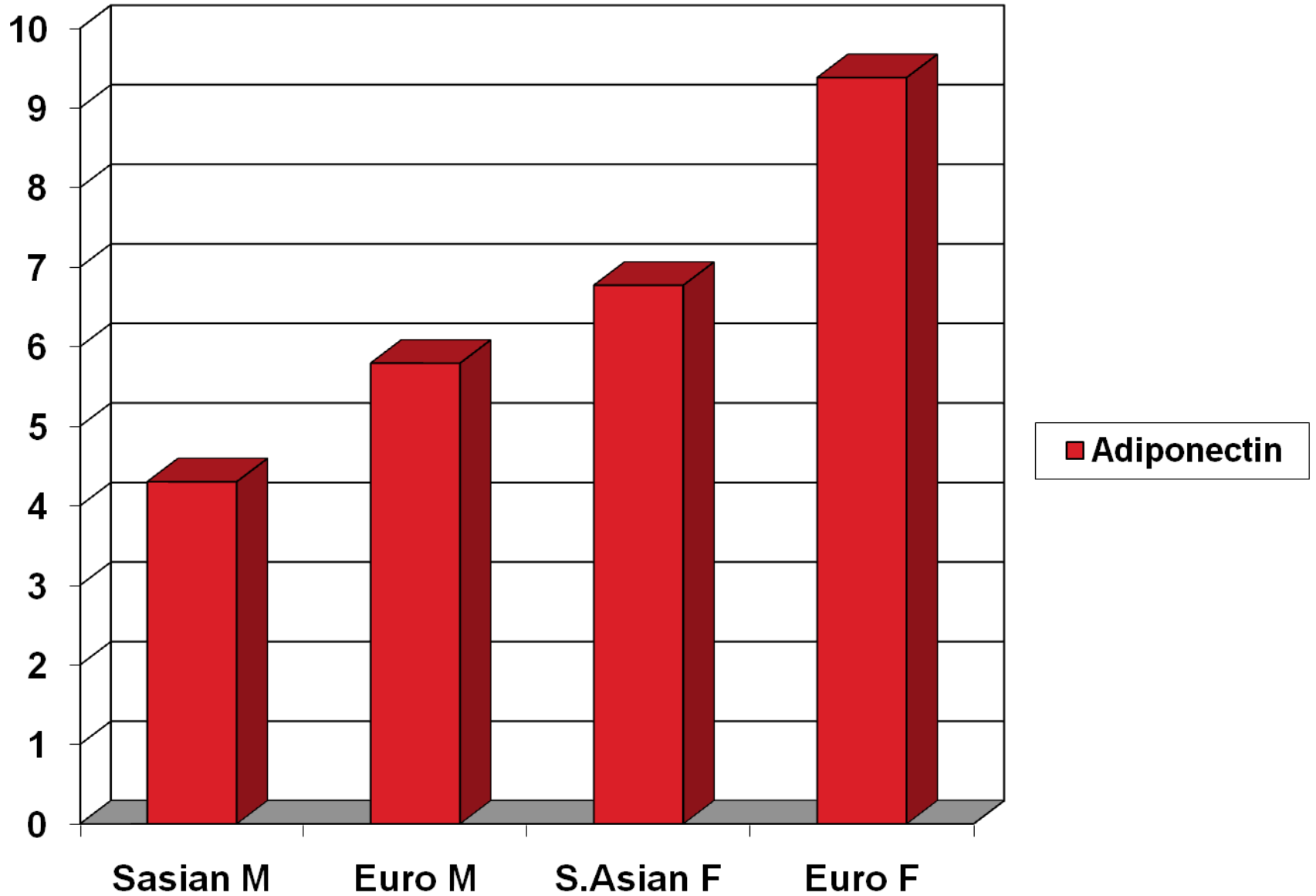
- Fasting Blood collection, 2 hr OGTT
- Dietary Assessment: FFQ/FR
- Physical Measurements (weight, height, WC, HC)
- Grip Strength, Fitness test
- DXA scan
- BIA
- MRI abdomen
- Fat biopsy, Muscle biopsy
- IMCL

South Asians vs Europeans - Baseline

	South Asian	European	p – value
Number of participants	56	52	
Age (years)	36	34	
Body Mass Index	26.4 (4.3)	28.2 (6.3)	0.05
Waist/Hip Ratio	0.88	0.86	0.05
Body Fat%	35.4	32.7	0.001
Adiponectin ug/mL	5.60	7.67	0.001

*age, sex adjusted

Adiponectin

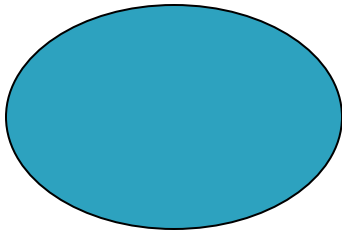


Age Adjust

Adipocyte Cell Size

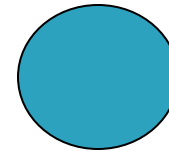
- South Asian

- Max diameter: 259.0
- Area: 451.8 units²



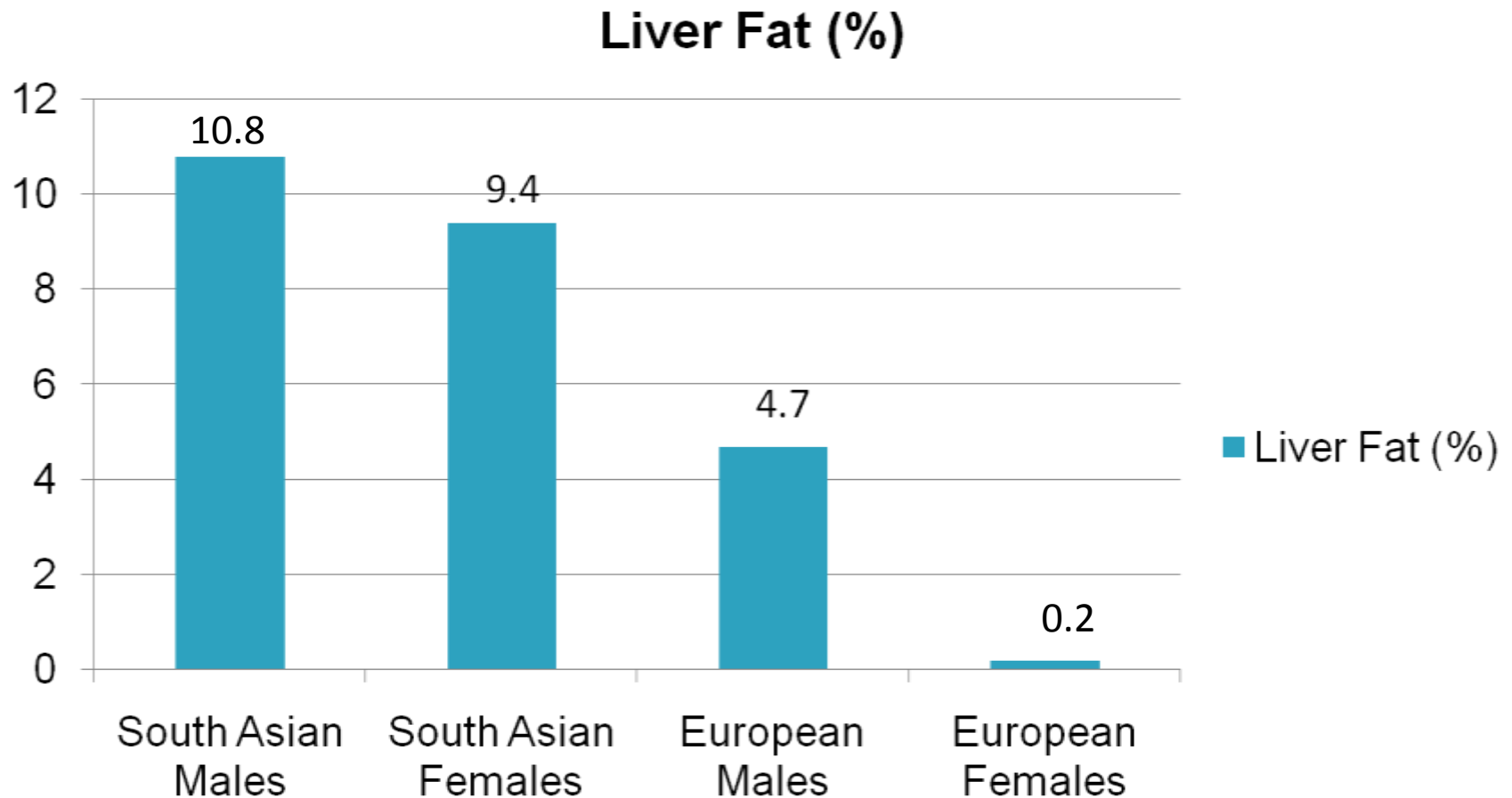
- Europeans

- Max diameter: 238.4
- Area: 387.7 units²



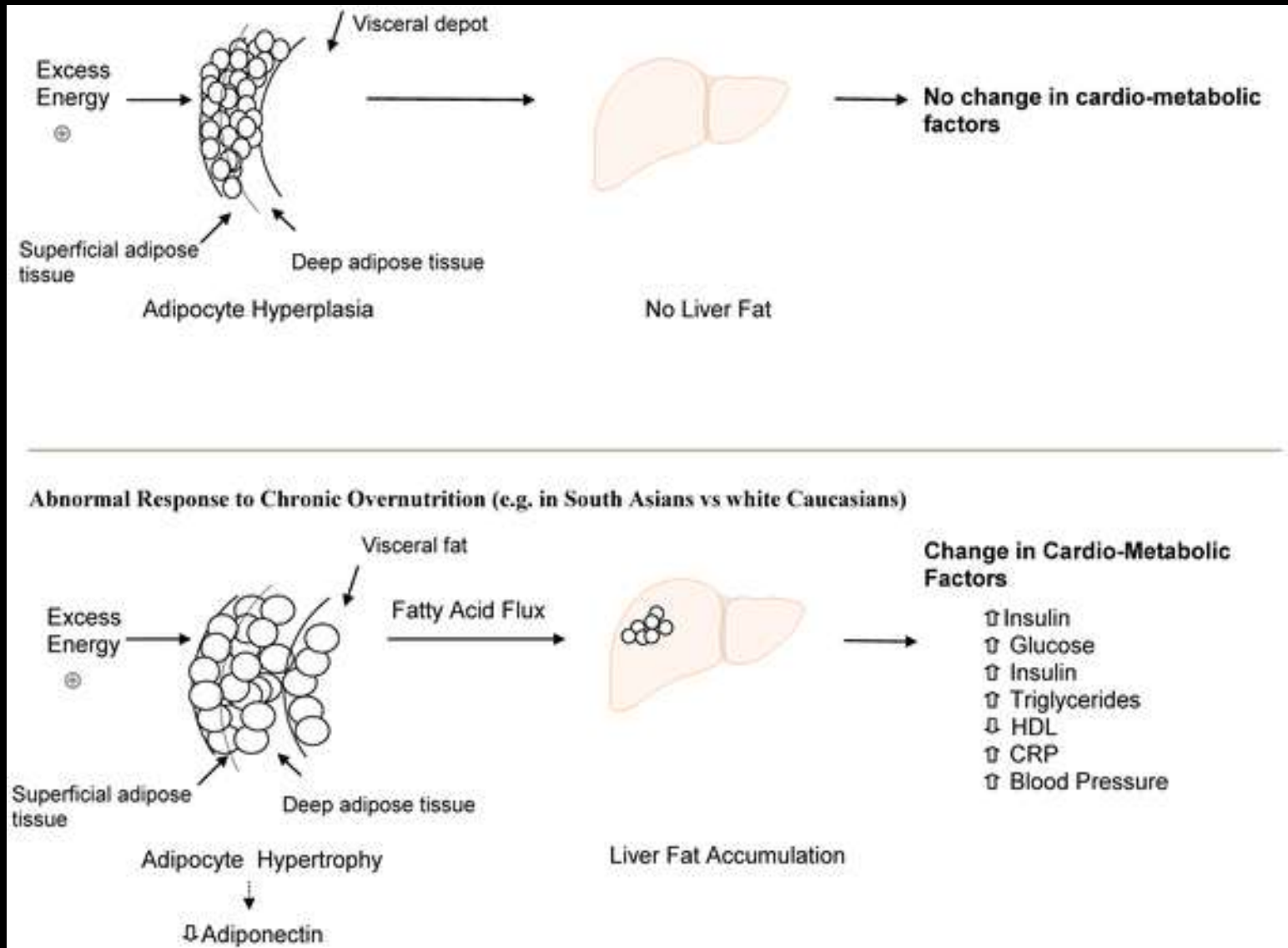
South Asians have larger adipocytes stuffed with triglycerides

Molecular SHARE – Liver Fat (%) by Ethnic and Sex Group



Between ethnicity $p=0.005$

South Asian Fat Overflow



Skinny-Fat People

Small Stature, but excess fat
including fatty liver

? Diet

? Genes



You are what you eat!



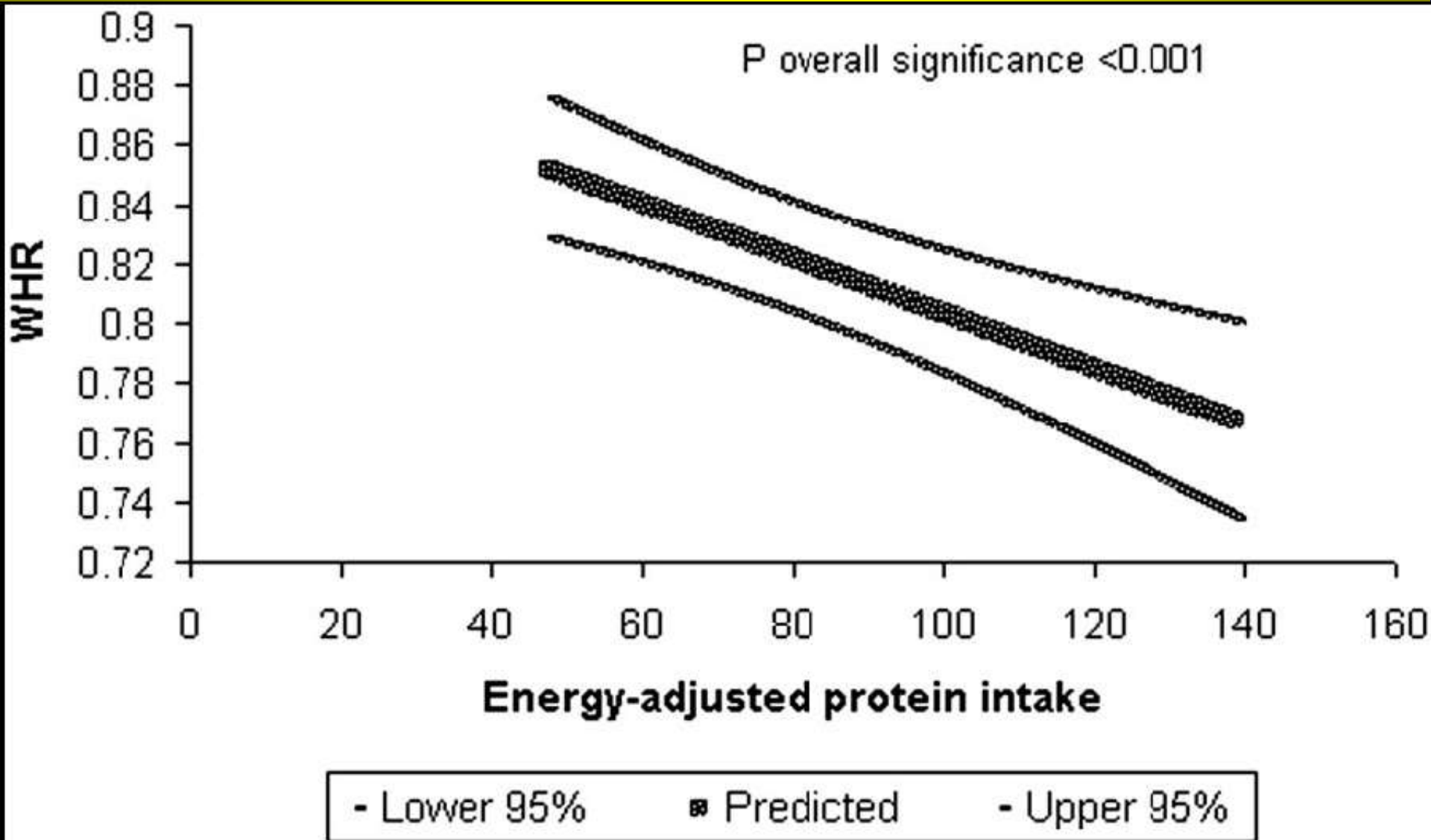
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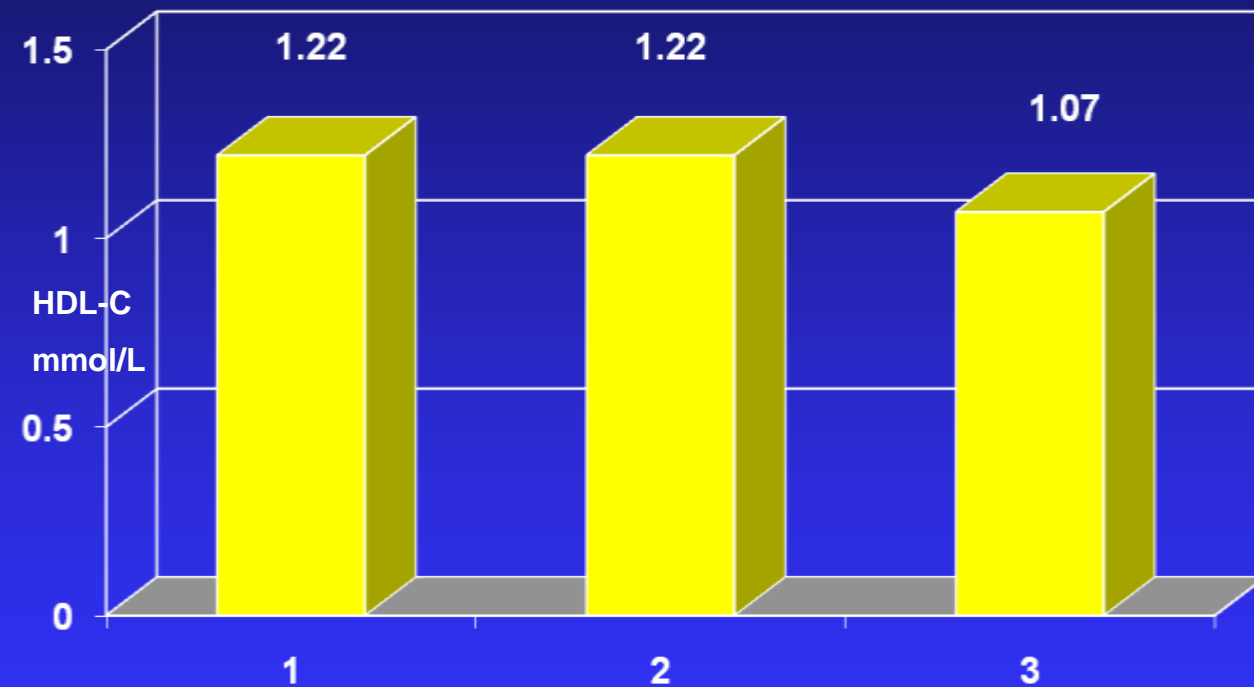
**↑Carbohydrate, ↓protein,
↑trans fats**

	South Asians	Chinese	Euro
N	173	167	185
Age	46.3	45.8	47.7
Calories/Day	1911	1898	2072
% Vegetarian	18.8	2.1	0.6
Carbohydrates g/day	298.8*	240.7	269.5
Protein g/day	70.1*	100.5*	78.0
Sugar g/day	11.2*	6.9	8.9
Trans Fats (g)	0.34	0.27	0.56
Saturated Fat g/day	19.6	17.3*	21.6

Protein Intake vs WHR



The effect of Carbohydrate intake on HDL-C



Tertile

CARBOHYDRATE INTAKE

*

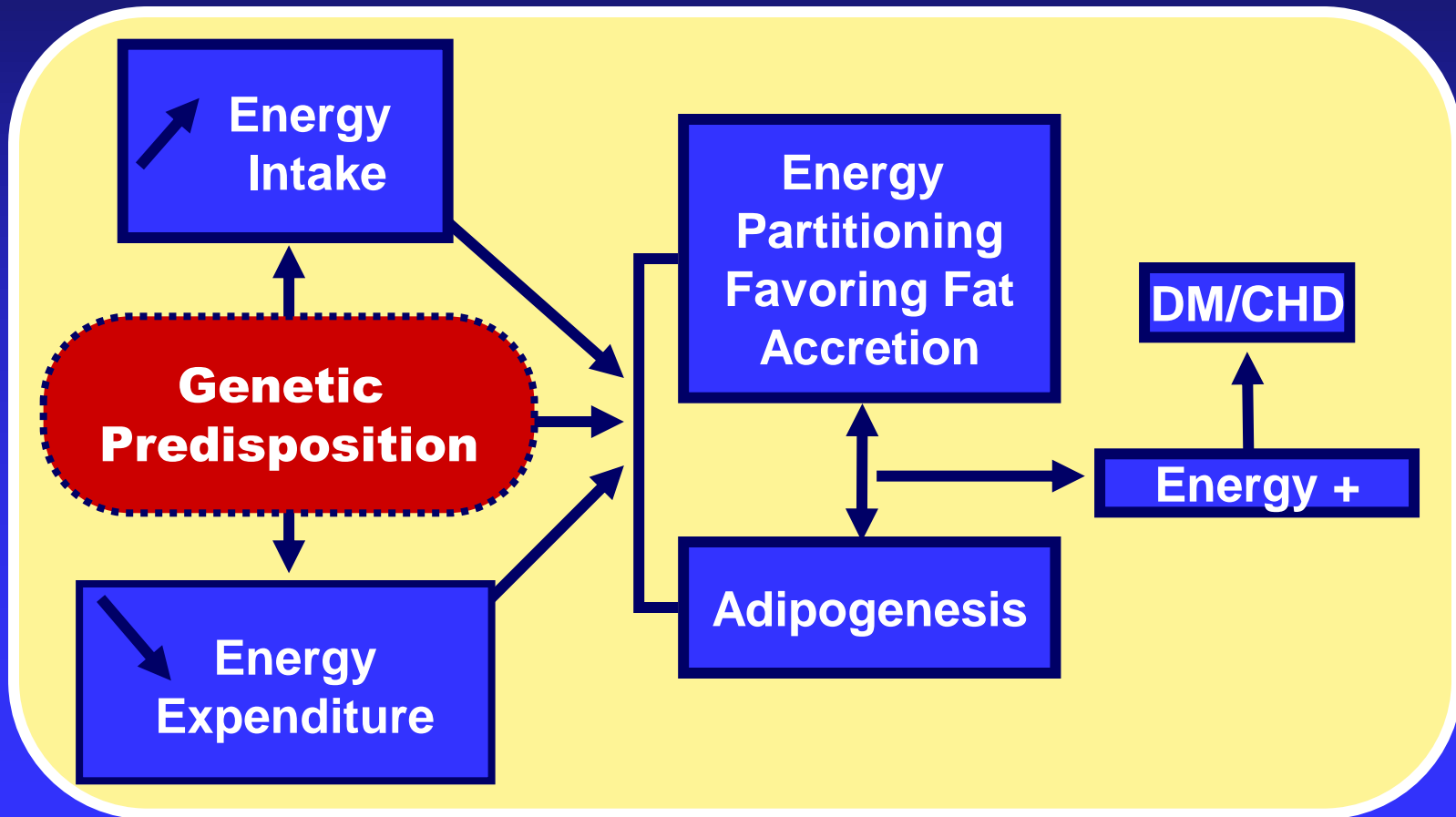
↓ 0.13 mmol/L
in HDL for every
100 g/d ↑ In
CHO

* P for trend
<0.001

* Adjusted for age, sex, ethnicity, physical activity, smoking, WHR, Etoh, total energy, protein, fiber, (excluded diabetes, any CVD)

Merchant et al J Nutr 2005

The search for Genes: Thrifty, Gluttonous, or Slothful... Energy Conservation



Early Origins Hypothesis

- Genetically Programmed to store excess energy in a way that we can quickly mobilize it during starvation and pregnancy
- i.e. insulin resistance provides glucose for the brain and fetus
- Maternal nutrition and low birth weight in Indian babies may predispose to an insulin resistant state and diabetes in adult life¹

¹ Fall C 2001

² Yajnik CS, 2003



START



South Asian biRth cohort



Peel Region, Ontario, Canada

Bangalore, India

Solur District, India



Why do South Asians develop Diabetes + Heart Disease?

- Diet: ↑ Carbo intake, ↑ Glycemic Load
- Genetics: Common SNPs associated with type 2 DM, fat transport, obesity
- Reduced subcutaneous storage capacity – overflow of fat into visceral depot and then liver + pancreas
- Various combinations of the above

If becoming energy+ is the problem

What can we do about it?

Advice: ↓ Carbohydrates and ↑ Activity

- Simple advice
- Difficult for individuals to maintain over time
- Food Addiction: Sweet, Salty, Fat
- Food as Stress Reliever
- “No-time” to be active – must drive, must work, must take care of others
- 1 lb weight gain per year

South Asian Exercise Class



Old



New



A multi-media based intervention aiming to provide culturally tailored health messaging and feedback to participants with the goal of reducing their cardiac risk score over a 6-month period.

<http://www.youtube.com/watch?v=SwZdUSmWBpo>

INTERHEART Modifiable Risk Score Report



Individual Participant IHRS

Participant ID: 99955
Participant Initials: JMM
Visit Date: 2011-09-13
Visit Number: 1

Lab Based Results

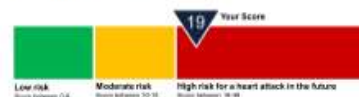
Risk Factor	Value	Score
Age & Sex:	You are a female, 64 years or younger	0
Apo B:A1 Ratio:	0.83	3
<i>Desirable Apo B:A1 Ratio: < 0.63</i>		
Smoking:	You are a non-smoker	0
Second Hand Smoke:	1 or more hours of exposure per week	2
Diabetes:	You have diabetes	6
Blood Pressure:	124 / 78	0
<i>Desirable Blood Pressure: 120/80 mmHg</i>		
Waist to Hip Ratio	Waist circumference: 96.60cm Hip circumference: 110.00cm WHR: 0.88	1
<i>Desirable Waist to Hip ratio: < 0.87</i>		
Psychosocial Factors		
General Stress	Several periods or permanent stress	3
Feeling sad or blue for 2 weeks or more in the past 12 months:	no	0
Diet		
Salty foods or snacks one or more times a day:	yes	1
Deep fried foods or snacks or fast foods 3 or more times a week:	yes	1
Vegetables one or more times a day:	yes	0
Fruit one or more times a day	yes	0
Meat and/or poultry 2 or more times a week	no	0
Physical Activity - Leisure time	Mainly sedentary or mild exercise	2

Your Score **19**

Your risk score indicates you are in the upper risk tertile (group) for developing heart disease. Please discuss these results with your physician.

Your Score Before:

Your Score After:



Genetic Risk Score Report

1 About this report

- This report outlines your future risk of suffering a heart attack. We estimated this based on your age, sex and changeable risk factors. These items were combined to create a personalized score, called the INTERHEART risk score, to estimate your risk of suffering a heart attack in the future.
- This report also outlines your genetic risk of having a heart attack in the future. It is based on a DNA test we performed from the blood sample you provided us. We are looking to see if you have a specific DNA marker (or allele) from one gene called 9p21, which is related to an increased heart attack risk. A person can have no risk alleles, one risk allele or two risk alleles. Your genetic risk is increased if you have either one or two of these markers present.

2 Your results

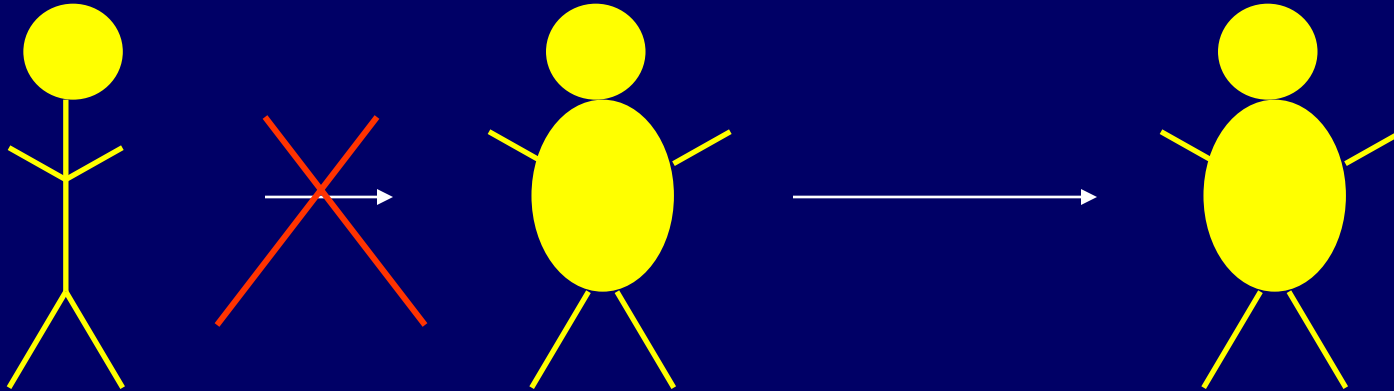
a) INTERHEART Risk Score Based on Age, Sex and Changeable Risk Factors:



b) Genetic Test:



Evolution of risk factors in South Asians



1. Weight gain → 2. pre-Diabetes → 3. Diabetes → 4. Heart Disease

- ↑ Activity
- ↓ Screen Time
- Begin in early adulthood

- Lipids
- Blood Pressure

5.? Some Cancer

Conclusions

- South Asians are a high risk group
- Extensive research has characterized their risk factors
- Using cardiac risk scoring and innovative technology to deliver health methods
- Attempt to change cardiac risk in primary prevention

Question 1- Answer

- What is the most common dyslipidemia in South Asians
- A: High LDL and low HDL cholesterol
- **B: High LDL, High triglycerides, and low HDL cholesterol**
- C: High HDL cholesterol
- D: High Triglycerides and low HDL cholesterol

Question 2: Answer

- 2) What is a better predictor of diabetes and CHD in S. Asians?
- A. Body Mass Index
- B. Waist Circumference
- **C. Waist to Hip Ratio**
- D. Percent Body Fat

Question 3- Answers

- When should a South Asian get their metabolic risk factors checked?
- A: In Hospital with their first MI
- **B. When abdominal obesity is apparent**
- C. For work or insurance purposes
- D. If they feel thirsty, polyuria and tired++

Question 4: Answer

- How best can we prevent T2DM in S. Asians?
- A: Have yearly blood glucose checked
- B: Become vegetarian
- C: Prevent weight gain by regular exercise and low carbohydrate intake
- D: Follow all of the advice our mothers give us