

INTERHEART: Aims

1. To evaluate the association (odds ratio) of risk factors for MI globally, and in each region; and among major ethnic groups in the world.
2. To quantify the impact of each risk factor alone and their combination on the population's risk (population attributable risk, PAR) overall and in each region, ethnic group, in males and females and in young and old.

Methods

Cases: First MI.

Controls: Matched to cases by age (+/-5 yr and sex) at each site

Data collected from 262 sites in 52 countries:

Questionnaire: demographics, lifestyle, health hx,
psychosocial, medications

Physical measures: height, weight, waist & hip circum,
blood pressure, heart rate

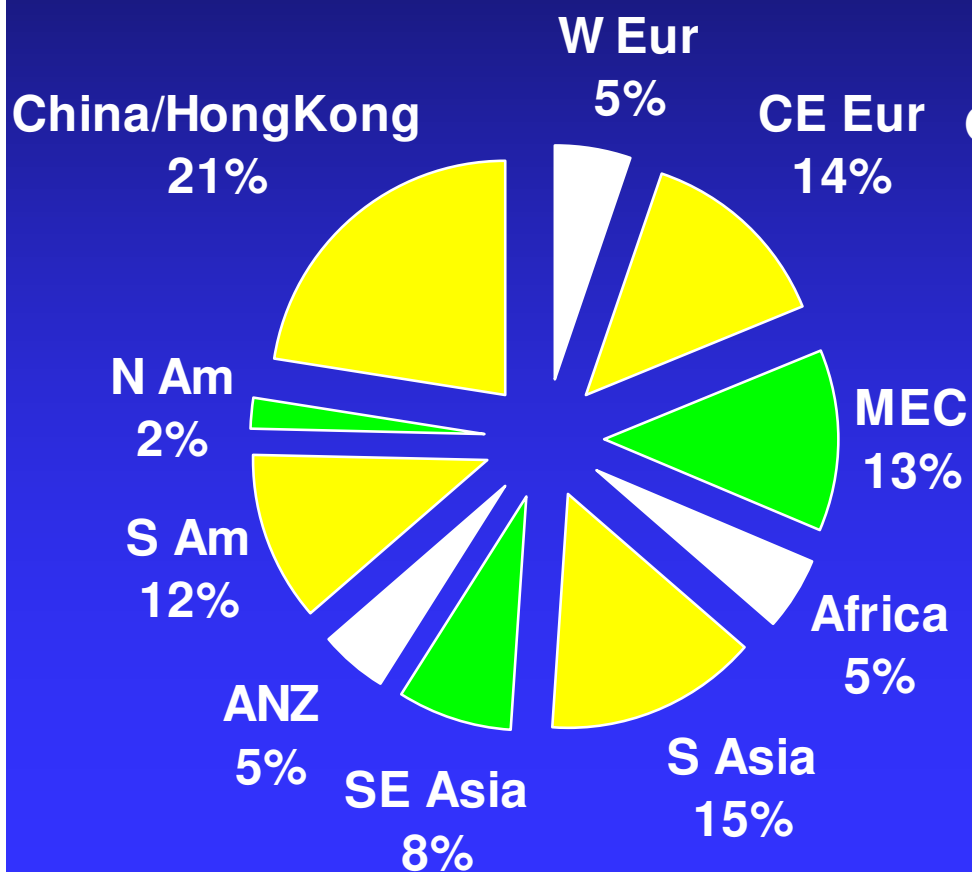
Blood sample: 20 ml

Statistical methods: OR and PAR both presented with 99% confidence intervals.
All analyses adjusted for age, sex and region.

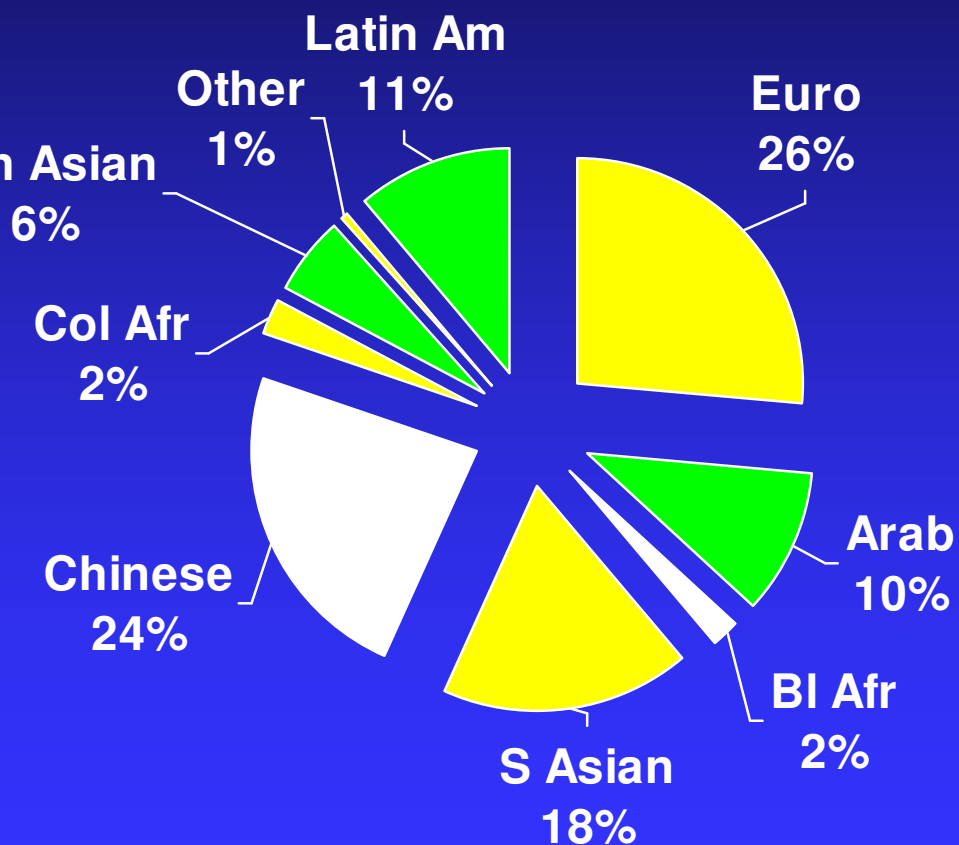
*Coordinated by the Population Health Research Institute,
McMaster University, Canada*

15,152 MI cases and 14,820 controls

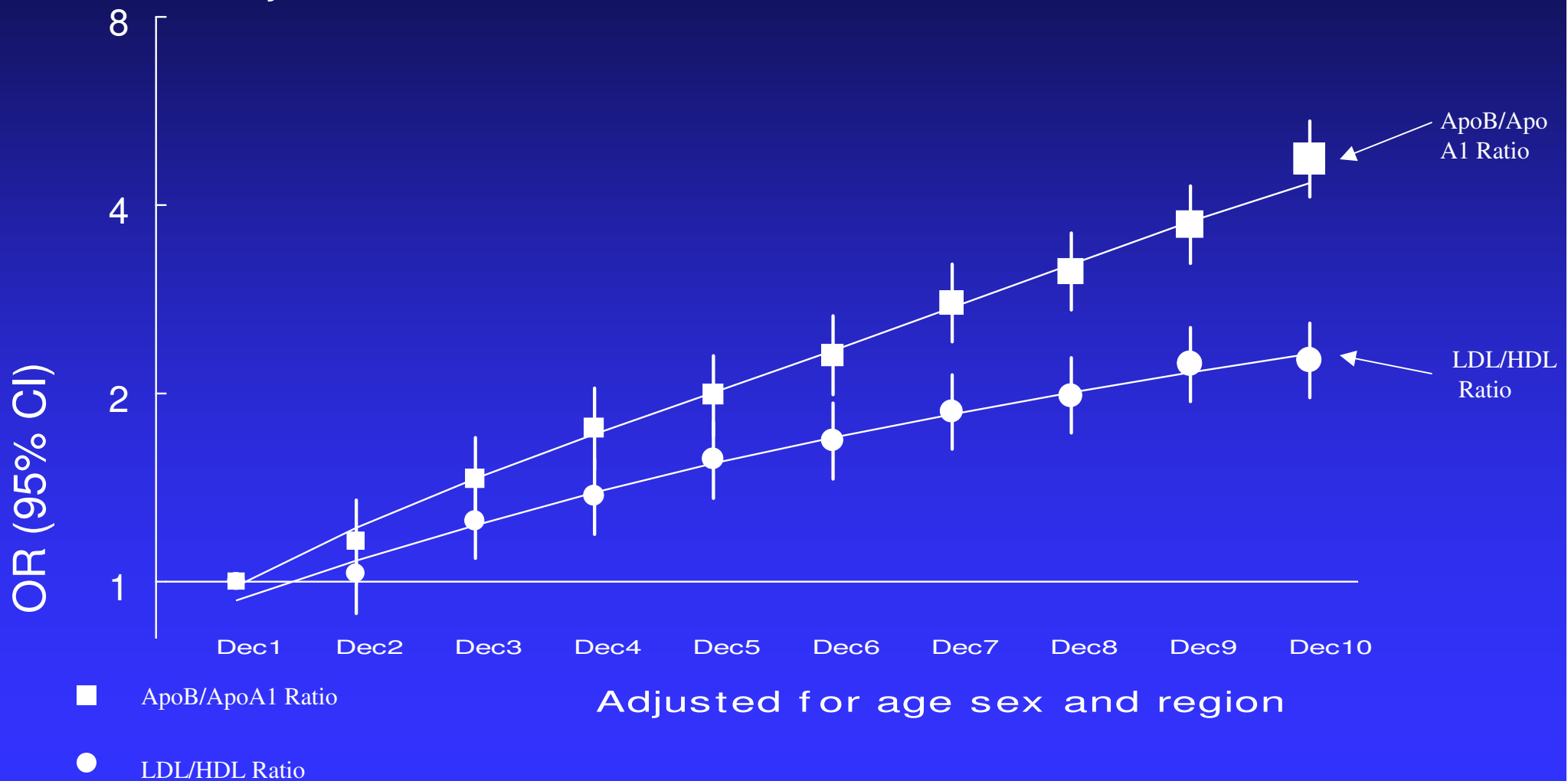
Distribution by region



Distribution by ethnicity

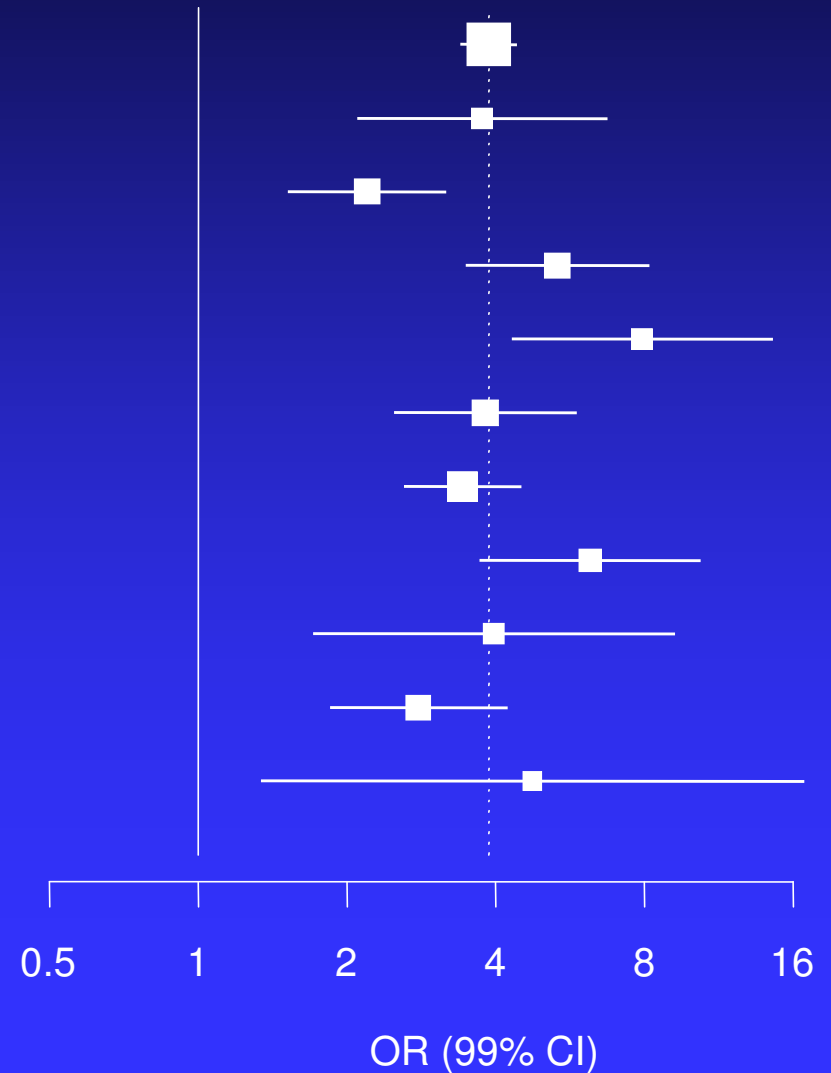


Odds ratios and 95% CIs for increasing Deciles of Blood Lipid Markers

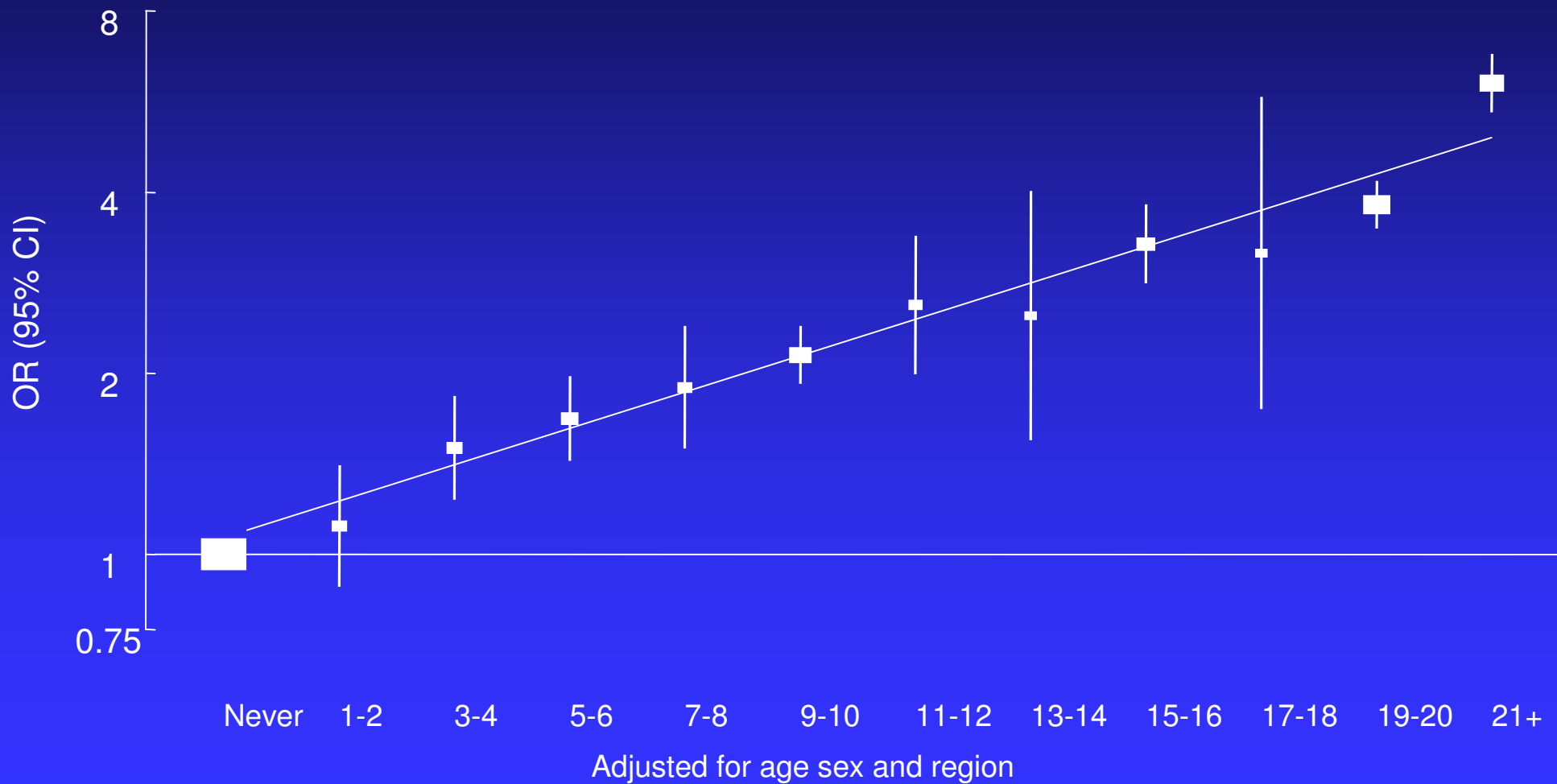


INTERHEART: ApoB/ApoA-1 ratio (top quintile vs lowest quintile) and MI

Region	N	Cont. %
Overall	21408	20.0
W Eur	1047	13.8
CE Eur	2618	20.3
MEC	3291	29.9
Afr	1037	18.0
S Asia	2820	27.7
China/HK	5400	7.3
SE Asia	1858	22.7
ANZ	487	13.8
S Am	2644	27.1
N Am	206	12.4

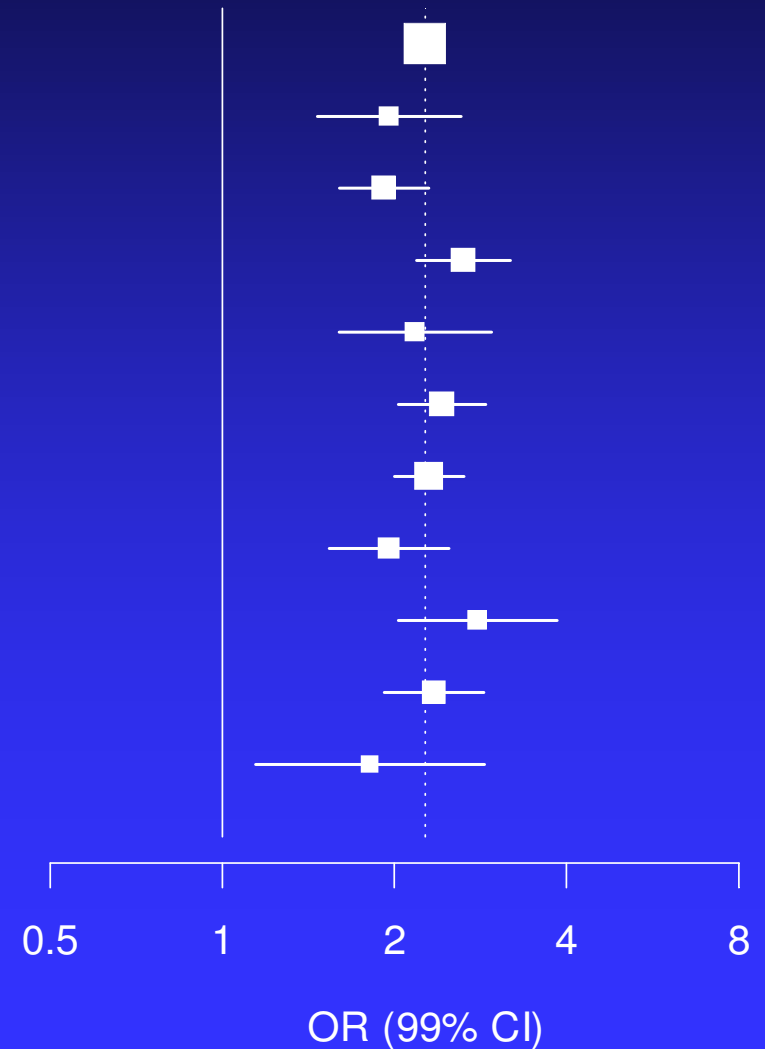


Low Levels of Smoking and MI

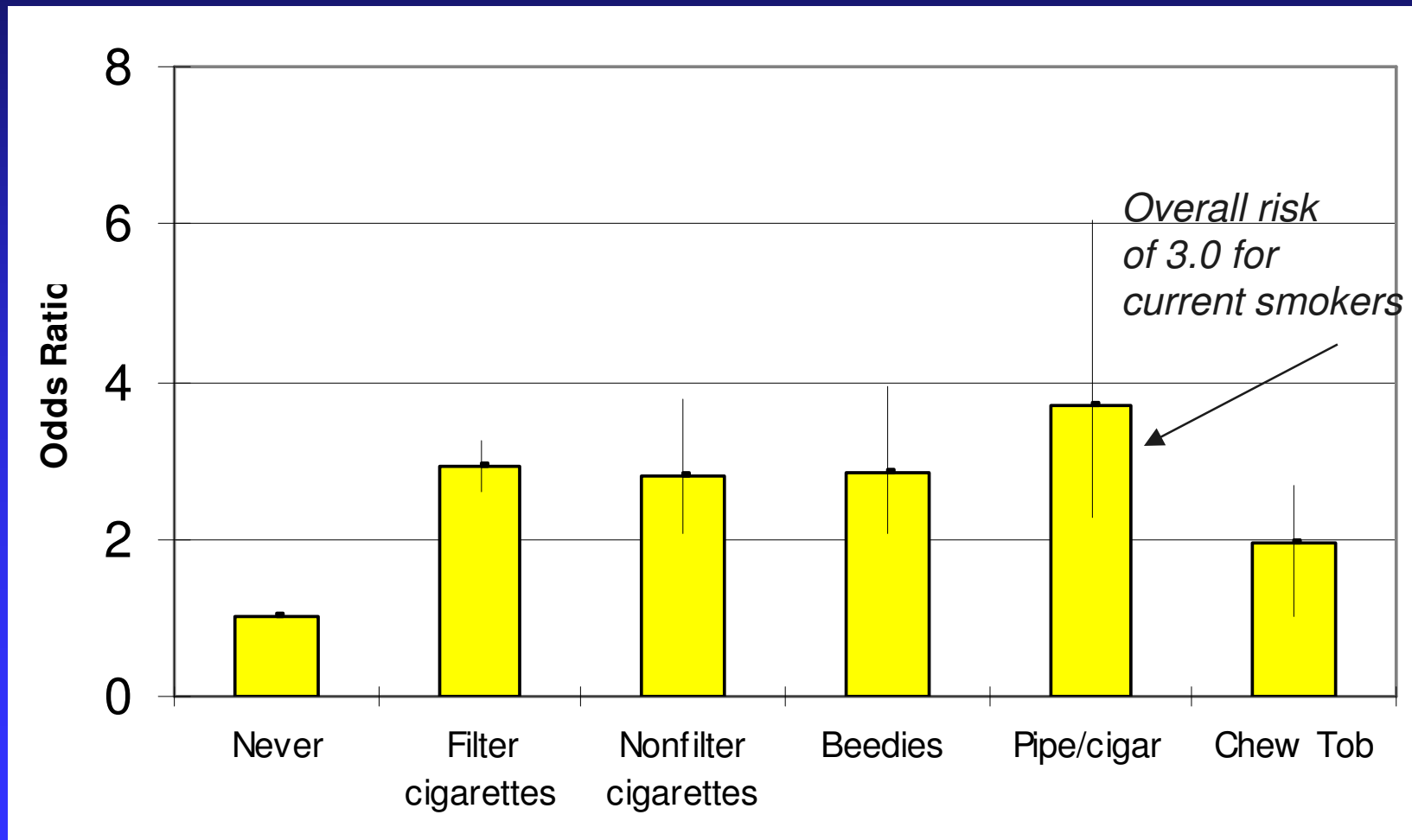


INTERHEART: Current or Former Smoking & MI

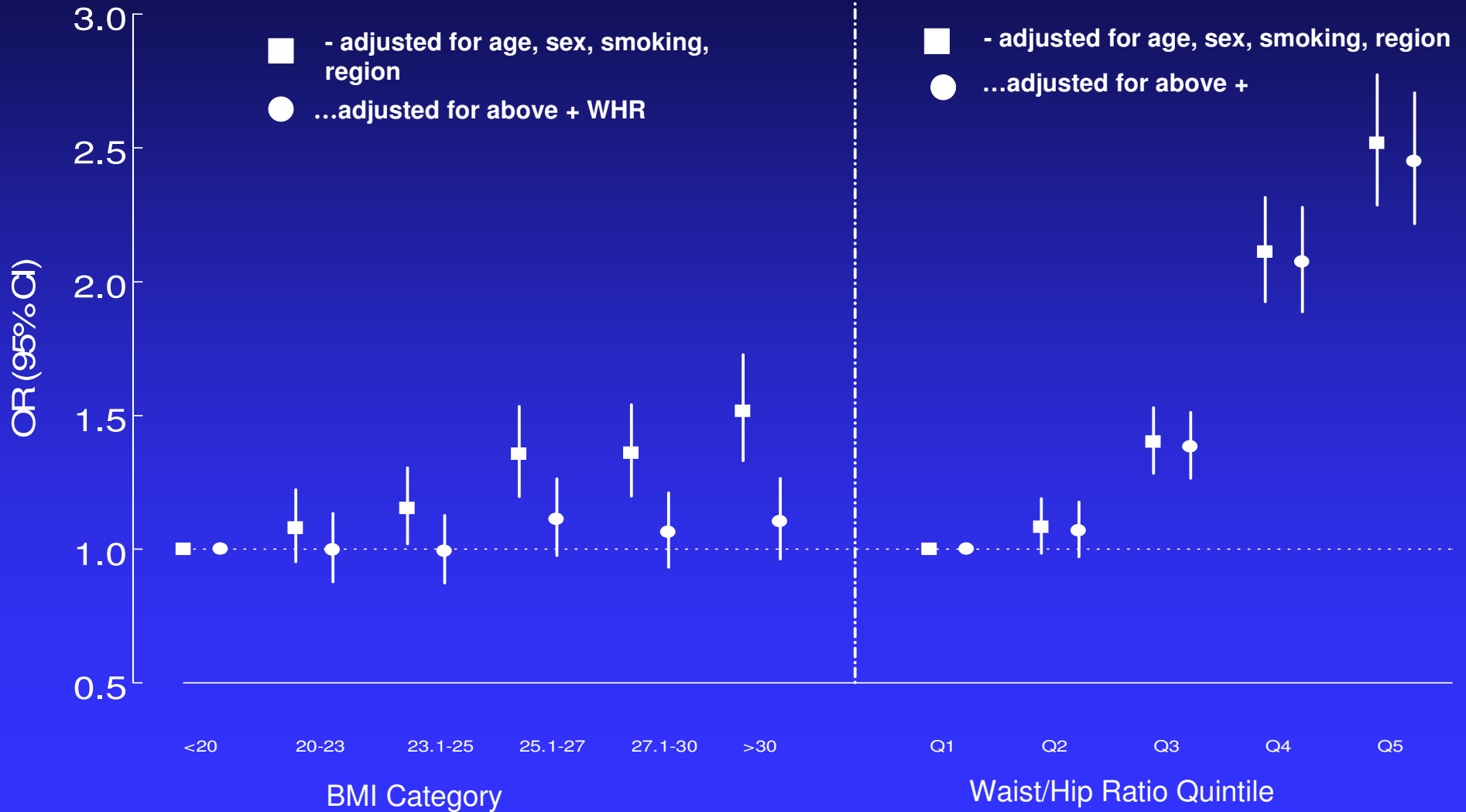
Region	N	Cont. %
Overall	26527	47.9
W Eur	1403	55.0
CE Eur	3624	54.2
MEC	3301	45.4
Afr	1339	53.8
S Asia	3706	41.0
China/HK	6062	42.7
SE Asia	2131	57.1
ANZ	1267	54.2
S Am	3068	48.9
N Am	626	64.6

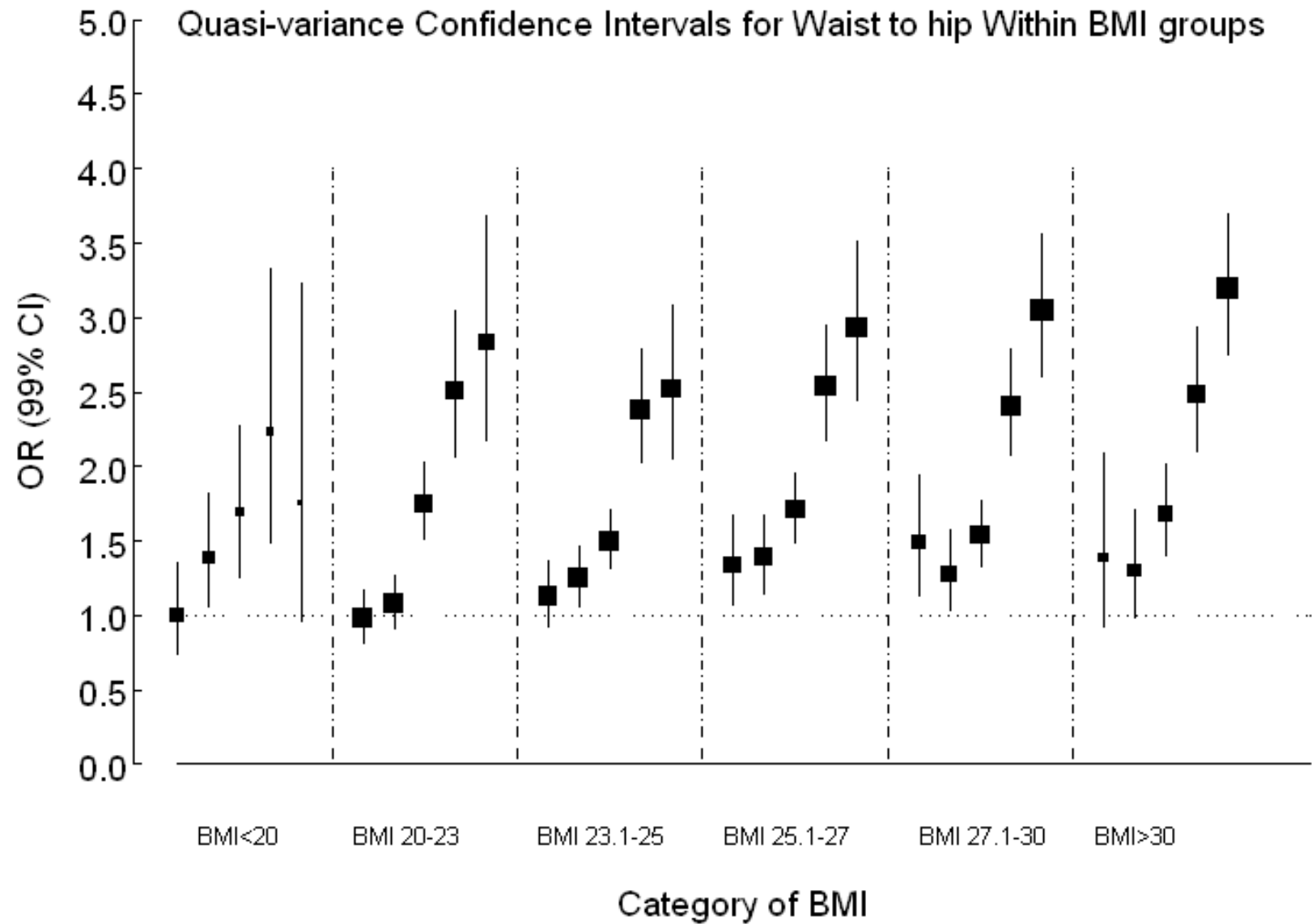


Excess risk of AMI associated with tobacco use by type of tobacco consumed (adjusted for age, sex region)



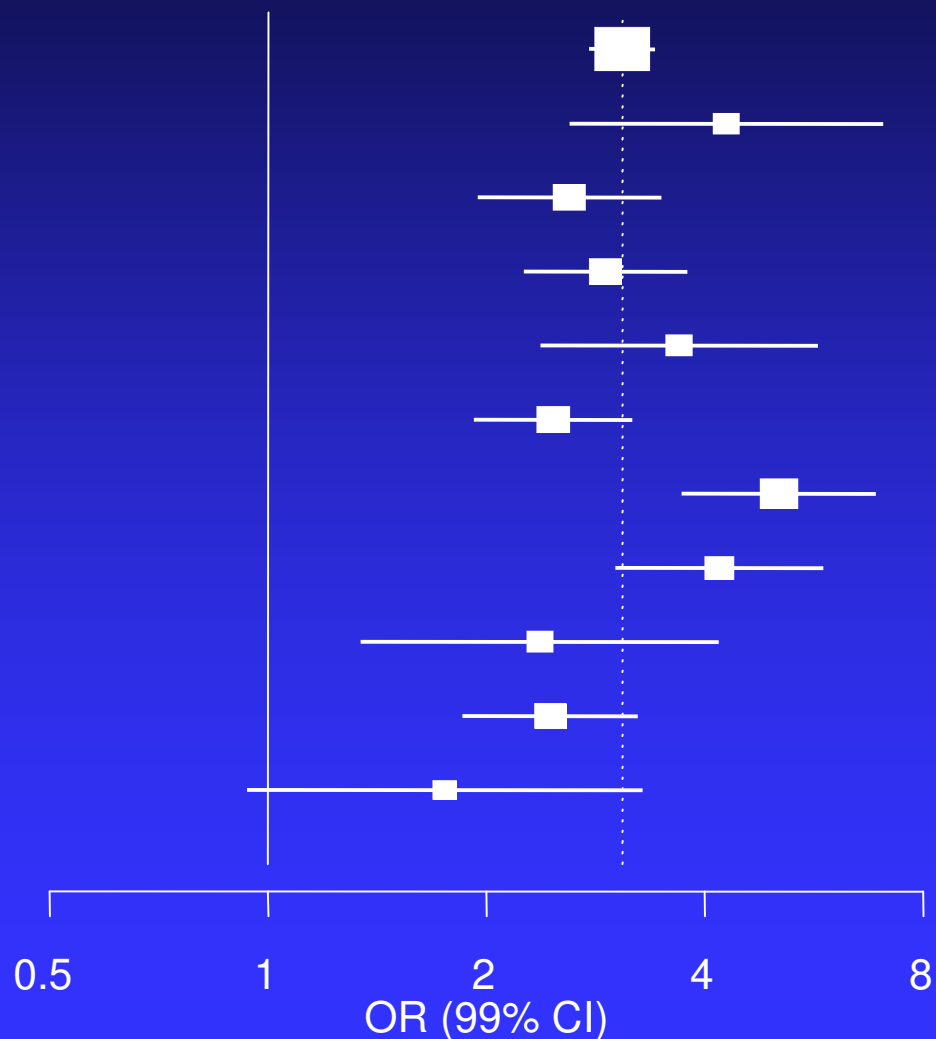
Association of BMI and WHR to AMI Risk





INTERHEART: Self-reported Diabetes and MI overall

Region	N	Cont.%
Overall	26903	7.6
W Eur	1422	4.2
CE Eur	3636	6.8
MEC	3401	11.6
Afr	1355	8.0
S Asia	3882	10.6
China/HK	6075	2.9
SE Asia	2140	9.2
ANZ	1269	4.8
S Am	3093	9.0
N Am	630	9.7

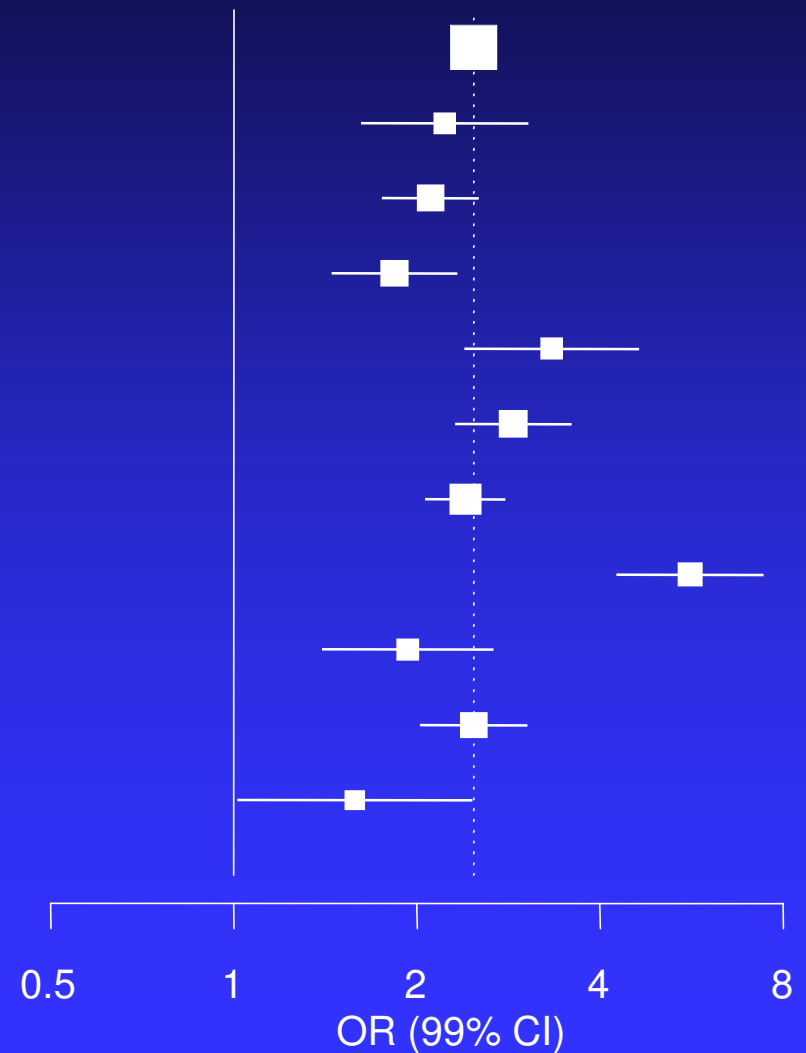


INTERHEART: Increased Risk of MI for 1% Rise in HbA1c

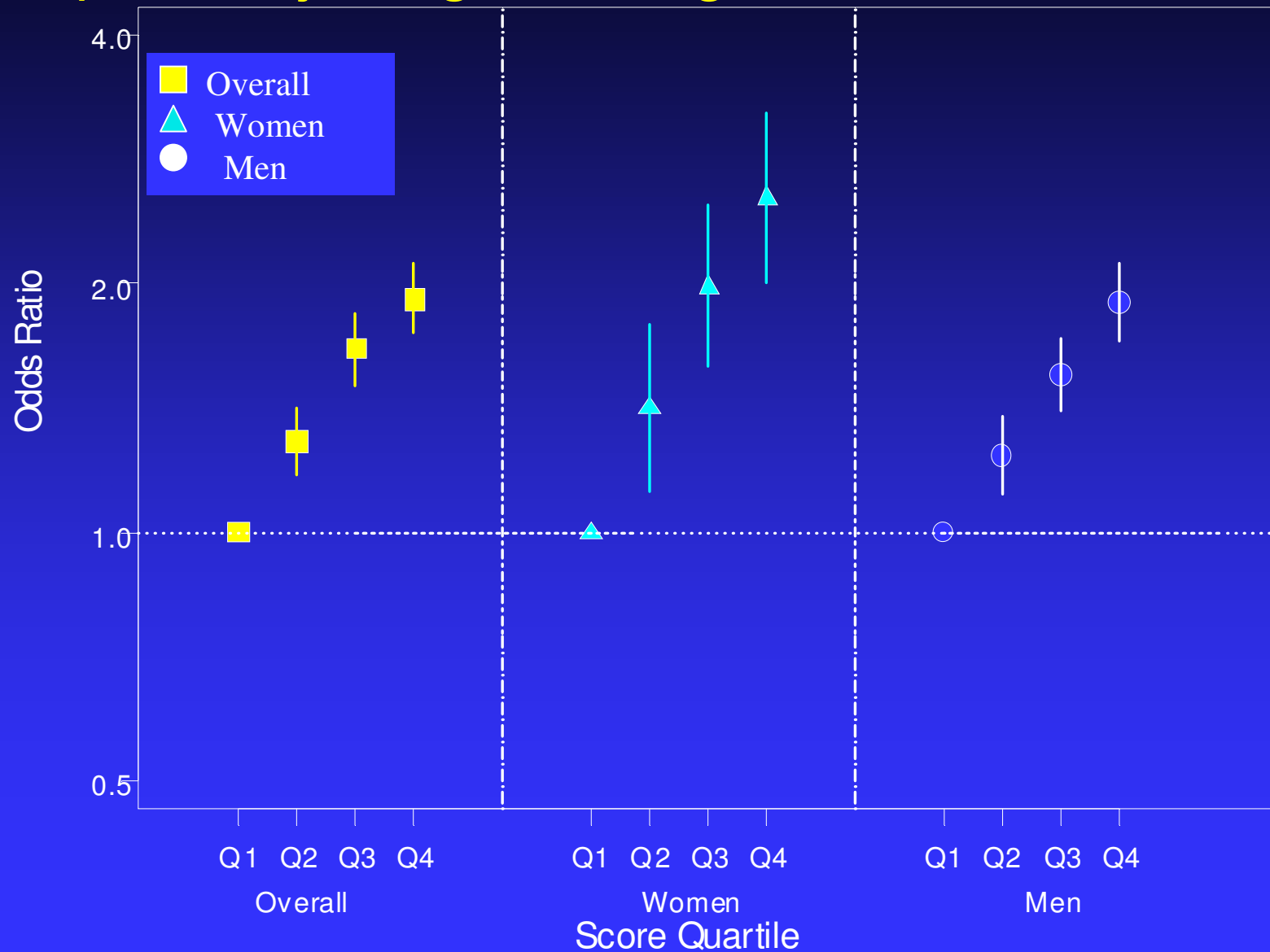
All Participants adjusted for:	OR	95% CI	P
Age, Sex, Region	1.40	(1.35, 1.45)	<0.0001
Age, Sex, Region, DM	1.25	(1.20, 1.30)	<0.0001
Age, Sex, Region, DM, WHR	1.23	(1.19, 1.28)	<0.0001
Age, Sex, All INTERHEART Risk Factors	1.19	(1.14, 1.24)	<0.0001

INTERHEART: Self-reported Hypertension and MI

Regions	N	Cont.%
	26916	22.3
	1425	16.4
	3636	32.7
	3404	20.2
	1355	21.6
	3881	13.8
	6075	21.1
	2141	15.3
	1269	22.0
	3100	27.7
	630	28.6

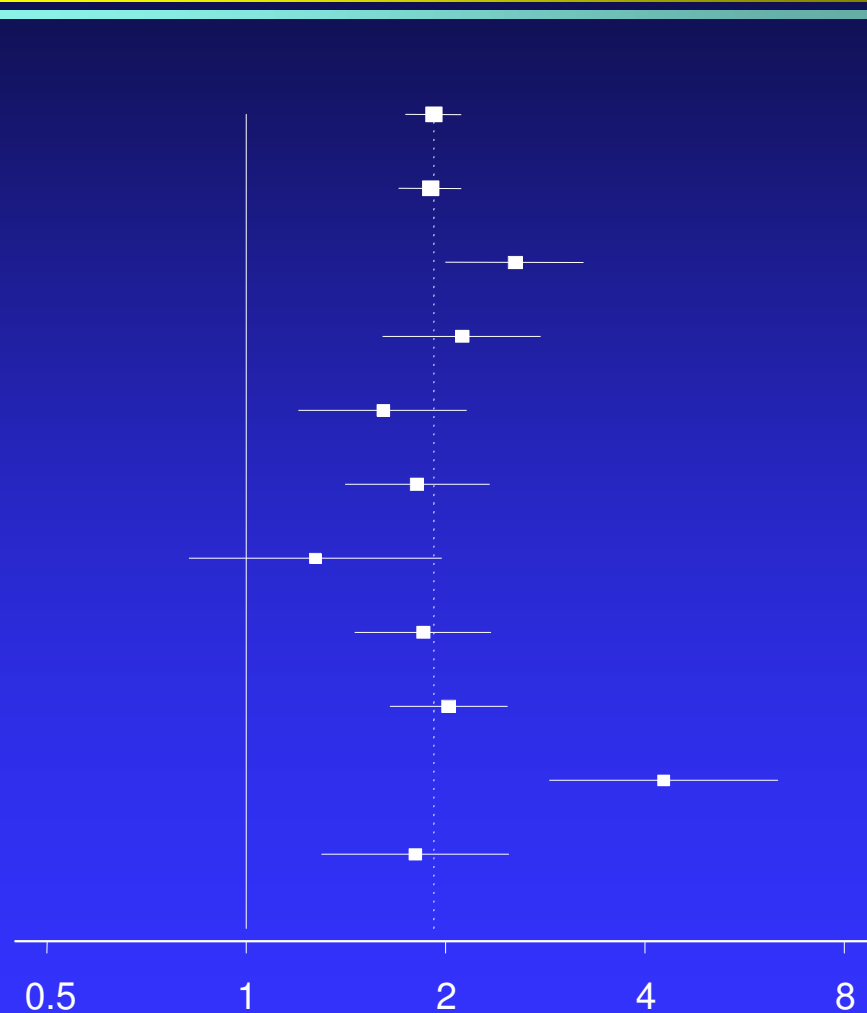


Risk of AMI associated with Quartiles of Dietary Risk Score (DRS) (95% CI) after adj for age, sex, region



Population Attributable Risk and Odds Ratios for AMI associated with Dietary Risk Score

	PAR	OR Q4 vs Q1
Overall ^a	0.30 (0.26-0.35)	1.92 (1.74-2.11)
Male ^b	0.28 (0.23-0.33)	1.90 (1.70-2.11)
Female ^b	0.39 (0.30-0.49)	2.55 (2.00-3.23)
N. America, W. Europe and Australia ^c	0.30 (0.17-0.42)	2.12 (1.61-2.78)
Central Europe ^c	0.31 (0.18-0.44)	1.61 (1.20-2.15)
Middle East ^c	0.28 (0.17-0.40)	1.81 (1.41-2.33)
Africa ^c	0.10 (-0.14-0.35)	1.27 (0.82-1.97)
South Asia ^c	0.29 (0.18-0.40)	1.85 (1.46-2.34)
China ^c	0.18 (0.07-0.29)	2.02 (1.65-2.48)
Southeast Asia ^c	0.58 (0.45-0.71)	4.27 (2.87-6.35)
S. America ^c	0.15 (-0.03-0.32)	1.80 (1.30-2.49)



^a adjusted for age, sex and regions

^b adjusted for age and regions

^c Adjusted for age and sex

OR (95% CI)

Iqbal et al. Unpublished

Association of leisure time related physical activity with AMI

Categories of physical activity	OR Model ^a	OR Model ^b	OR Model ^c
Mild to moderate activity vs. mainly sedentary	0.82 (0.77-0.87)	0.84 (0.76-0.92)	0.86 (0.78-0.96)
Strenuous activity vs. mainly sedentary	0.66 (0.61-0.71)	0.73 (0.65-0.83)	0.80 (0.70-0.91)

a Model adjusted for age and sex

b Model adjusted for age, sex, region, smoking status, alcohol, household income, BMI

c Model adjusted for age, BMI, sex, region, smoking status, alcohol intake, household income, education, subject hypertension, subject diabetes, psychosocial factors, fruit intake, vegetable intake

Association (OR) of ownership status and risk of AMI

Ownership status	OR Model ^a	OR Model ^b
<i>Car</i>	1.30 (1.19-1.42)	1.24 (1.11-1.38)
Bicycle	1.02 (0.95-1.11)	1.01 (0.92-1.12)
Computer	1.00 (0.91-1.10)	1.02 (0.91-1.15)
<i>TV</i>	1.17 (1.00-1.36)	1.17 (0.97-1.41)
Radio	0.96 (0.87-1.08)	1.01 (0.88-1.17)
Motorbike	0.97 (0.87-1.07)	0.98 (0.87-1.11)

Model a: adjusted for age, BMI, sex, region, smoking status, alcohol intake, household income, education, hypertension, diabetes, psychosocial factors, fruit intake, vegetable intake

Model b: Model a + overall physical activity

Association (OR) of ownership status and risk of AMI

Ownership status	OR Model ^a	OR Model ^b
Car and TV	1.47 (1.18-1.44)	1.41 (1.07-1.87)

Results were consistent across regions of the world and in young/old

Risk of AMI associated with Risk Factors in the Overall Population

Risk factor	% Cont	% Cases	PAR 1 (99% CI)	PAR 2 (99% CI)
ApoB/ApoA-1 (5 v 1)	20.0	33.5	54.1 (49.6, 58.6)	49.2 (43.8, 54.5)
Curr smoking	26.8	45.2	36.4 (33.9, 39.0)	35.7 (32.5, 39.1)
Diabetes	7.5	18.5	12.3 (11.2, 13.5)	9.9 (8.5, 11.5)
Hypertension	21.9	39.0	23.4 (21.7, 25.1)	17.9 (15.7, 20.4)
Abd Obesity (3 v 1)	33.3	46.3	33.7 (30.2, 37.4)	20.1 (15.3, 26.0)
Psychosocial	-	-	28.8 (22.6, 35.8)	32.5 (25.1, 40.8)
Veg & fruits daily	42.4	35.8	12.9 (10.0, 16.6)	13.7 (9.9, 18.6)
Exercise	19.3	14.3	25.5 (20.1, 31.8)	12.2 (5.5, 25.1)
Alcohol	24.5	24.0	13.9 (9.3, 20.2)	6.7 (2.0, 20.2)
Combined	-	-	90.4 (88.1, 92.4)	90.4 (88.1, 92.4)

Risk Factor Impact by Age

	Odds Ratio		PAR	
	Young	Old	Young	Old
Smoking	3.33	2.44*	40.7	33.1
Fruit/Veg	0.69	0.72	16.9	11.9
Exercise	0.95	0.79	7.5	13.4
Alcohol	1.00	0.85	-4.1	11.1
Hypertension	2.24	1.72*	19.2	17.0
Diabetes	2.96	2.05*	12.4	8.6
Abd Obesity	1.79	1.50	24.8	18.1
All Psych	2.87	2.43	43.5	25.2
ApoB/ApoA-1	4.35	2.50*	58.9	43.6
All 9 RF	216.47	81.99*	93.8	87.9

P for interactions: *p<0.001

**Why do South Asians have a
higher risk of AMI?**

INTERHEART: Mean Age of First MI in S. Asia v Other Countries

	Years	% < 40 yrs
Other Countries	58.8	5.6%
South Asia	53.0	8.9%
India	53.0	11.7%
Pakistan	53.3	8.9%
S. Lanka	57.7	5.9%
Bangladesh	51.9	10.5%
Nepal	58.9	3.7%

Joshi (INTERHEART) JAMA 2007

Prevalence of Risk Factors <60 yrs in S. Asia v Other Countries (1)

	S. Asia	Other Countries
<u>ApoB/ApoA1*</u>		
<40	5.2%	2.4%
40-49	13.8%	7.1%
50-59	13.8%	9.0%
<u>Diabetes</u>		
<40	0.2%	0.1%
40-49	2.4%	0.9%
50-59	3.8%	2.1%
<u>Hi WHR*</u>		
<40	2.9%	1.6%
40-49	9.6%	6.2%
50-59	11.3%	8.9%

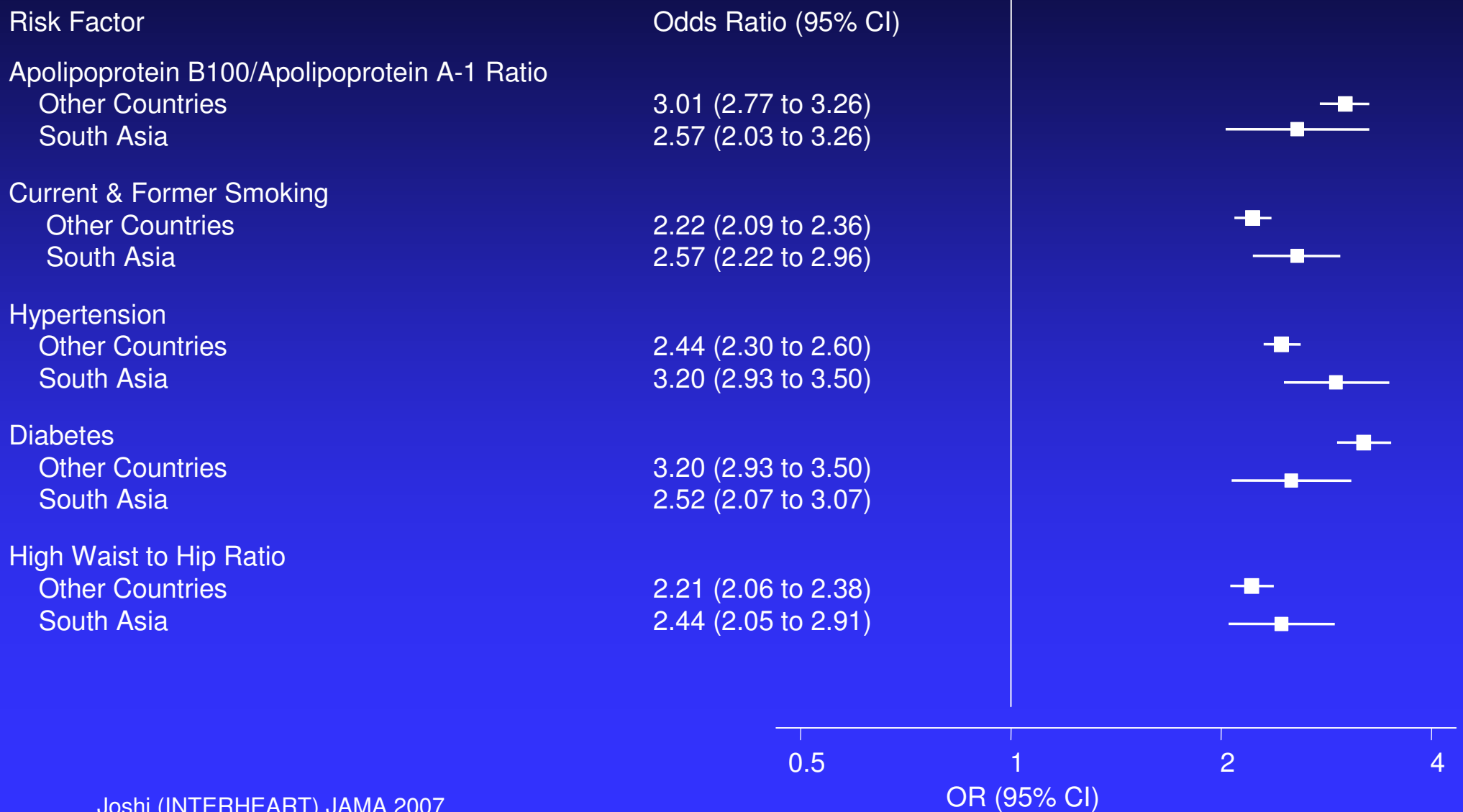
*Top tertile of global distribution

Joshi (INTERHEART) JAMA 2007

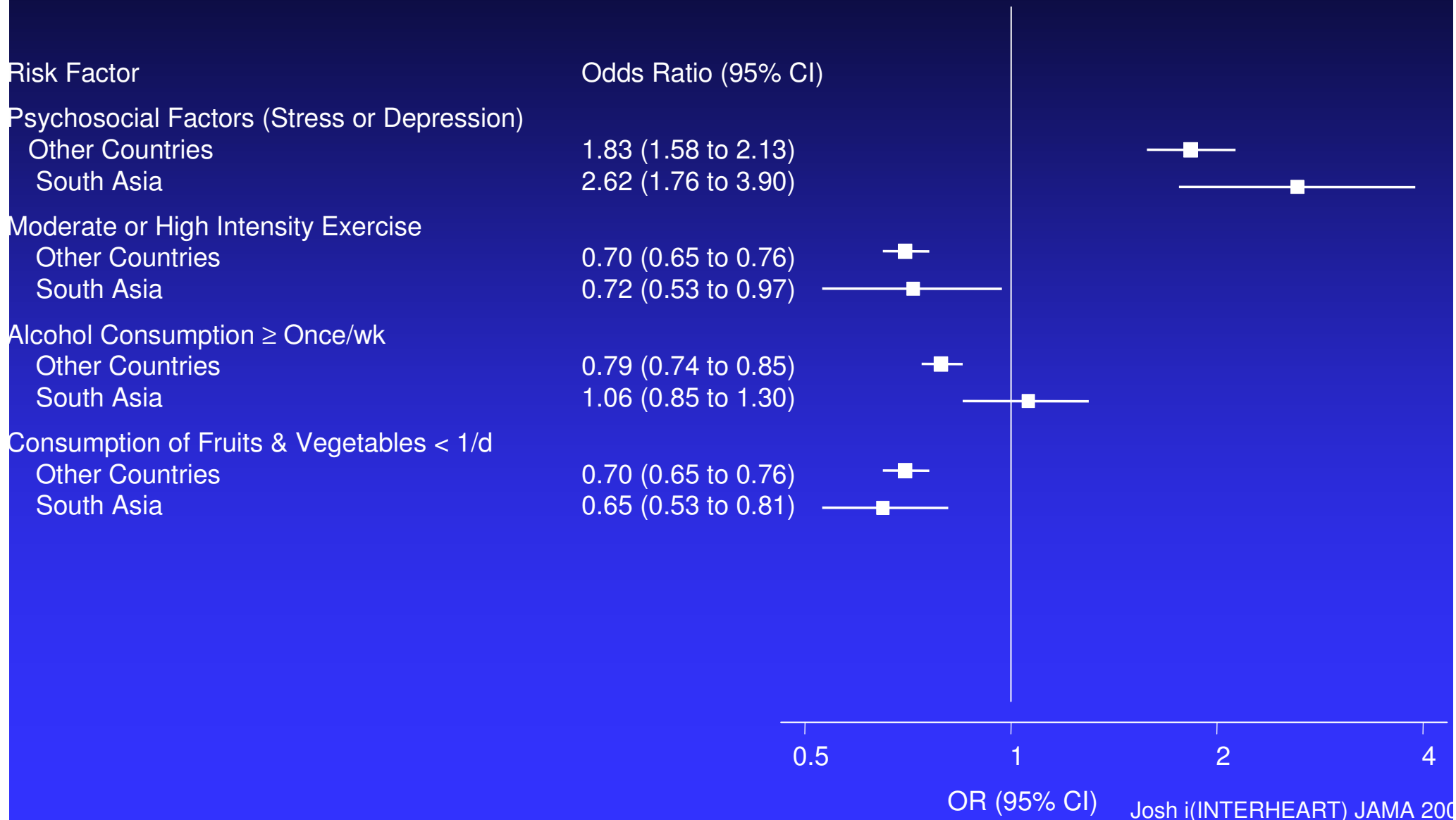
Prevalence of Risk Factors <60 yrs in S. Asia v Other Countries (Controls only) (2)

	S. Asia	Other Countries
<u>Mod/Intense exercise</u>		
<40	0.7%	1.4%
40-49	1.9%	4.5%
50-59	1.9%	5.7%
<u>Alcohol \geq 1/wk</u>		
<40	1.7%	1.9%
40-49	3.8%	6.1%
50-59	3.6%	7.9%
<u>Fr/veg >1/day</u>		
<40	2.6%	2.6%
40-49	8.5%	8.6%
50-59	7.4%	12.1%
\geq 60	8.0%	21.8%

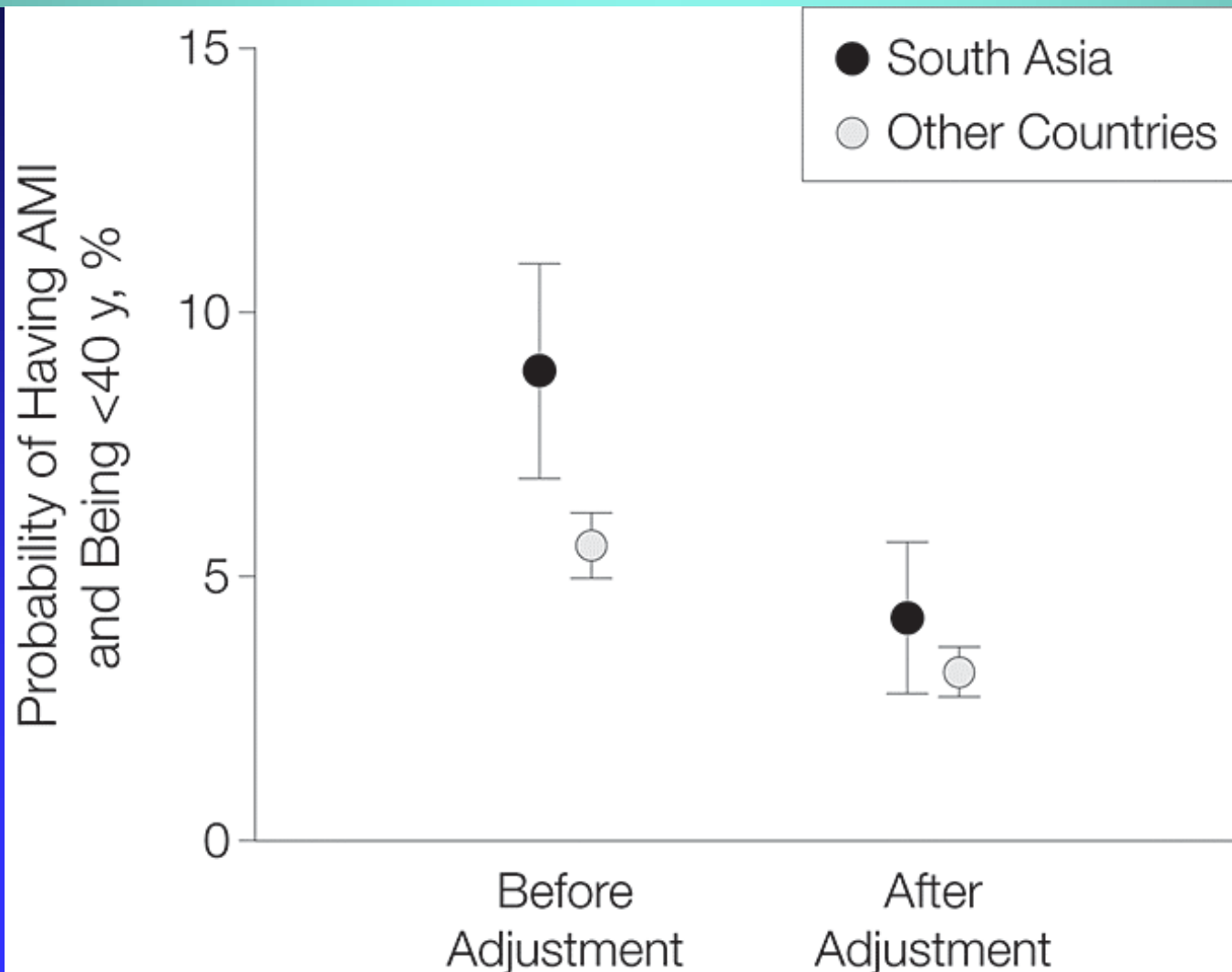
Risk Factors Associated with AMI in S. Asians Compared with Other Participants in the INTERHEART Study



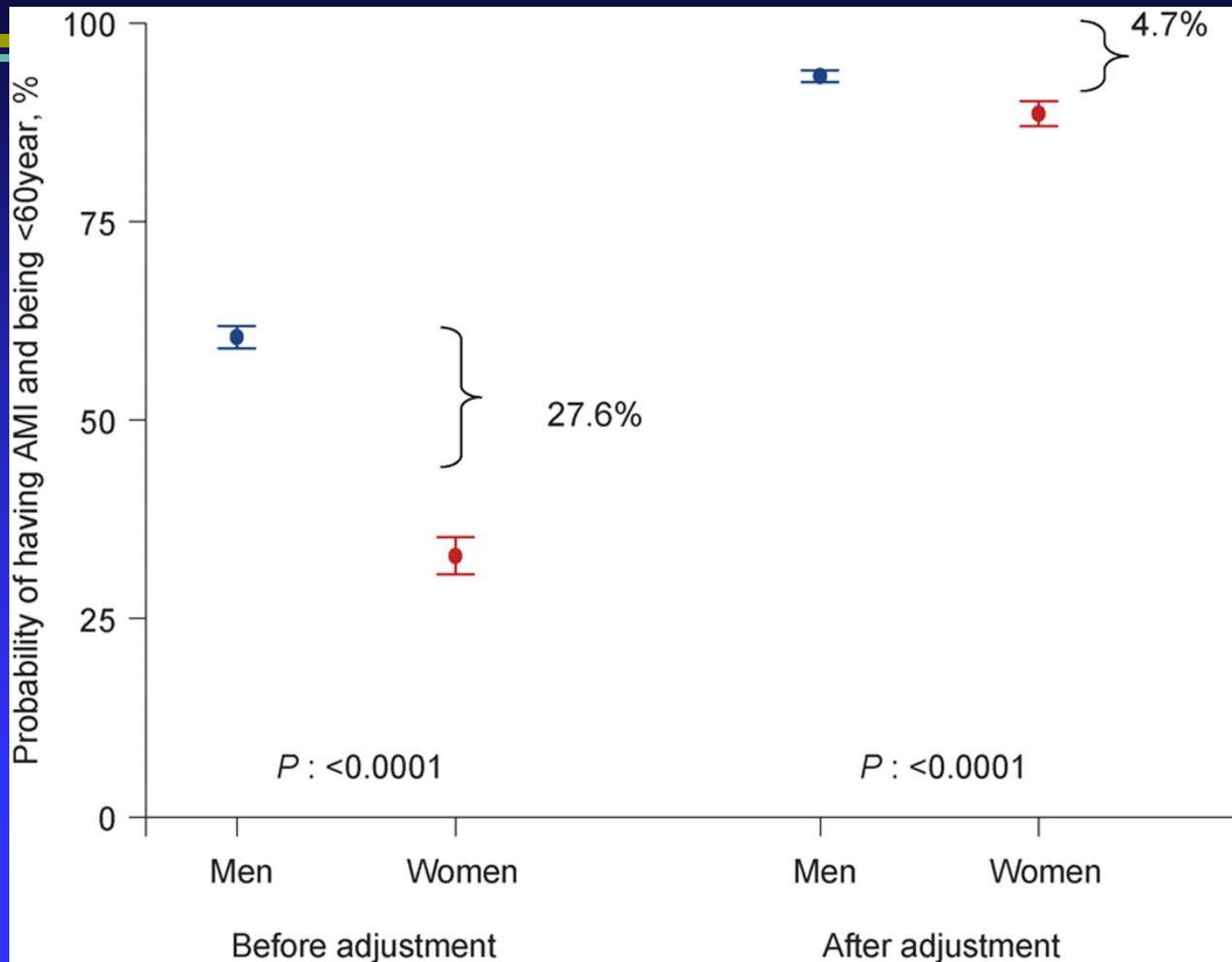
Risk Factors Associated with AMI in S. Asians Compared with Other Participants in the INTERHEART Study



Predicted Probability of Acute MI at a Younger Age in S. Asians Compared with Individuals from Other Countries



Differences in Predicted Probability of Infarction Cases <60 years comparing Men and Women



Genetic Variants Associated with Acute Myocardial Infarction Risk in Five Ethnic Groups: The INTERHEART Genetics Study

S. Anand, C. Xie, A. Montpetit, D. Serre,
B. Keavney, H. Cordell, M. McQueen,
S. Yusuf, T. Hudson, J. Engert
McMaster, McGill, Newcastle Universities

STAGED APPROACH OF SNPs RELATED TO MI

Interm. Phenotype	Number of SNPs	P cutoff	SNPs to Stage 2	Associated with MI
ApoB/A	669	0.00007	11	3
Diabetes	189	0.0002	0	
Hyperten.	164	0.0003	0	
Abdo Obesity	212	0.0002	0	
Smoking	43	0.001	0	
Exercise	17	0.0029		
Fruit and Vegetable	1	0.048	1	
Alcohol	13	0.0036	2	
Depressn	23	0.0022	0	
TOTAL	941		14	3*

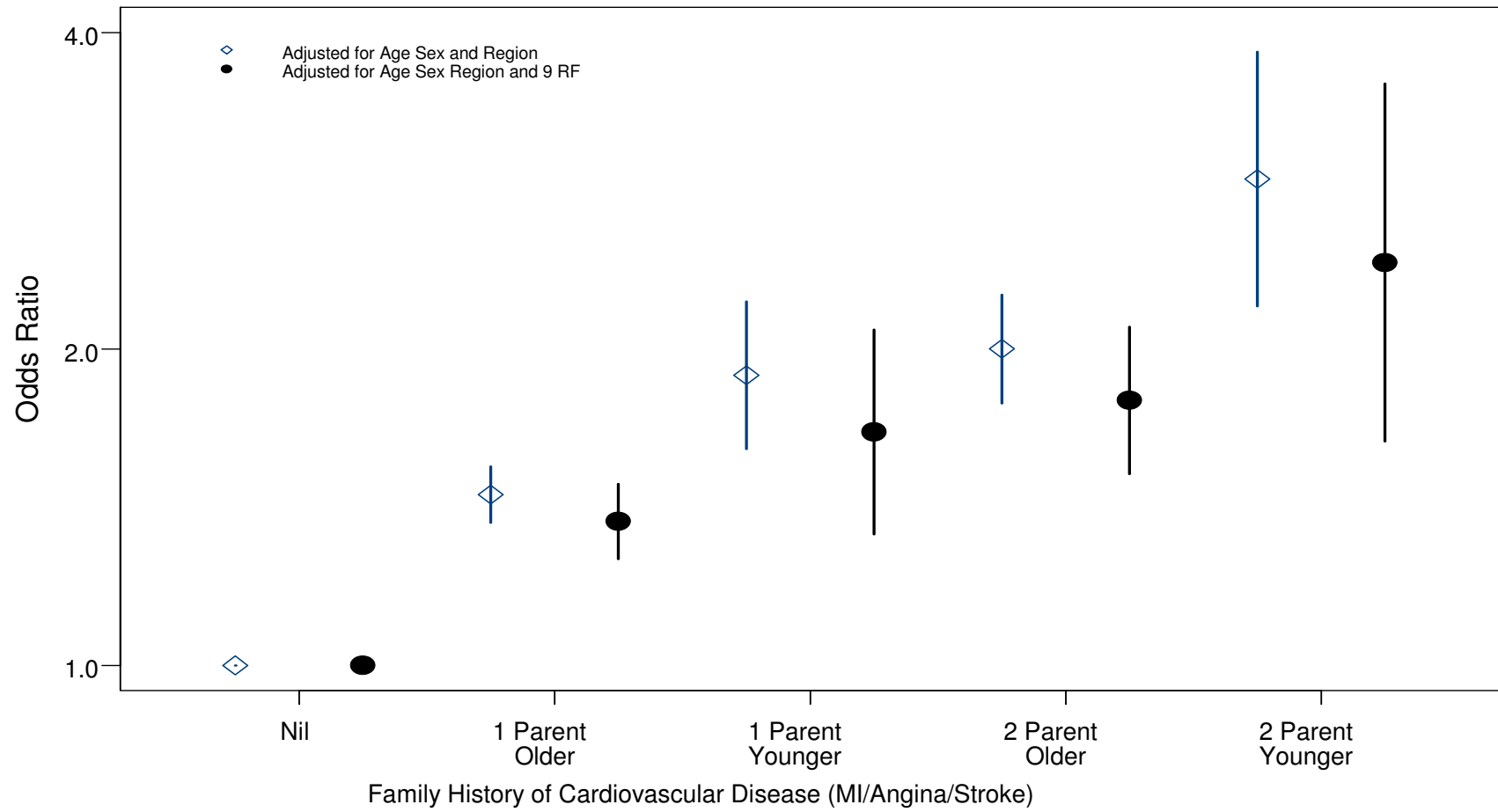
Adjusted for age, sex, ethnicity

Do the 3 SNPs Add to the Total PAR Predicted by the 9 Risk Factors?

- The PAR of the nine INTERHEART risk factors for MI = 89.6 (95% CI: 86.4 - 92.2)
- The PAR increased to 91.2 (95% CI: 88.3- 93.8) with the addition of the LDLR SNP rs1433099

**Why does family history of CVD
increase the risk of MI?**

Family History of CVD and Risk of MI



Risk of MI Associated with Family History of CVD and Risk Factors Adjusted for Genotype Score and 9 INTERHEART Risk Factors

	OR – age/sex/region adjusted	OR – age/sex/region/ genotype score adjusted	OR – age/sex/region/9 INTERHEART risk factors	OR – age/sex/region, all 9 RFs and genotype score adjusted
<u>Family History of MI</u>				
Mother	1.75 (1.46-2.09)	1.74 (1.45-2.08)	1.69 (1.38-2.09)	1.68 (1.36-2.07)
Father	1.60 (1.39-1.84)	1.62 (1.40-1.86)	1.54 (1.31-1.81)	1.56 (1.32-1.84)
Mother or Father	1.64 (1.45-1.85)	1.65 (1.46-1.86)	1.60 (1.39-1.84)	1.60 (1.39-1.85)

Chow et al. Unpublished

INTERHEART: Summary

1. Nine simple risk factors are strongly associated with AMI worldwide
2. These risk factors are even more important in the young, with consistent effects in men and women, across all ethnic groups and all regions.
3. Abnormal Apo-B/ApoA-1 ratio and smoking are the most important risk factors and account for $>2/3$ of the PAR. All 9 risk factors account for $>90\%$ of the PAR globally and in most regions.
4. The impact of these risk factors is underestimated in INTERHEART and so these data imply that the majority of the PAR can be accounted for *if these risk factors are causal.*

IMPLICATIONS: Implementing preventive strategies based on our current knowledge could avert the majority of premature CHD worldwide.

Where is our work headed to?

- Understand the “causes of the causes”: early development of CV risk factors(FAMILY), societal influences on behaviours, and interactions with genes to cause risk factors and CVD (PURE).
- Risk factors for stroke globally(INTERSTROKE).
- Maximizing the benefits from current approaches, eg polypipi (HOPE 3,TIPS-1, 2 and 3).
- Tackling emerging manifestations of CVD(vasc cog impair)
- Tackling the unfinished agenda of CVD due to poverty:(TB pericarditis, Chagas).