



INTERHEART: Background

- Over 80% of the CVD burden occurs in low (L) and middle income countries (MIC), but there are few data on risk factors for CVD from these countries
- Current thinking suggests that “only 50%” of the risk of CHD is accounted by known risk factors



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*



INTERHEART: History (1991 to 2004)

1. Single center case-control study (300 + 300) in India 1991-1994
2. Multicenter study in India (1200 + 2400) 1994-2003
3. Idea and protocol development of INTERHEART 1997-1999
4. Vanguard phase 1999-2000
5. Full scale recruitment 2000-2003
6. Data analysis/publications 2004



INTERHEART

Funded by 39 sources:

- *The Canadian Institutes of Health Research*
- *Heart and Stroke Foundation of Ontario*
- *The International Clinical Epidemiology Network, and*
- *Generous donations from pharmaceutical companies:*
 - Astra Zeneca
 - Bristol Myers Squibb
 - Novartis
 - King
 - Aventis
 - Knoll
 - Sanofi Synthelabo

Plus multiple sources in various countries.



52 Countries Representing Every Inhabited Continent

Argentina	Croatia	Kuwait	Russia
Australia	Czech Rep	Malaysia	Seychelles
Bahrain	Egypt	Mexico	Singapore
Bangladesh	Germany	Mozambique	S Africa
Benin	Greece	Nepal	Spain
Botswana	Guatemala	New Zealand	Sri Lanka
Brazil	Hungary	Netherlands	Sultanate of Oman
Cameroon	India	Nigeria	Sweden
Canada	Iran	Pakistan	Thailand
Chile	Israel	Philippines	UAE
China/Hong Kong	Italy	Poland	UK
Colombia	Japan	Portugal	USA
	Kenya	Qatar	Zimbabwe

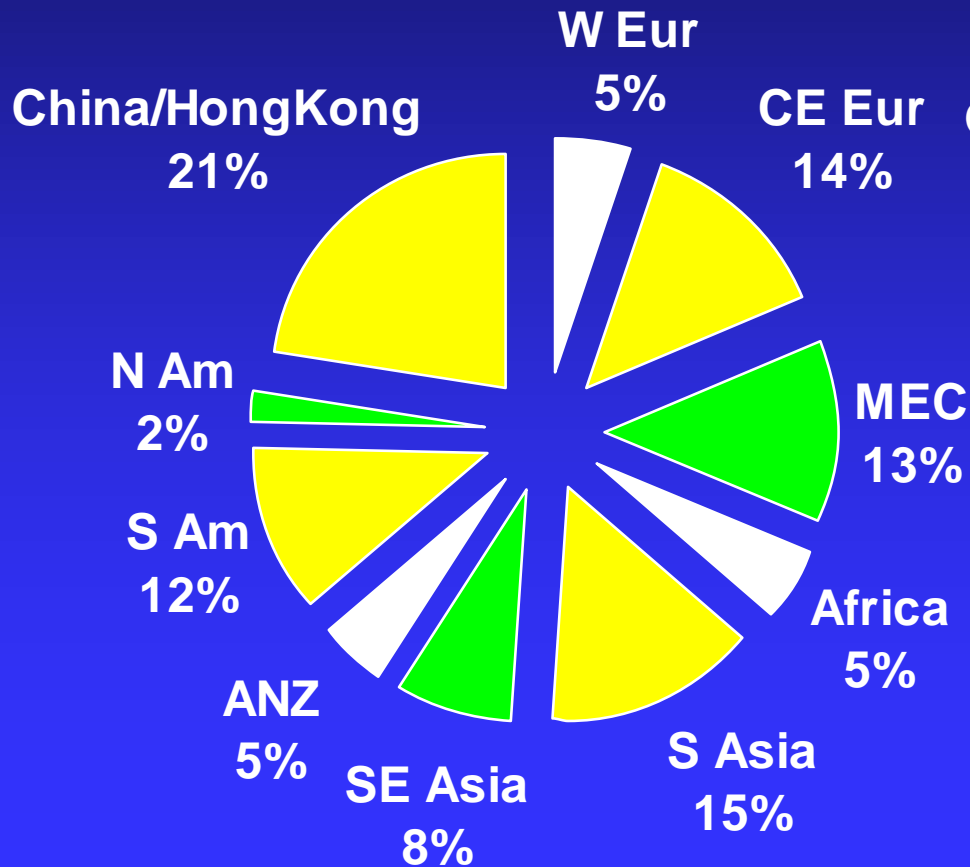


National Coordinators

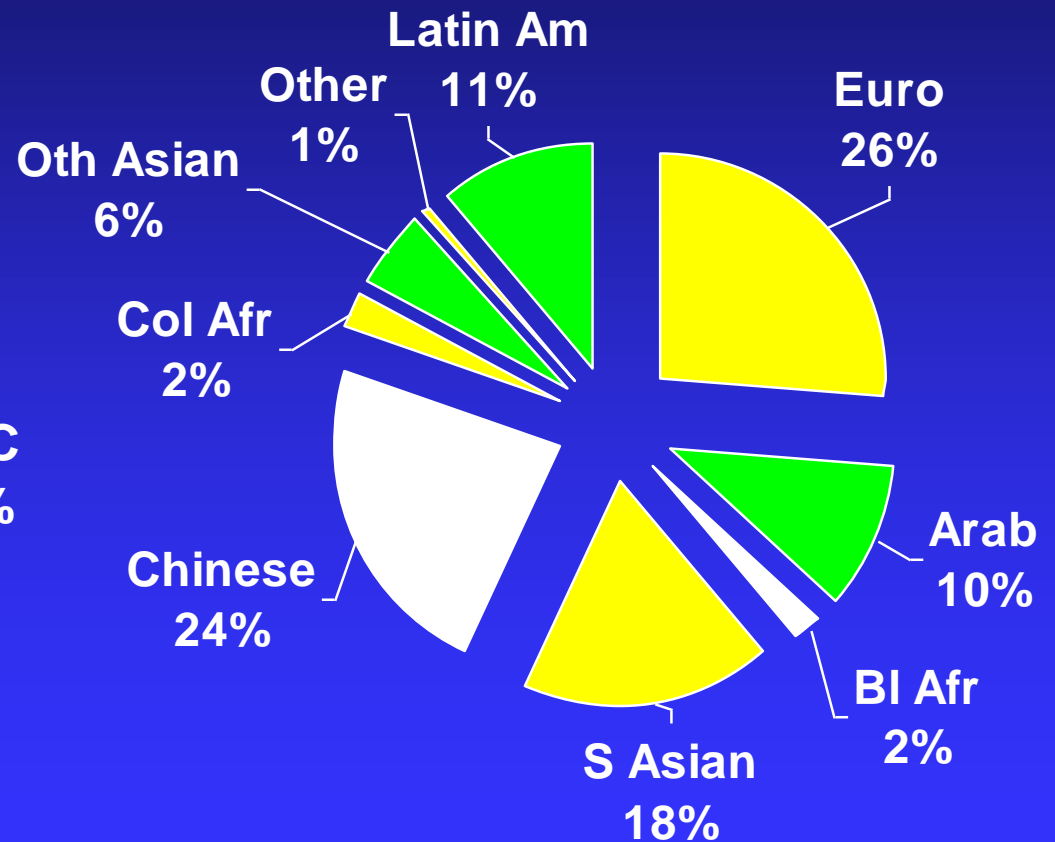
Argentina: Paolasso, Diaz; **ANZ:** Varigos, Hunt; **Bahrain:** Halim;
Bangladesh: Haque; **Benin:** Agboton; **Botswana:** Onen; **Brazil:** Avezum,
Piegas; **Cameroon:** Blackett; **Canada:** Yusuf, Teo; **Chile:** Lanas; **China:** Liu
Lisheng; **Colombia:** Bautista; **Croatia:** Rumboldt; **Czech:** Widimsky; **Egypt:**
Khedr; **Germany:** Wittlinger, Rupprecht; **Greece:** Karatzas; **Guatemala:**
Luna; **HK:** Sanderson; **Hungary:** Keltai; **India:** Reddy, Pais; **Iran:** Hasani,
Mirkhani; **Israel:** Lewis, Halon; **Italy:** Tognoni, Franzosi; **Japan:** Hori, Sato;
Kenya: Ogola, Wangai; **Kuwait:** Zubaid; **Malaysia:** Lang; **Mexico:** Ramos-
Corrales; **Mozambique:** Damasceno; **Nepal:** Pandey; **Netherlands:** Peters;
Nigeria: Akinroye; **Pakistan:** Kazmi; **Philippines:** Dans; **Poland:**
Ceremuzynski, Budaj; **Portugal:** Morais; **Qatar:** Gehani; **Russia:** Volkova;
Seychelles: Panovsky; **Singapore:** Johan; **S Africa:** Steyn; Commerford;
Sliwa; **Spain:** Valentin; **S Lanka:** Mendis, Jayalath; **Oman:** Al Hinai;
Sweden: Rosengren; **Thailand:** Sitthi-Amorn; **UAE:** Almahmeed; **UK:** Fox,
Flather; **USA:** Probstfield; **Zimbabwe:** Chifamba

15,152 MI cases and 14,820 controls

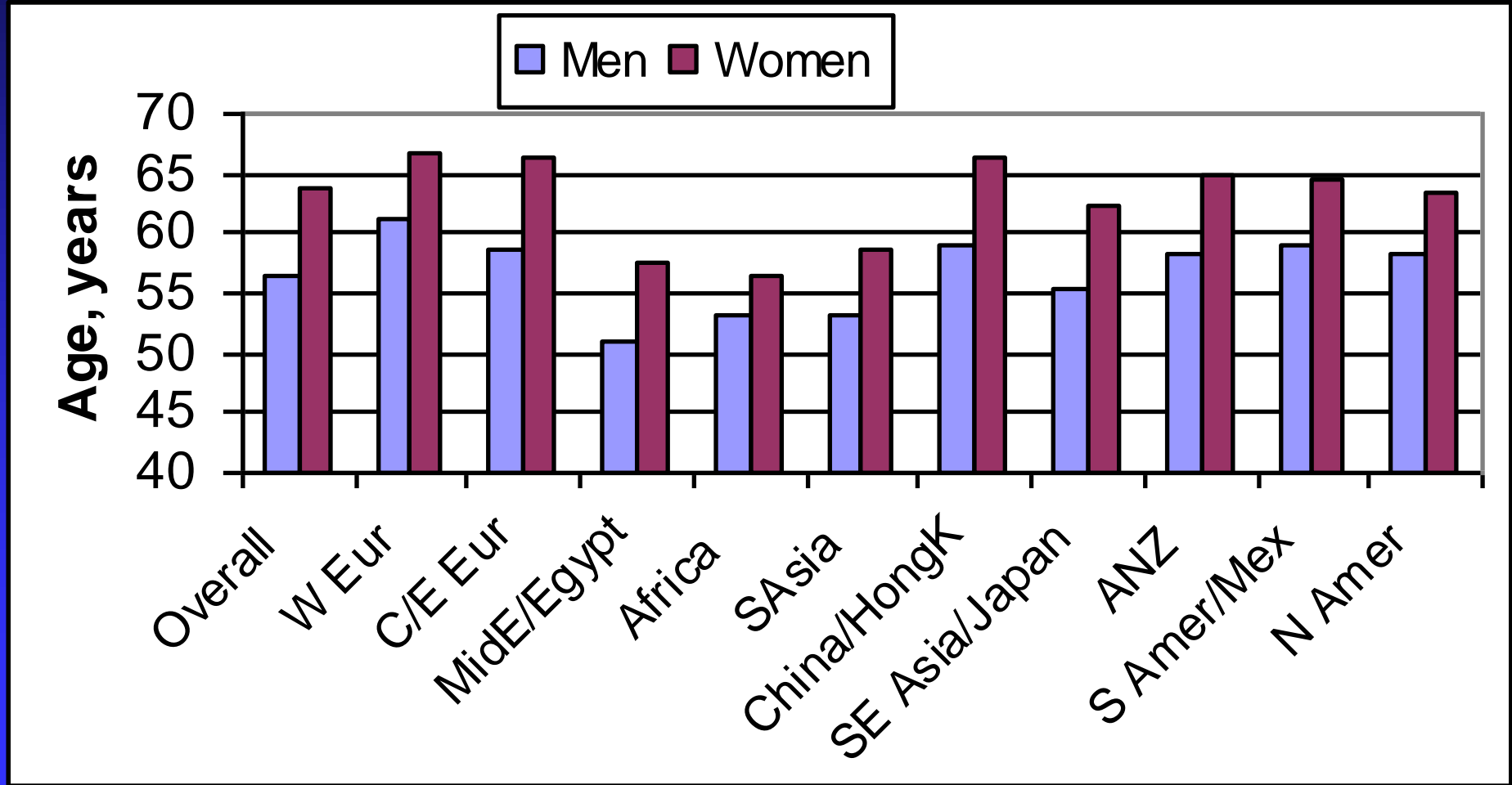
Distribution by region



Distribution by ethnicity

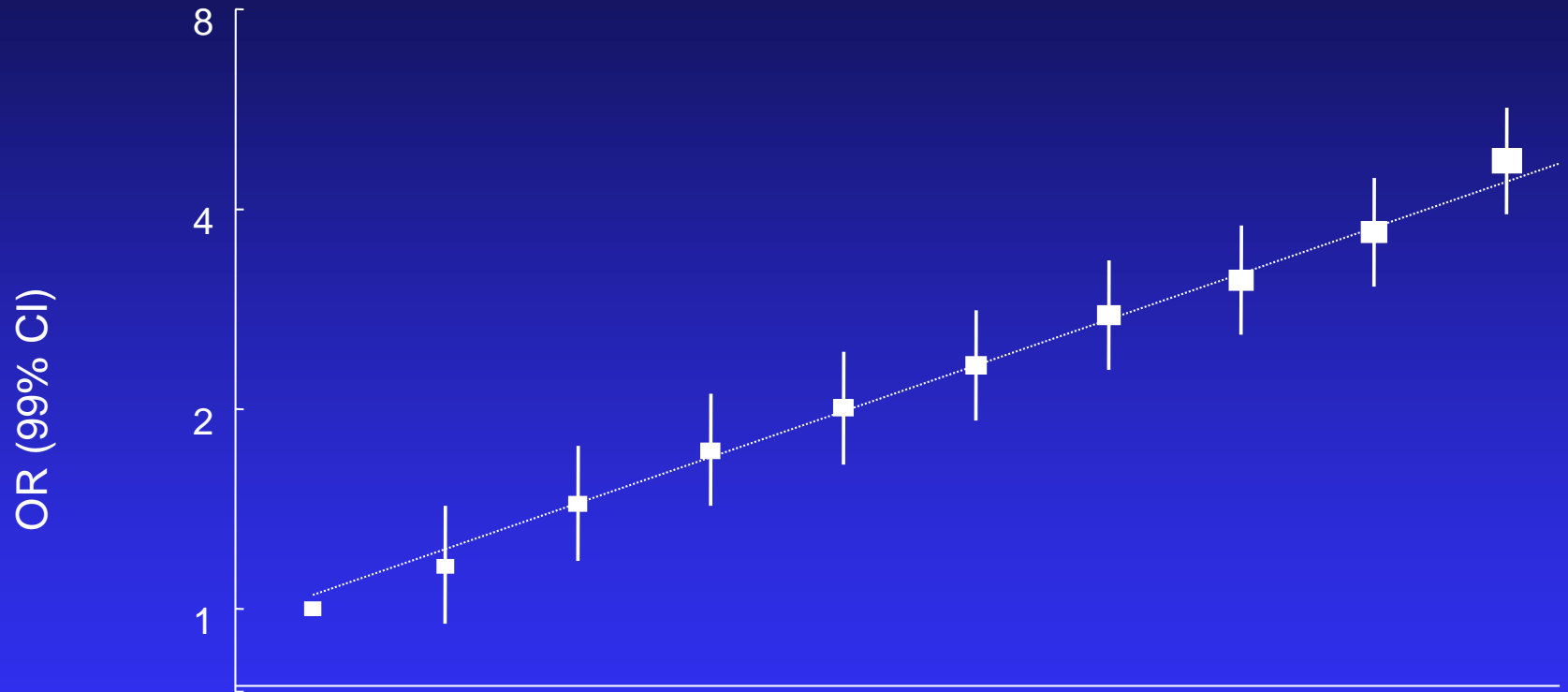


Mean age of male and female cases, overall and by region





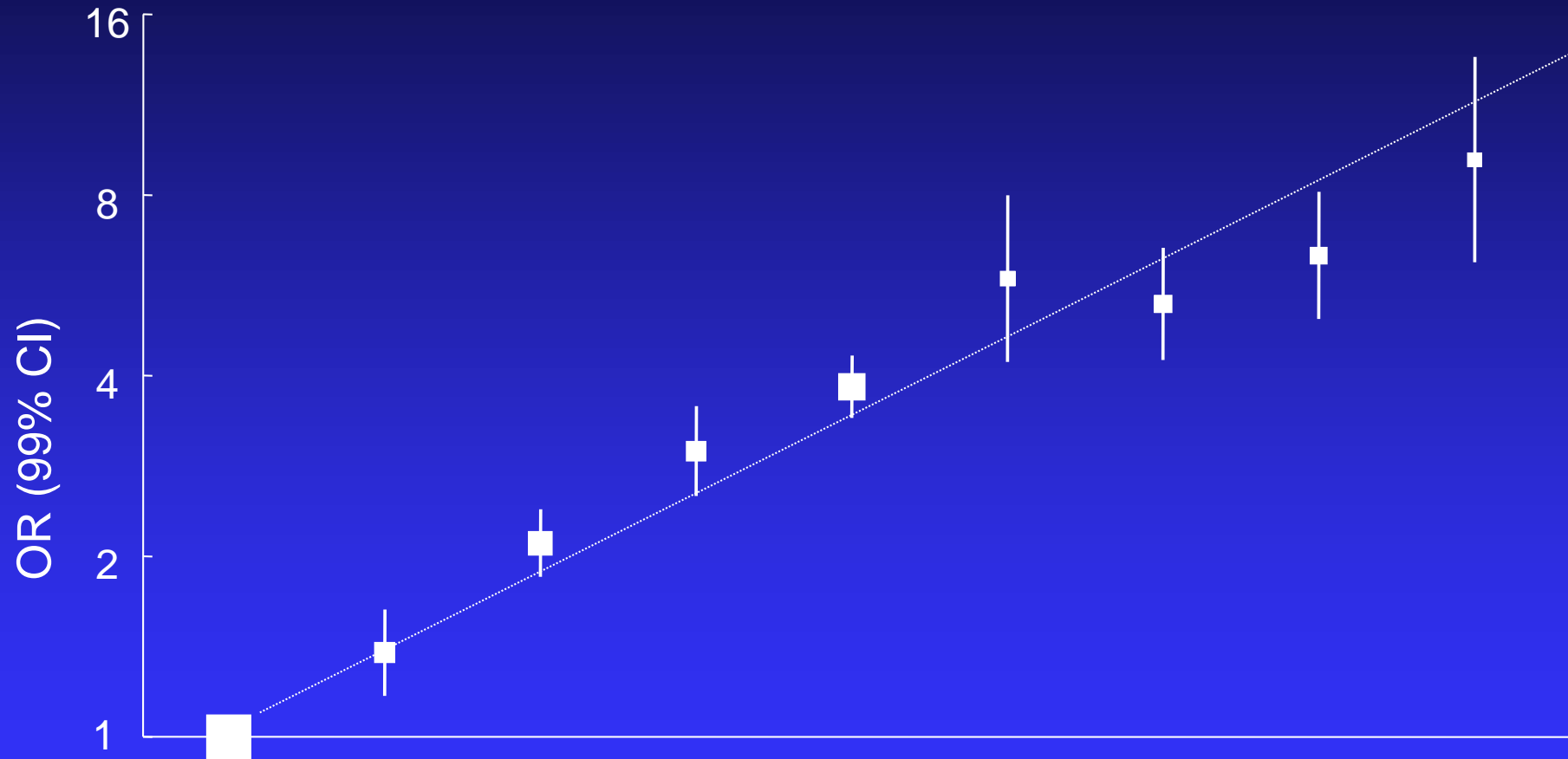
INTERHEART: Apolipoprotein B/A-1 and MI



Deciles:	1	2	3	4	5	6	7	8	9	10
Cont	1210	1206	1208	1207	1210	1209	1207	1208	1208	1209
Cases	435	496	610	720	790	893	1063	1196	1366	1757
Median	0.43	0.53	0.60	0.66	0.72	0.78	0.85	0.93	1.04	1.28



INTERHEART: Smoking and MI



	Never	1-5	6-10	11-15	16-20	21-25	26-30	31-40	41+
Cont	7489	727	1031	446	1058	96	230	168	56
Cases	4223	469	1021	623	1832	254	538	459	218
OR	1	1.38	2.10	2.99	3.83	5.80	5.26	6.34	9.16



Risk of AMI associated with Risk Factors in the Overall Population

Risk factor	% Cont	% Cases	OR (99% CI) adj for age, sex, smok	OR (99% CI) adj for all
ApoB/ApoA-1 (5 v 1)	20.0	33.5	3.87 (3.39, 4.42)	3.25 (2.81, 3.76)
Curr smoking	26.8	45.2	2.95 (2.72, 3.20)	2.87 (2.58, 3.19)
Diabetes	7.5	18.4	3.08 (2.77, 3.42)	2.37 (2.07, 2.71)
Hypertension	21.9	39.0	2.48 (2.30, 2.68)	1.91 (1.74, 2.10)
Abd Obesity (3 v 1)	33.3	46.3	2.22 (2.03, 2.42)	1.62 (1.45, 1.80)
Psychosocial	-	-	2.51 (2.15, 2.93)	2.67 (2.21, 3.22)
Veg & fruits daily	42.4	35.8	0.70 (0.64, 0.77)	0.70 (0.62, 0.79)
Exercise	19.3	14.3	0.72 (0.65, 0.79)	0.86 (0.76, 0.97)
Alcohol Intake	24.5	24.0	0.79 (0.73, 0.86)	0.91 (0.82, 1.02)
All combined	-	-	129.2 (90.2, 185.0)	129.2(90.2, 185.0)
All combined (extremes)			333.7 (230.2, 483.9)	333.7 (230.2, 483.9)

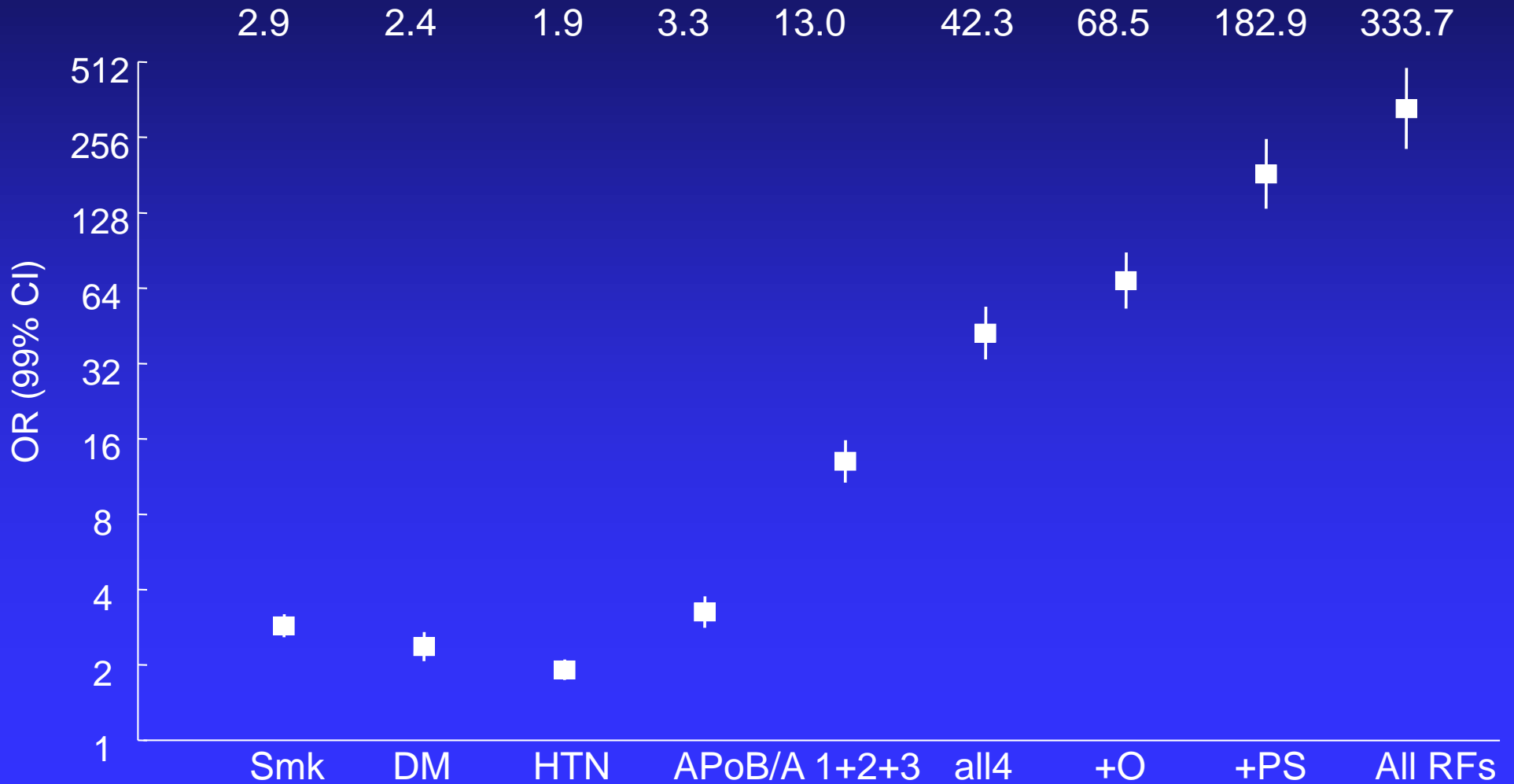


Risk of AMI associated with Risk Factors in the Overall Population

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)

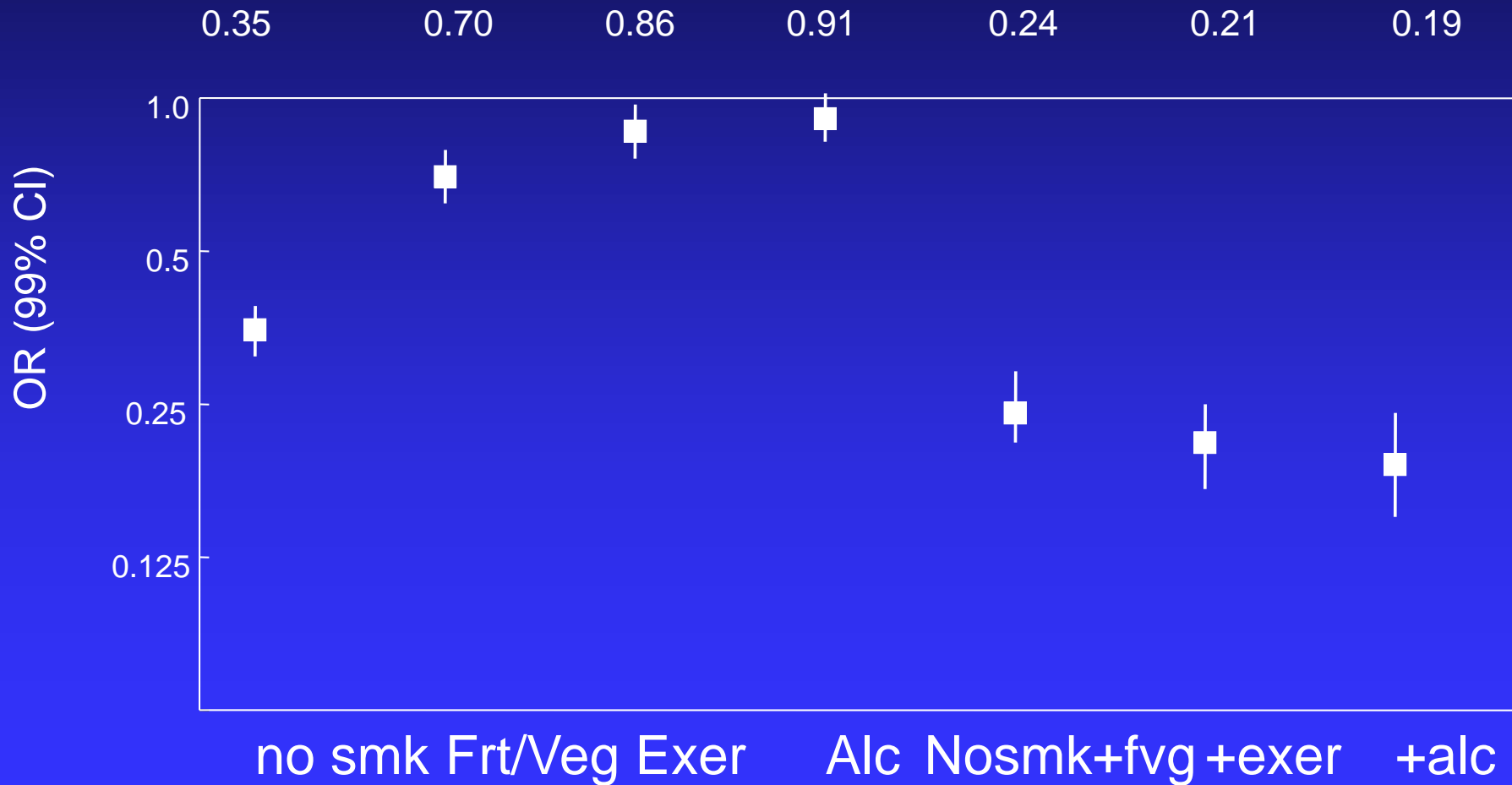


INTERHEART: Risk of AMI with Multiple Risk Factors





INTERHEART: Decreased Risk of AMI with Avoidance of Smoking; Daily Fruits/Veg, Reg Phys Activity & Alcohol





Population Attributable Risk by Region and Overall

LIFESTYLE FACTORS

Region	Smoke %	Fr/vg %	Exer %	Alc %	All LS
W. Europe	28.9	12.9	38.8	18.9	67.8
E/C Europe	30.2	10.2	11.3	12.9	49.6
Middle East	44.8	8.1	4.0	-4.4	45.5
Africa	38.0	3.8	11.1	27.3	63.2
S. Asia	37.5	18.4	24.3	-5.3	55.2
China	35.8	17.8	21.1	5.3	62.4
S.E. Asia	36.2	11.2	31.4	27.9	69.9
Australia/NZ	44.7	10.7	23.8	18.5	65.8
S. America	38.5	6.7	27.2	-3.1	56.9
N. America	26.3	19.8	25.3	25.3	59.8
Overall 1	36.2	12.9	25.5	13.9	62.8
Overall 2	35.7	13.7	12.2	6.7	54.6



Population Attributable Risk by Region and Overall

NON-LIFESTYLE RISK FACTORS

Region	HTN %	Diab %	Abd Obes %	All PS%	Lipids %	All 9 RF
W. Europe	22.0	14.9	63.6	38.9	44.6	94.0
E/C Europe	24.5	9.1	28.0	4.9	35.0	72.5
Middle East	9.7	15.5	26.7	41.6	70.5	95.0
Africa	29.9	17.1	58.3	40.0	74.1	97.4
S. Asia	19.4	12.1	37.0	15.9	58.7	89.4
China	22.1	10.0	5.5	35.6	43.8	89.9
S.E. Asia	38.4	21.0	58.0	26.7	67.7	93.7
Australia/NZ	22.8	7.2	61.6	28.9	43.4	89.5
S. America	32.8	12.8	45.4	35.6	47.6	89.4
N. America	18.9	7.9	59.6	51.4	50.5	98.7
Overall 1	23.4	12.4	33.7	28.8	53.8	90.4
Overall 2	17.9	9.9	20.1	32.5	49.2	90.4

Risk Factor Impact by Age

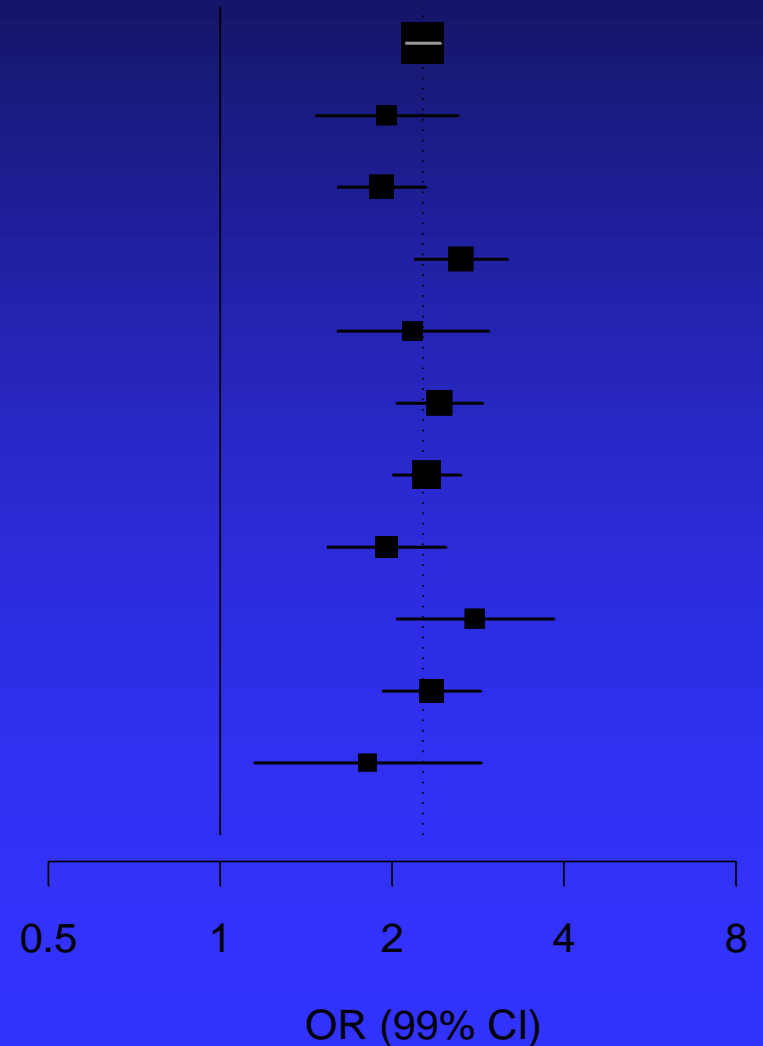
	Odds Ratio		PAR	
	Young	Old	Young	Old
Smoking	3.33	2.44*	40.7	33.1
Fruit/Veg	0.69	0.72	16.9	11.9
Exercise	0.95	0.79	7.5	13.4
Alcohol	1.00	0.85	-4.1	11.1
Hypertension	2.24	1.72*	19.2	17.0
Diabetes	2.96	2.05*	12.4	8.6
Abd Obesity	1.79	1.50	24.8	18.1
All Psych	2.87	2.43	43.5	25.2
ApoB/ApoA-1	4.35	2.50*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

P for interactions: *p<0.001



INTERHEART: Current or Former Smoking & MI

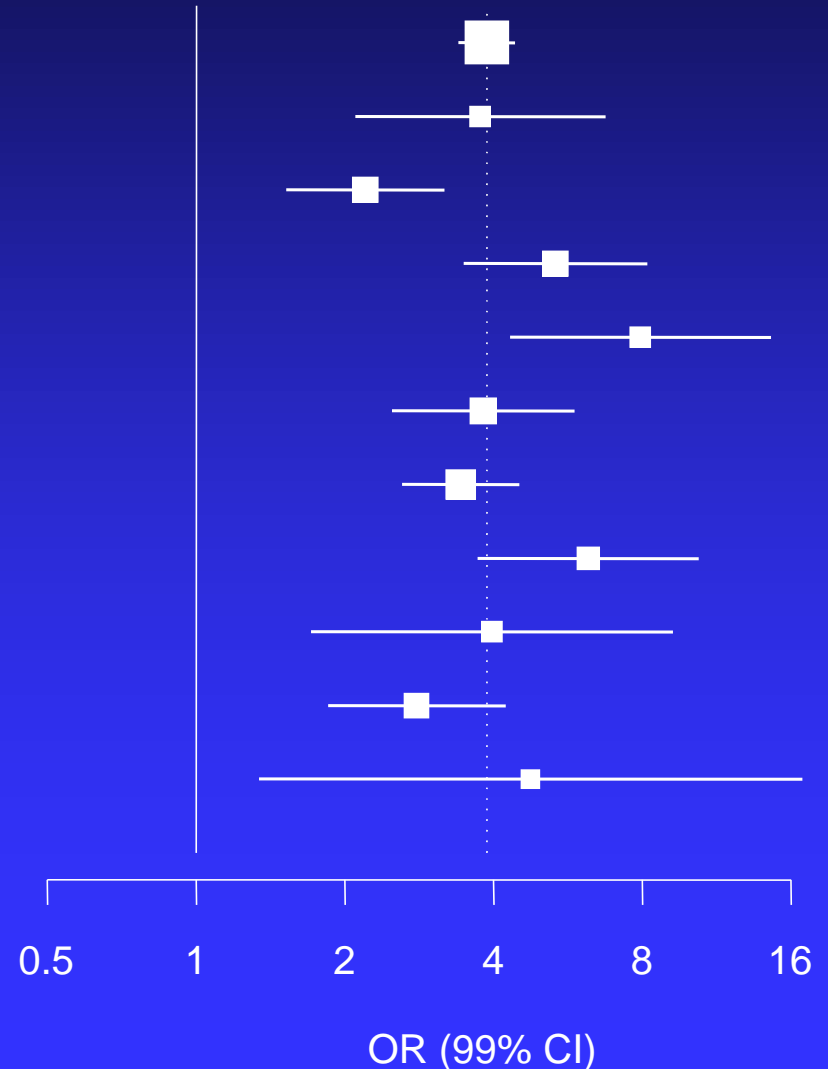
Region	N	Cont. %
Overall	26527	47.9
W Eur	1403	55.0
CE Eur	3624	54.2
MEC	3301	45.4
Afr	1339	53.8
S Asia	3706	41.0
China/HK	6062	42.7
SE Asia	2131	57.1
ANZ	1267	54.2
S Am	3068	48.9
N Am	626	64.6





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

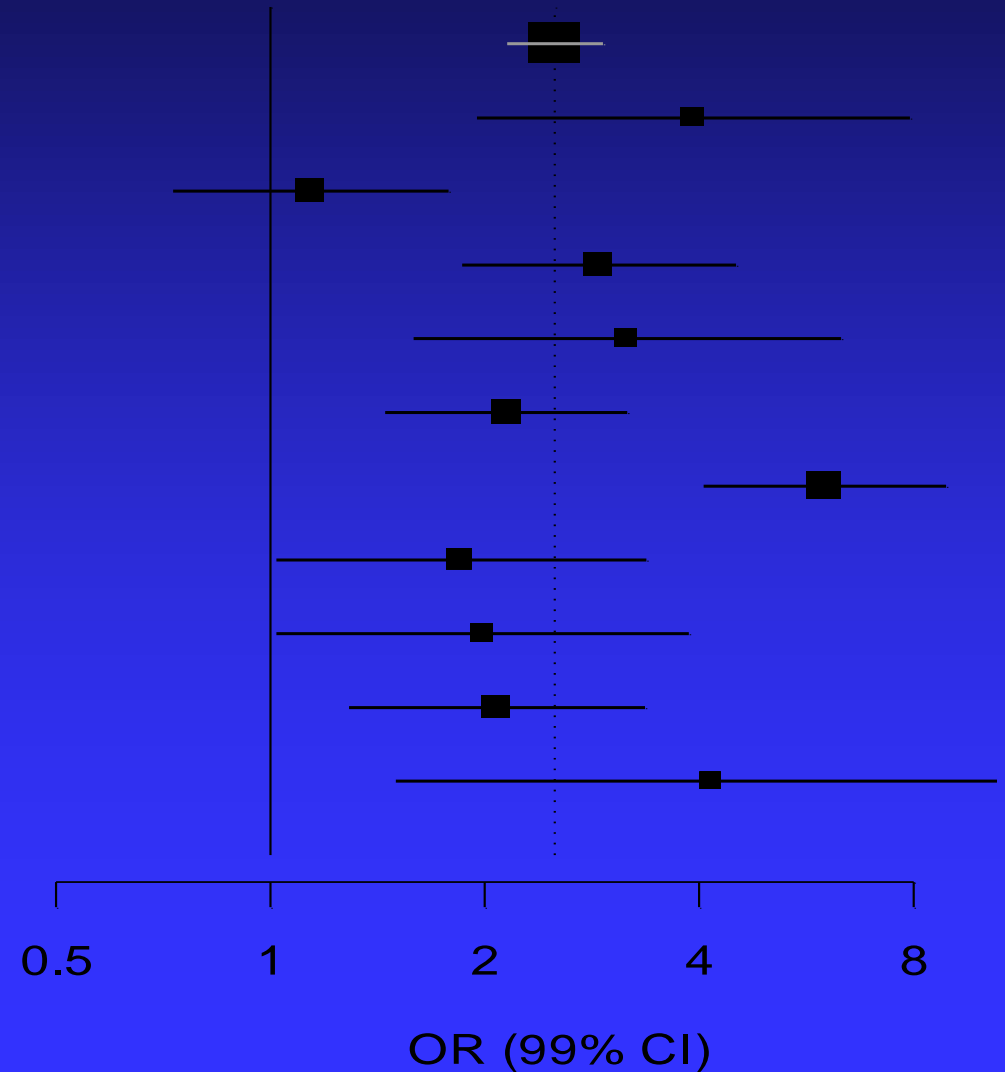
Region	N	Cont. %
Overall	21408	20.0
W Eur	1047	13.8
CE Eur	2618	20.3
MEC	3291	29.9
Afr	1037	18.0
S Asia	2820	27.7
China/HK	5400	7.3
SE Asia	1858	22.7
ANZ	487	13.8
S Am	2644	27.1
N Am	206	12.4





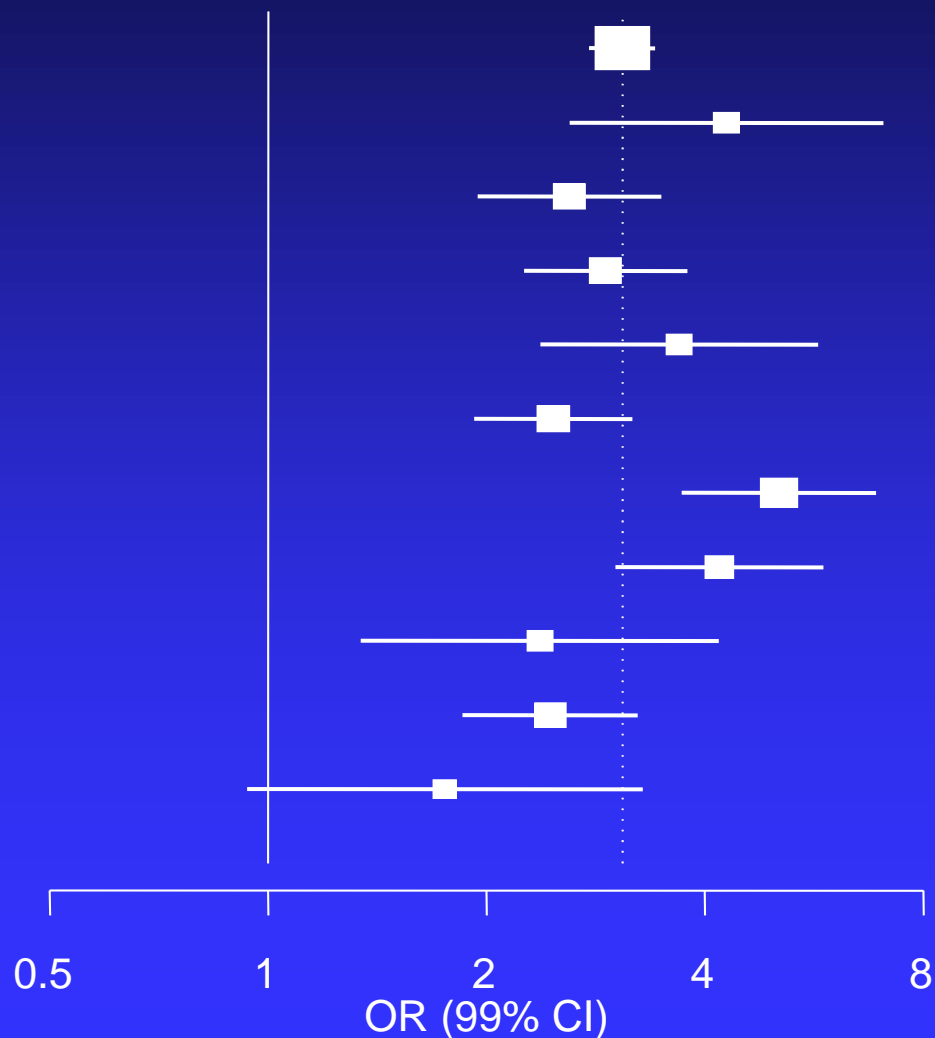
INTERHEART: Composite Psychosocial Index and MI

Region	N	OR
Overall	24767	3.11
W.Eur	1375	4.76
C.E.Eur	3473	1.31
M East	2892	3.21
Africa	1259	4.34
S.Asia	3300	2.47
China/HK	5894	7.72
SE Asia	1921	2.76
ANZ	1255	2.81
S.Am.	2783	2.80
N.Am.	615	4.11



INTERHEART: Self-reported Diabetes and MI overall

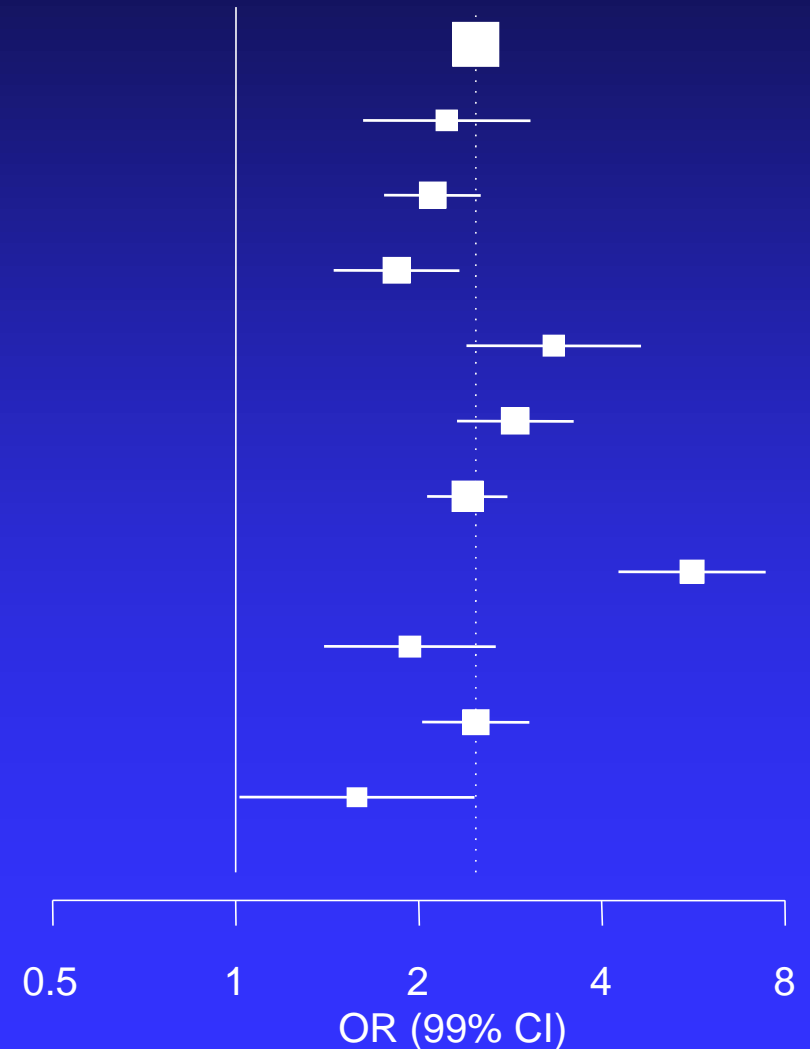
Region	N	Cont. %
Overall	26903	7.6
W Eur	1422	4.2
CE Eur	3636	6.8
MEC	3401	11.6
Afr	1355	8.0
S Asia	3882	10.6
China/HK	6075	2.9
SE Asia	2140	9.2
ANZ	1269	4.8
S Am	3093	9.0
N Am	630	9.7





INTERHEART: 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





Recruitment by Region

	MI Cases	Controls
	Actual	Actual
W Eur	664	761
C/E Eur	1,758	1,927
MiddleE/Egypt	1,651	1,789
Africa	579	788
S Asia	1,742	2,204
China/HongKong	3,056	3,056
SE Asia/Japan	968	1,199
ANZ	592	681
S Amer/Mexico	1,246	1,888
N Amer	297	340



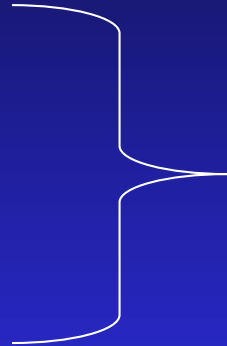
INTERHEART: Analysis of Markers of Obesity and MI

1. Prevalence of obesity in cases & controls overall and in various regions using:
 - BMI as a marker of overall obesity
 - WHR as a marker of abdominal obesity
2. To assess the association of BMI alone, WHR alone and the two together to MI.
3. To assess regional variations in OR and PAR for obesity



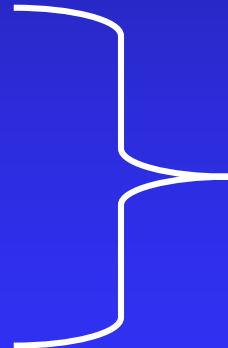
Measurements taken for INTER-HEART

- Height
- Weight



Body Mass Index (BMI)

- Waist circumference
- Hip circumference

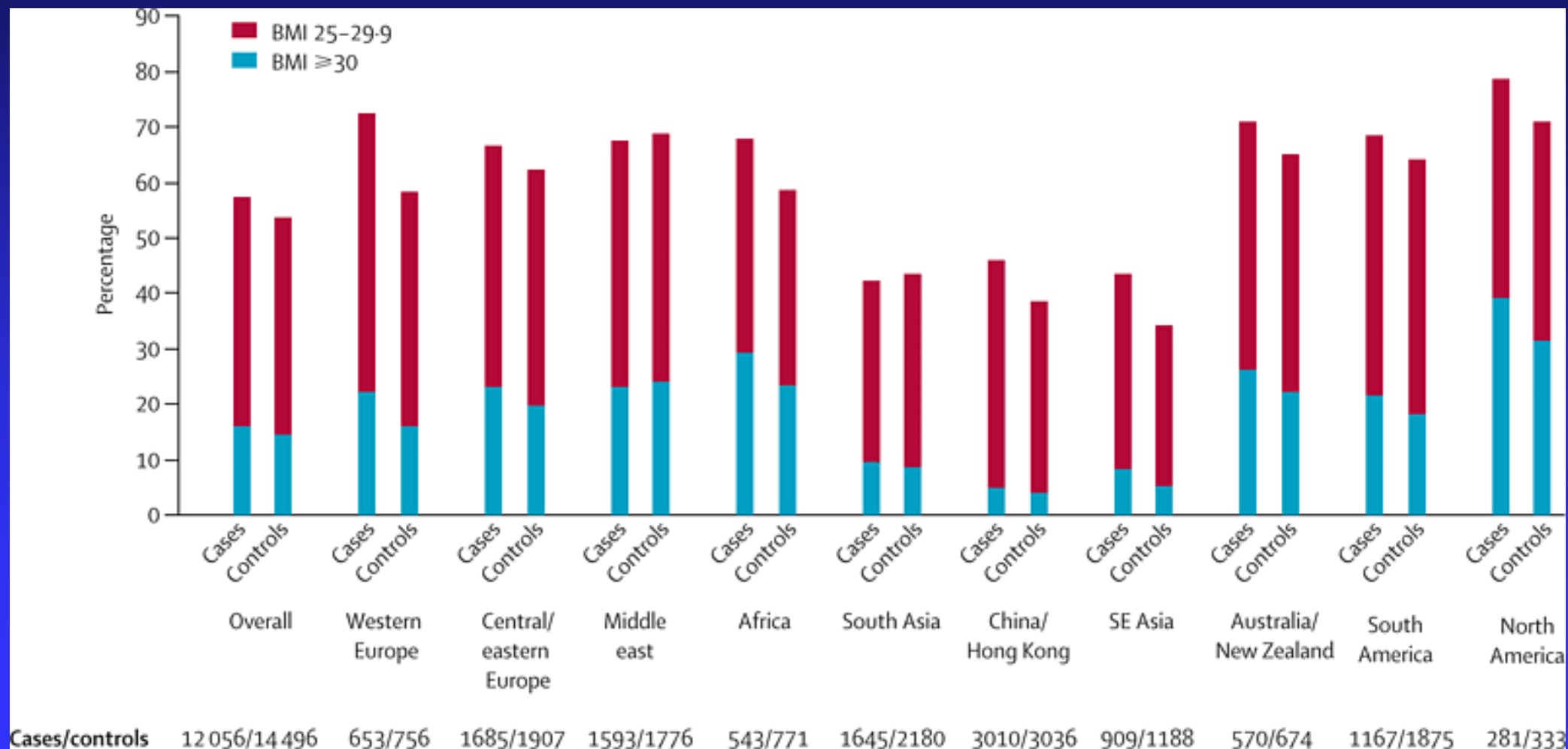


Waist to hip ratio (WHR)



A Global Study of Risk Factors
in Acute Myocardial Infarction

Proportion of cases and controls who are obese or overweight





Waist –to-hip ratio Quintile cut points:

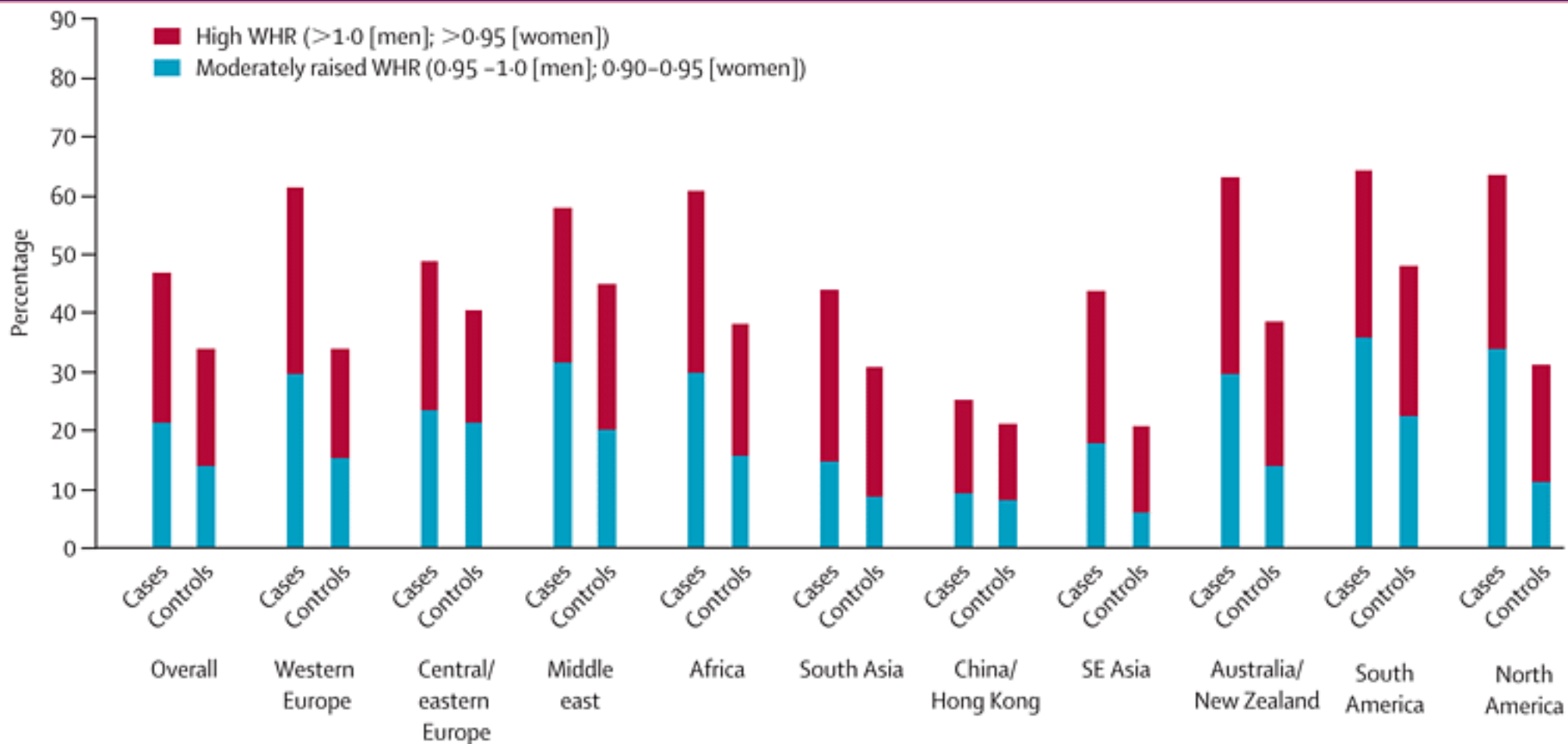
Women

1. WHR < 0.80
2. 0.80 – 0.85
3. 0.85 – 0.90
4. 0.90 – 0.95
5. > 0.95

Men

1. WHR < 0.85
2. 0.85 – 0.90
3. 0.90 – 0.95
4. 0.95 – 1.00
5. >1.00

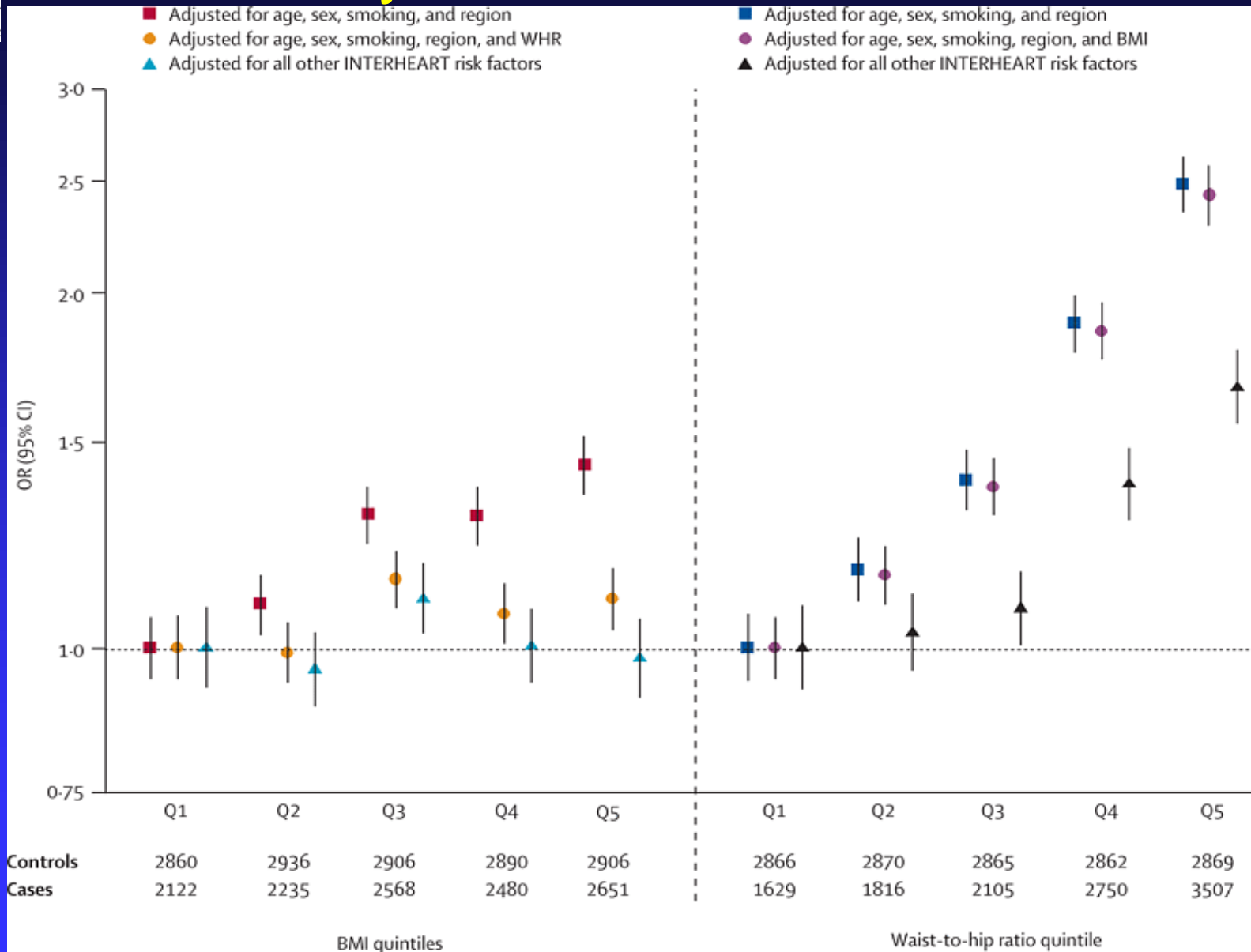
Percentage (age-adjusted) of cases and controls with abdominal obesity (waist-to-hip ratio) overall and by region





A Global Study of Risk Factors
in Acute Myocardial Infarction

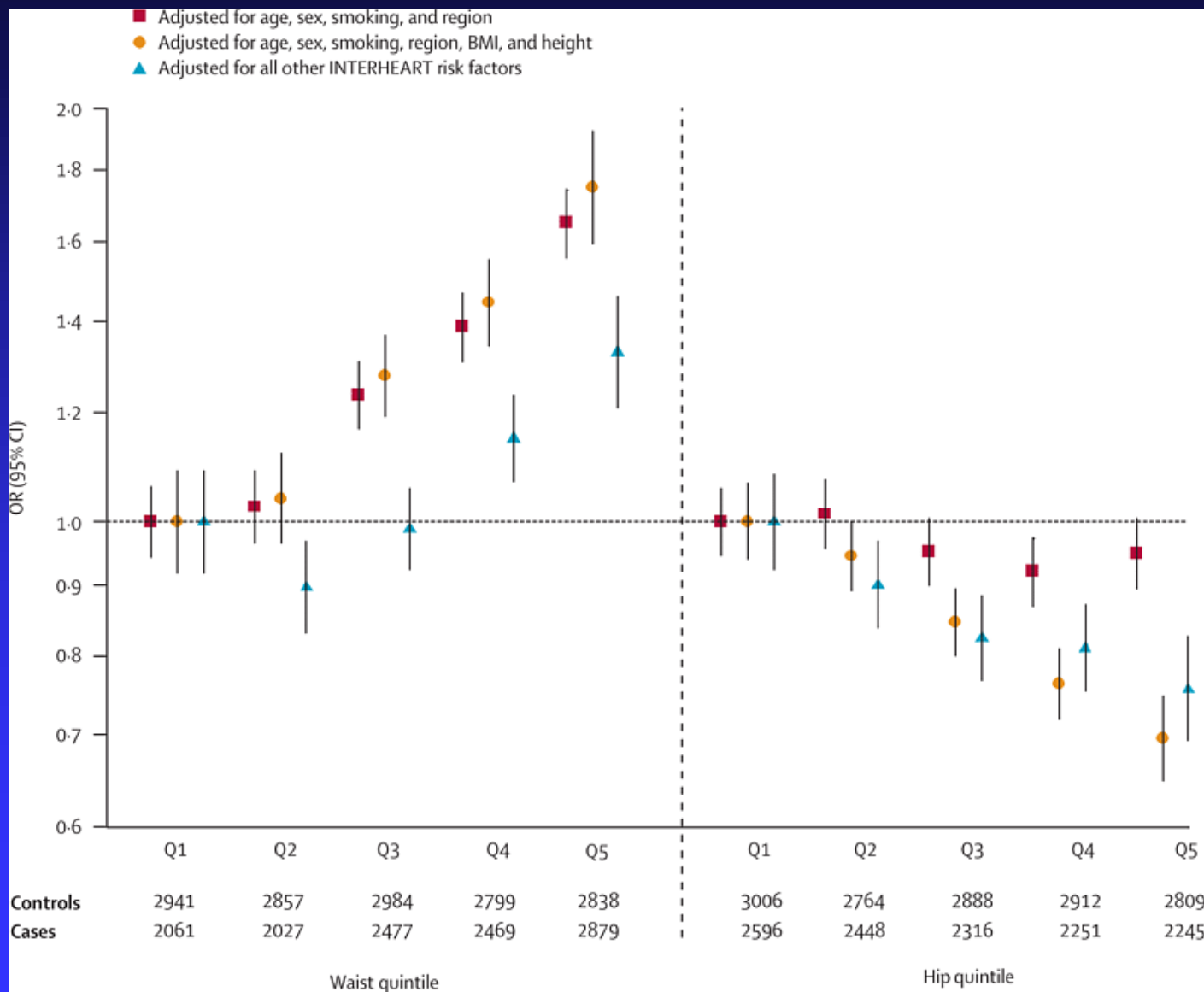
Association of BMI and waist-to-hip ratio with myocardial infarction risk





A Global Study of Risk Factors
in Acute Myocardial Infarction

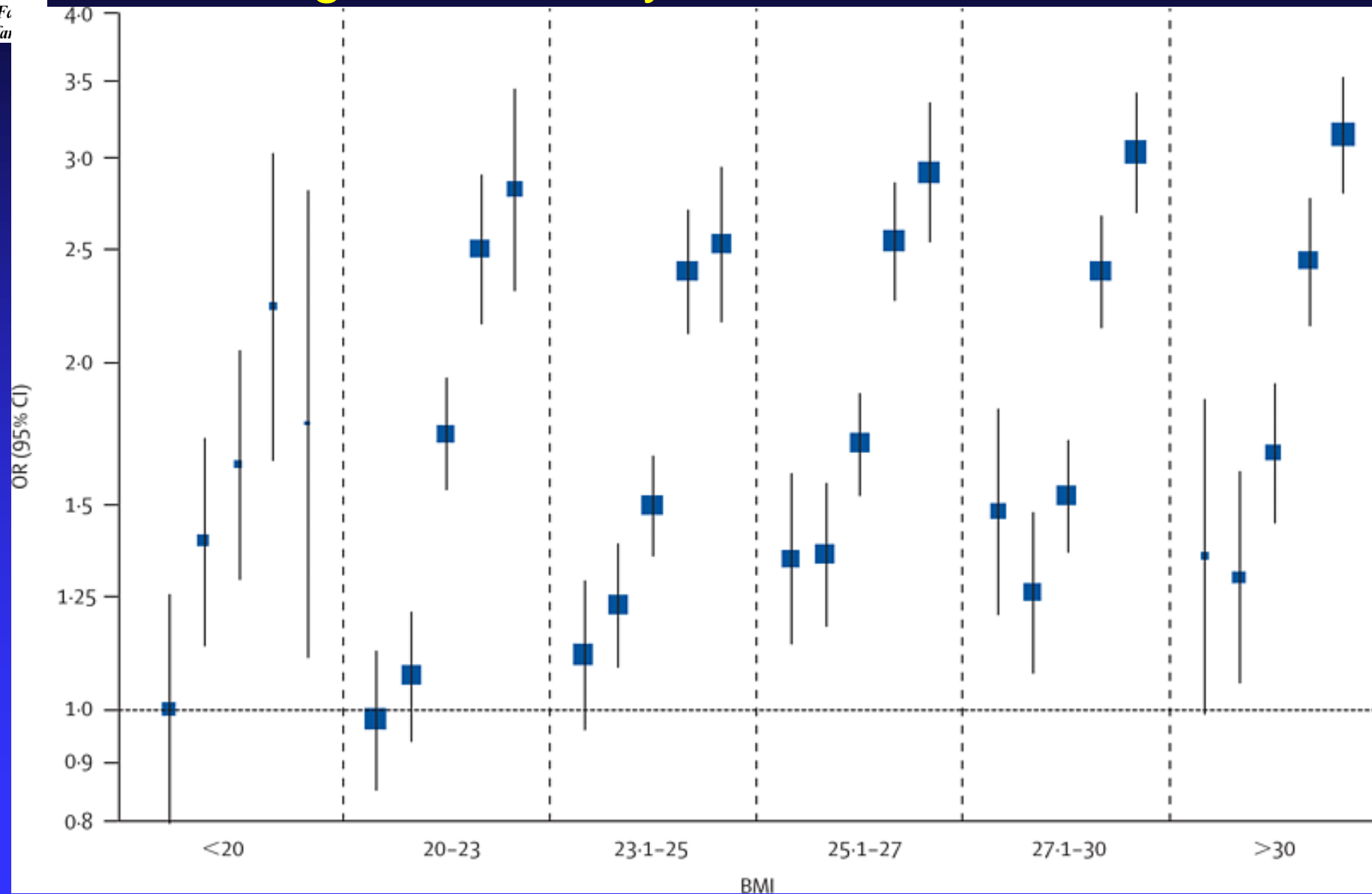
Risk of MI associated with increasing waist circumference and hip circumference



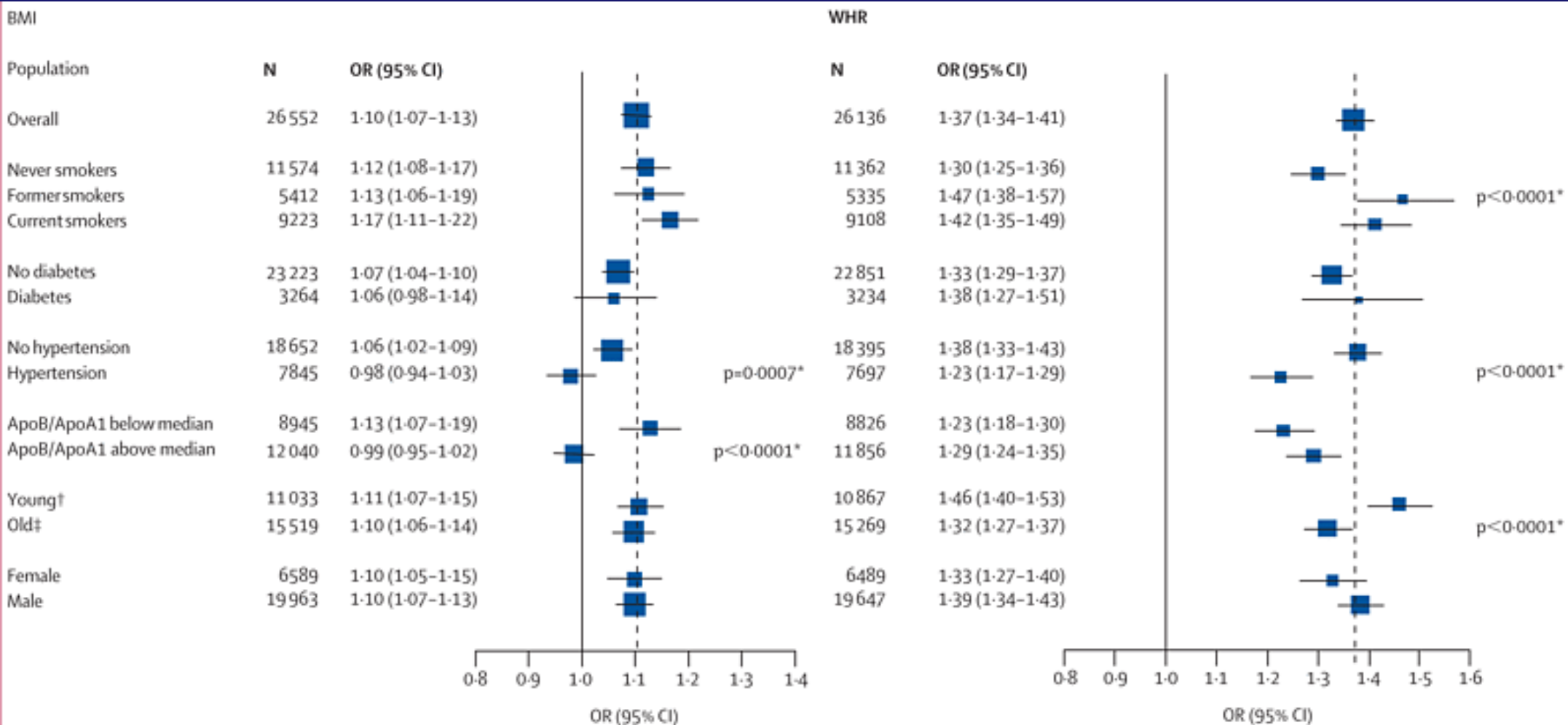


A Global Study of Risk Factors in Acute Myocardial Infarction

Association of waist-to-hip ratio within BMI categories with myocardial infarction risk



Odds ratio for myocardial infarction for 1 SD increase



Summary - Obesity

1. Waist circumference and waist to hip ratio which are measures of abdominal obesity, but not BMI, closely correlate with risk of AMI globally, and in all ethnic groups.
2. Markers of obesity (especially WHR) demonstrate a graded relationship with AMI risk, even at levels currently considered to be “normal”.
3. Obesity accounts for 34% of PAR overall (36% women, 32% men). It is more important than smoking in high income countries (e.g. North America), whereas it is less important in some regions (e.g. China)

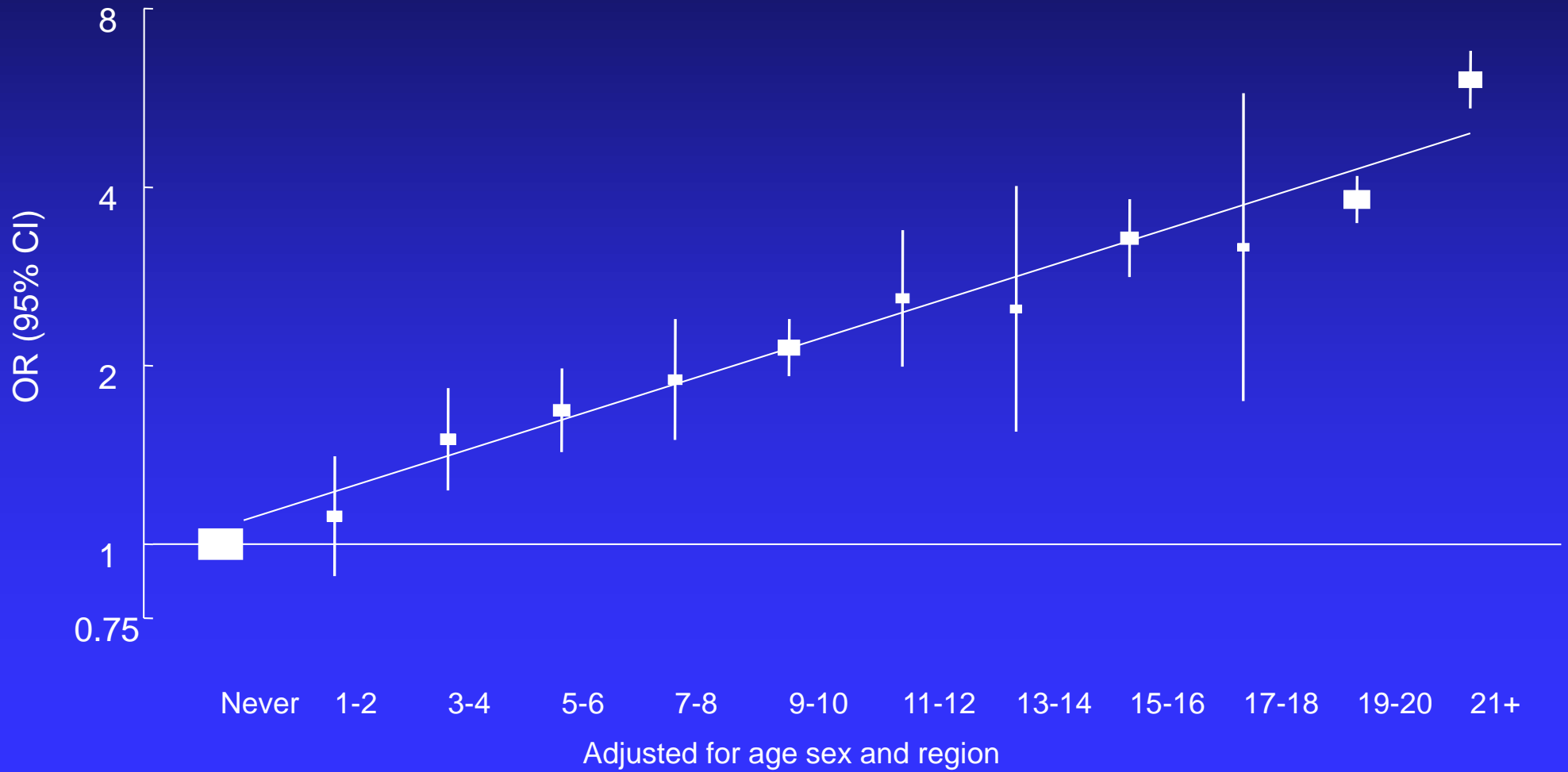


Conclusion

- Abdominal obesity is highly predictive of increased risk for acute myocardial infarction and other cardiovascular disease. Measures to reduce obesity should be part of risk factor modification.
- In assessment risk factors in patients, there should be routine measurement of waist circumference and waist to hip ratio in order to more precisely identify this important risk factor.



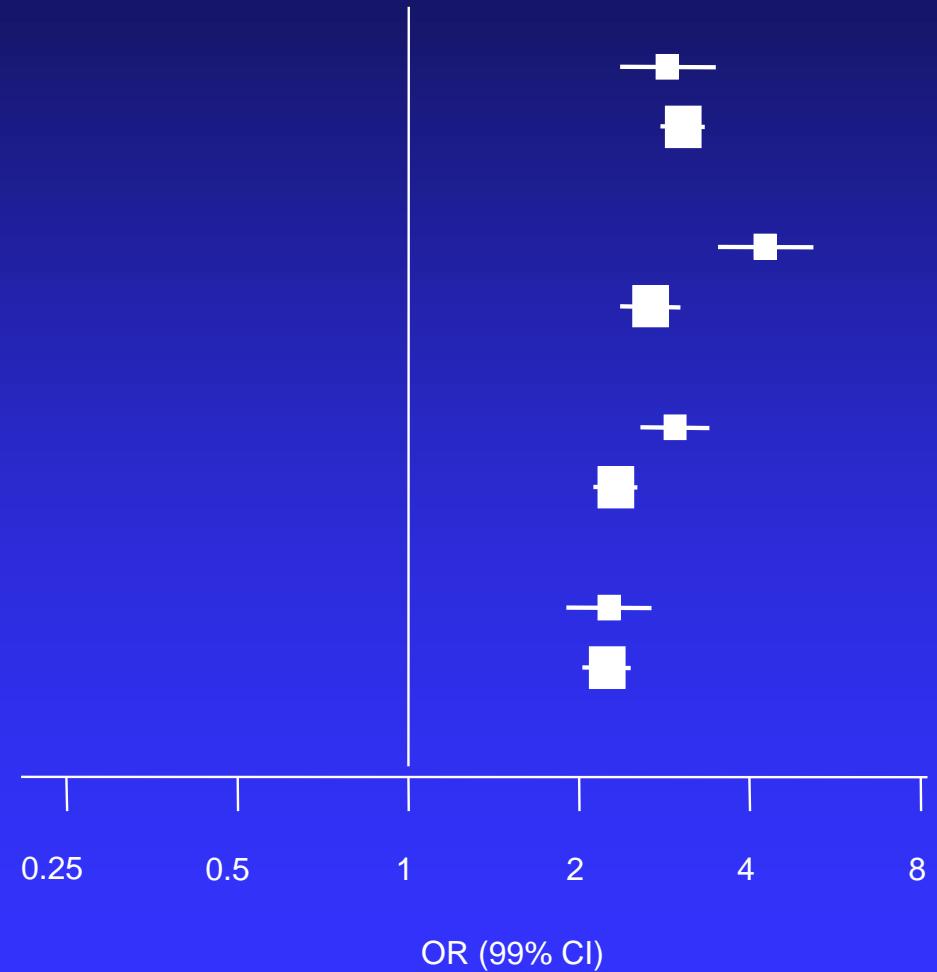
Low Levels of Smoking and MI





INTERHEART: Association of Risk Factors with AMI in Men & Women (1)

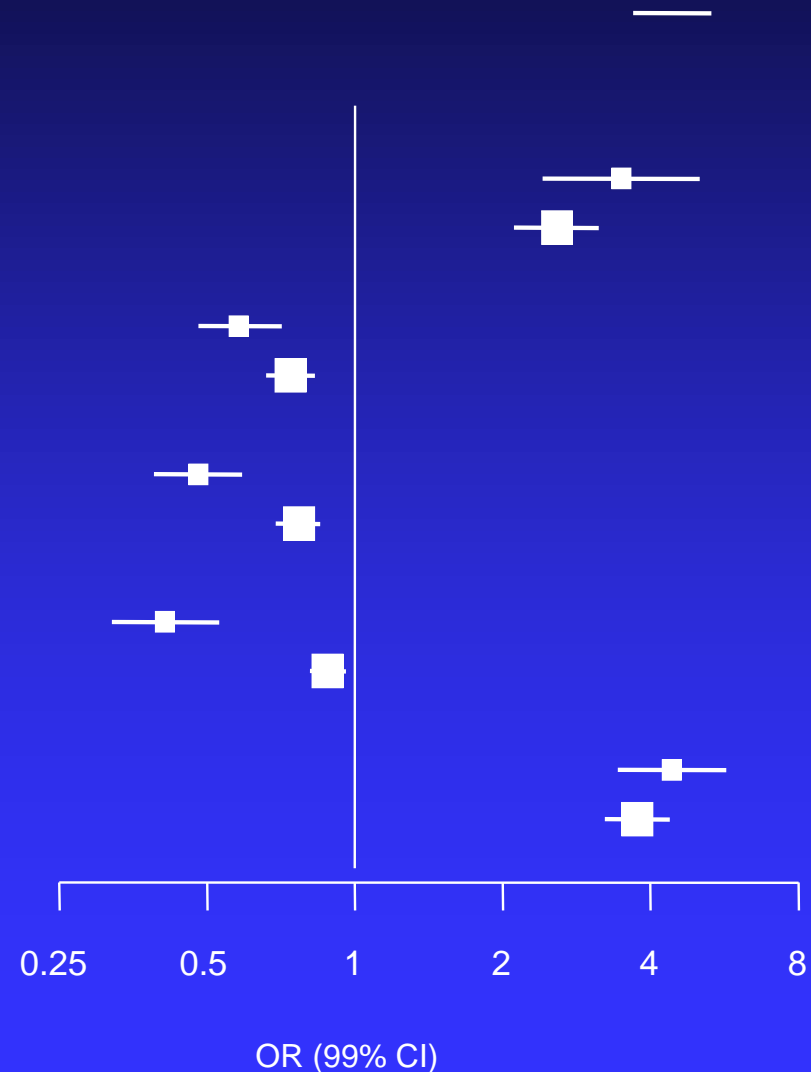
Risk Factor	Gender	Cont. %
Curr Smok	F	9.3
	M	33.0
Diabetes	F	7.9
	M	7.4
Hypertension	F	28.3
	M	19.7
Abd Obesity	F	33.3
	M	33.3





INTERHEART: Association of Risk Factors with AMI in Men & Women (2)

Risk Factor	Gender	Cont. %
PS Index	F	-
	M	-
Fruits/Veg	F	50.3
	M	39.6
Exercise	F	16.5
	M	20.3
Alcohol	F	11.2
	M	29.1
ApoB/ApoA-1 Ratio	F	14.1
	M	21.9





INTERHEART: Summary

1. Nine simple risk factors are strongly associated with AMI worldwide.
2. These risk factors are even more important in the young, and their effects are consistent in men and women, and across 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.

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



INTERHEART: Implications

1. Current knowledge provides a basis for a global strategy for prevention of CHD and suggests the potential for preventing the large majority of premature MI. These strategies can utilize similar principles in various regions of the world, but with consideration for the prevalence of risk factors and local economic and cultural factors.
2. Future research is likely to be particularly fruitful if focussed on why known risk factors develop and how they can be substantially modified.