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

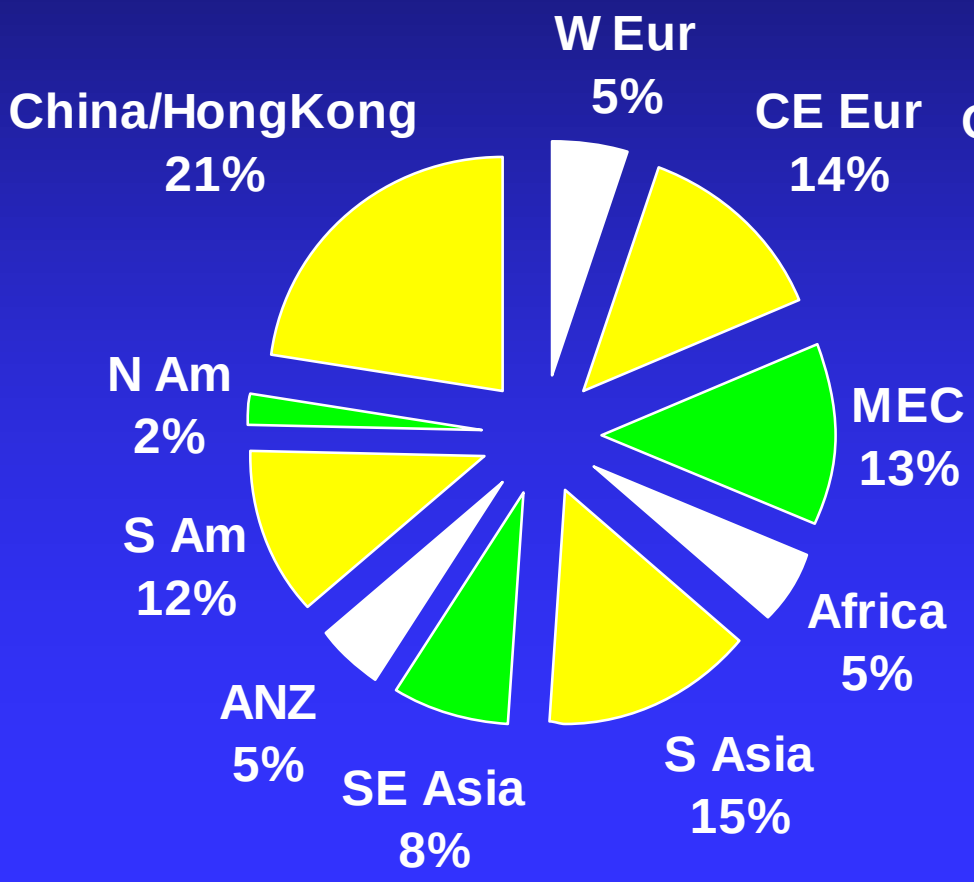
National Coordinators

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

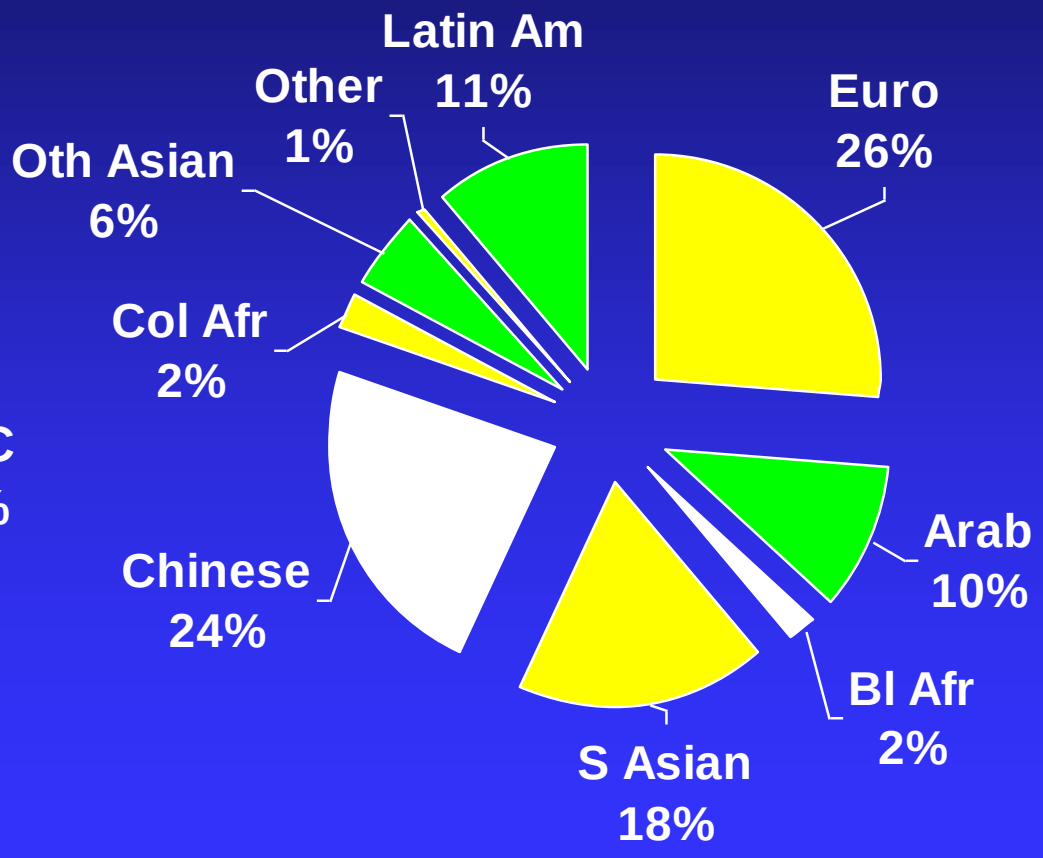
INTER-HEART
A Global Study of Risk Factors in Acute Myocardial Infarction

15,152 MI cases and 14,820 controls

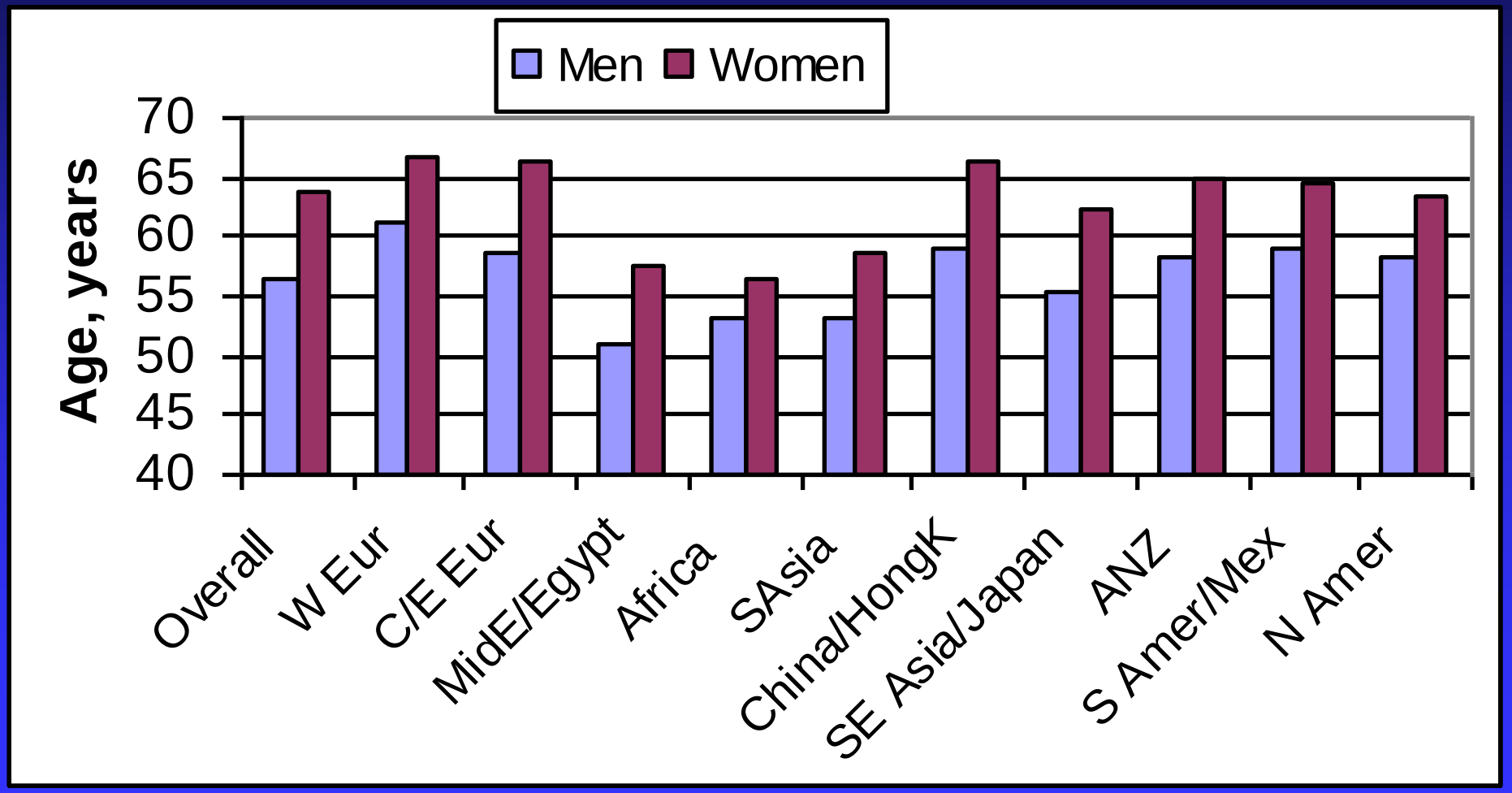
Distribution by region



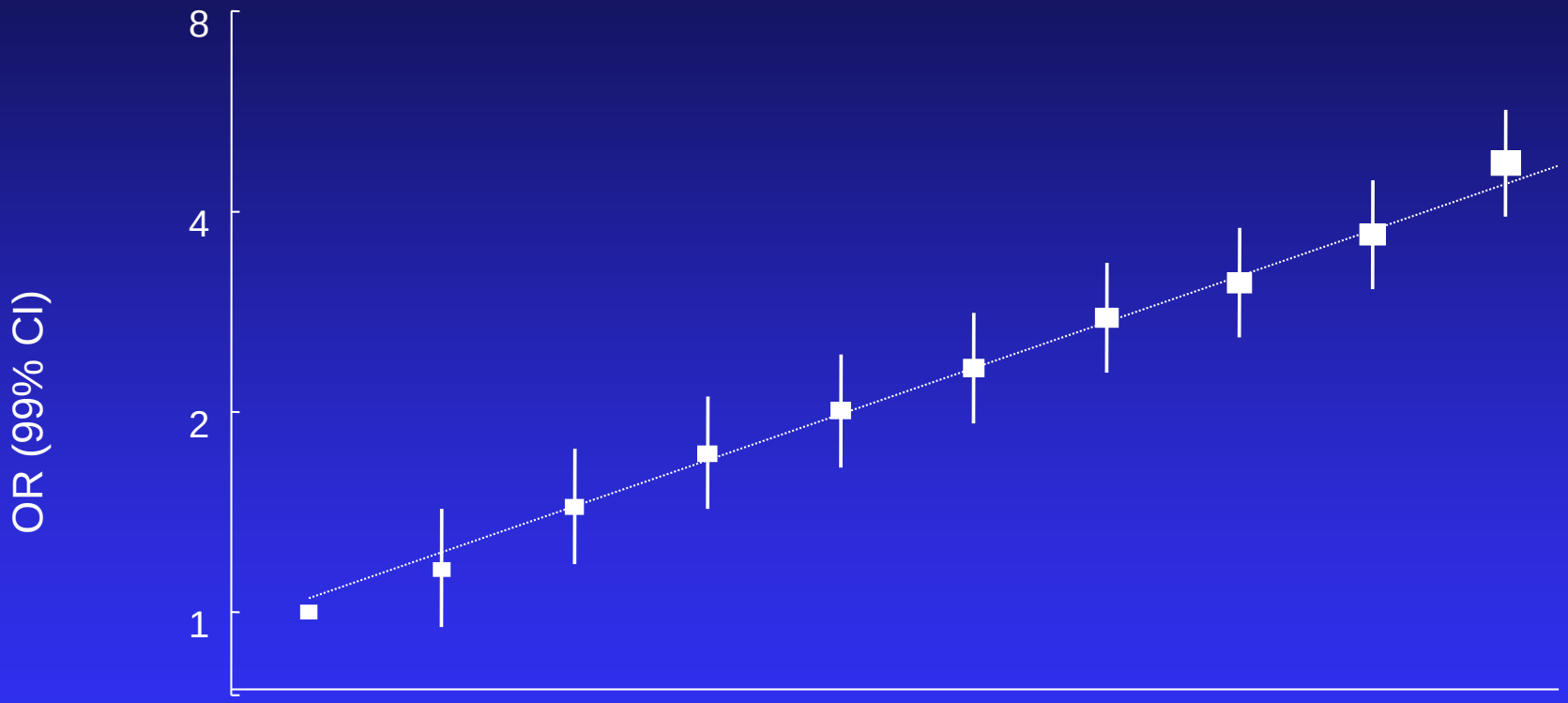
Distribution by ethnicity



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



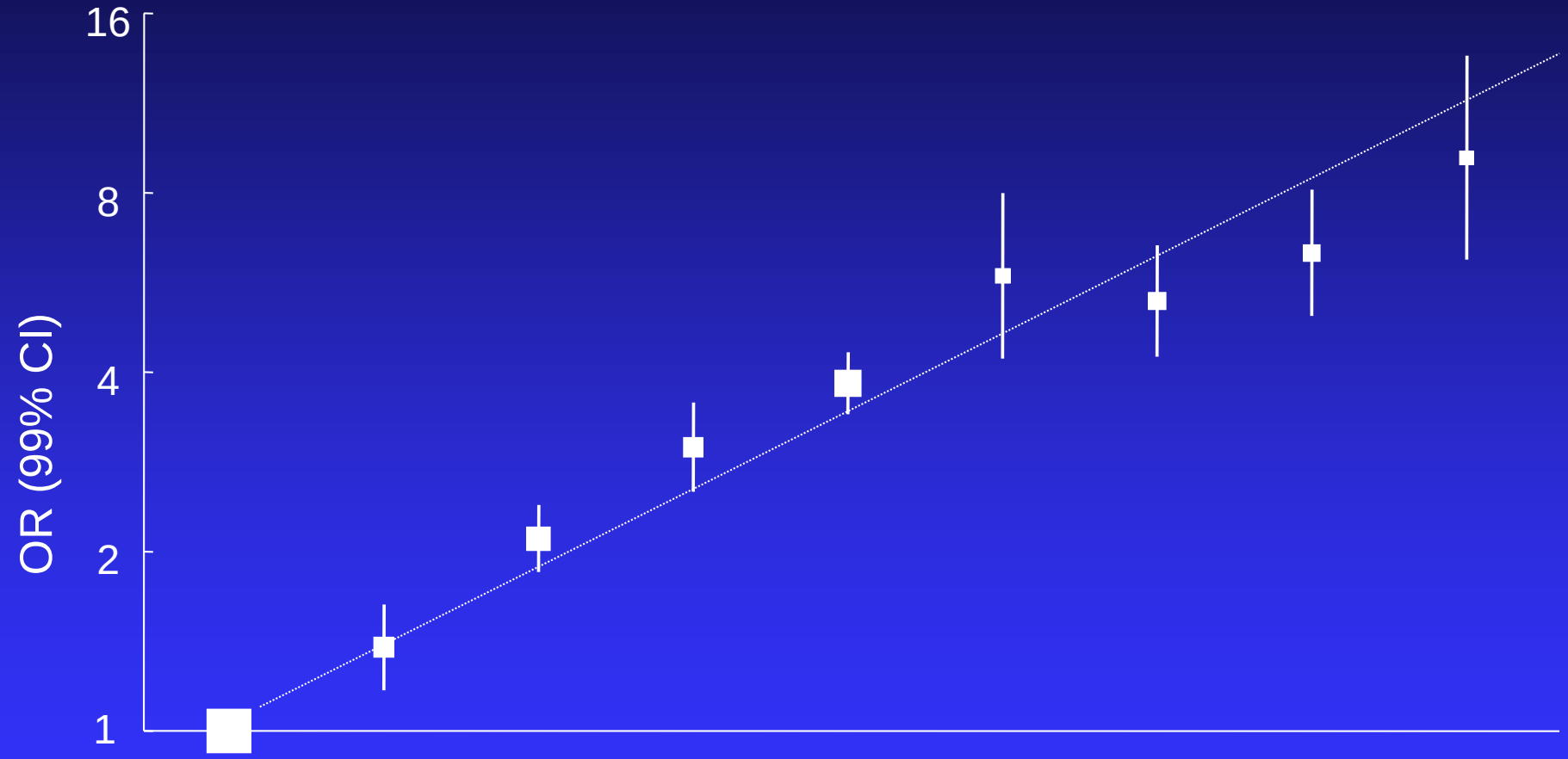
INTERHEART: Apolipoprotein B/A-1 and MI



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

A Global Study of Risk Factors in Acute Myocardial Infarction



	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

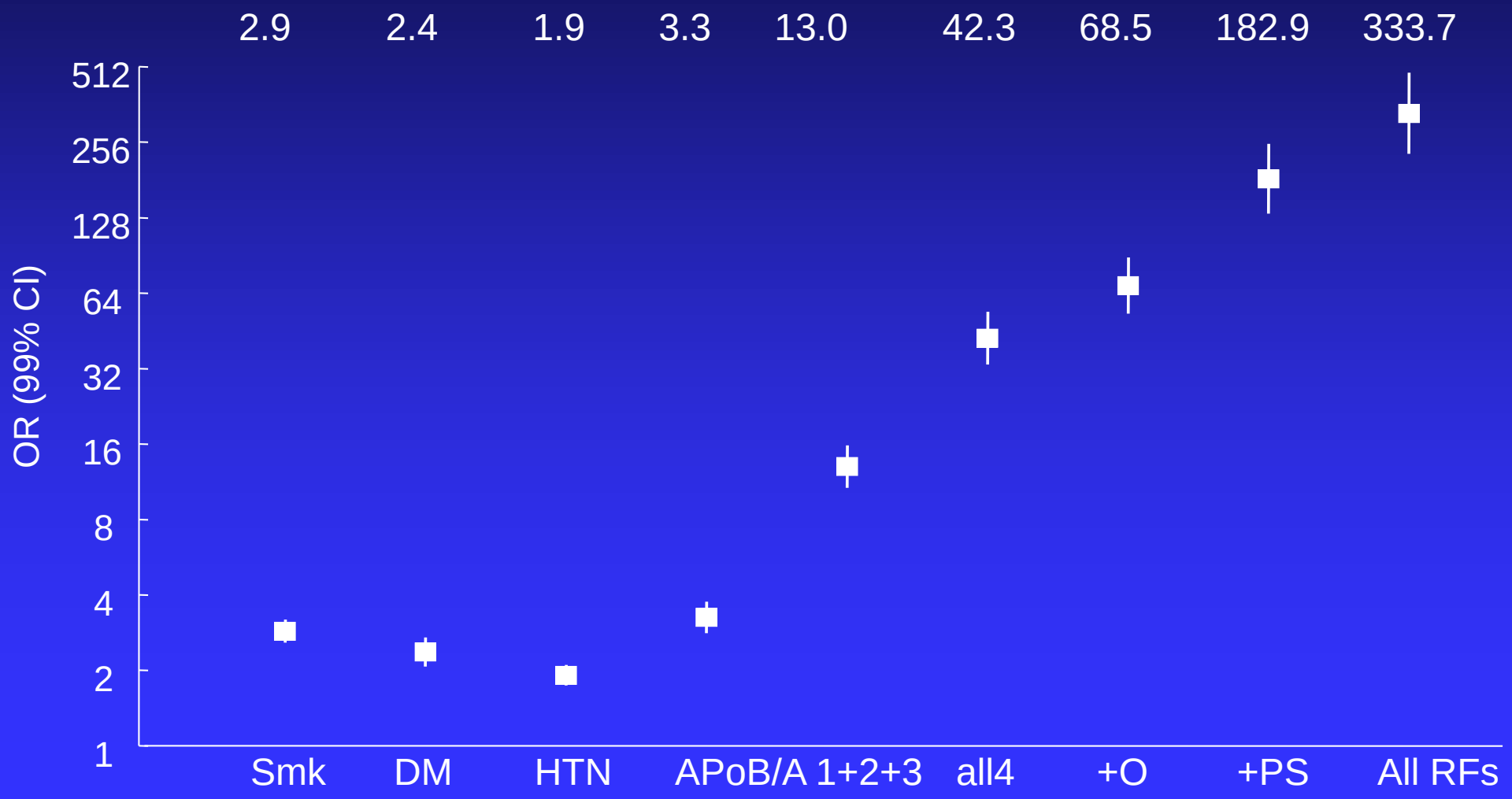
Risk factor	% Cont	% Cases	OR (99% CI) adj for age, sex, smok	OR (99% CI) adj for all
ApoB/ApoA-1 (5 v 1)	20.0	33.5	3.87 (3.39, 4.42)	3.25 (2.81, 3.76)
Curr smoking	26.8	45.2	2.95 (2.72, 3.20)	2.87 (2.58, 3.19)
Diabetes	7.5	18.4	3.08 (2.77, 3.42)	2.37 (2.07, 2.71)
Hypertension	21.9	39.0	2.48 (2.30, 2.68)	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

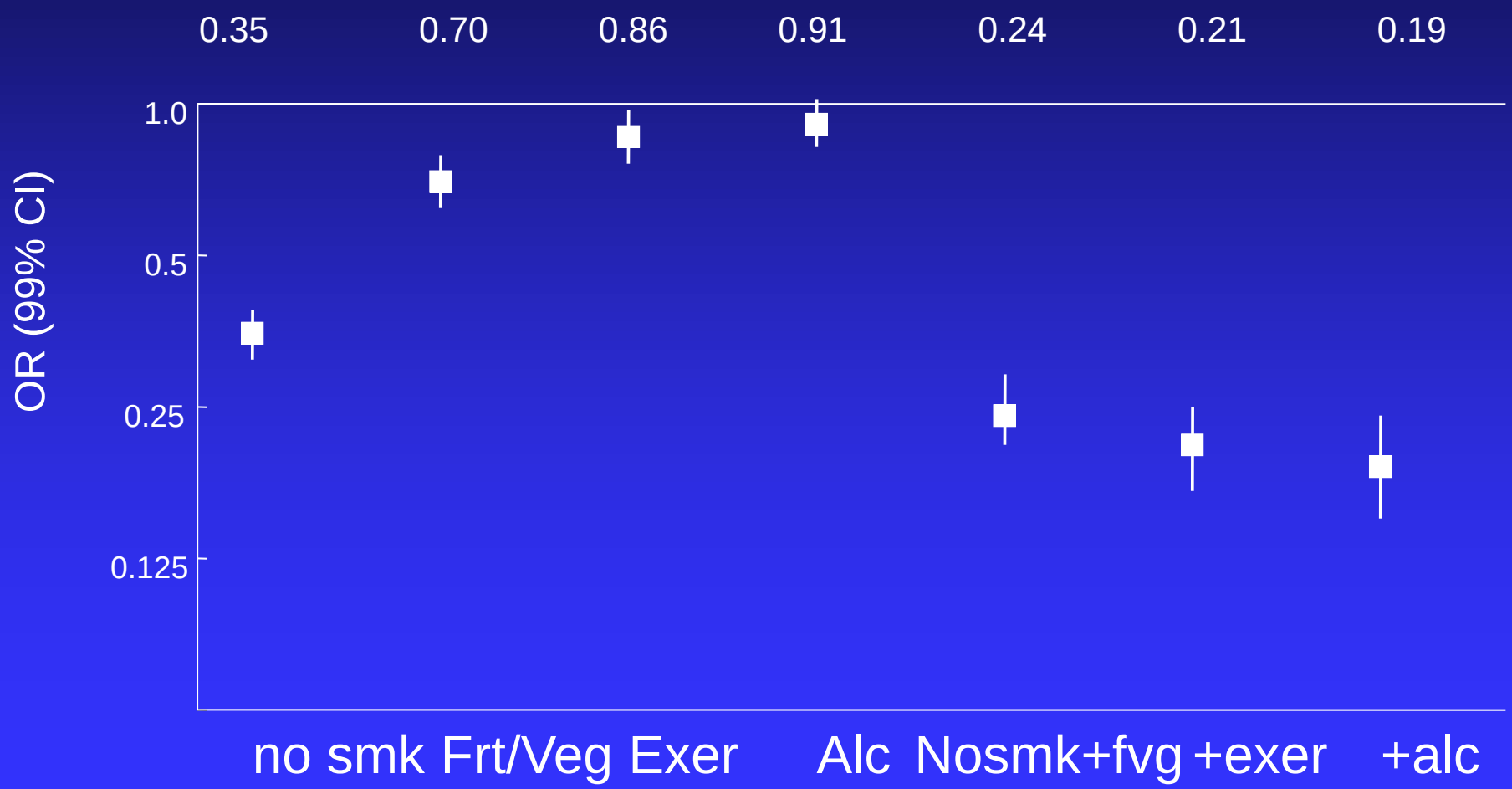
Risk factor	% Cont	% Cases	PAR 1 (99% CI)	PAR 2 (99% CI)
ApoB/ApoA-1(5 v 1)	20.0	33.5	54.1 (49.6, 58.6)	49.2 (43.8, 54.5)
Curr smoking	26.8	45.2	36.4(33.9,39.0)	35.7,(32.5,39.1)
Diabetes	7.5	18.5	12.3 (11.2, 13.5)	9.9 (8.5, 11.5)
Hypertension	21.9	39.0	23.4 (21.7, 25.1)	17.9 (15.7, 20.4)
Abd Obesity (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

A Global Study of Risk Factors in Acute Myocardial Infarction



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**

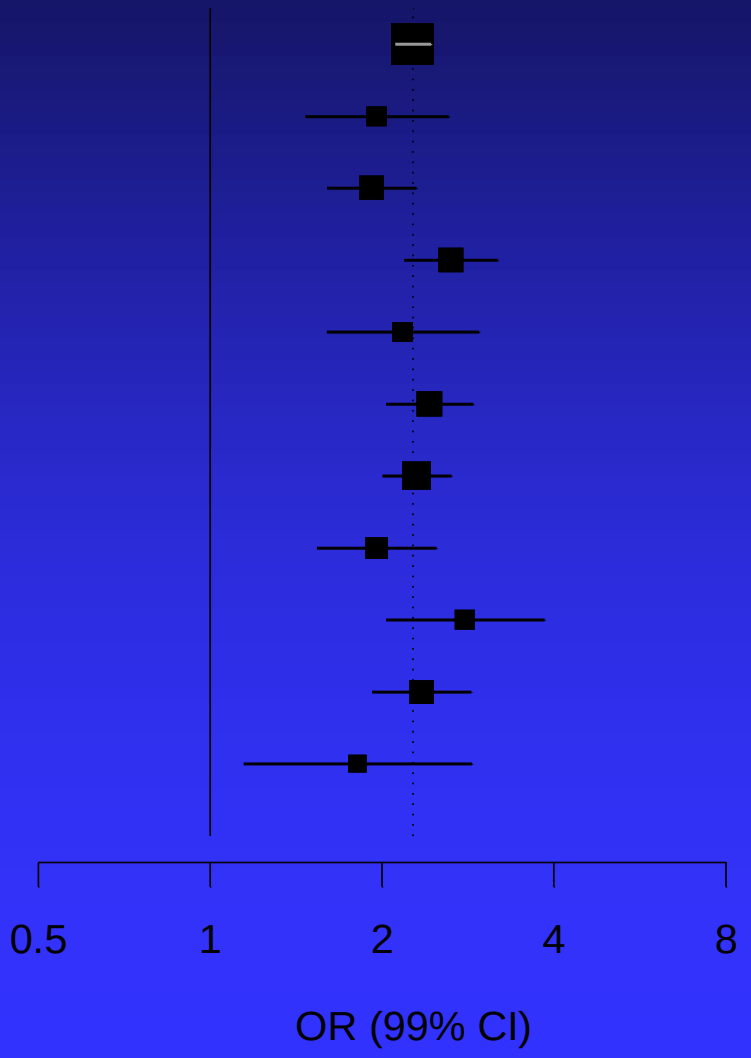
Risk Factor Impact by Age

	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

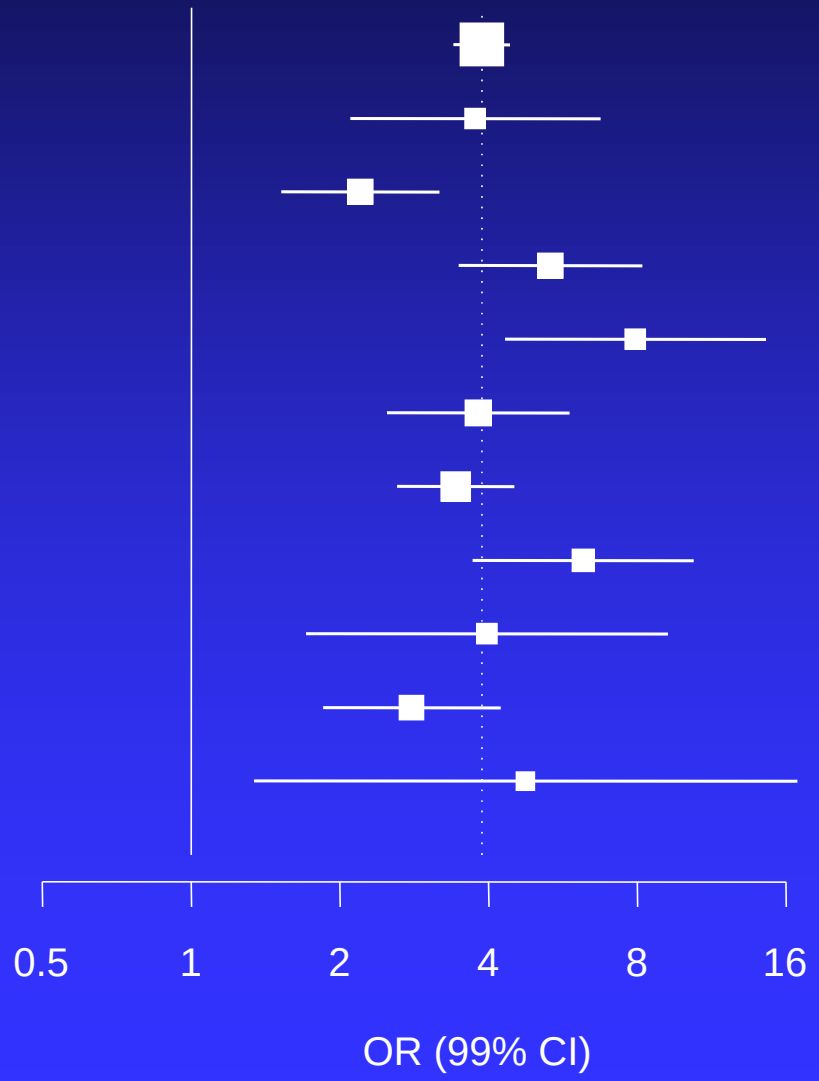
INTERHEART: Current or Former Smoking & MI

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

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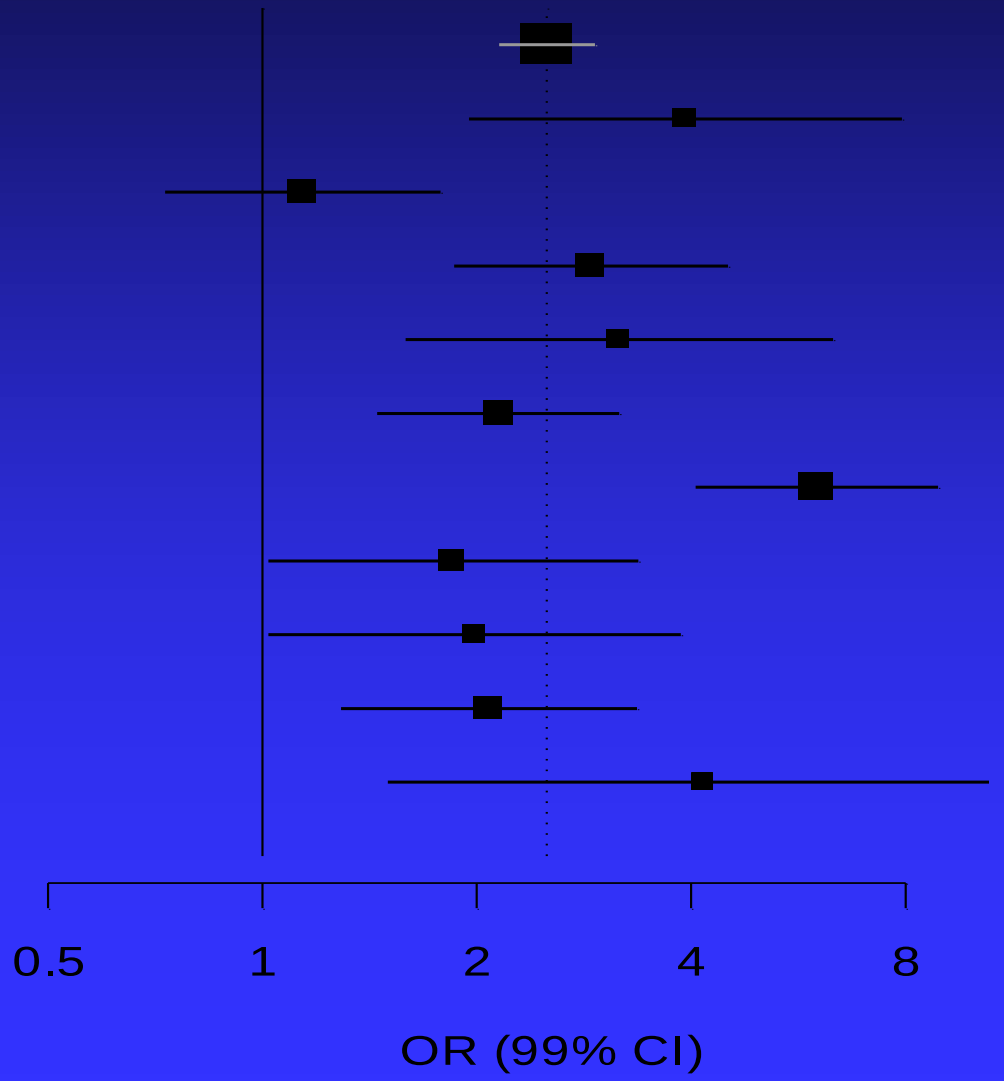
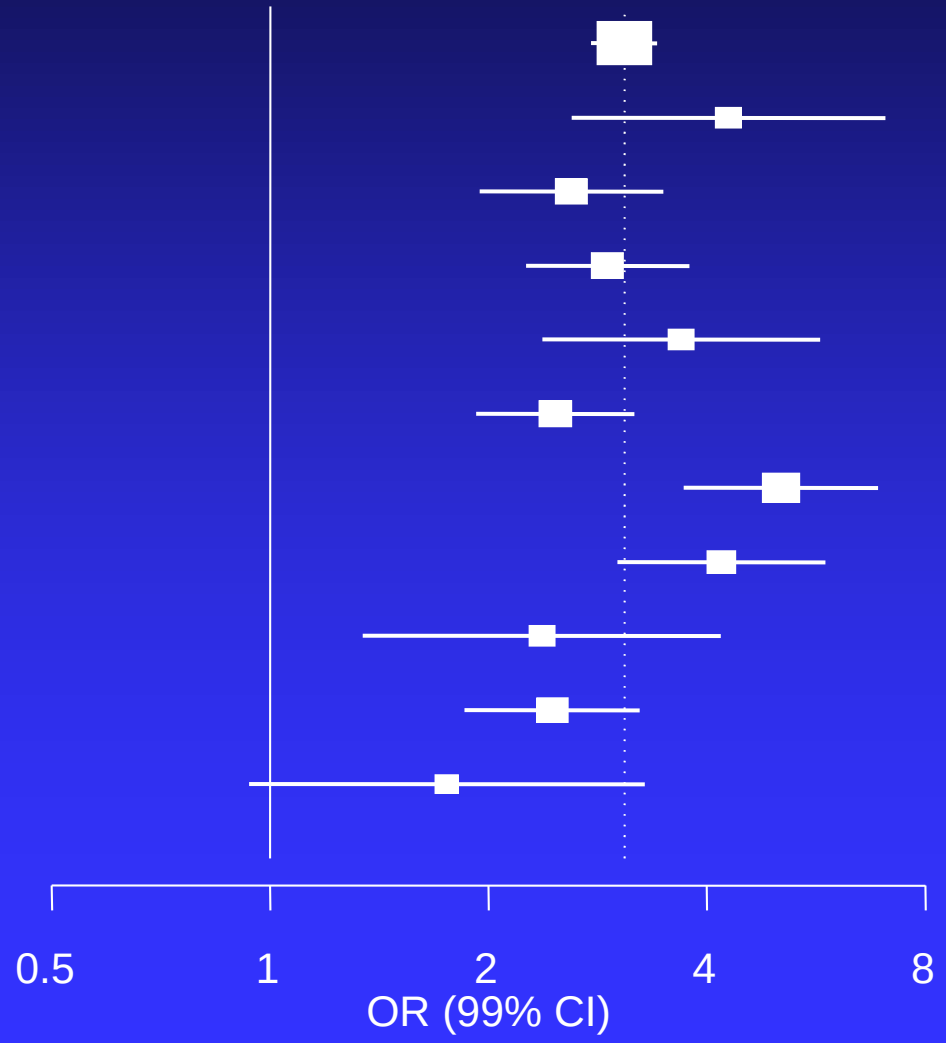
Region	N	OR
Overall	24767	3.11
W.Eur	1375	4.76
C.E.Eur	3473	1.31
M East	2892	3.21
Africa	1259	4.34
S.Asia	3300	2.47
China/HK	5894	7.72
SE Asia	1921	2.76
ANZ	1255	2.81
S.Am.	2783	2.80
N.Am.	615	4.11



INTERHEART: Self-reported Diabetes and MI overall

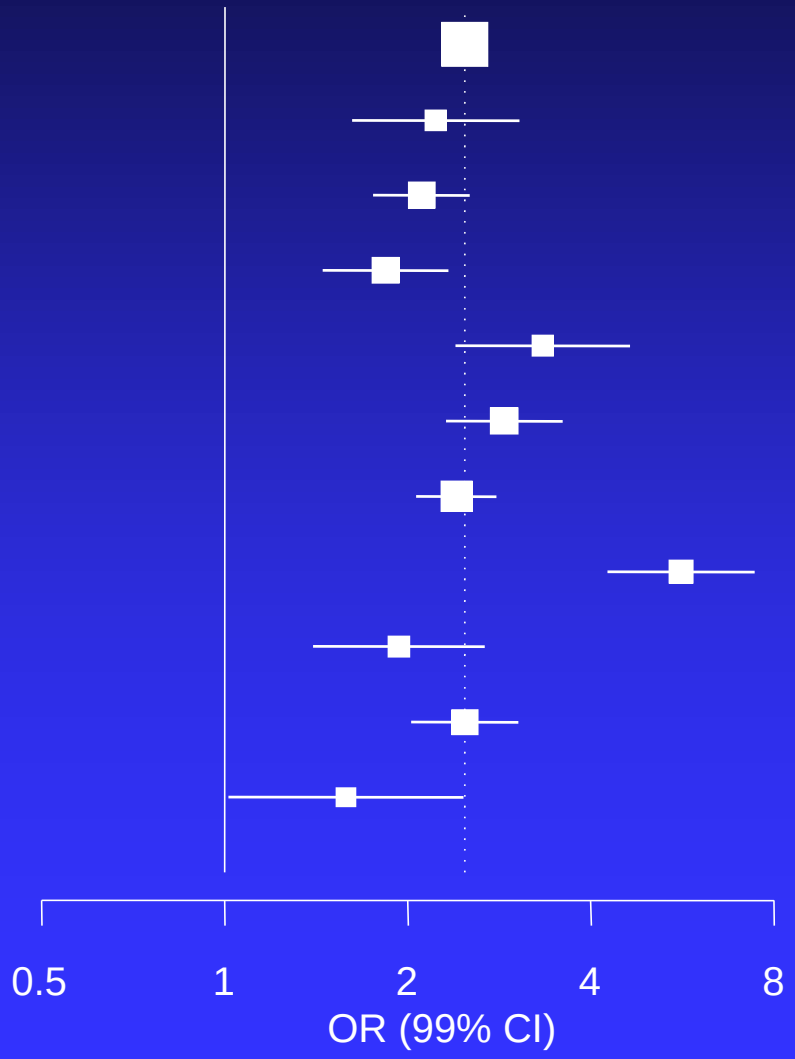
A Global Study of Risk Factors in Acute Myocardial Infarction

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 Actual	Controls 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)

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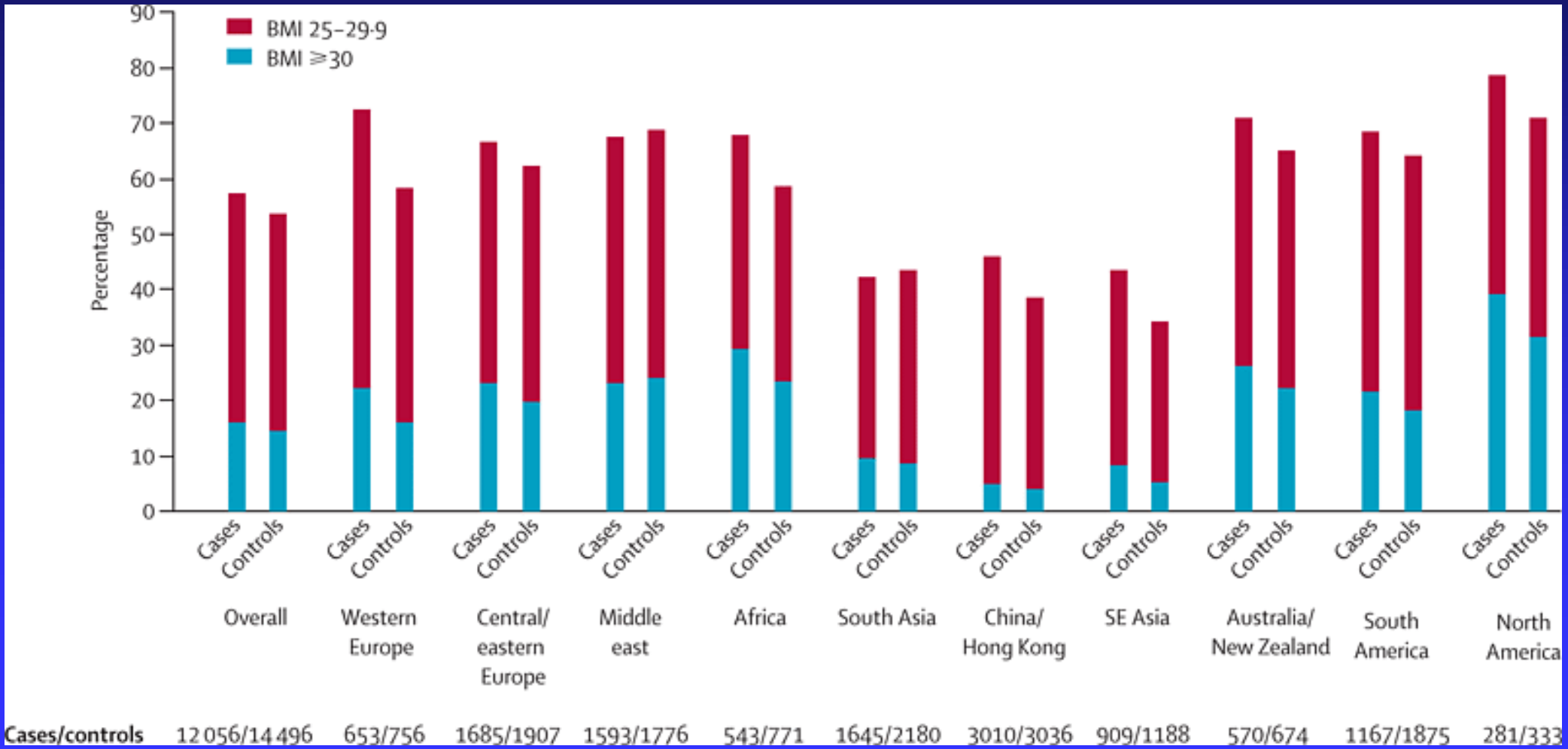
Proportion of cases and controls who are obese or overweight



	Overall	Western Europe	Central/ eastern Europe	Middle east	Africa	South Asia	China/ Hong Kong	SE Asia	Australia/ New Zealand	South America	North America
Cases/controls	12 056/14 496	653/756	1685/1907	1593/1776	543/771	1645/2180	3010/3036	909/1188	570/674	1167/1875	281/333

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

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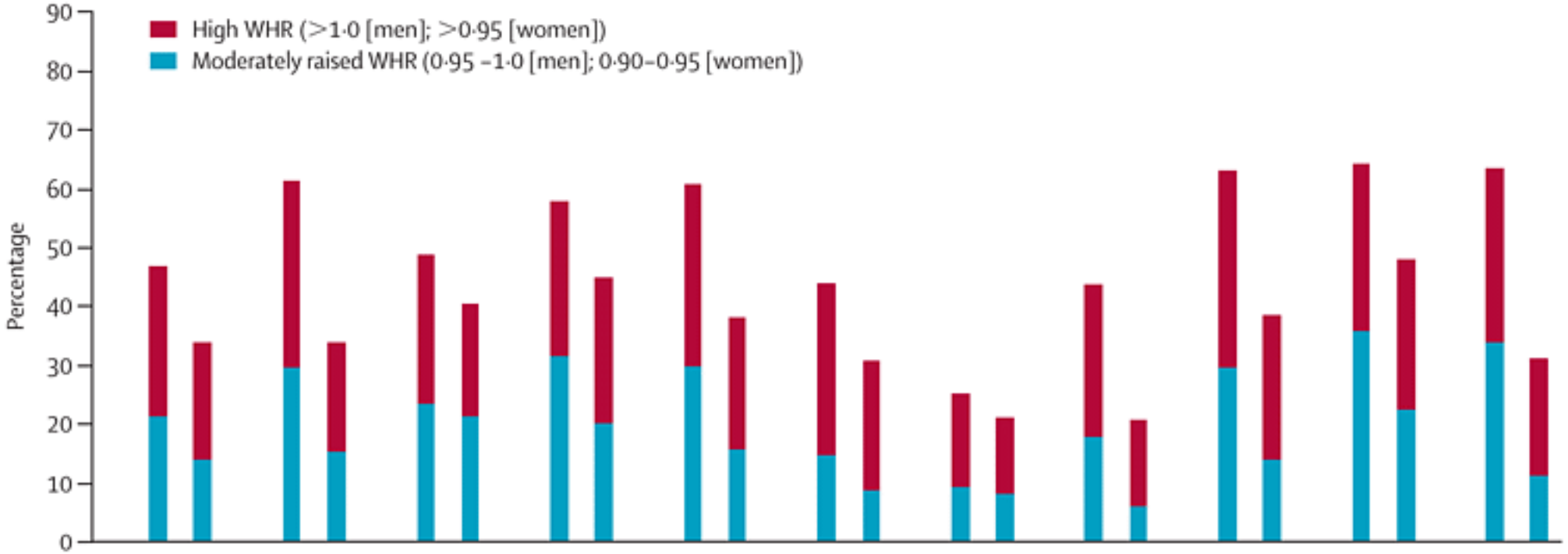
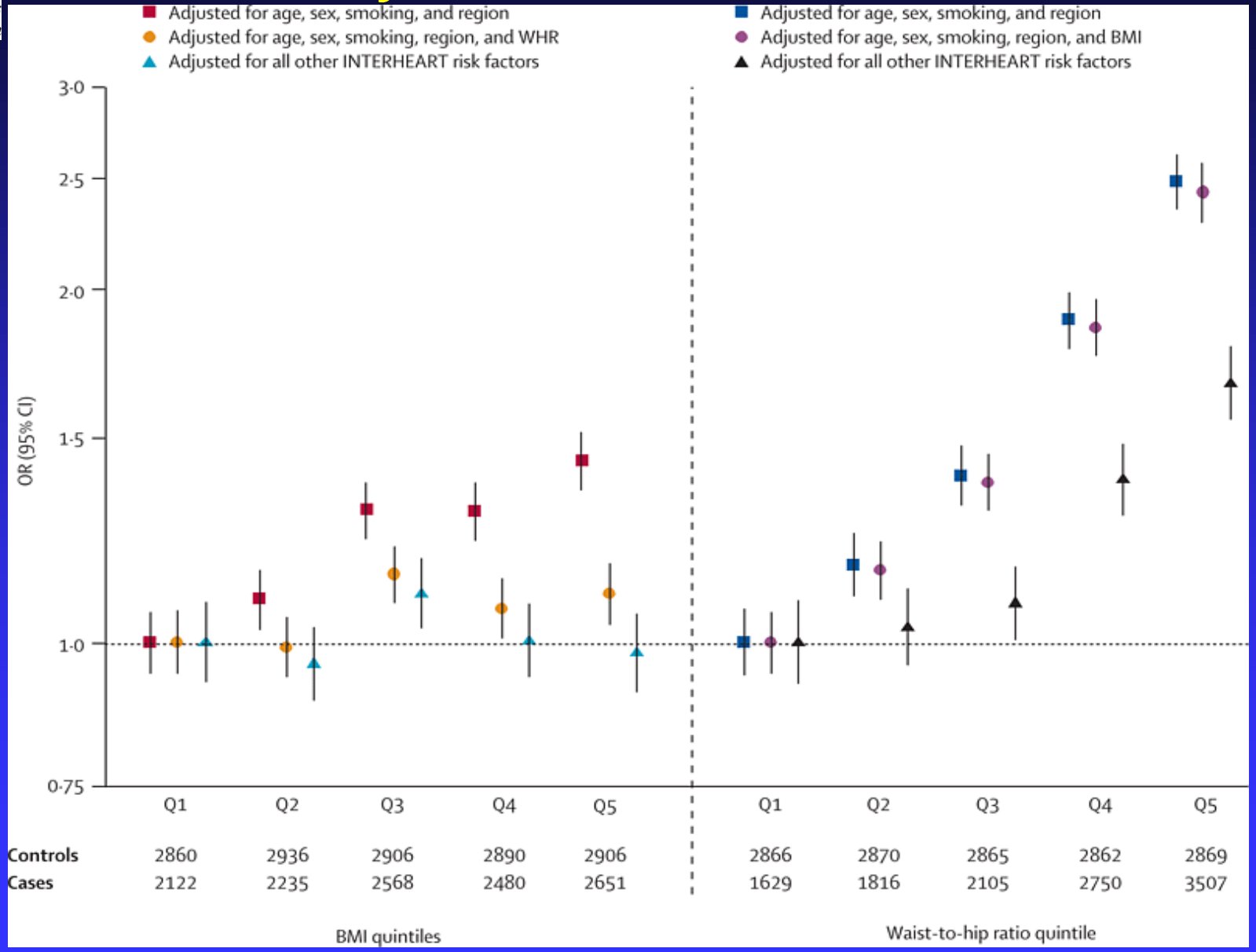
Percentage (age-adjusted) of cases and controls with abdominal obesity (waist-to-hip ratio) overall and by region



	Overall	Western Europe	Central/ eastern Europe	Middle east	Africa	South Asia	China/ Hong Kong	SE Asia	Australia/ New Zealand	South America	North America
Cases/controls	11 807/14 329	597/709	1643/1895	1553/1756	528/737	1644/2177	2989/3029	914/1187	554/670	1118/1841	267/328

INTER-HEART
A Global Study of Risk Factors in Acute Myocardial Infarction

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



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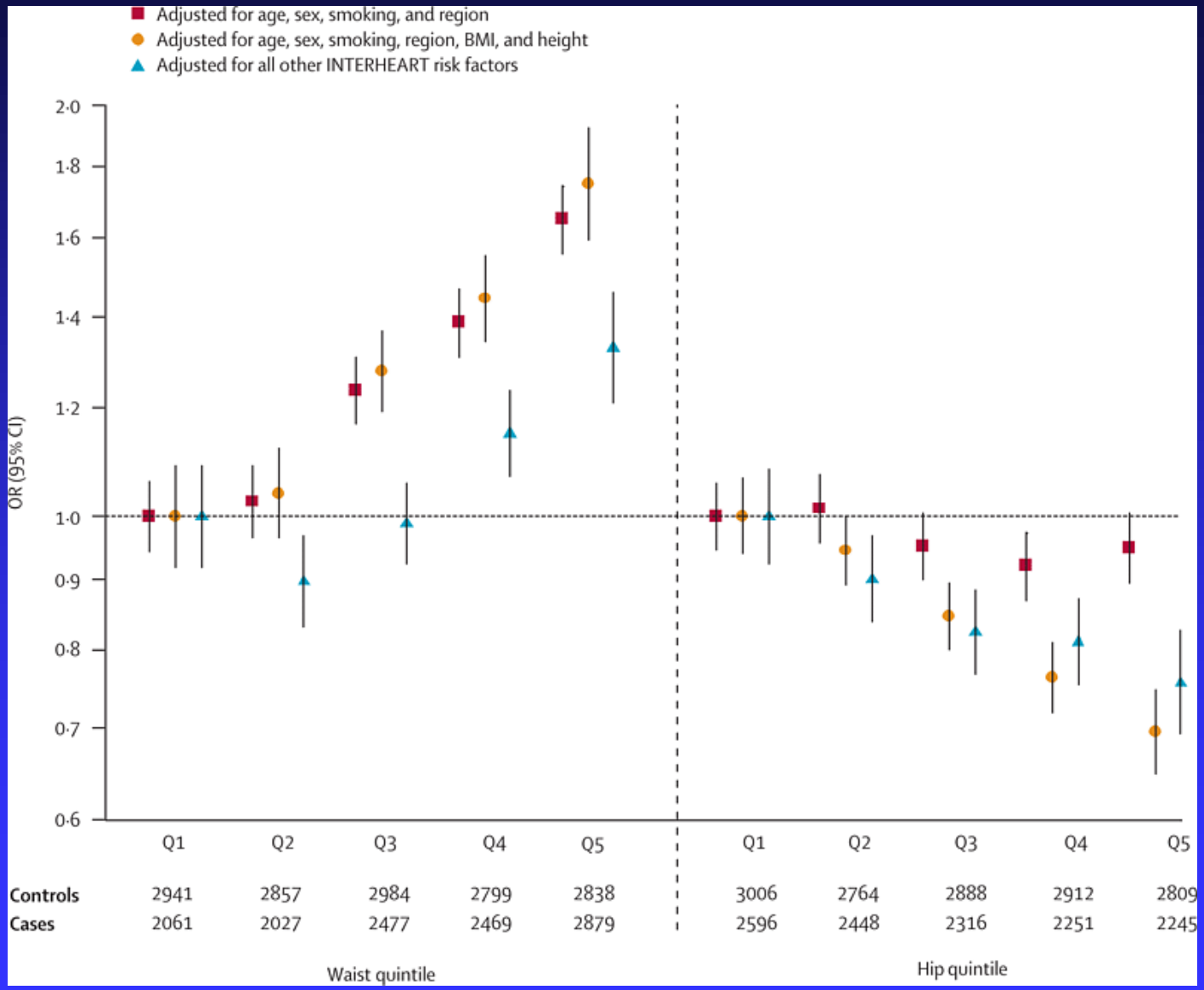
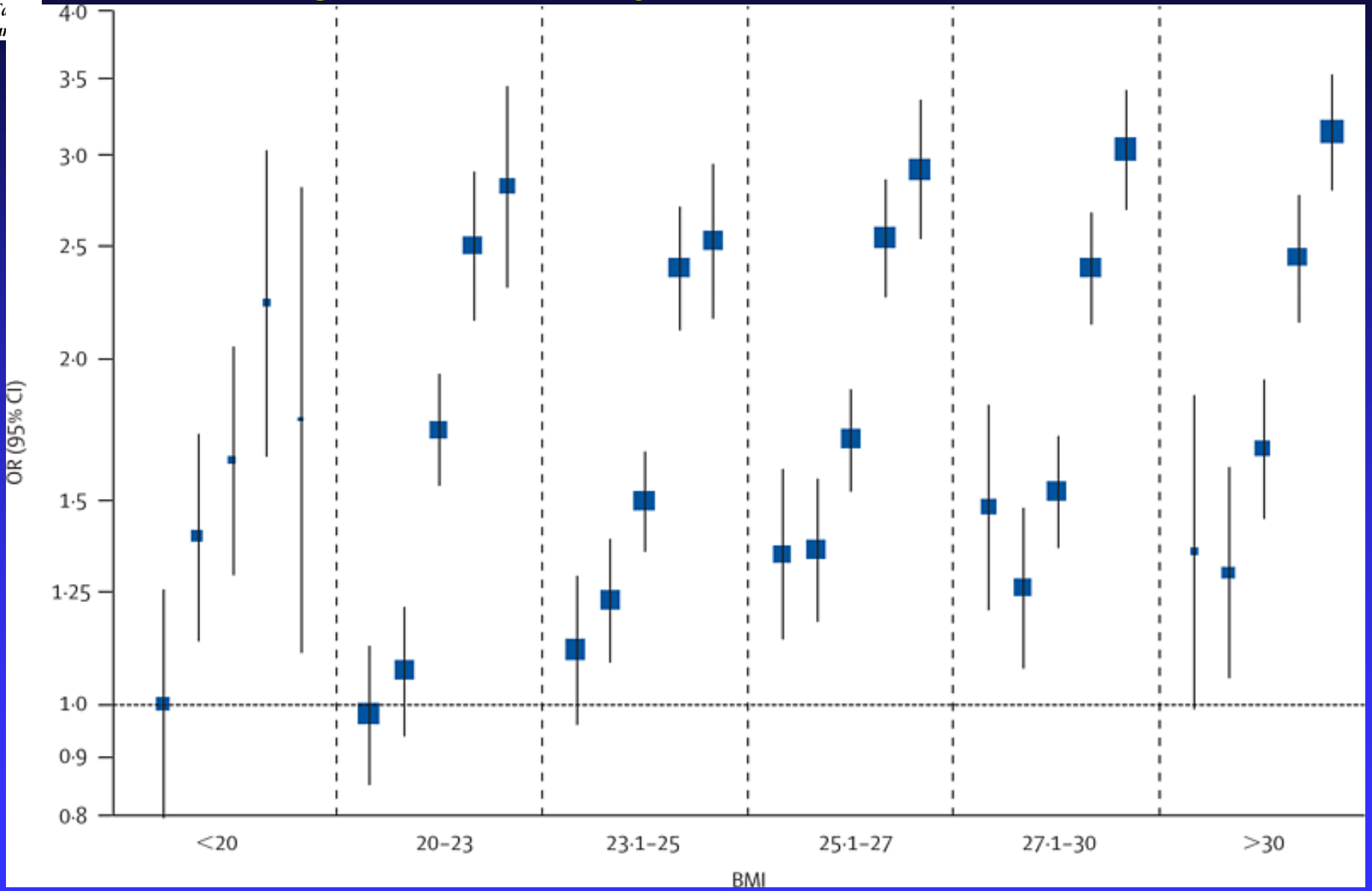
Risk of MI associated with increasing waist circumference and hip circumference



INTER-HEART

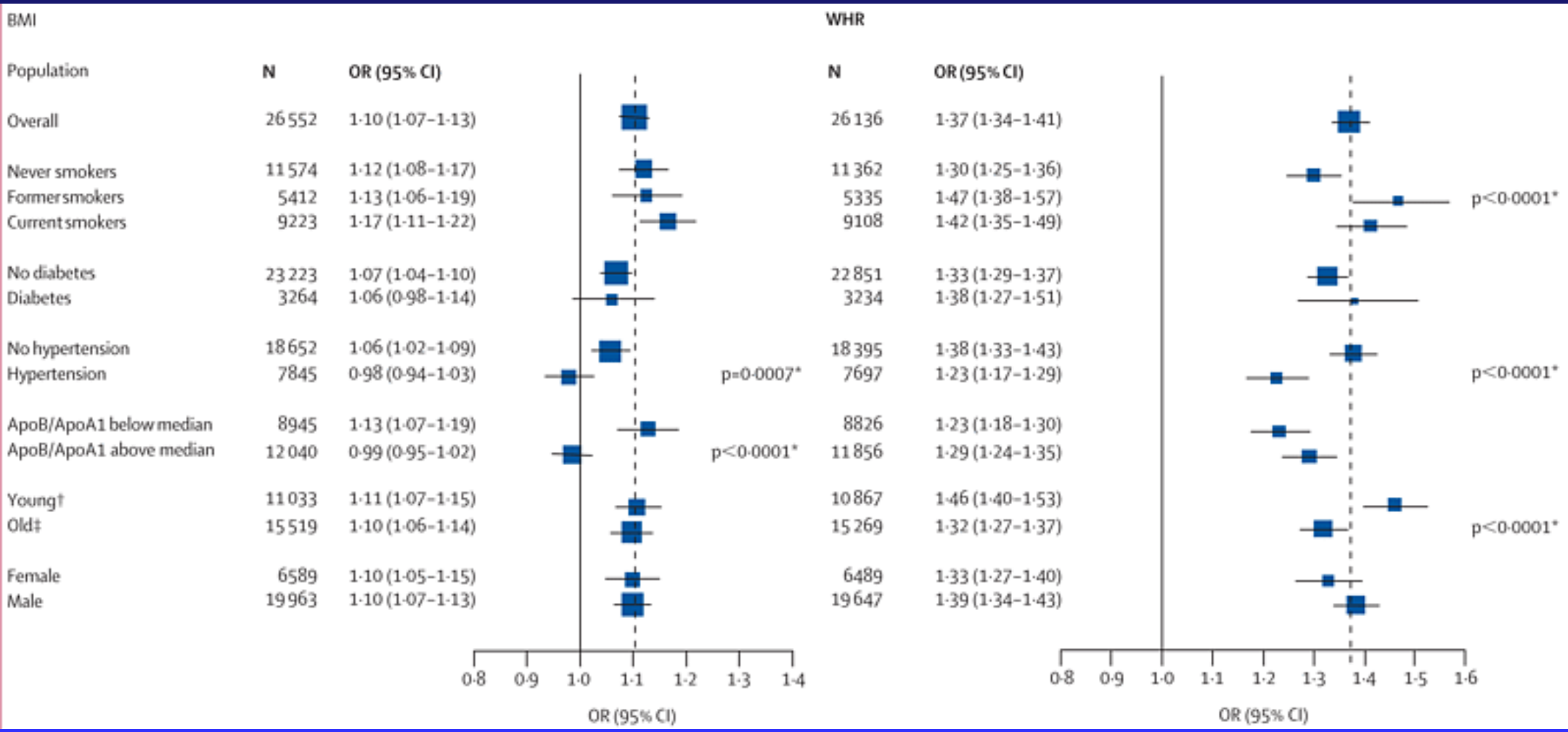
A Global Study of Risk Fa
in Acute Myocardial Infa

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



INTER-HEART
A Global Study of Risk Factors in Acute Myocardial Infarction

Odds ratio for myocardial infarction for 1 SD increase



INTER-HEART
A Global Study of Risk Factors in Acute Myocardial Infarction

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)

INTER-HEART
A Global Study of Risk Factors in Acute Myocardial Infarction

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.

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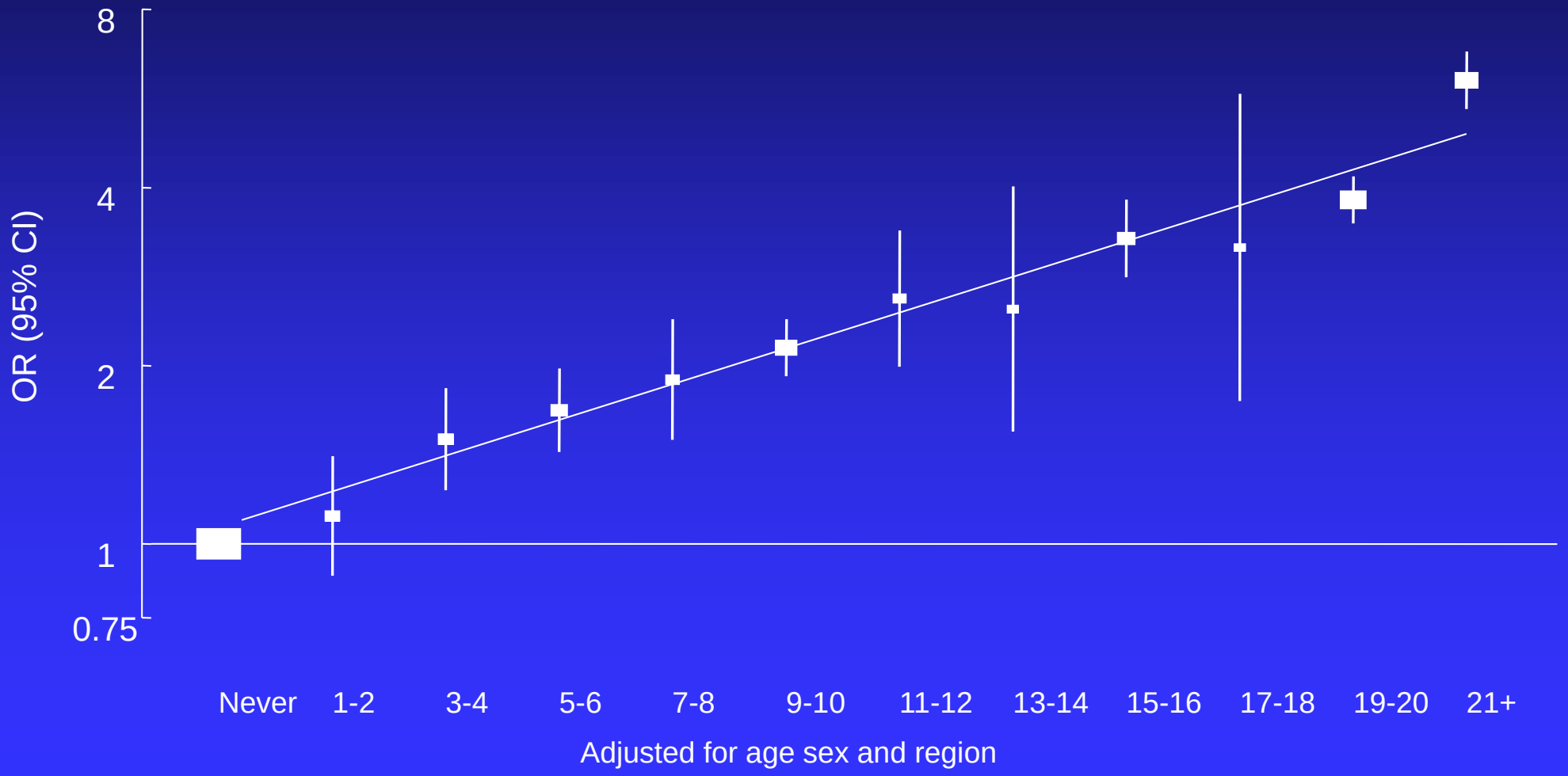
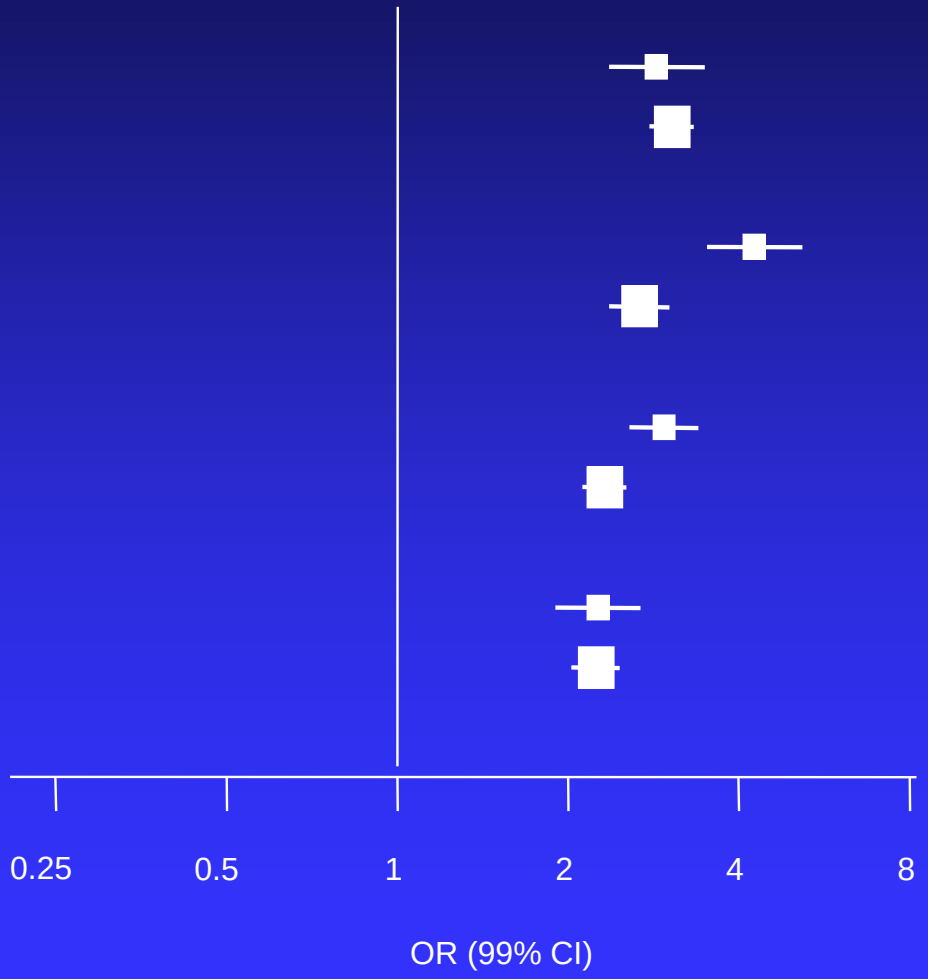
Low Levels of Smoking and MI



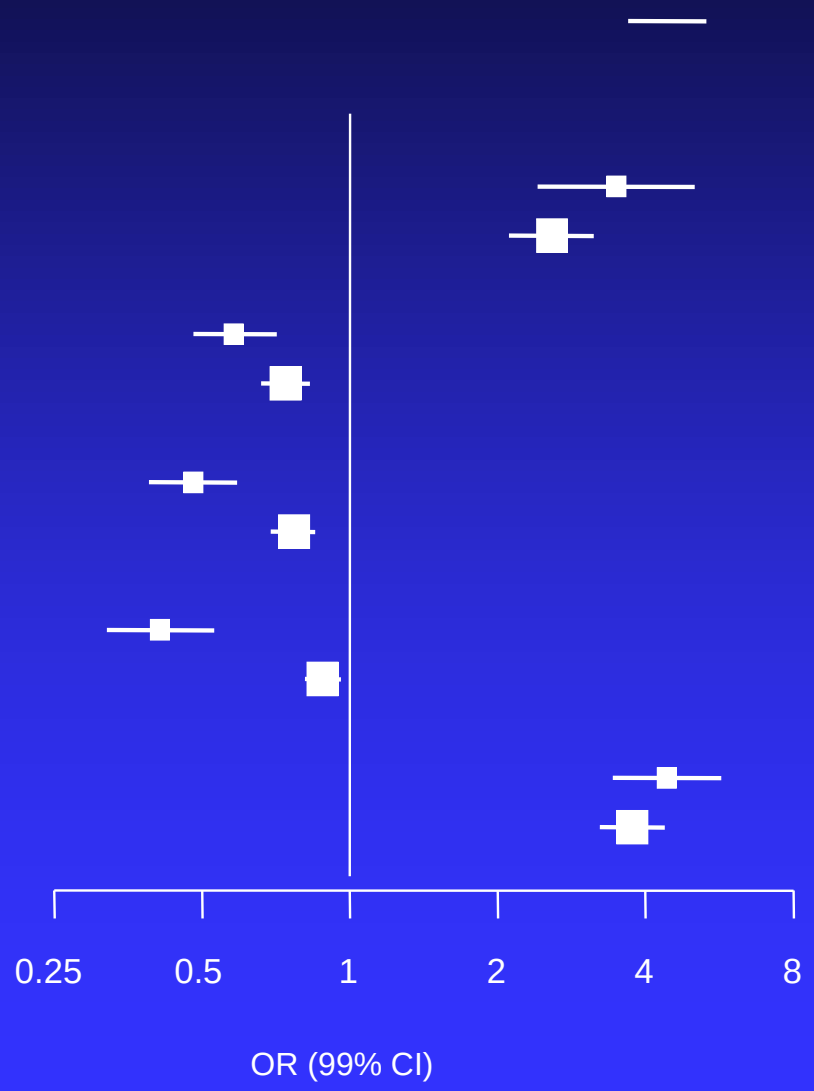
INTERHEART: Association of Risk Factors with AMI in Men & Women (1)

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.