LDL-Cholesterol lowering
an endocrinologist perspective

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INSERM CIC

DOI 2014-2017

	Speaking fees	Expertise / Sc Board participation	Investigator honorarium	Invitations to meetings	Other support / research
AADAIRC					x
AstraZeneca/BMS	x	x	x	x	
Abbott		x			x
Boehringer Ingelheim	x	x	x		
Eli-Lilly	x	x	x		
Dinno Santé					x
Janssen	x		x	x	
LVL				x	
Merck Sharpe Dome	x	x		x	
Novartis	x				x
Novo Nordisk	x	x	x		
Sanofi	x	x	x	x	

- ✓ EPIDEMIOLOGY OF CV DISEASE
- ✓ CV RISK STRATIFICATION

- ✓ **EPIDEMIOLOGY OF CV DISEASE**
- ✓ **CV RISK STRATIFICATION**

EPIDEMIOLOGY OF CV DISEASE

- Do we really lack knowledge on risk factors for Myocardial Infarction ?
  - INTERHEART
- Do we have new data on CV, nonCV and all cause death regarding CV risk factors ?
  - PURE program

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

Questionnaire:	demographics, lifestyle, health hx, psychosocial, medications
Physical measures:	height, weight, waist & hip circum, blood pressure, heart rate
Blood sample:	20 ml

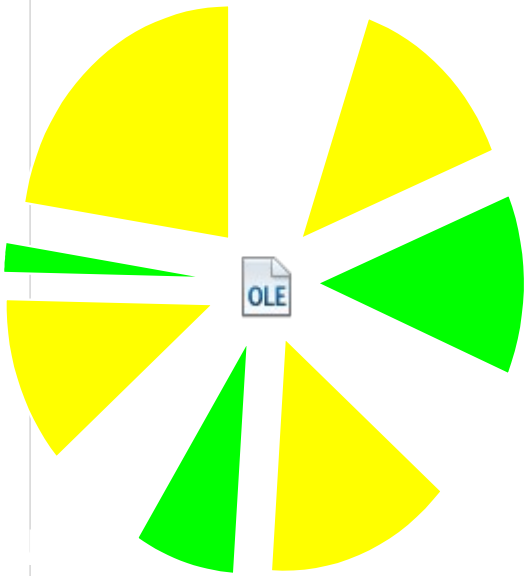
Statistical methods:	OR and PAR both presented with 99% confidence intervals. All analyses adjusted for age, sex and region.

52 Countries Representing Every Inhabited Continent

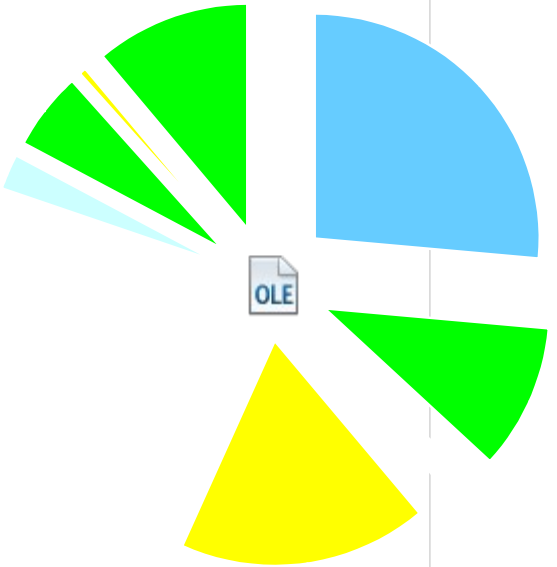
Argentina
Australia
Bahrain
Bangladesh
Benin
Botswana
Brazil
Cameroon
Canada
Chile
China/Hong Kong
Croatia
Czech Rep
Egypt
Germany
Greece
Guatemala
Hungary
India
Iran
Israel
Italy
Japan
Kuwait
Malaysia
Mexico
Mozambique
Nepal
New Zealand
Netherlands
Nigeria
Pakistan
Philippines
Poland
Portugal
Russia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

15,152 MI cases and 14,820 controls

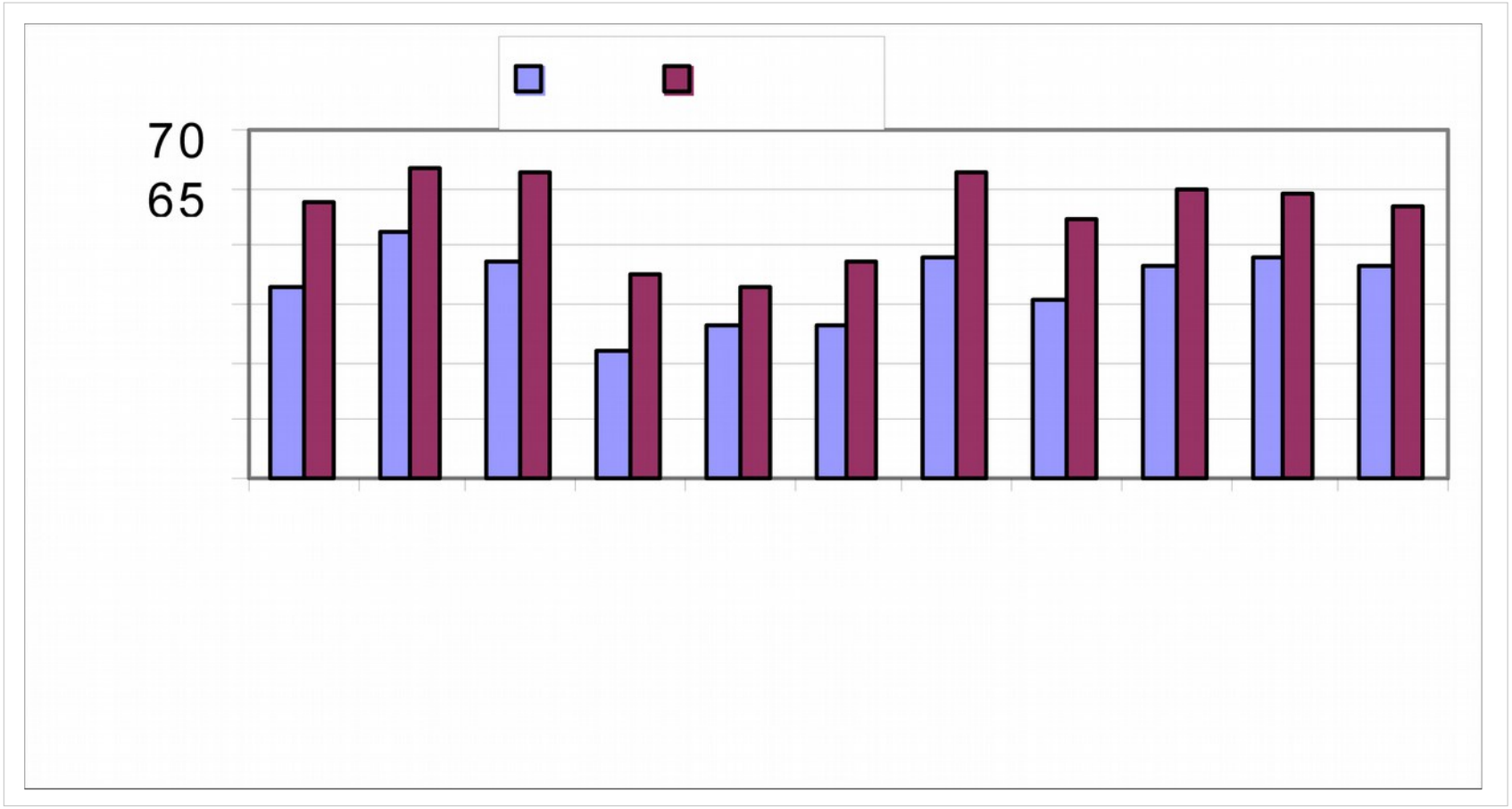
Distribution by region



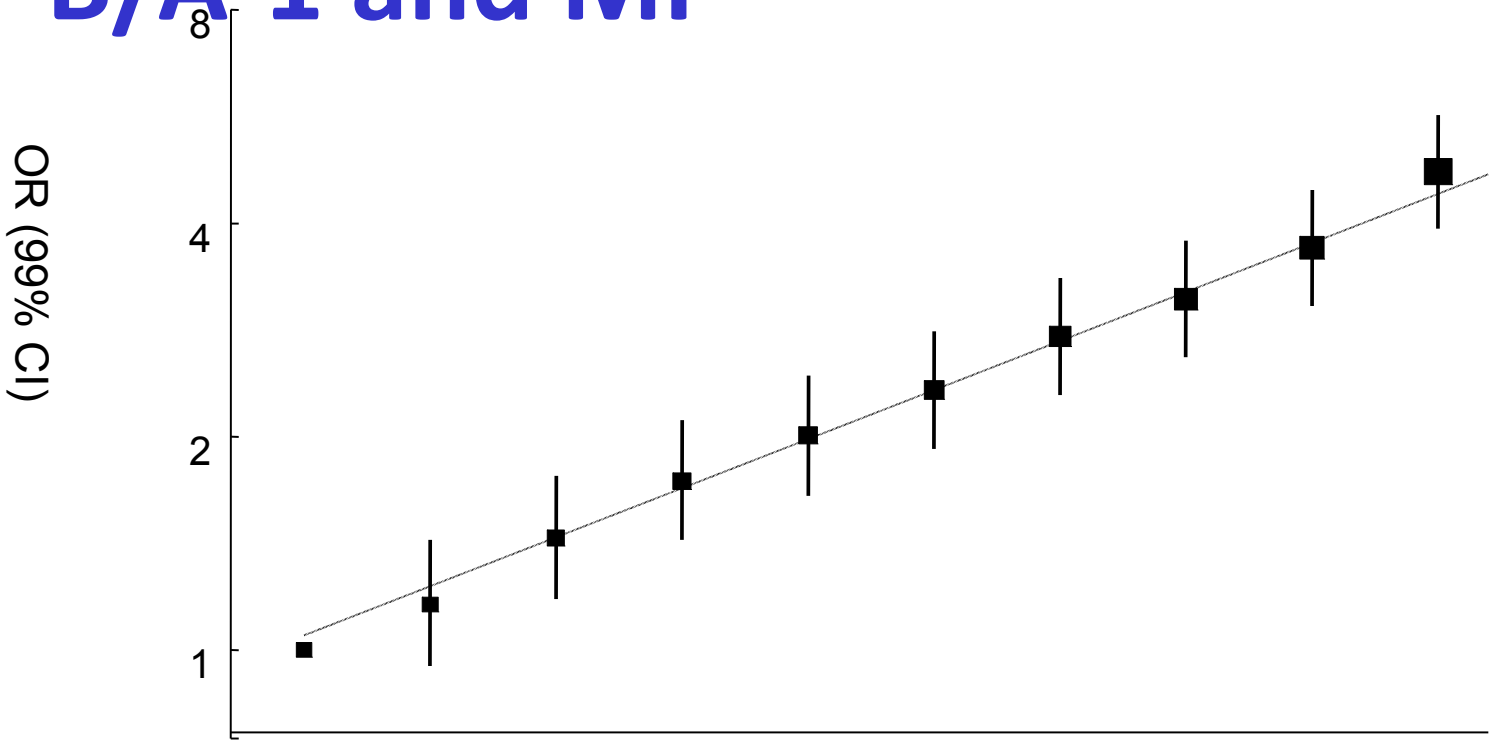
Distribution by ethnicity



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

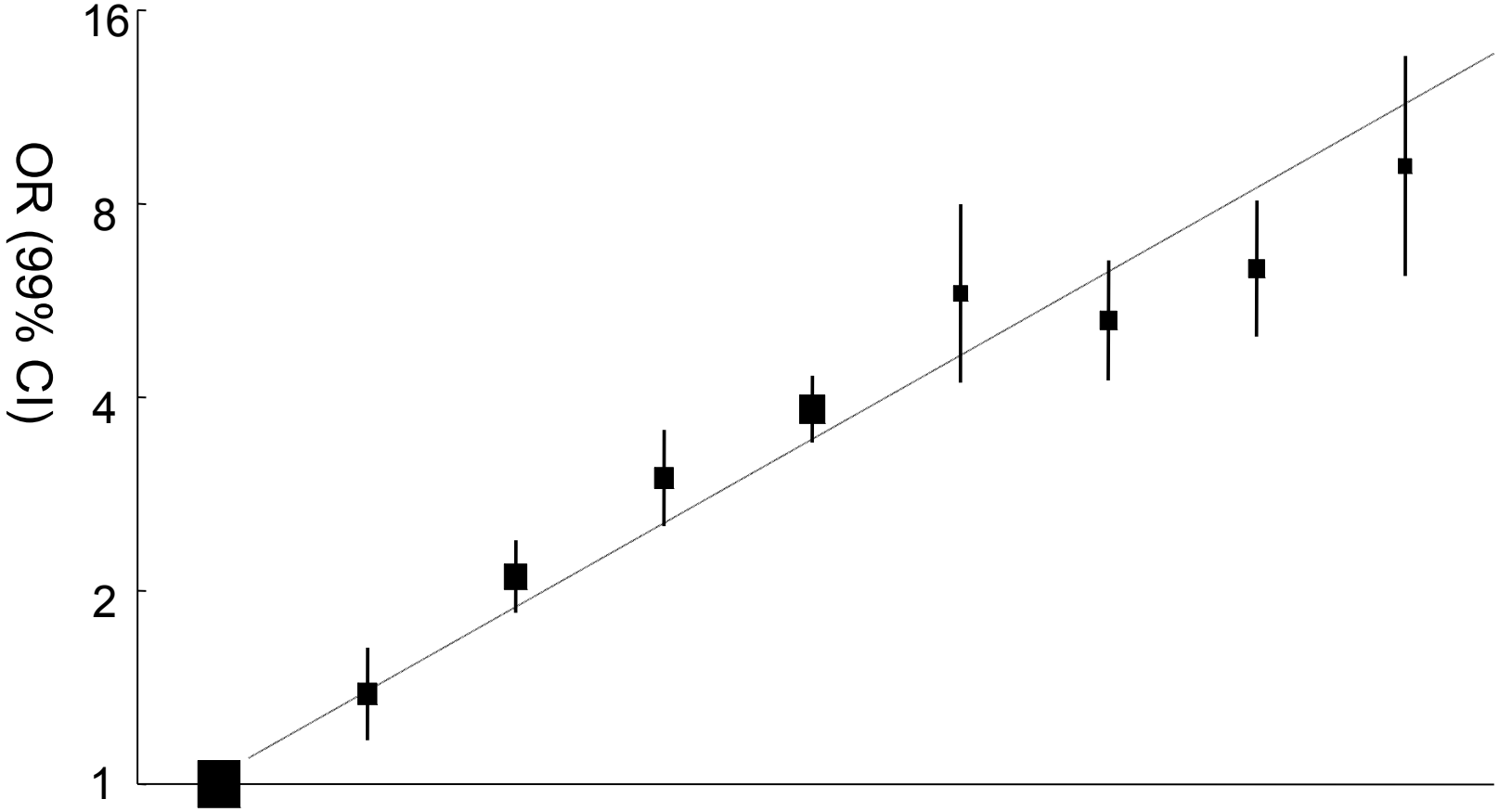


INTERHEART: Apolipoprotein B/A-1 and MI



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

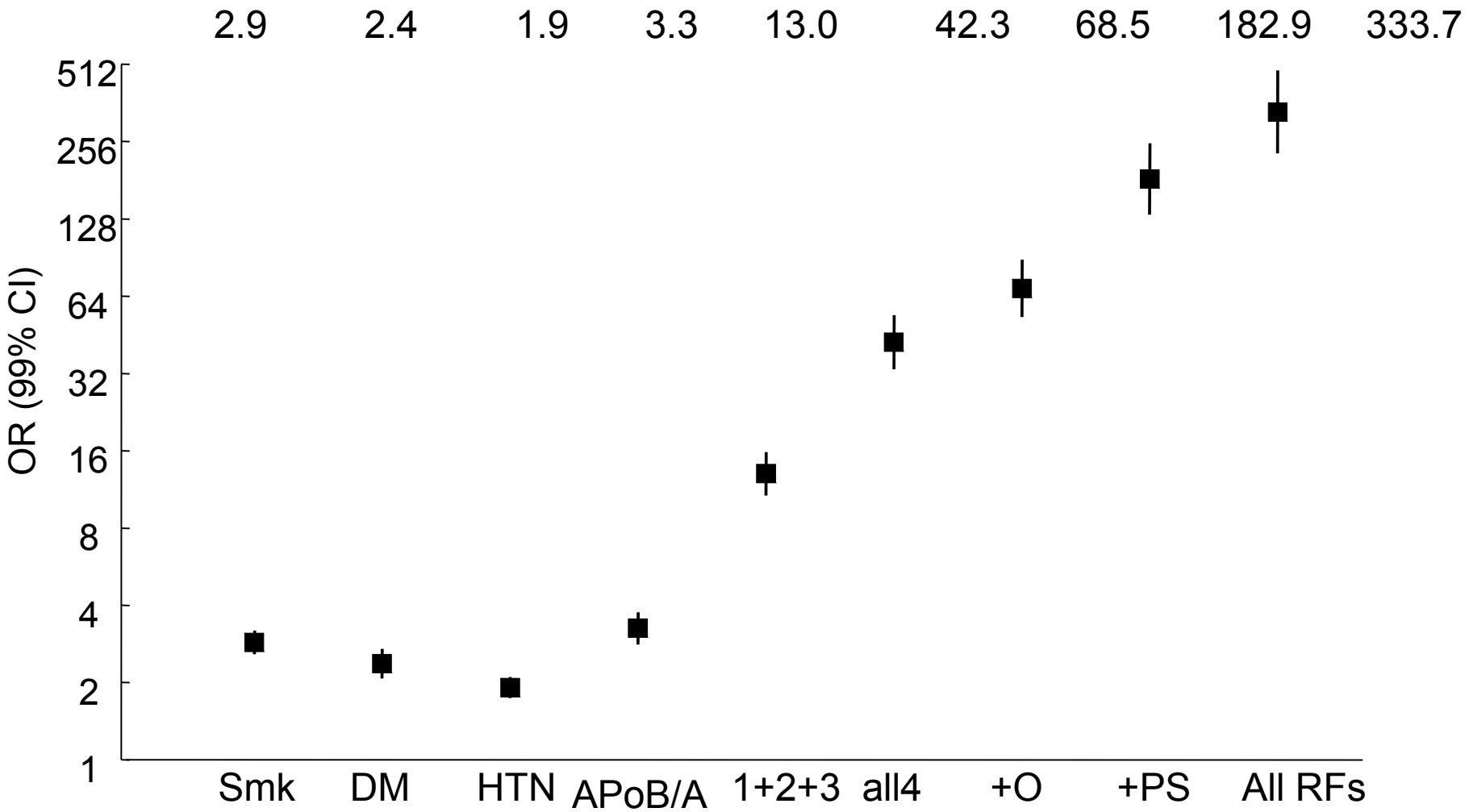


	Never	1-5	6-10	11-15	16-20	21-25	26-30	31-40	41+
Cont	7489	727	1031	446	1058	96	230	168	56
Cases	4223	469	1021	623	1832	254	538	459	218
OR	1	1.38	2.10	2.99	3.83	5.80	5.26	6.34	9.16

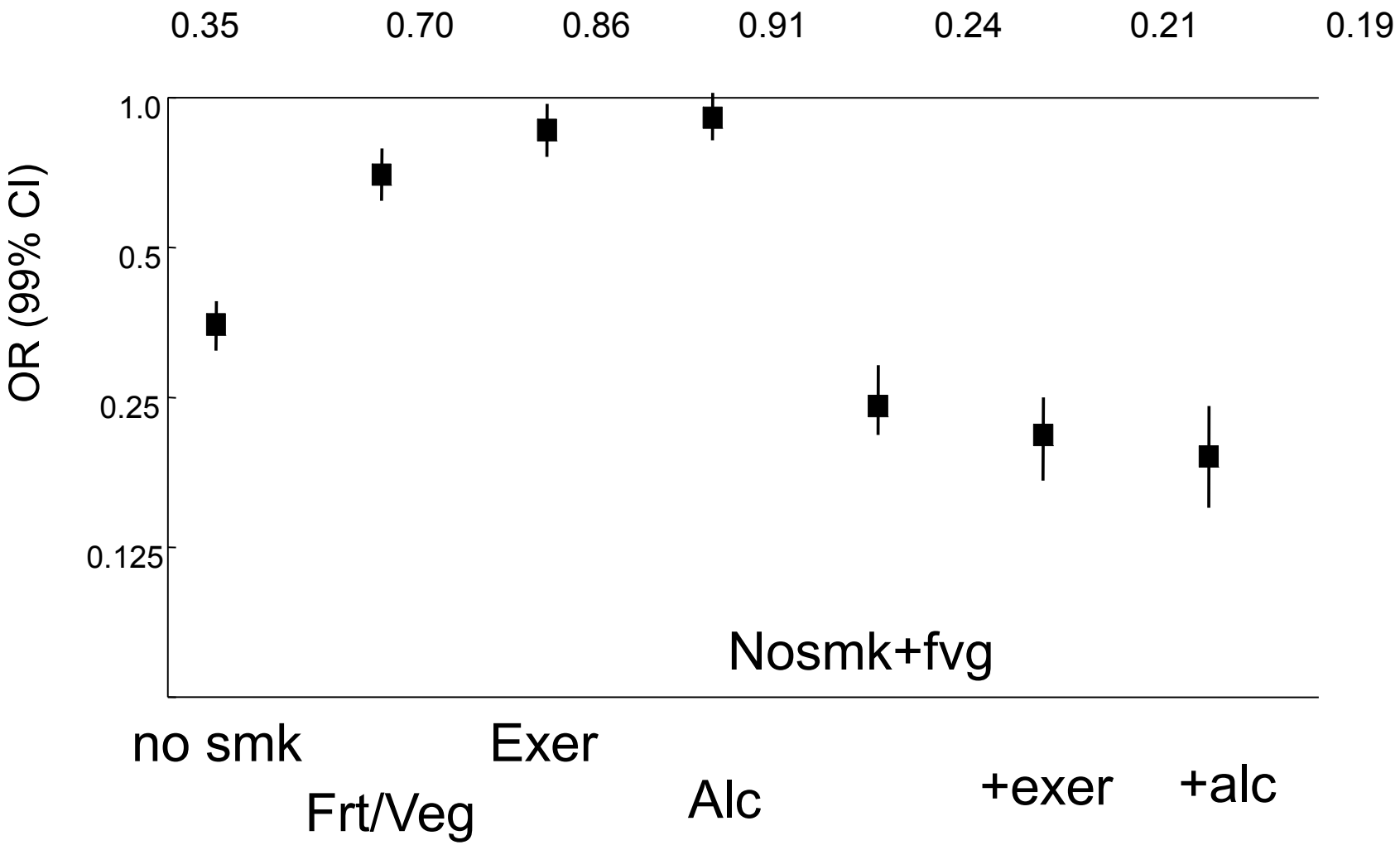
Risk of AMI associated with Risk Factors in the Overall Population

Risk factor	% Cont	% Cases	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**

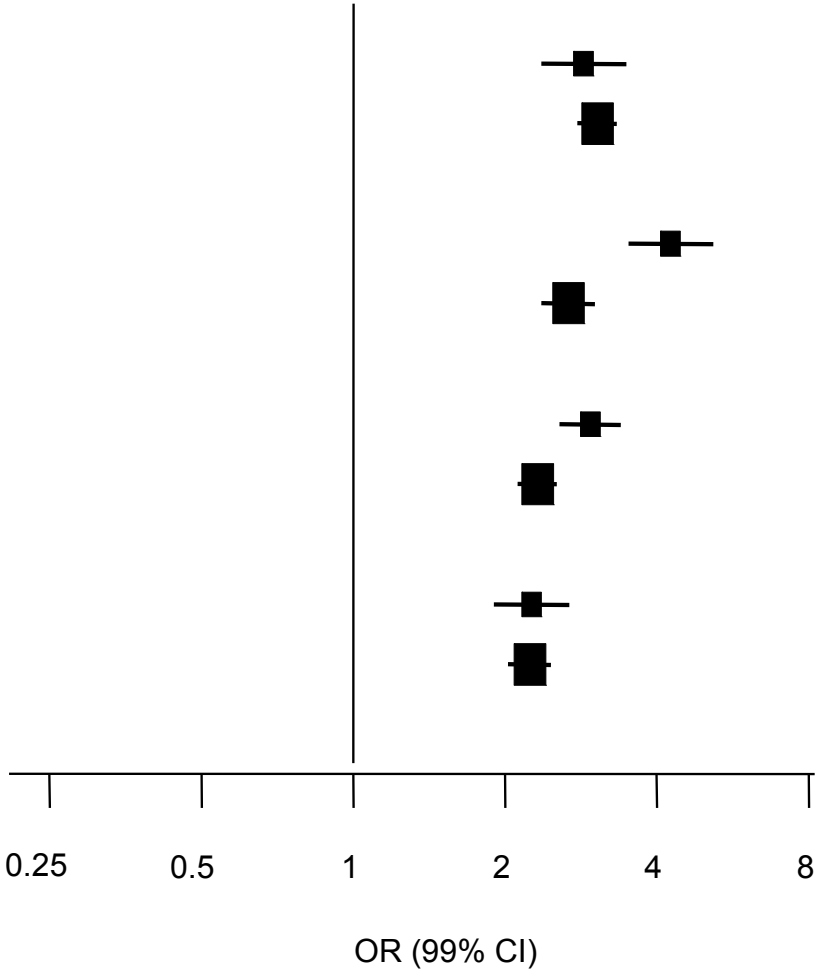
Risk Factor Impact by Age

	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 PF	216.47	81.99*	93.8	87.9

P for interactions: *p<0.001

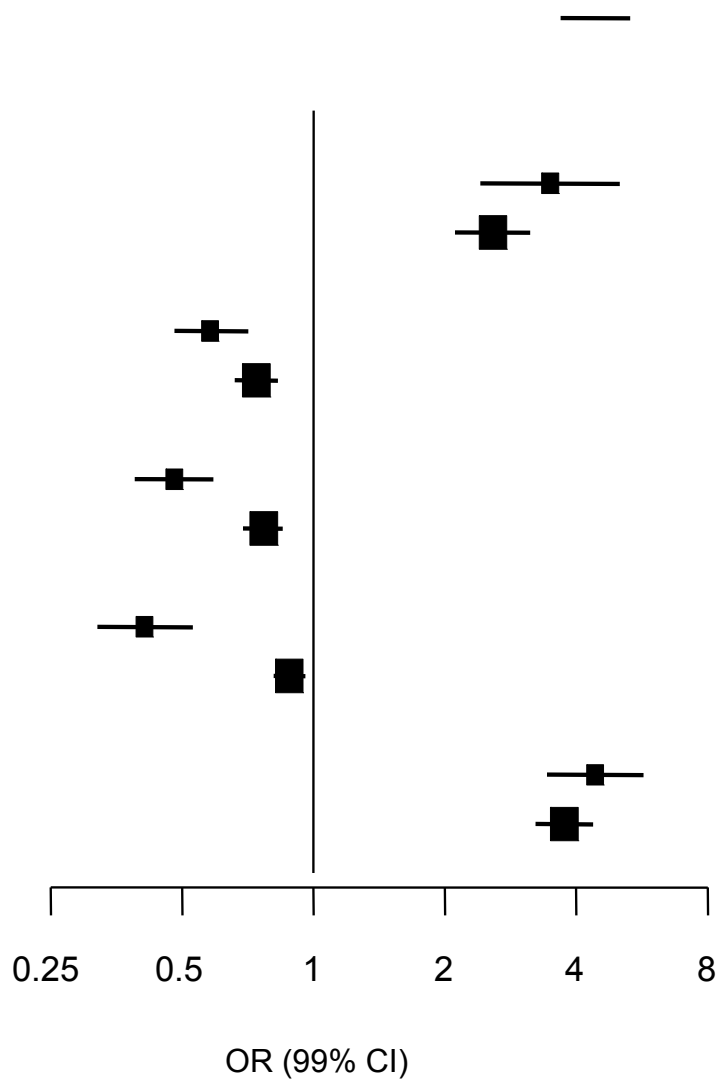
INTERHEART: Association of Risk Factors with AMI in Men & Women (1)

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



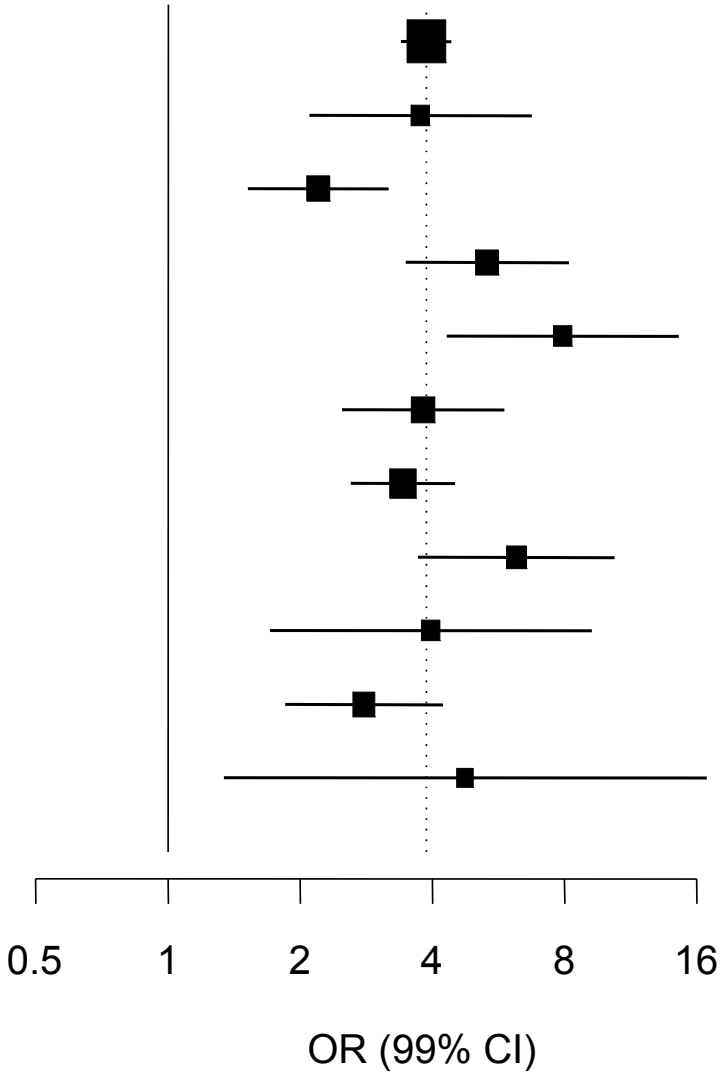
INTERHEART: Association of Risk Factors with AMI in Men & Women (2)

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: 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



PURE Program

Prospective Urban Rural Epidemiology

Epidemiology of CVD events, nonCV, CV and all-cause death – A global approach

- Beyond data from EU/North America for CV related health outcomes
- If found in other settings, other ethnicities MORE CHANCE for a given factor TO BE TRULY ASSOCIATED
- Participants aged 35-70 yrs
- F-Up at 3, 6, 9 yrs ; median 7.4 yrs
- Endpoints adjudicated

Epidemiology of CVD events, nonCV, CV and all-cause death – A global approach

- 3 high-income: Canada, Sweden, and United Arab Emirates,
- 11 middle-income: Argentina, Brazil, Chile, China, Colombia, Iran, Malaysia, occupied Palestinian territory, Poland, South Africa, and Turkey
- 4 low-income countries: Bangladesh, India, Pakistan, and Zimbabwe

PURE physical activity

The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study

Scott A Lear, Weihong Hu, Sumathy Rangarajan, Danijela Gasevic, Darryl Leong, Romaina Iqbal, Amparo Casanova, Sumathi Swaminathan, R M Anjana, Rajesh Kumar, Annika Rosengren, Li Wei, Wang Yang, Wang Chuangshi, Liu Huaxing, Sanjeev Nair, Rafael Diaz, Hany Swidon, Rajeev Gupta, Noushin Mohammadifard, Patricio Lopez-Jaramillo, Aytekin Oguz, Katarzyna Zatonska, Pamela Seron, Alvaro Avezum, Paul Poirier, Koon Teo, Salim Yusuf

www.thelancet.com **Published online September 21, 2017 http://dx.doi.org/10.1016/S0140-6736(17)31634-3**

In the Prospective Urban Rural Epidemiologic (PURE) study done in 17 countries of various income levels, we examined whether physical activity is associated with lower risk of mortality and CVD in countries at varying economic levels and whether these associations differ by type of physical activity.

	Overall (n=130 843)	Low physical activity* (n=23 631)	Moderate physical activity† (n=49 348)	High physical activity‡ (n=57 864)
Age (years)	50·2 (9·7)	51·0 (10·1)	50·5 (9·7)	49·7 (9·5)
Male	54 621 (41·7%)	11 080 (46·9%)	18 224 (36·9%)	25 317 (43·8%)
Urban resident	69 993 (53·5%)	12 983 (54·9%)	28 525 (57·8%)	28 485 (49·2%)
Country income level				
High	13 546 (10·4%)	1435 (6·1%)	4991 (10·1%)	7120 (12·3%)
Upper middle	34 625 (26·5%)	7479 (31·6%)	11 922 (24·2%)	15 224 (26·3%)
Lower middle	53 841 (41·1%)	8620 (36·5%)	22 648 (45·9%)	22 573 (39·0%)
Low	28 831 (22·0%)	6097 (25·8%)	9787 (19·8%)	12 898 (22·4%)
Education				
None, primary, or unknown	54 635 (41·9%)	10 642 (45·2%)	19 085 (38·8%)	24 908 (43·1%)
Secondary	50 500 (38·7%)	9035 (38·3%)	19 746 (40·1%)	21 719 (37·6%)
Trade, college, or university	25 396 (19·5%)	3885 (16·5%)	10 412 (21·1%)	11 099 (19·2%)
Family history of heart disease or stroke	36 812 (31·3%)	4911 (23·5%)	13 605 (30·5%)	18 296 (35·0%)
Hypertension	47 752 (39·0%)	9053 (42·6%)	18 364 (39·7%)	20 335 (36·9%)
Diabetes	12 740 (9·7%)	2898 (12·3%)	5102 (10·3%)	4740 (8·2%)
Smoker (current and former)	40 955 (31·5%)	7093 (30·3%)	13 695 (28·0%)	20 167 (35·0%)
Alternate Healthy Eating Index score	35·1 (8·0)	34·9 (7·6)	35·5 (7·9)	34·8 (8·3)
Body-mass index (kg/m^2)	25·7 (5·1)	25·9 (5·4)	25·9 (5·0)	25·4 (5·1)

Data are mean (SD) or n (%). MET=metabolic equivalents. *Low physical activity=<600 MET x min per week and <150 min per week of moderate intensity physical activity. †Moderate physical activity=600–3000 MET x min per week and 150–750 min per week of moderate intensity physical activity. ‡High physical activity=>3000 MET x min per week and >750 min per week of moderate intensity physical activity.

Table 1: **Participant characteristics stratified by total physical activity**

	High-income countries (n=13 546)	Upper-middle-income countries (n=34 625)	Lower-middle-income countries (n=53 841)	Low-income countries (n= 28 831)	p value (for heterogeneity)	p value (for trend)
Total physical activity*	..	..	..	..	<0·0001	<0·0001
MET × min per week	3227 (1485–6426)	2436 (750–5979)	2340 (960–5177)	2520 (721–6442)	..	..
Min per week	807 (371–1607)	609 (188–1495)	585 (240–1294)	630 (180–1611)	..	..
Recreational physical activity*	..	..	..	..	<0·0001	<0·0001
MET × min per week	518 (50–1386)	0 (0–320)	99 (0–693)	0 (0–0)	..	..
Min per week	130 (12–347)	0 (0–80)	25 (0–173)	0 (0–0)	..	..
Non-recreational physical activity*	..	..	..	..	<0·0001	0.7762
MET × min per week	2115 (806–4980)	1983 (578–5400)	1748 (693–4186)	2297 (594–6222)	..	..
Min per week	529 (202–1245)	496 (144–1350)	437 (173–1047)	574 (149–1556)	..	..
Low physical activity†	1435 (10·6%)	7479 (21·6%)	8620 (16·0%)	6097 (21·1%)	<0·0001	..
Moderate physical activity‡	4991 (36·8%)	11 922 (34·4%)	22 648 (42·1%)	9787 (33·9%)	..	..
High physical activity§	7120 (52·6%)	15 224 (44·0%)	22 573 (41·9%)	12 947 (44·9%)	..	..
Meeting physical activity guidelines¶	12 111 (89·4%)	27 146 (78·4%)	45 221 (84·0%)	22 734 (78·9%)	<0·0001	<0·0001

Data are median (IQR) or n (%). p value for heterogeneity was calculated by χ^2 test for categorical variable and Kruskal-Wallis for continuous variable. p value for trend was calculated by Cochran-Armitage test for categorical variable and Jonckheere-Terpstra test for continuous variable.[15,16] MET=metabolic equivalents. *Moderate intensity physical activity. †Low physical activity <600 MET x min per week and <150 min per week of moderate intensity physical activity. ‡Moderate physical activity 600–3000 MET x min per week and 150–750 min per week of moderate intensity physical activity. §High physical activity >3000 MET x min per week and >750 min per week of moderate intensity physical activity. ¶Meeting physical activity guidelines ≥600 MET x min per week and ≥150 min per week of moderate intensity physical activity.

***Table 2*: Physical activity by country income level**

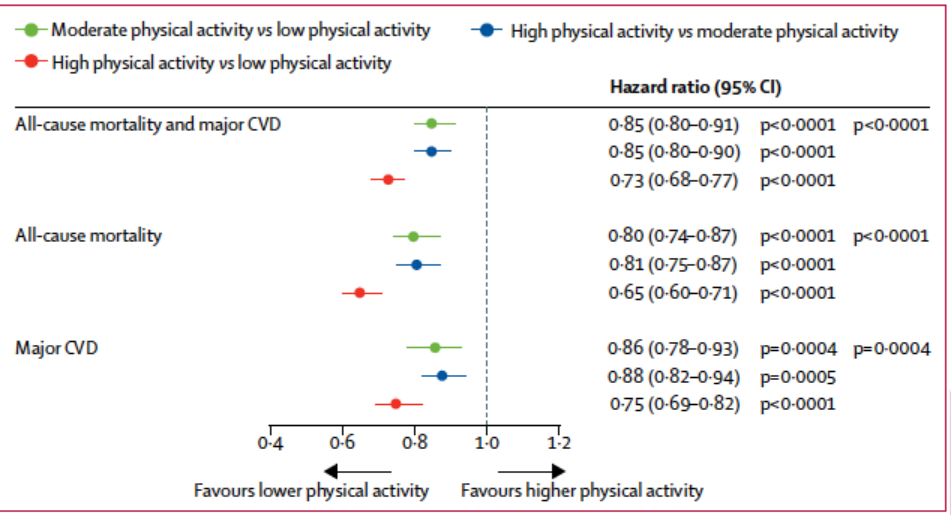


***Figure 1*: Hazard ratios and 95% CI for all-cause mortality and major CVD, all-cause mortality, or major CVD by level of physical activity**

Data adjusted for age, sex, education, country income level, urban or rural residency, family history of CVD, and smoking status; taking into account household, community, and country clustering. There were 3155 events for all-cause mortality and major CVD, 2041 events for all-cause mortality, and 1723 events for major CVD. The p values of the first column show the significance of each comparison. p values of the second column show the significance of the overall effect of physical activity. Low physical activity=<600 MET × min per week. Moderate physical activity=600–3000 MET × min per week. High physical activity=>3000 MET × min per week. CVD=cardiovascular disease. Major CVD=CVD mortality plus incident myocardial infarction, stroke, or heart failure. MET=metabolic equivalents.

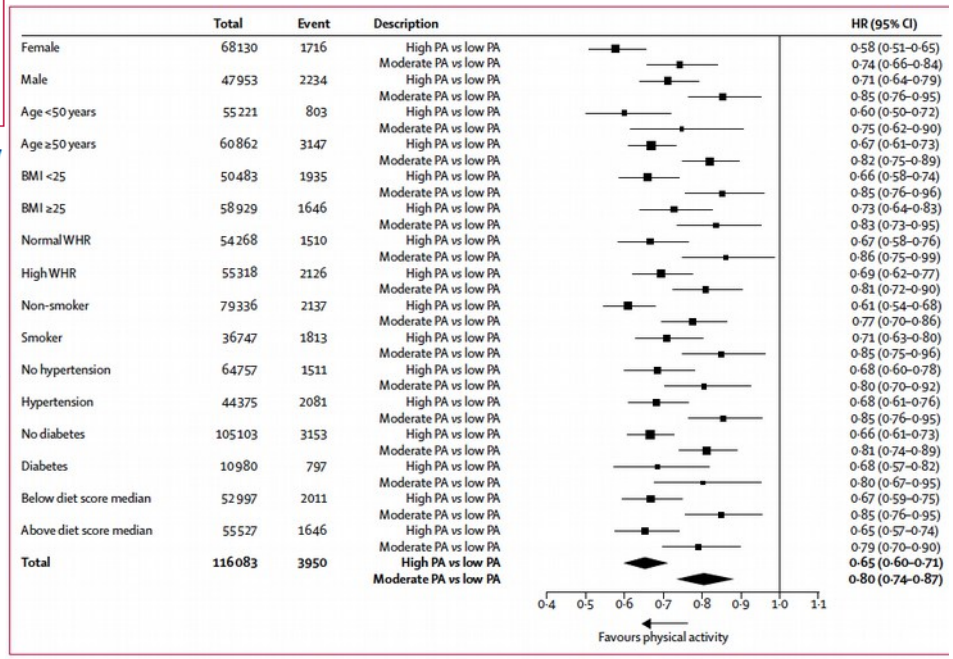
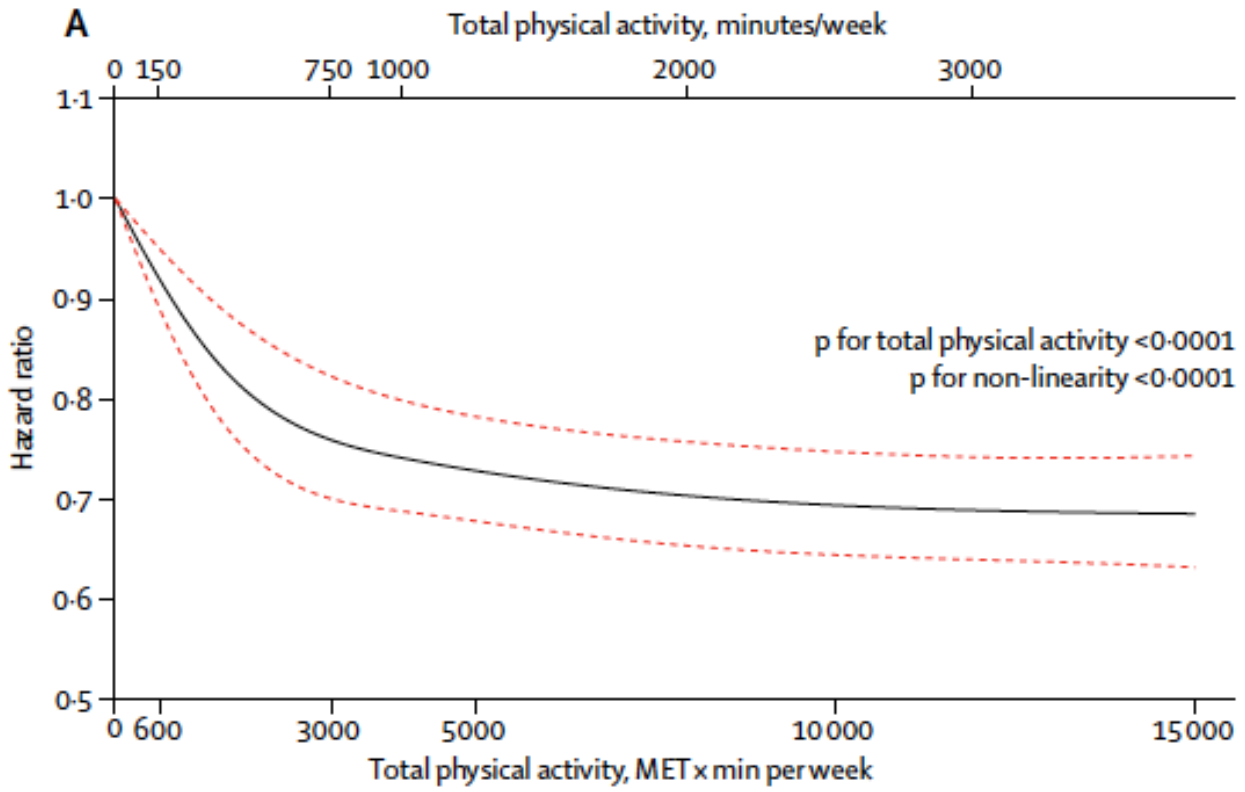


***Figure 2*: Hazard ratios and 95% CI of total physical activity for mortality**



Interval (MET x min per week)	0–600	600–3000	3000–5000	5000–10 000	10 000–15 000	>15 000
Total	21 690	46 409	18 781	20 801	8566	6420
Number of events	1941	3007	1028	1247	507	446

PURE physical activity

Implications of all the available evidence

Physical activity is associated with reduced risk of mortality and incident cardiovascular disease in all regions of the world. The greatest reductions occurred at the lowest and continued to be present at very high levels of physical activity with no indication of a ceiling effect. In addition, both recreational and non-recreational physical activity were associated with lower risks. Physical activity is a low-cost approach to reducing deaths and cardiovascular disease that is applicable globally with potential large impact.

PURE Fruits & Veg

Fruit, vegetable, and legume intake, and cardiovascular disease and deaths in 18 countries (PURE): a prospective cohort study

*Victoria Miller, Andrew Mente, Mahshid Dehghan, Sumathy Rangarajan, Xiaohe Zhang, Sumathi Swaminathan, Gilles Dagenais, Rajeev Gupta, Viswanathan Mohan, Scott Lear, Shrikant I Bangdiwala, Aletta E Schutte, Edelweiss Wentzel-Viljoen, Alvaro Avezum, Yuksel Altuntas, Khalid Yusoff, Noorhassim Ismail, Nasheeta Peer, Jephat Chifamba, Rafael Diaz, Omar Rahman, Noushin Mohammadifard, Fernando Lana, Katarzyna Zatonska, Andreas Wielgosz, Afzalhussein Yusufali, Romaina Iqbal, Patricio Lopez-Jaramillo, Rasha Khatib, Annika Rosengren, V Raman Kutty, Wei Li, Jiankang Liu, Xiaoyun Liu, Lu Yin, Koon Teo, Sonia Anand, Salim Yusuf, on behalf of the Prospective Urban Rural Epidemiology (PURE) study investigators**

www.thelancet.com **Published online August 29, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32253-5**

Currently, most dietary guidelines do not differentiate between raw and cooked vegetable intake, despite potential differences in nutritional composition and digestibility.[6,7] Therefore, guidelines that are largely based on European and US data might not necessarily apply to other regions of the world. In this study, we investigated the association of fruit, vegetable, and legume consumption with cardiovascular outcomes and total mortality in a prospective cohort study from 18 countries from seven geographical regions: North America and Europe, South America, the Middle East, south Asia, China, southeast Asia, and Africa. This allowed us to investigate relationships across a broad range of intakes including very low consumption of fruits and vegetables, and high consumption of legumes. Additionally, we examined the associations of raw and cooked vegetable intake independently from each other with cardiovascular disease events and total mortality.

	<1 per day (n=9082)	≥1 to <2 per day (n=19 036)	≥2 to <3 per day (n=35 128)	≥3 to <4 per day (n=24 485)	≥4 to <5 per day (n=14 849)	≥5 to <6 per day (n=9790)	≥6 to <7 per day (n=6945)	≥7 to <8 per day (n=4857)	≥8 per day (n=11 163)
Age (year)	49·0 (41·0–58·0)	49·0 (40·0–58·0)	50·0 (42·0–58·0)	50·0 (42·0–57·0)	50·0 (42·0–58·0)	50·0 (42·0–58·0)	50·0 (43·0–58·0)	50·0 (43·0–58·0)	51·0 (44·0–59·0)
Female sex	5303 (58%)	11 218 (59%)	20 260 (58%)	14 156 (58%)	8592 (58%)	5618 (57%)	4048 (58%)	2862 (59%)	6856 (61%)
Urban location	2901 (32%)	7771 (41%)	16 447 (47%)	13 988 (57%)	9313 (63%)	5976 (61%)	4260 (61%)	3227 (66%)	7417 (66%)
Education level									
Less than graduation from high-school	6027/9031 (66%)	10 514/18 953 (55%)	14 625/35 033 (42%)	8838/24 436 (36%)	5393/14 825 (36%)	3809/9769 (39%)	2693/6933 (39%)	1769/4852 (36%)	3770/11 149 (34%)
High-school graduate	2502/9031 (28%)	6476/18 953 (34%)	15 737/35 033 (45%)	10 791/24 436 (44%)	5795/14 825 (39%)	3315/9769 (34%)	2206/6933 (32%)	1513/4852 (31%)	3395/11 149 (30%)
Some college or more	502/9031 (6%)	1963/18 953 (10%)	4671/35 033 (13%)	4807/24 436 (20%)	3637/14 825 (24%)	2645/9769 (27%)	2034/6933 (29%)	1570/4852 (32%)	3984/11 149 (36%)
Currently a smoker	2676/9031 (29%)	4480/18 953 (24%)	7836/35 033 (22%)	4982/24 436 (20%)	2883/14 825 (19%)	1761/9769 (18%)	1280/6933 (18%)	814/4852 (17%)	1698/11 149 (15%)
High physical activity level*	3253/7388 (36%)	7947/16 738 (42%)	13 817/33 335 (39%)	10 115/23 398 (41%)	5954/14 162 (40%)	4200/9272 (43%)	3168/6560 (46%)	2274/4606 (47%)	5346/10 486 (48%)
Waist-to-hip ratio	0·859 (0·086)	0·865 (0·090)	0·868 (0·081)	0·871 (0·082)	0·877 (0·086)	0·882 (0·086)	0·882 (0·088)	0·881 (0·088)	0·878 (0·088)
Energy intake (kcal/day)†	1442 (1077–1906)	1698 (1322–2205)	1847 (1461–2338)	2017 (1618–2517)	2160 (1726–2698)	2254 (1817–2767)	2363 (1923–2903)	2498 (2036–3054)	2869 (2305–3559)
Vegetable intake (servings per day)	0·27 (0·23)	0·76 (0·39)	1·60 (0·55)	1·86 (0·54)	2·18 (0·75)	2·67 (1·01)	3·13 (1·27)	3·63 (1·49)	4·91 (2·67)
Fruit intake (servings per day)	0·19 (0·22)	0·43 (0·35)	0·62 (0·35)	1·23 (0·60)	1·82 (0·83)	2·27 (1·13)	2·76 (1·40)	3·24 (1·58)	5·21 (3·03)
Legume intake (servings per day)	0·14 (0·16)	0·35 (0·33)	0·30 (0·36)	0·37 (0·41)	0·45 (0·49)	0·53 (0·57)	0·57 (0·60)	0·59 (0·60)	0·71 (0·77)
Starch intake (g/day)	604·8 (465·4)	659·6 (478·3)	507·7 (340·8)	491·8 (318·8)	510·8 (325·1)	506·4 (314·2)	505·0 (306·2)	506·9 (301·0)	544·5 (331·8)
Red meat intake (g/day)	32·8 (58·2)	37·7 (62·4)	57·2 (67·8)	71·6 (73·8)	75·3 (73·0)	83·2 (76·5)	88·0 (74·6)	89·7 (72·3)	93·8 (76·9)
White meat intake (g/day)	16·2 (30·0)	21·3 (33·2)	18·5 (30·6)	24·3 (36·4)	36·7 (47·8)	38·5 (44·9)	42·9 (44·8)	47·9 (48·7)	57·1 (62·2)

Total number of participants=135 335. Data are median (IQR), n (%), n/N (%), or mean (SD). *Defined as ≥3000 metabolic equivalent of task-min per week. †Plausible energy intake between ≥500 kcal/day and ≤5000 kcal/day.

***Table 1*: Participants' characteristics divided by number of fruit, vegetable, and legume servings per day**

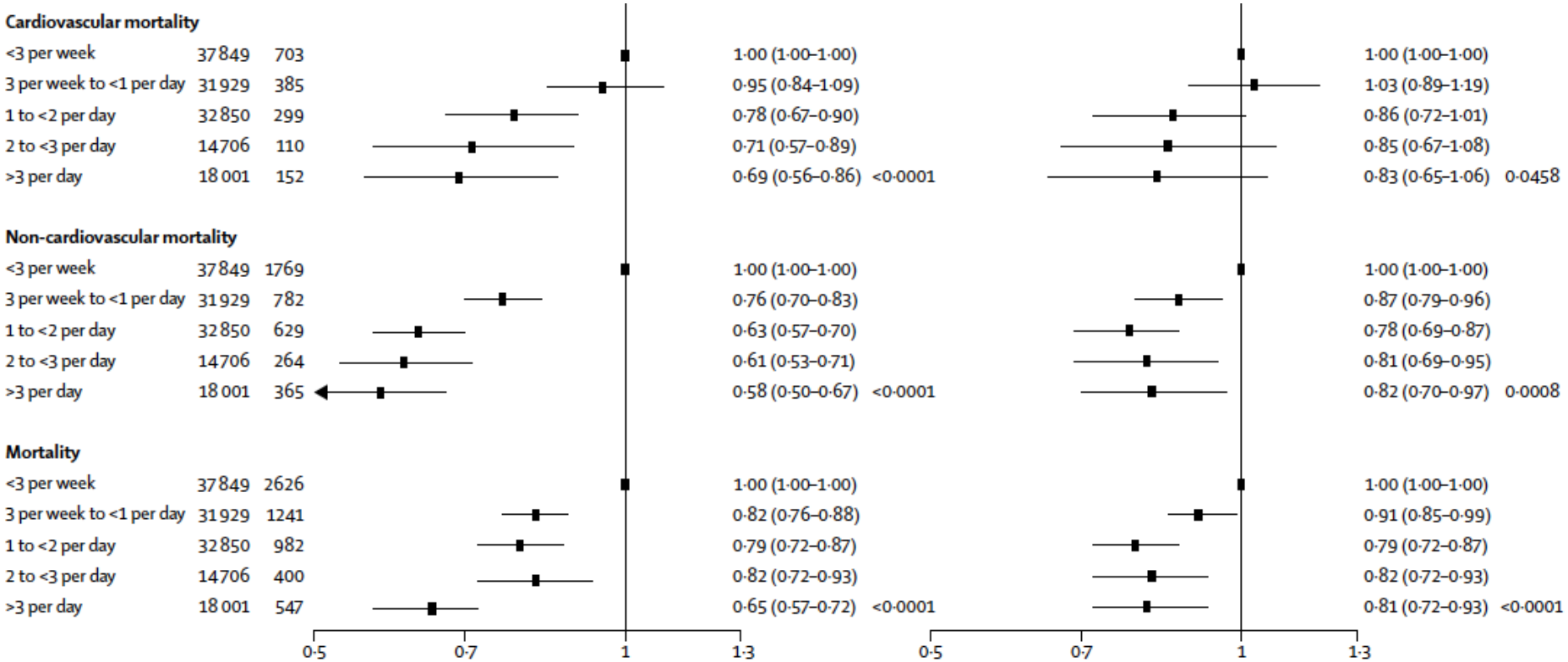


***Figure 2*: Association of fruit intake with cardiovascular outcomes and mortality**

(A) Adjusted for age, sex, and centre (random effect). (B) Adjusted for age, sex, centre (random effect), energy intake, current smoker, diabetes, urban or rural location, physical activity, education level, and tertiles of white meat, red meat, and intake of breads, cereals, and vegetables. Crude event rates are shown. Additional sensitivity analyses with waist-to-hip ratio, hypertension status, and statin medication used in the model did not substantially change estimates of association (appendix). HR=hazard ratio. Major cardiovascular disease events=death from cardiovascular causes and non-fatal myocardial infarction, stroke, and heart failure.

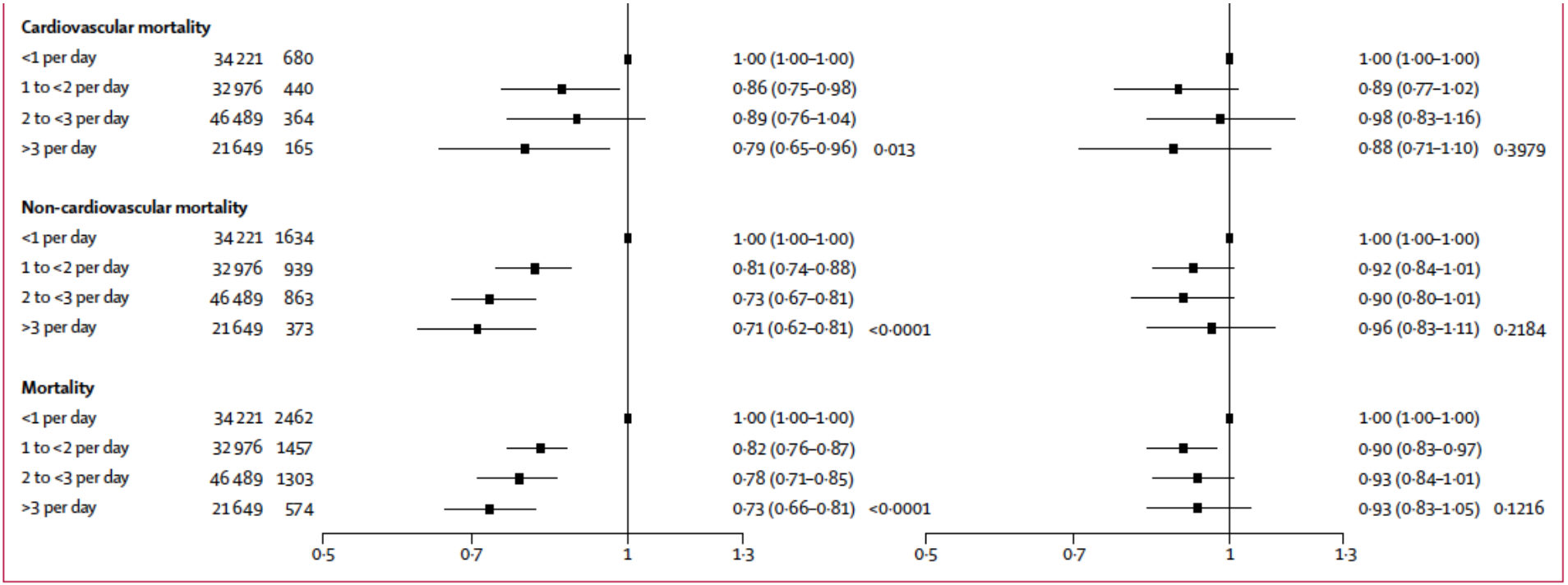


***Figure 3*: Association of vegetable intake with cardiovascular outcomes and mortality**

(A) Adjusted for age, sex, and centre (random effect). (B) Adjusted for age, sex, centre (random effect), energy intake, current smoker, diabetes, urban/rural location, physical activity, education level, and tertiles of white meat, red meat, and intake of breads, cereals, and fruit. Crude event rates are shown. Additional sensitivity analyses with waist-to-hip ratio, hypertension status, and statin medication used in the model did not substantially change estimates of association (appendix). HR=hazard ratio. Major cardiovascular disease events=death from cardiovascular causes and nonfatal myocardial infarction, stroke, and heart failure.

PURE Fruits & Veg

Implications of all the available evidence

Many dietary guidelines recommend a minimum of 400 g/day of fruits and vegetables, which might not be achievable globally since fruits and vegetables have previously been shown to be unaffordable in low-income and lower-middle income countries. Our findings that even three servings per day (375 g/day) show similar benefit against the risk of non-cardiovascular and total mortality as higher intakes indicates that optimal health benefits can be achieved with a more modest level of consumption, an approach that is likely to be more affordable in poor countries.

PURE Carbs & Fats

Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study

*Mahshid Dehghan, Andrew Mente, Xiaohe Zhang, Sumathi Swaminathan, Wei Li, Viswanathan Mohan, Romaina Iqbal, Rajesh Kumar, Edelweiss Wentzel-Viljoen, Annika Rosengren, Leela Itty Amma, Alvaro Avezum, Jephat Chifamba, Rafael Diaz, Rasha Khatib, Scott Lear, Patricio Lopez-Jaramillo, Xiaoyun Liu, Rajeev Gupta, Noushin Mohammadifard, Nan Gao, Aytekin Oguz, Anis Safura Ramli, Pamela Seron, Yi Sun, Andrzej Szuba, Lungiswa Tsolekile, Andreas Wielgosz, Rita Yusuf, Afzal Hussein Yusufali, Koon K Teo, Sumathy Rangarajan, Gilles Dagenais, Shrikant I Bangdiwala, Shofiqul Islam, Sonia S Anand, Salim Yusuf, on behalf of the Prospective Urban Rural Epidemiology (PURE) study investigators**

www.thelancet.com **Published online August 29, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32252-3**

concern. In this study, our primary aim was to assess the association of fats (total, saturated fatty acids, and unsaturated fats) and carbohydrate with total mortality and cardiovascular disease events. The secondary aim was to examine associations between these nutrients and myocardial infarction, stroke, cardiovascular disease mortality, and non-cardiovascular disease mortality.

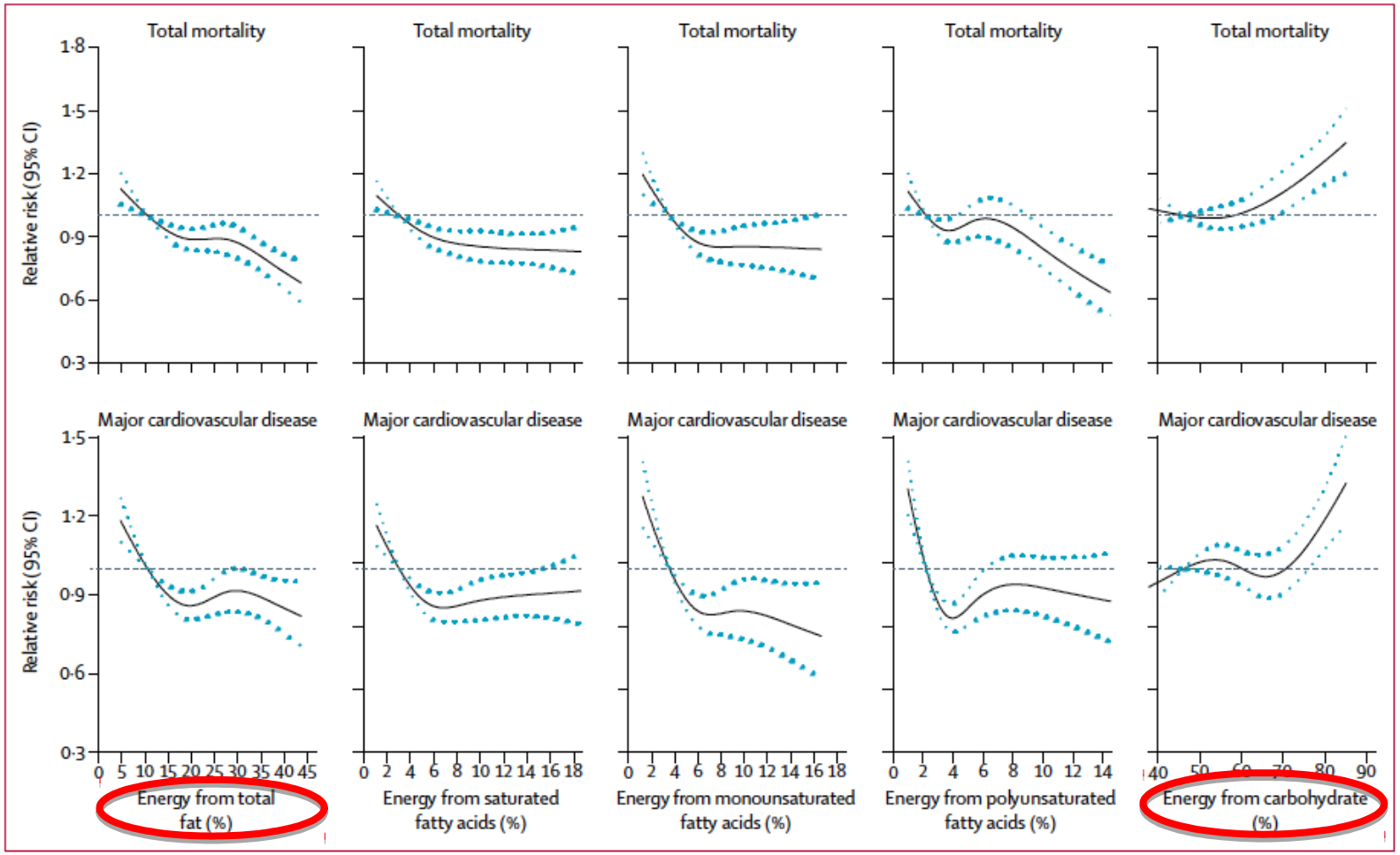
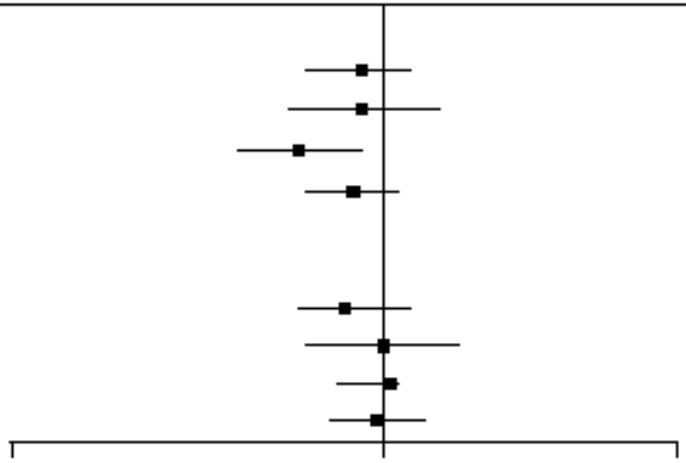


Figure 1: **Association between estimated percentage energy from nutrients and total mortality and major cardiovascular disease (n=135 335)**
Adjusted for age, sex, education, waist-to-hip ratio, smoking, physical activity, diabetes, urban or rural location, centre, geographical regions, and energy intake. Major cardiovascular disease=fatal cardiovascular disease+myocardial infarction+stroke+heart failure.

A

Carbohydrate replaced by	HR (95% CI)
Total mortality	
Saturated fatty acids	0·97 (0·90–1·04)
Monounsaturated fatty acids	0·97 (0·88–1·08)
Polyunsaturated fatty acids	0·89 (0·82–0·97)
Protein	0·96 (0·90–1·02)
Major cardiovascular disease	
Saturated fatty acids	0·95 (0·89–1·04)
Monounsaturated fatty acids	1·00 (0·90–1·11)
Polyunsaturated fatty acids	1·01 (0·94–1·02)
Protein	0·99 (0·93–1·06)



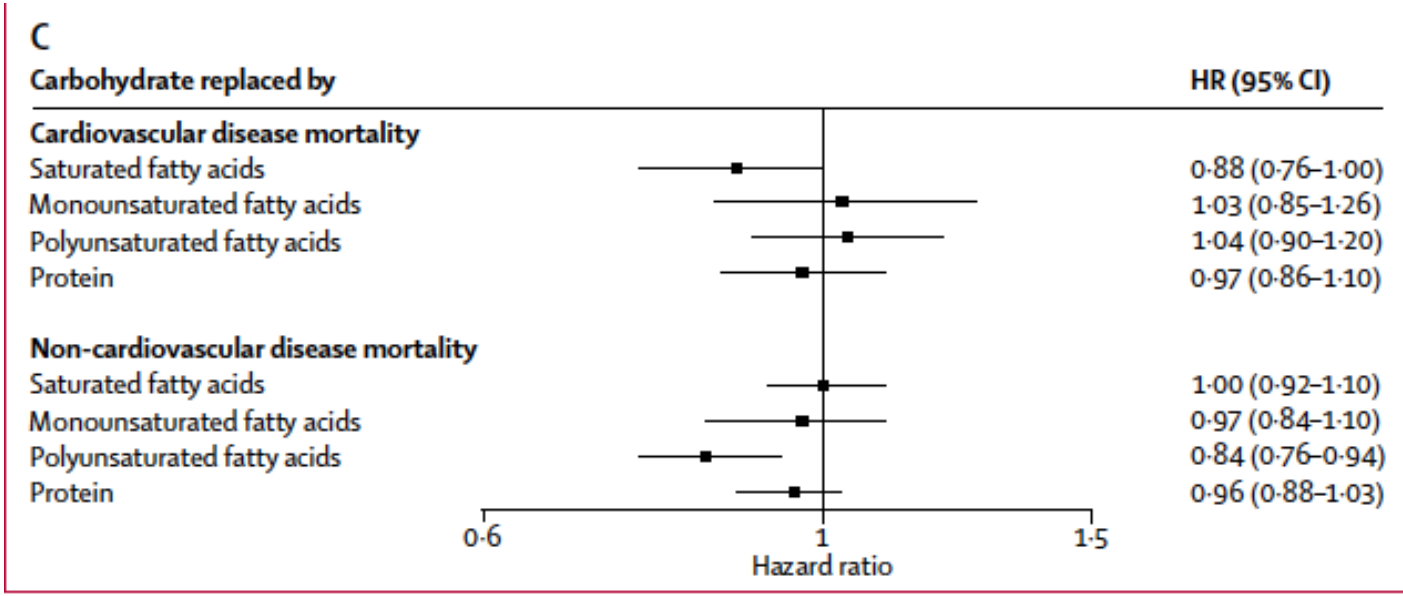


Figure 3: **Risk of clinical outcomes associated with isocaloric (5% of energy) replacement of carbohydrate with other nutrients (n=135 335)**

Hazard ratios (HRs) and 95% CIs are adjusted for age, sex, education, waist-to-hip ratio, smoking, physical activity, diabetes, urban or rural location, and energy intake. Centre was also included as a random effect and frailty models were used. Major cardiovascular disease=fatal cardiovascular disease+myocardial infarction+stroke+heart failure.

PURE Carbs & Fats

Implications of all the available evidence

Removing current restrictions on fat intake but limiting carbohydrate intake (when high) might improve health. Dietary guidelines might need to be reconsidered in light of consistent findings from the present study, especially in countries outside of Europe and North America.

CONCLUSION #1

- A LOT OF MI RISK FACTORS IS ESTABLISHED
- RELATIONSHIP bw LIPIDS AND CV RISK
  - BLOOD CONCENTRATION
  - NUTRITION INTAKE
- PHYSICAL ACTIVITY
- FRUITS & VEGETABLE

✓ EPIDEMIOLOGY OF CV DISEASE

✓ **CV RISK STRATIFICATION**

Cardio-Vascular risk stratification

2016 European Guidelines on cardiovascular disease prevention in clinical practice

The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts).

Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR).

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Councils: Council on Cardiovascular Nursing and Allied Professions, Council for Cardiology Practice, Council on Cardiovascular Primary Care.
Working Groups: Cardiovascular Pharmacotherapy

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European Heart Journal 2016 ;37:2315–2381-doi:10.1093/eurheartj/ehw106

ESC Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/ is indicated.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered.
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered.
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended.

European Heart Journal 2016;37:2315–2381-doi:10.1093/eurheartj/ehw106

ESC Levels of evidence

Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of Evidence C	Consensus of opinion of the experts and/ or small studies, retrospective studies, registries.

European Heart Journal 2016;37:2315–2381-doi:10.1093/eurheartj/ehw106

Cardiovascular risk assessment

Recommendations	Class	Level
Systematic CV risk assessment is recommended in individuals at increased CV risk, i.e. with family history of premature CVD, familial hyperlipidaemia, major CV risk factors (such as smoking, high BP, DM or raised lipid levels) or comorbidities increasing CV risk.	I	C
It is recommended to repeat CV risk assessment every 5 years, and more often for individuals with risks close to thresholds mandating treatment.	I	C
Systematic CV risk assessment may be considered in men >40 years of age and in women >50 years of age or post-menopausal with no known CV risk factors.	IIb	C
Systematic CV risk assessment in men <40 of age and women <50 years of age with no known CV risk factors is not recommended.	III	C

European Heart Journal 2016;37:2315–2381-doi:10.1093/eurheartj/ehw106

How to estimate cardiovascular risk

Recommendations	Class	Level
Total CV risk estimation, using a risk estimation system such as SCORE, is recommended for adults >40 years of age, unless they are automatically categorised as being at *high-risk* or *very high-risk* based on documented CVD, DM (>40 years of age), kidney disease or highly elevated single risk factor.	I	C

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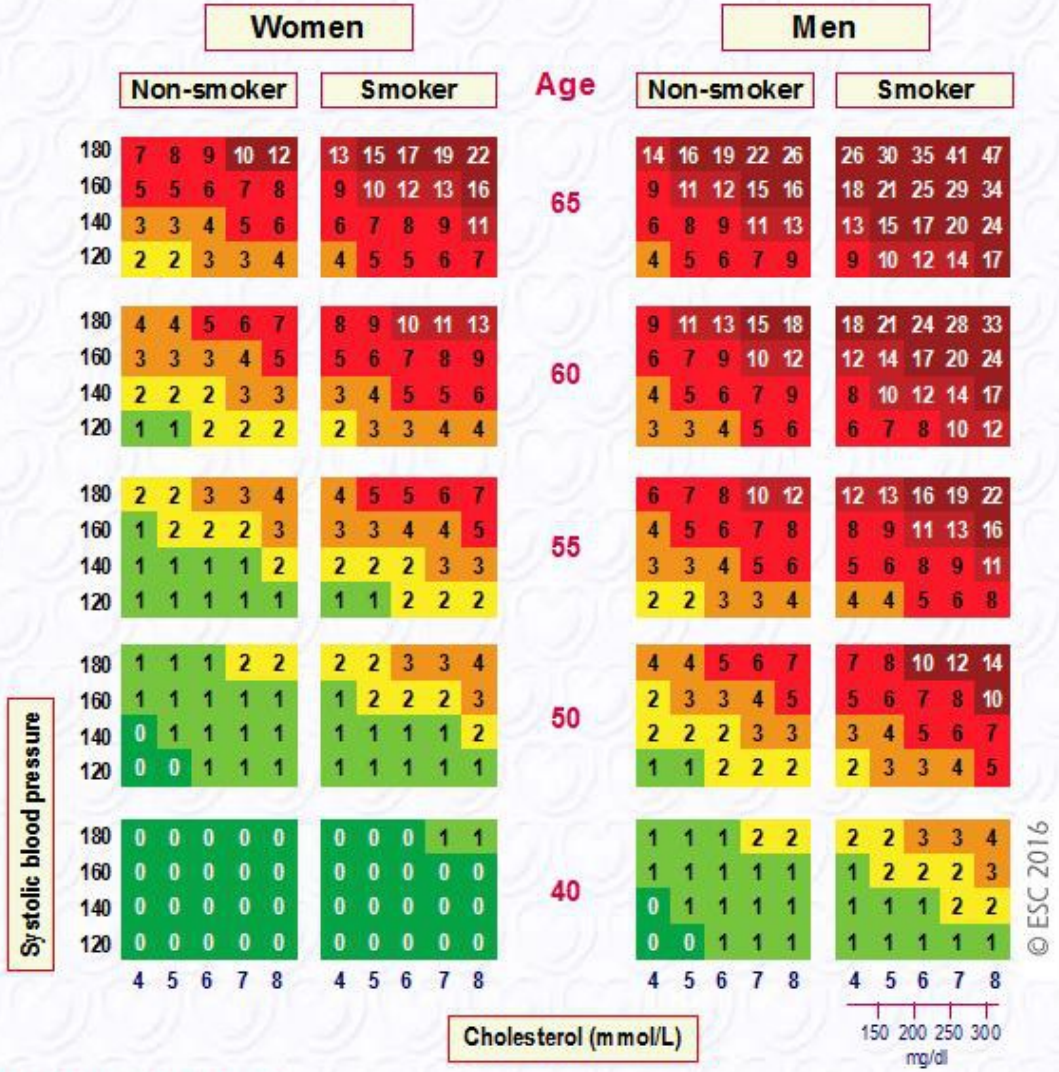
SCORE chart: 10-year risk of fatal cardiovascular disease in populations of countries at high cardiovascular risk



SCORE

- 15% and over
- 10%-14%
- 5%-9%
- 3%-4%
- 2%
- 1%
- <1%

10-year risk of fatal CVD in populations at **High CVD risk**

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European Heart Journal 2016;37:2315–2381-doi:10.1093/eurheartj/ehw106

Risk categories

Very high-risk	Subjects with any of the following: • Documented CVD, clinical or unequivocal on imaging. Documented clinical CVD includes previous AMI, ACS, coronary revascularization and other arterial revascularization procedures, stroke and TIA, aortic aneurysm and PAD. Unequivocally documented CVD on imaging includes significant plaque on coronary angiography or carotid ultrasound. It does NOT include some increase in continuous imaging parameters such as intima–media thickness of the carotid artery. • DM with target organ damage such as proteinuria or with a major risk factor such as smoking or marked hypercholesterolaemia or marked hypertension. • Severe CKD (GFR <30 mL/min/1.73 m^2). • A calculated SCORE ≥10%.
High-risk	Subjects with: • Markedly elevated single risk factors, in particular cholesterol >8 mmol/L (>310 mg/dL) (e.g. in familial hypercholesterolaemia) or BP ≥180/110 mmHg. • Most other people with DM (with the exception of young people with type 1 DM and without major risk factors that may be at low or moderate risk). • Moderate CKD (GFR 30–59 mL/min/1.73 m^2). • A calculated SCORE ≥5% and <10%.
Moderate-risk	SCORE is ≥1% and <5% at 10 years. Many middleaged subjects belong to this category.
Low-risk	SCORE <1%.

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