L’importanza della nutrizione

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NFI – Nutrition Foundation of Italy

Possibili conflitti di interesse

Collaborazioni/Consulenze (negli ultimi 24 mesi) con:

- MSD
- SANOFI
- ERREKAPPA

Presidente di NFI, associazione non profit supportata da 18 grandi aziende alimentari

PLOS | MEDICINE

RESEARCH ARTICLE

Association between intake of less-healthy foods defined by the United Kingdom's nutrient profile model and cardiovascular disease: A population-based cohort study

Oliver T. Mytton[1], Nita G. Forouhi[1], Peter Scarborough[2], Marleen Lentjes[3], Robert Luben[3], Mike Rayner[2], Kay Tee Khaw[3], Nicholas J. Wareham[1], Pablo Monsivais[1,4]*

We used data from the European Prospective Investigation of Cancer (EPIC)-Norfolk cohort study in adults (n = 25,639) aged 40-79 years who completed a 7-day diet diary between 1993 and 1997. Incident CVD (primary outcome), cardiovascular mortality, and all-cause mortality (secondary outcomes) were identified using record linkage to hospital admissions data and death certificates up to 31 March 2015.

Association between intake of less-healthy foods and cardiovascular disease.

Table 1. Baseline characteristics of participants: The European Prospective Investigation of Cancer (EPIC)-Norfolk study (n = 22,992).

	Quintile group of less-healthy food and beverage consumption (proportion of energy consumed from foods and beverages categorised as 'less-healthy')				
Measures of dietary quality (mean consumption per day)					
Fruit (g)	218 (169)	187 (135)	171 (125)	156 (113)	132 (106)
Vegetables (g)	178 (95)	160 (74)	151 (71)	141 (66)	127 (68)
Fish (g)	32.5 (33.0)	29.7 (27.2)	27.8 (26.4)	25.1 (23.8)	22.0 (24.6)
Processed meat (g)	17.4 (18.9)	21.3 (19.8)	22.5 (19.9)	24.3 (21.2)	25.9 (24.1)
Alcohol (units)	2.35 (3.12)	1.86 (2.35)	1.48 (1.91)	1.13 (1.56)	0.72 (1.15)
Energy (kJ)	7,210 (2,020)	7,895 (2,025)	8,242 (2,016)	8,606 (2,079)	9,121 (2,309)
Percentage of energy from saturated fat (%)	10.2 (2.5)	12.1 (2.4)	13.0 (2.4)	13.8 (2.6)	15.2 (3.0)
Ratio of saturated to unsaturated fat	1.81 (0.72)	1.99 (0.69)	2.11 (0.77)	2.23 (0.82)	2.52 (1.01)
Sodium (mg)	2,400 (780)	2,690 (820)	2,770 (790)	2,900 (810)	3,020 (900)
Fibre (g)	16.2 (6.3)	15.5 (5.4)	15.1 (5.4)	14.7 (5.1)	13.9 (5.2)
Characteristics of diet defined by FSA-Ofcom model					
Mean energy-weighted nutrient profile score	3.99 (1.52)	5.99 (1.10)	7.05 (1.12)	8.07 (1.21)	9.50 (1.56)
Less-healthy food (g/d)	181 (76)	258 (84)	298 (87.5)	343 (99)	405.5 (125)
Less-healthy food (kJ/d)	2,091 (795)	3,109 (850)	3,716 (959)	4,355 (1,133)	5,319 (1,498)
Healthy food (kJ/d)	3,973 (1,113)	3,717 (965)	3,508 (893)	3,312 (838)	2,891 (870)
Less-healthy beverage (kJ/d)	81 (153)	133 (213)	177.5 (265)	246.2 (338)	435 (501)

Mytton OT et al, Plos Med 2018

Association between intake of less-healthy foods and cardiovascular disease.

		Quintile group of consumption of less-healthy food and beverages				
		Q1—lowest (n = 4,760)	Q2 (n = 4,760)	Q3 (n = 4,760)	Q4 (n = 4,760)	Q5—highest (n = 4,759)
Proportion of energy consumed from foods and beverages categorised as less-healthy (Range, %)		<37.1	37.1–44.4	44.4–50.2	50.2–57.0	57.0–92.7
Cardiovascular mortality	Deaths	484	497	493	551	530
	Unadjusted	1.00	1.02 (0.90–1.17)	1.02 (0.90–1.16)	1.07 (0.94–1.21)	1.12 (0.99–1.27)
	Model 1	1.00	0.91 (0.80–1.04)	**0.84 (0.74–0.96)**	**0.86 (0.76–0.99)**	**0.86 (0.75–0.98)**
	Model 2	1.00	0.94 (0.82–1.07)	0.92 (0.80–1.04)	0.96 (0.84–1.09)	0.99 (0.87–1.14)
All-cause mortality	Deaths	1,268	1,379	1,389	1,493	1,610
	Unadjusted	1.00	**1.09 (1.00–1.18)**	**1.10 (1.01–1.19)**	**1.19 (1.10–1.29)**	**1.31 (1.21–1.41)**
	Model 1	1.00	0.99 (0.91–1.07)	0.94 (0.87–1.02)	1.00 (0.93–1.10)	1.04 (0.96–1.13)
	Model 2	1.00	0.99 (0.92–1.08)	0.98 (0.90–1.06)	1.05 (0.97–1.14)	**1.11 (1.02–1.20)**

Mytton OT et al, Plos Med 2018

Association between intake of less-healthy foods and cardiovascular disease.

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	Model 1	1.00	0.99 (0.91–1.07)	0.94 (0.87–1.02)	1.00 (0.93–1.10)	1.04 (0.96–1.13)
	Model 2	1.00	0.99 (0.92–1.08)	0.98 (0.90–1.06)	1.05 (0.97–1.14)	**1.11 (1.02–1.20)**

only adjusting for sociodemographic and behavioural risk factors (Model 1). Given that CVD accounts for a third of all deaths (35.7%) and the absence of associations for CVD, it might be more appropriate to put greater emphasis on the Model 1 findings for the all-cause mortality analyses. Given this and having undertaken multiple tests of significance, we suggest the all-

Mytton OT et al, Plos Med 2018

Association between intake of less-healthy foods and cardiovascular disease.

Table 4. Hazard ratios of incident cardiovascular disease by quintile group of proportional fruit and vegetable consumption in the European Prospective Investigation of Cancer (EPIC)-Norfolk ($n = 22{,}992$).

	Quintile group of fruit and vegetable consumption (proportion of food weight consumed as fruit and vegetables)					
	Q1—lowest ($n = 4599$)	Q2 ($n = 4598$)	Q3 ($n = 4{,}599$)	Q4 ($n = 4{,}598$)	Q5—highest ($n = 4{,}598$)	Test for linear trend
Weight of fruit and vegetables (Range, g/d)	0–185	185–262	262–339	339–448	448–2,441	
Cases	1,092	1,021	1,003	959	890	
Unadjusted model	1.00	**0.91 (0.83–0.99)**	**0.88 (0.81–0.96)**	**0.83 (0.76–0.91)**	**0.76 (0.69–0.83)**	**<0.001**
Model 1	1.00	0.94 (0.86–1.03)	0.95 (0.87–1.03)	0.93 (0.85–1.02)	**0.88 (0.80–0.96)**	**0.01**
Model 2	1.00	0.92 (0.84–1.00)	0.92 (0.84–1.00)	**0.89 (0.81–0.97)**	**0.84 (0.76–0.92)**	**<0.001**

Model 1 is adjusted for age, sex, alcohol consumption, physical activity, smoking status, education level, and total dietary energy. Model 2 is adjusted for Model 1 covariates plus blood pressure-lowering medication, lipid-lowering medication, diabetes, hypertension, hypercholesterolemia, past cancer diagnosis, family history of heart attack, family history of stroke, and family history of diabetes.

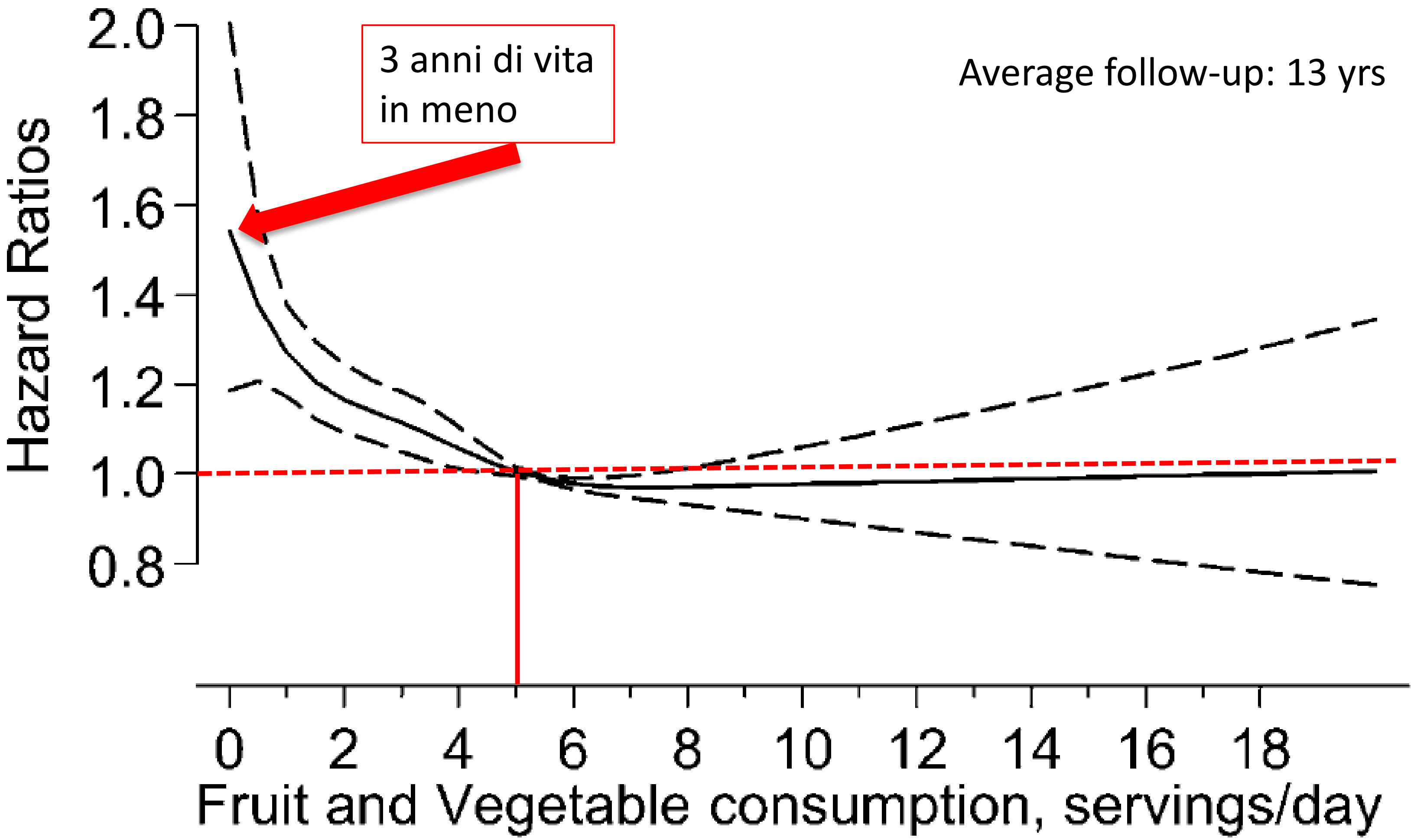
Mytton OT et al, Plos Med 2018

PURE Healthy Diet Score: Foods

Foods	Least Healthy: Quintile (Number of Servings per Day)	Most Healthy: Quintile 5 (Number of Servings per Day)
Fruits and vegetables	1.8	8.4
Nuts and legumes	0.7	2.5
Dairy	0.6	3.0
Red meat	0.3	1.4
Fish	0.2	0.3

PURE Study group, ESC 2018, unpublished

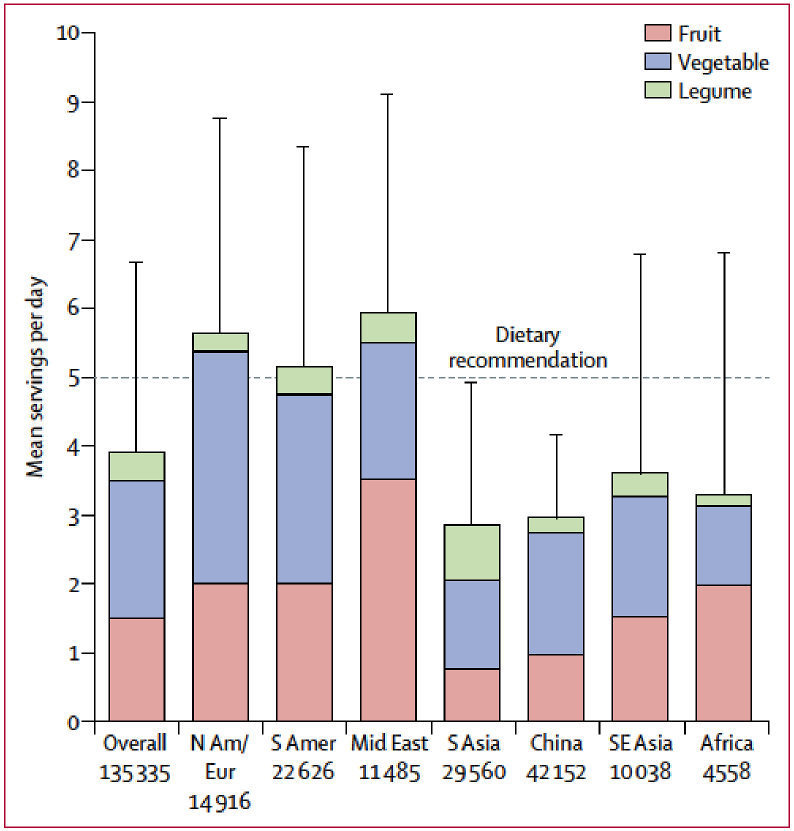
Fruit and vegetable consumption and all-cause mortality: a dose response analysis in 71,000 swedish men and women



Bellavia A et al, Am J Clin Nutr 2013

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

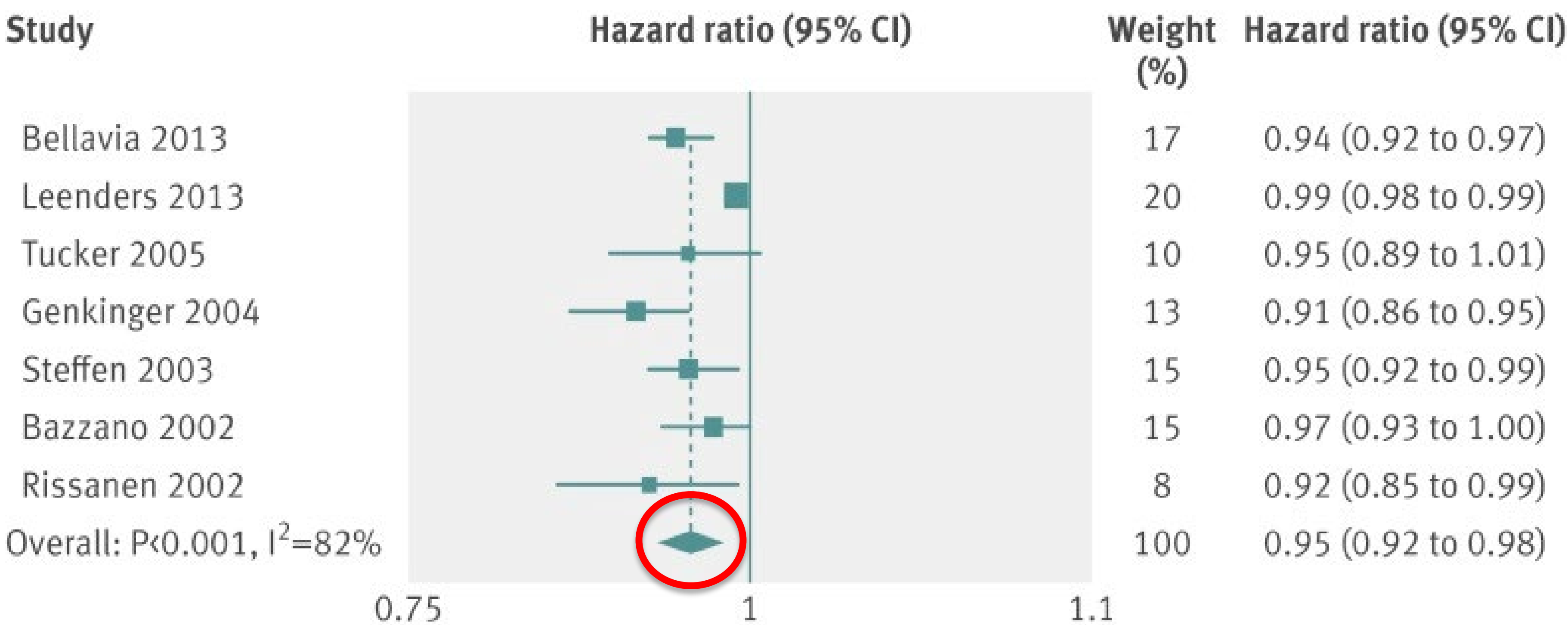
*Victoria Miller, Andrew Mente, Mahshid Dehghan, Sumathy Rangarajan, Xiaohe Zhang, Sumathi Swaminathan, Gilles Dagenais, Rajeev Gupta, Viswanathan Mohan, Scott Lear, Shrikant I Bangdiwala, Aletta E Schutte, Edelweiss Wentzel-Viljoen, Alvaro Avezum, Yuksel Altuntas, Khalid Yusoff, Noorhassim Ismail, Nasheeta 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**



Higher fruit, vegetable, and legume consumption was associated with a lower risk of non-cardiovascular, and total mortality. Benefits appear to be maximum for both non-cardiovascular mortality and total mortality at three to four servings per day (equivalent to 375–500 g/day).

Lancet, 2017

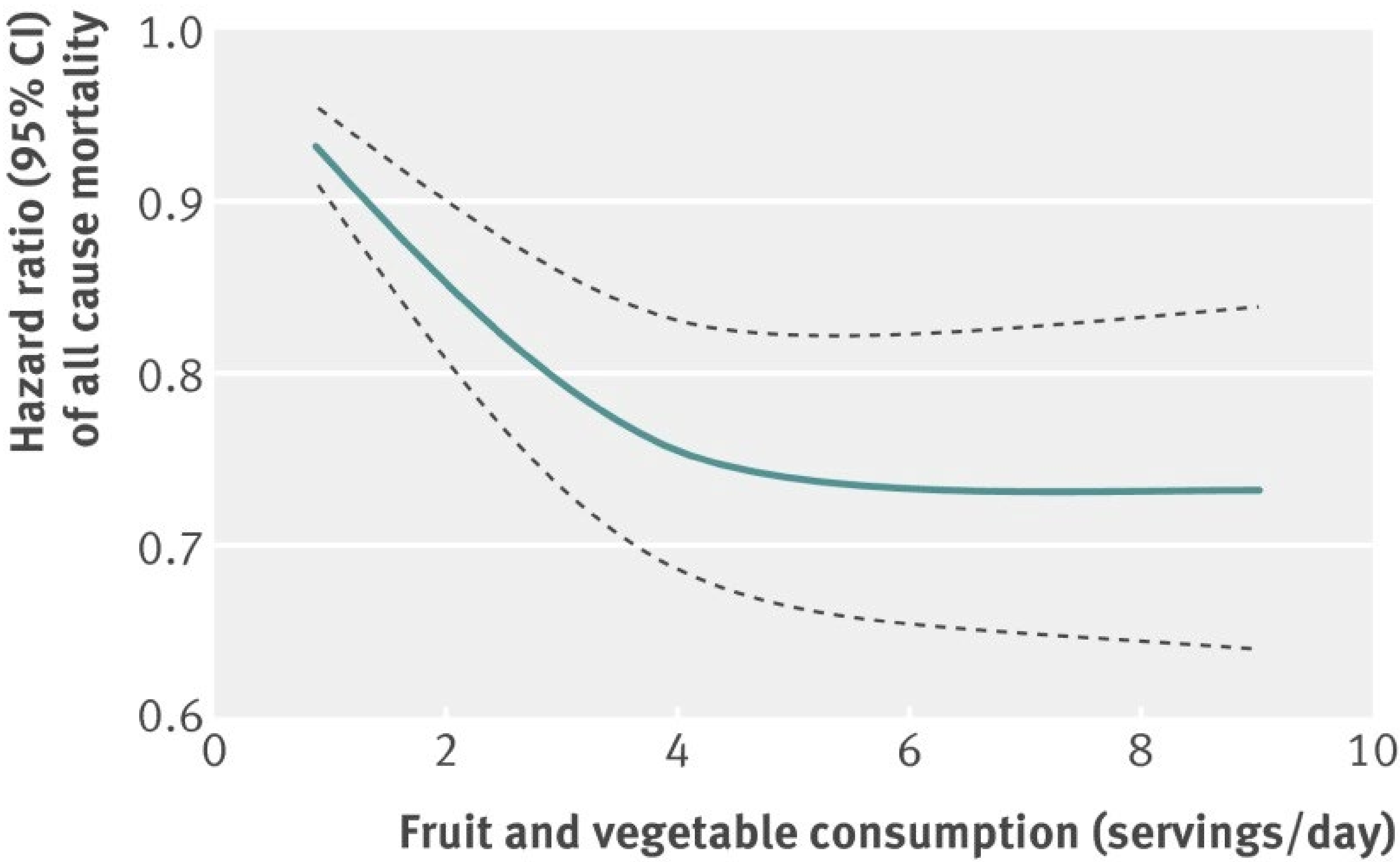
Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies



RR of all cause mortality associated with an additional serving/day of fruit and vegetables

Wang X et al, BMJ 2014

Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: systematic review and dose-response meta-analysis of prospective cohort studies



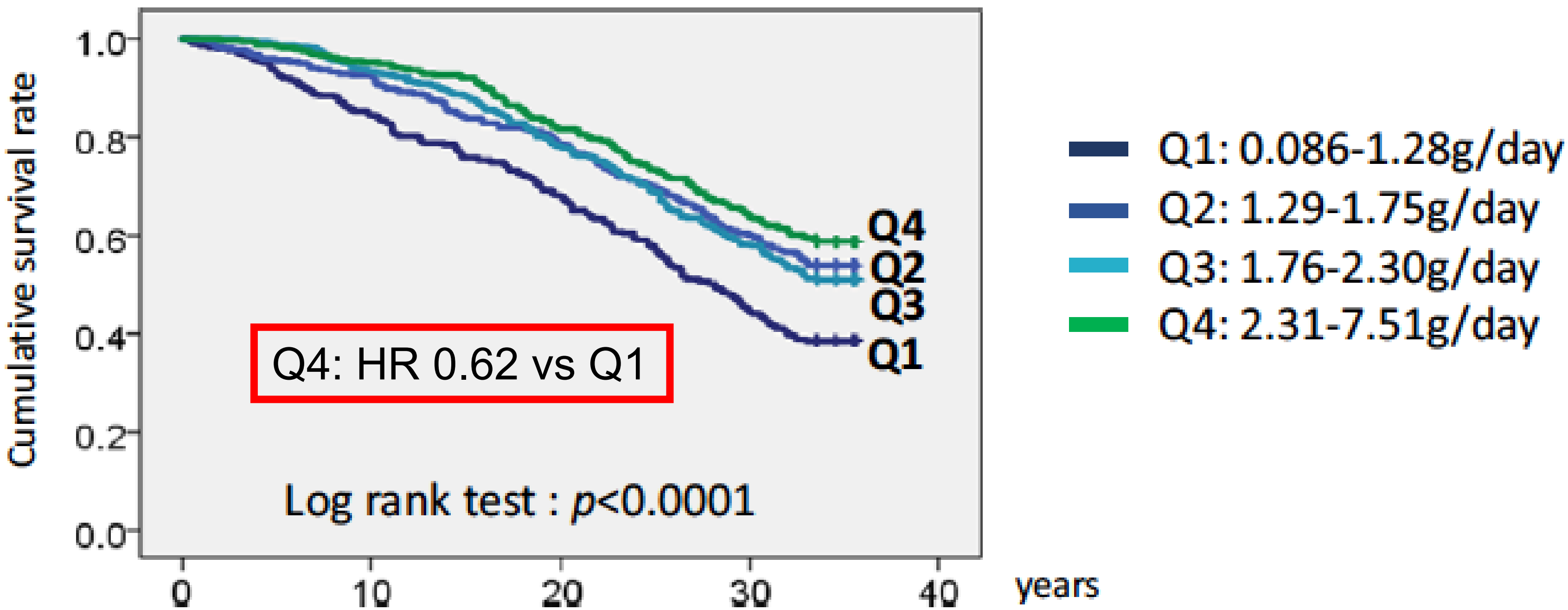
Relative Risk of all cause mortality associated with intake (servings/day) of fruit and vegetables

Wang X et al, BMJ 2014

Perché il consumo di frutta e verdura ha effetti favorevoli sulla salute?

- F&V hanno un certo potere saziante e lasciano comunque meno spazio ad alimenti con effetti di salute meno favorevoli
- Sono ricche di Potassio
- Sono ricche di Polifenoli
  - *Azione antiossidante ed antinfiammatoria*
  - *Azione prebiotica*
- Sono ricche di fibra alimentare
  - *Azione prebiotica*
  - *Azione metabolica*
- Sono ricche di

Twenty-four-Hour Urinary Potassium Excretion, But Not Sodium Excretion, Is Associated With All-Cause Mortality in a General Population

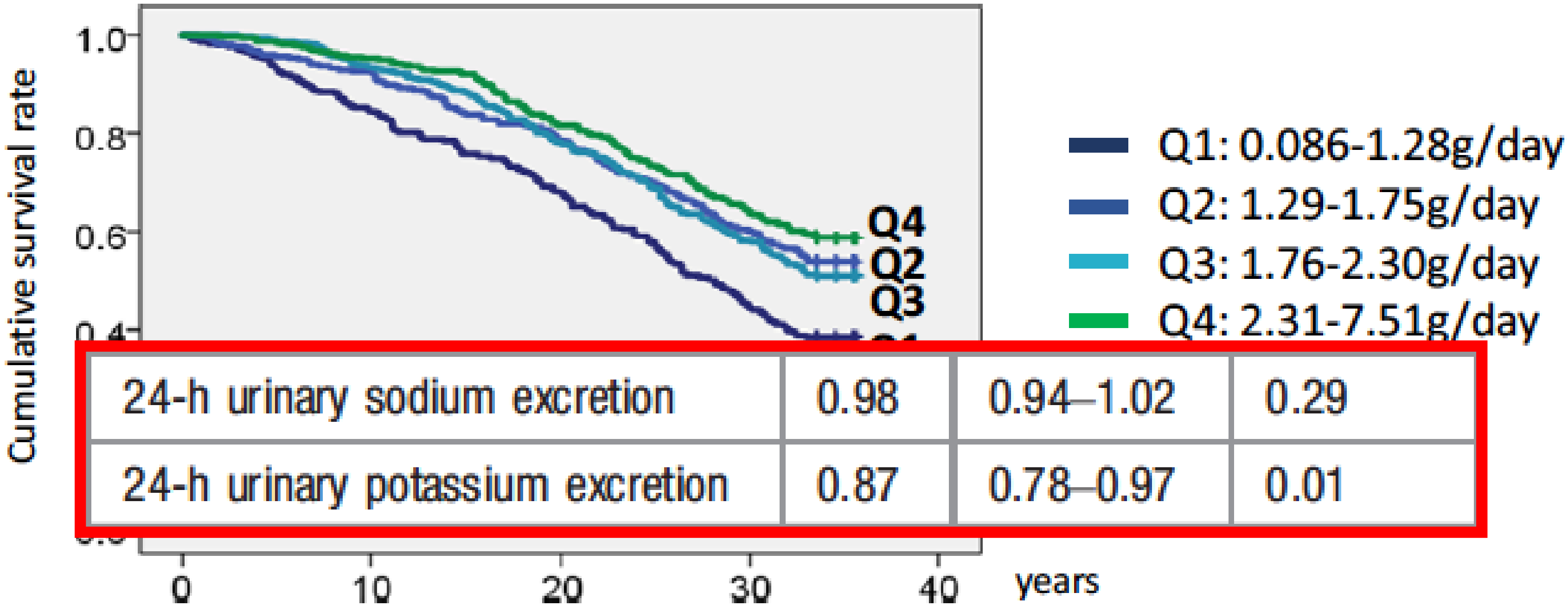


No. at Risk	0	10	20	30	40
Q1	283	239	192	126	109
Q2	295	273	231	177	159
Q3	302	282	235	176	154
Q4	308	293	251	196	181
p value		<0.0001	0.0002	<0.0001	<0.0001

1291 participants, 21-85 yrs, follow-up 27.5 yrs

Nohara-Shitama Y et al, J Am Heart Assoc 2018

Twenty-four-Hour Urinary Potassium Excretion, But Not Sodium Excretion, Is Associated With All-Cause Mortality in a General Population



24-h urinary sodium excretion	0.98	0.94–1.02	0.29
24-h urinary potassium excretion	0.87	0.78–0.97	0.01

No. at Risk					
Q1	283	239	192	126	109
Q2	295	273	231	177	159
Q3	302	282	235	176	154
Q4	308	293	251	196	181
p value		<0.0001	0.0002	<0.0001	<0.0001

1291 participants, 21-85 yrs, follow-up 27.5 yrs

Nohara-Shitama Y et al, J Am Heart Assoc 2018

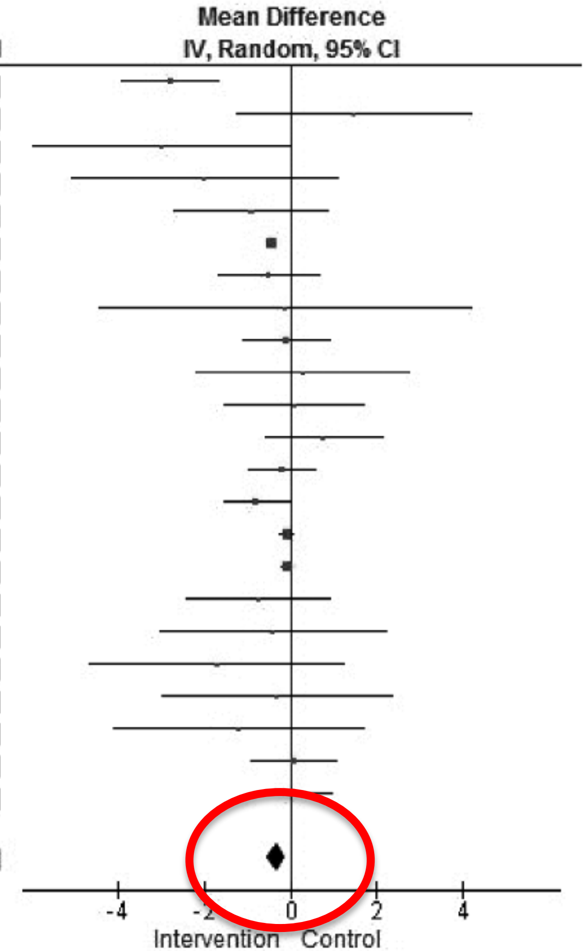
Effects of fruit and vegetable consumption on inflammatory biomarkers: a meta-analysis

CRP

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Aalami-Harandi 2015 (60)	-1.42	2.67	22	1.36	0.45	22	3.4%	-2.78 [-3.91, -1.65]
Baldrick 2011 (1)	0.71	4.52	29	-0.76	5.92	29	0.7%	1.47 [-1.24, 4.18]
Basu 2014 (28)	-1.2	0.9	15	1.8	5.8	15	0.6%	-3.00 [-5.97, -0.03]
Basu 2014 (28)	-0.2	1.93	15	1.8	5.8	15	0.5%	-2.00 [-5.09, 1.09]
Buscemi 2012 (30)	-1.6	2.61	19	-0.7	2.96	19	1.5%	-0.90 [-2.67, 0.87]
Davidson 2009 (33)	-0.39	0.21	146	0.06	0.37	143	19.0%	-0.45 [-0.52, -0.38]
Dow 2013 (35)	-0.1	2.06	37	0.4	2.8	32	3.2%	-0.50 [-1.68, 0.68]
Freese 2004 (11)	-1.92	5.04	19	-1.8	8.14	19	0.3%	-0.12 [-4.42, 4.18]
Guo 2014 (37)	-0.1	2.38	44	0	2.49	43	4.0%	-0.10 [-1.12, 0.92]
Kanellos 2017 (57)	0.8	3.56	22	0.5	3.74	14	0.8%	0.30 [-2.16, 2.76]
Kent 2017 (56)	0.1	2.3	24	0	3.35	25	1.8%	0.10 [-1.50, 1.70]
Kolehmainen 2012 (41)	0.06	1.37	11	-0.71	1.98	13	2.5%	0.77 [-0.58, 2.12]
McCall 2011 (12)	-0.32	1.37	35	-0.13	1.67	29	6.2%	-0.19 [-0.95, 0.57]
McCall 2011 (12)	-0.92	1.31	34	-0.13	1.67	29	6.3%	-0.79 [-1.54, -0.04]
Riso 2013 (47)	-0.02	0.24	18	0.06	0.24	18	17.7%	-0.08 [-0.24, 0.08]
Riso 2013 (47)	-0.08	0.22	17	0	0.13	17	18.4%	-0.08 [-0.20, 0.04]
Sohrab 2014 (50)	-1.45	3.33	22	-0.71	2.2	22	1.7%	-0.74 [-2.41, 0.93]
Tomé-Carneiro 2012 (51)	0	3.2	25	0.4	5.9	25	0.7%	-0.40 [-3.03, 2.23]
Tomé-Carneiro 2012 (51)	-1.3	4.45	25	0.4	6.05	25	0.6%	-1.70 [-4.64, 1.24]
Tomé-Carneiro 2012 (51)	0.1	3.05	25	0.4	6.05	25	0.7%	-0.30 [-2.96, 2.36]
Tomé-Carneiro 2012 (51)	-0.8	4.5	25	0.4	5.9	25	0.6%	-1.20 [-4.11, 1.71]
Vidal 2012 (52)	0.09	2.9	65	0.01	2.96	68	4.1%	0.08 [-0.92, 1.08]
Vidal 2012 (52)	0.04	2.77	75	0.01	2.94	75	4.7%	0.03 [-0.88, 0.94]
Total (95% CI)			**769**			**747**	**100.0%**	**-0.33 [-0.56, -0.10]**

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 69.39$, $df = 22$ ($P < 0.00001$); $I^2 = 68\%$

Test for overall effect: $Z = 2.81$ ($P = 0.005$)



Hosseini B et al, Am J Clin Nutr 2018

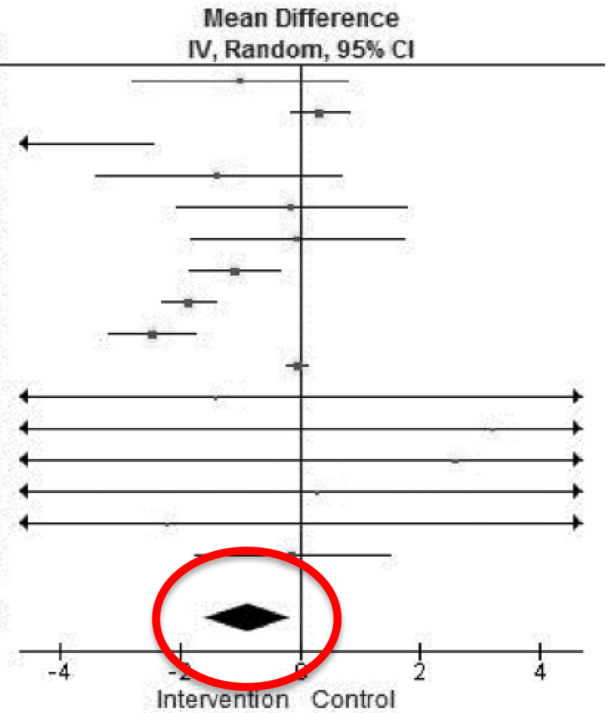
Effects of fruit and vegetable consumption on inflammatory biomarkers: a meta-analysis

TNF-alfa

Study or Subgroup	Intervention Mean	Intervention SD	Intervention Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
Briviba 2004 (14)	-0.6	1.89	15	0.4	3.02	15	7.2%	-1.00 [-2.80, 0.80]
Buscemi 2012 (30)	0.08	0.78	19	-0.25	0.78	19	12.3%	0.33 [-0.17, 0.83]
Ghavipour 2013 (4)	-8.25	21.9	53	0.08	0.14	53	1.3%	-8.33 [-14.23, -2.43]
Han 2016 (38)	-2	4.06	26	-0.63	3.31	24	6.4%	-1.37 [-3.42, 0.68]
Han 2016 (38)	-0.78	3.62	26	-0.63	3.31	24	6.8%	-0.15 [-2.07, 1.77]
Knab 2014 (67)	-0.12	2.19	9	-0.07	1.62	9	7.3%	-0.05 [-1.83, 1.73]
Lamprecht 2007 (13)	-0.82	1.2	21	0.27	1.28	21	11.4%	-1.09 [-1.84, -0.34]
Lamprecht 2013 (68)	-0.63	0.77	21	1.22	0.76	20	12.4%	-1.85 [-2.32, -1.38]
Leelarungrayub 2016 (44)	-2.11	1.56	29	0.35	1.18	29	11.6%	-2.46 [-3.17, -1.75]
Riso 2013 (47)	0.02	0.27	17	0.06	0.24	17	12.9%	-0.04 [-0.21, 0.13]
Sohrab 2014 (50)	-6.6	26.03	22	-5.2	27.2	22	0.2%	-1.40 [-17.13, 14.33]
Tomé-Carneiro 2012 (51)	2.2	15.2	25	-1	14.75	25	0.7%	3.20 [-5.10, 11.50]
Tomé-Carneiro 2012 (51)	1.3	14.8	25	-1.3	14.75	25	0.7%	2.60 [-5.59, 10.79]
Tomé-Carneiro 2012 (51)	-1	21.3	25	-1.3	14.75	25	0.5%	0.30 [-9.86, 10.46]
Tomé-Carneiro 2012 (51)	-3.2	20.7	25	-1	14.75	25	0.5%	-2.20 [-12.16, 7.76]
Zunino 2013 (81)	-0.18	2.9	24	-0.05	2.86	24	7.8%	-0.13 [-1.76, 1.50]
Total (95% CI)			**382**			**377**	**100.0%**	**-0.87 [-1.59, -0.15]**

Heterogeneity: $Tau^2 = 1.04$; $Chi^2 = 106.66$, df = 15 ($P < 0.00001$); $I^2 = 86\%$

Test for overall effect: Z = 2.36 (P = 0.02)



Hosseini B et al, Am J Clin Nutr 2018

I molteplici effetti dei polifenoli

- Effetto antiossidante
- Effetti sulla trascrizione genica
- Inibizione dell’attività delle amilasi
- Effetti sul microbiota (con formazione di metaboliti secondari)
- Effetto antiinfiammatorio
- ….

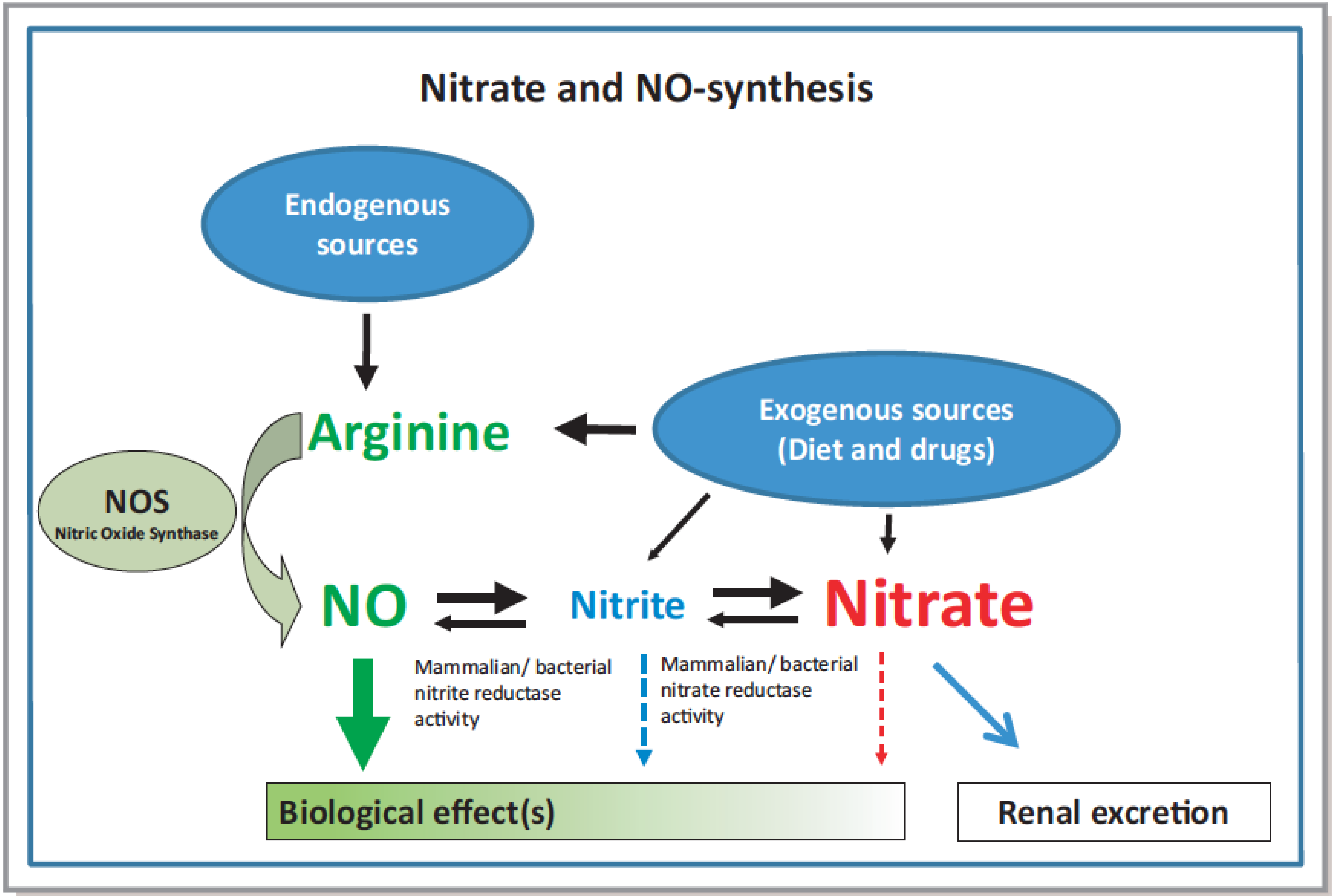
Mol. Nutr. Food Res. 2015, *0*, 1–18 DOI 10.1002/mnfr.201500313

REVIEW

A 'green' diet-based approach to cardiovascular health? Is inorganic nitrate the answer?

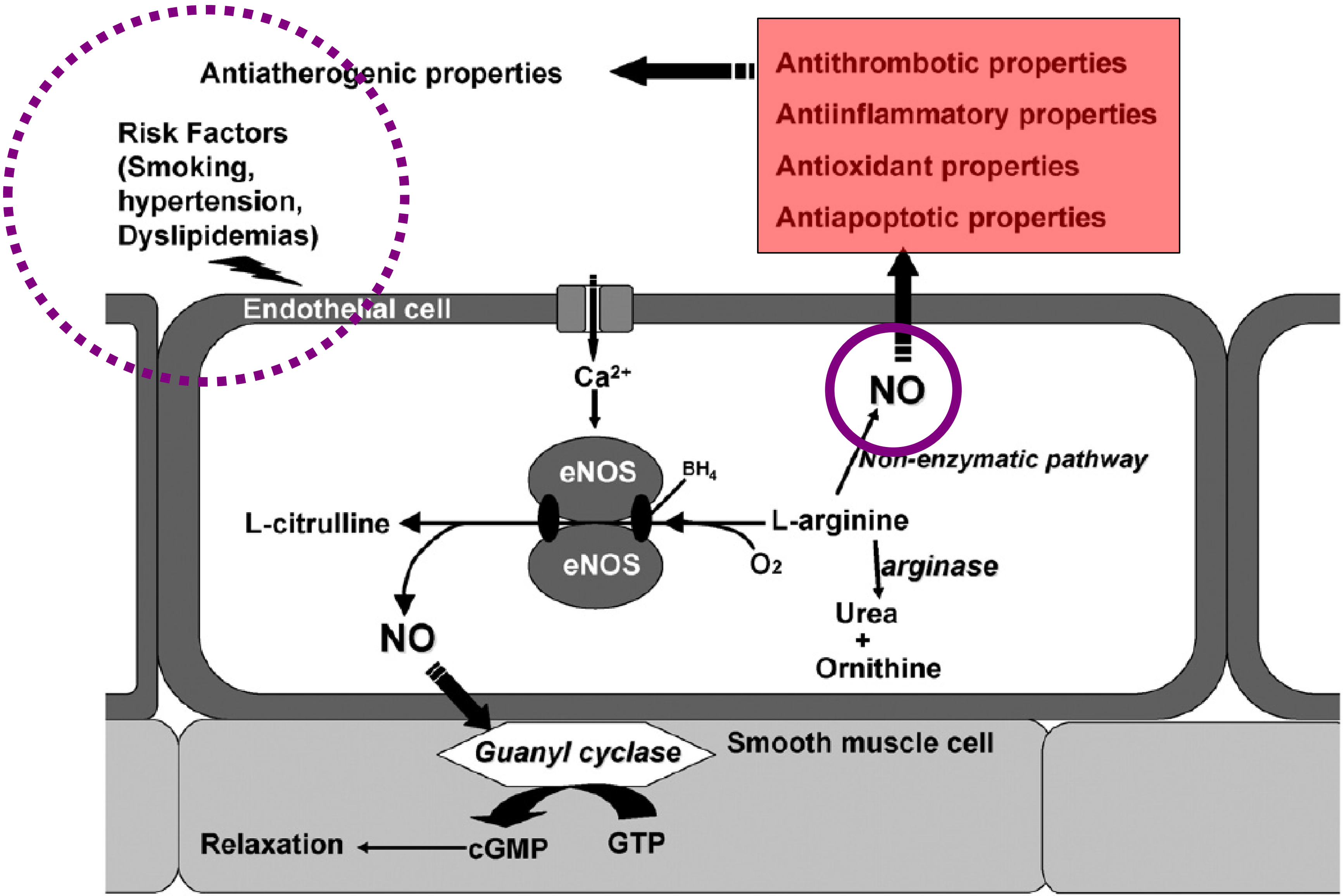
Krishnaraj Sinhji Rathod, Shanti Velmurugan* and Amrita Ahluwalia*

William Harvey Research Institute, Barts NIHR Cardiovascular Biomedical Research Unit, Barts & The London Medical School, Queen Mary University of London, Charterhouse Square, London, UK

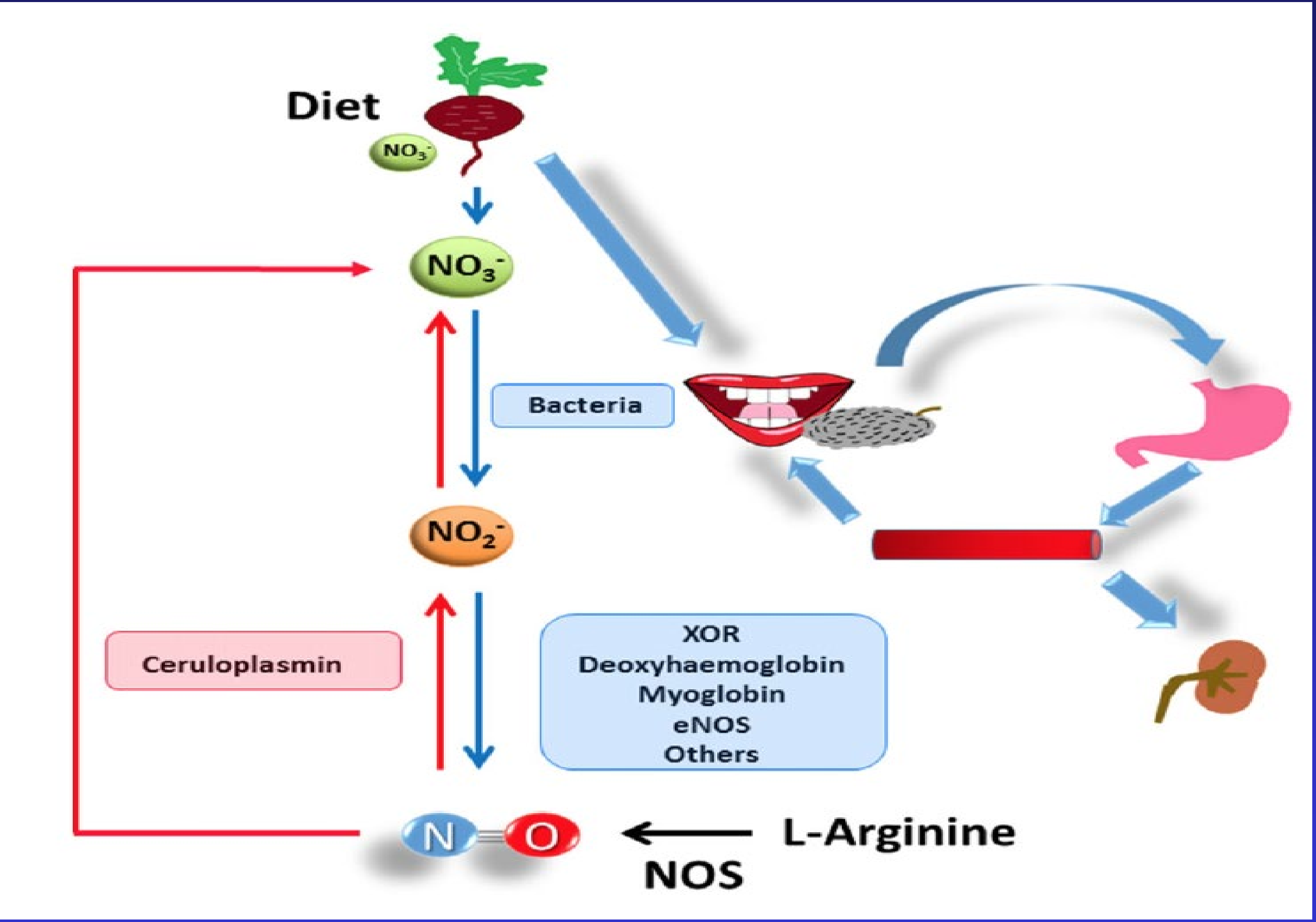


Maas R et al, J Am Heart Assoc 2017

L'arginina e le vie del Nitrossido (NO)



Dietary nitrates as a source of NO: a good reason to eat fruit and vegetables?



Rathod KS et al, Mol Nutr Food Res 2015

Nitrate concentrations in vegetables

Vegetable group	Examples	Sample size	Nitrate concentration (mg/kg)		
			Median	Mean	Range (P5–P95)
Leafy	Spinach Lettuce Rucola (rocket) Beet	25,306	1,140	1,614	66–4,556
Herb	Basil Parsley Dill Chives	492	791	1,240	10–4,040
Stem	Asparagus Fennel Celery Rhubarb	1,379	302	698	3–2,923
Root and tuber	Potato Beetroot Carrot Celeriac	7,579	152	506	15–2,302
Brassica	Broccoli Cabbage Kale Cauliflower	3,192	241	279	7–758
Legume	Beans Peas String beans	882	56	221	1–748
Bulb	Garlic Onions	243	60	159	1–601
Fruiting	Cucumber Tomato Aubergine Pumpkin	2,822	83	149	1–486
Fungi	Mushroom	12	41	59	31–100

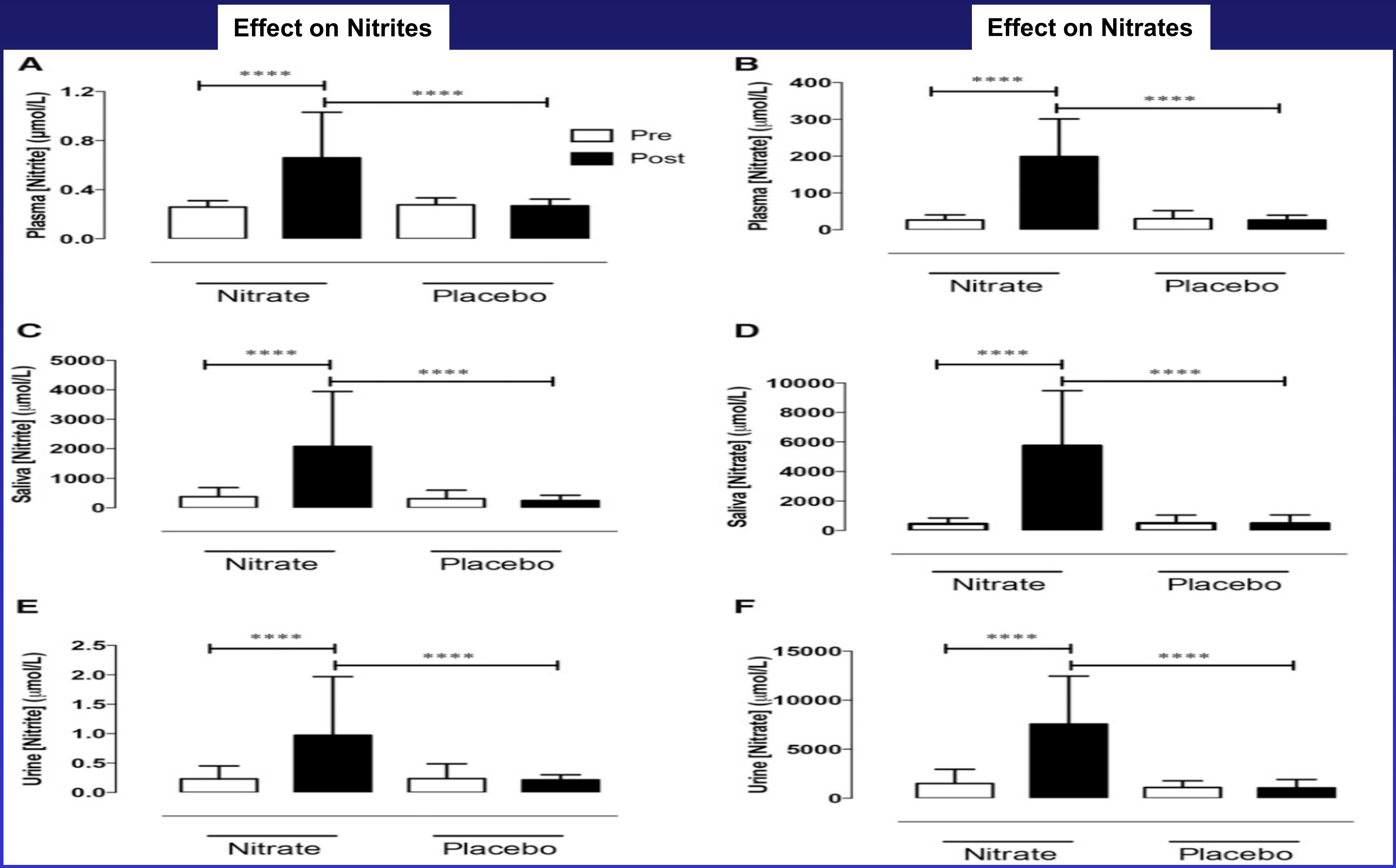
Eur Food Saf, EFSA J 2008

Nitrate concentrations in fruits

Common name	Scientific name	Production system	Season	Nitrate (mg/kg FW)	
				Mean	Min-max
Apple	*Malus pumila* Mill.	Conventional	May–Oct	3.3	(0.2–15)
		Conventional	Unspecified	11	
Banana	*Musa spp.*	Conventional	Unspecified	45	
		Conventional	Unspecified	153	(peeled–61.9%)
Grape	*Vitis vinifera* L.	Conventional	May–Oct	5.6	(0.5–19)
		Conventional	Unspecified	46	
Kiwi	*Actinidia spp.*	Conventional	Unspecified	0	(peeled)
Nectarine	*Prunus persica* (L.) Batsch *var. nucipersica* (Borkh.) C.K.Schneid	Conventional	Unspecified	12	
Peach	*Prunus persica* (L.) Batsch	Conventional	May–Oct	4	(ND–12)
		Conventional	Unspecified	10	
Pear	*Pyrus* L.	Conventional	May–Oct	2.8	(1.4–4.5)
		Conventional	Unspecified	14	
Orange	*Citrus sinensis* L.	Conventional	Unspecified	8	
		Conventional	Unspecified	13	

Colla G et al, Sci Hort 2018

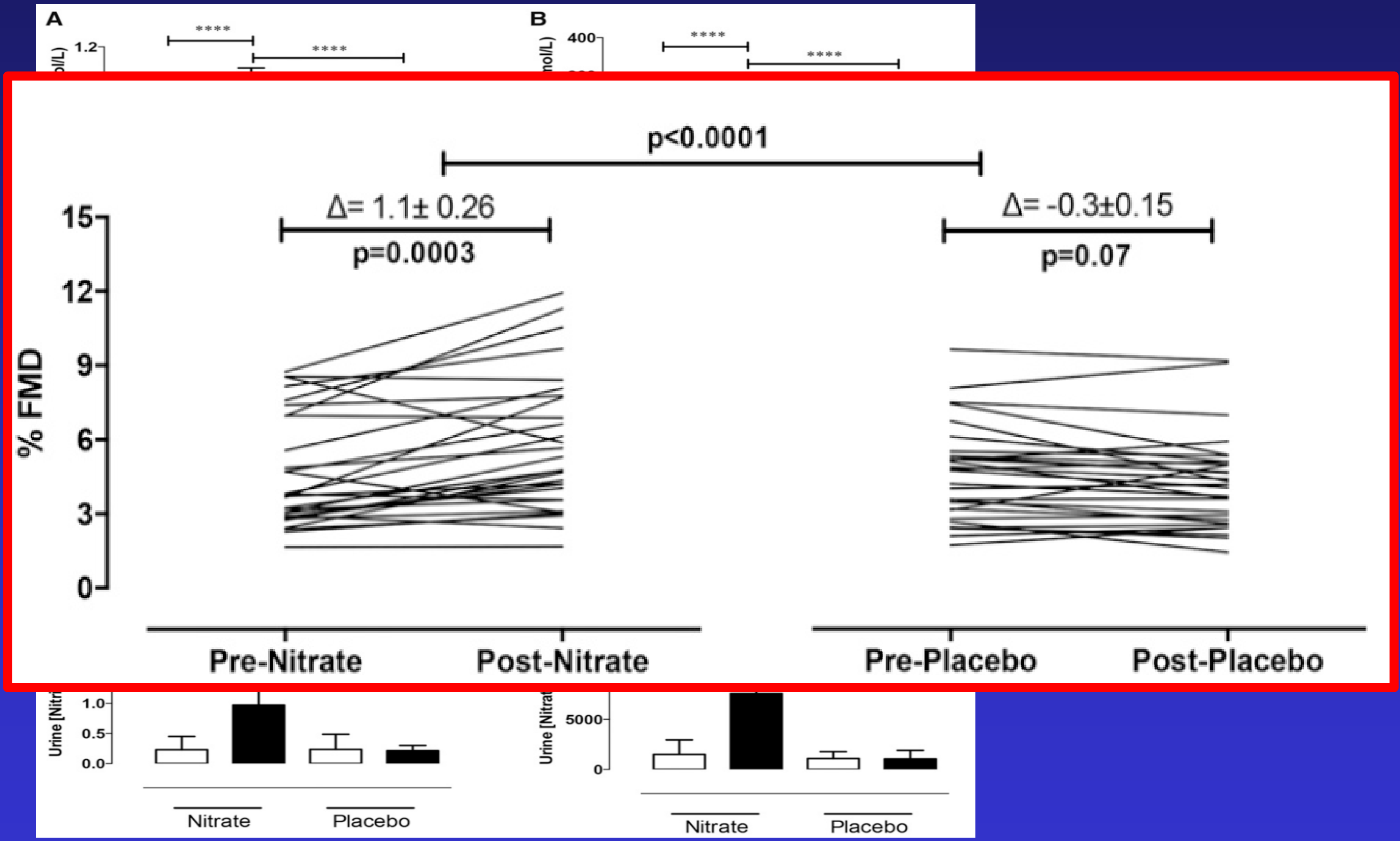
Dietary nitrates and FMD in hypercholesterolemic patients: a RCT



250 ml of nitrate rich beetroot juice

Velmurugan S et al, Am J Clin Nutr 2015

Dietary nitrates and FMD in hypercholesterolemic patients: a RCT



Velmurugan S et al, Am J Clin Nutr 2015

Nitrate-Rich Fruit and Vegetable Supplement Reduces Blood Pressure in Normotensive Healthy Young Males without Significantly Altering Flow-Mediated Vasodilation: A RCT

Nutrient	FVS	PRU
Calories	30	45
Total carbohydrates	6 g	11 g
Dietary fiber	1 g	<1 g
Sugars	2 g	6 g
Protein	1 g	<1 g
Dietary nitrates	240–280 mg	<0.6 mg
Total polyphenols	51 mg	133 mg

[1]FVS: fruit and vegetable extract; PRU: prune juice. FVS data from manufacture; PRU data from http://sunsweet.com.

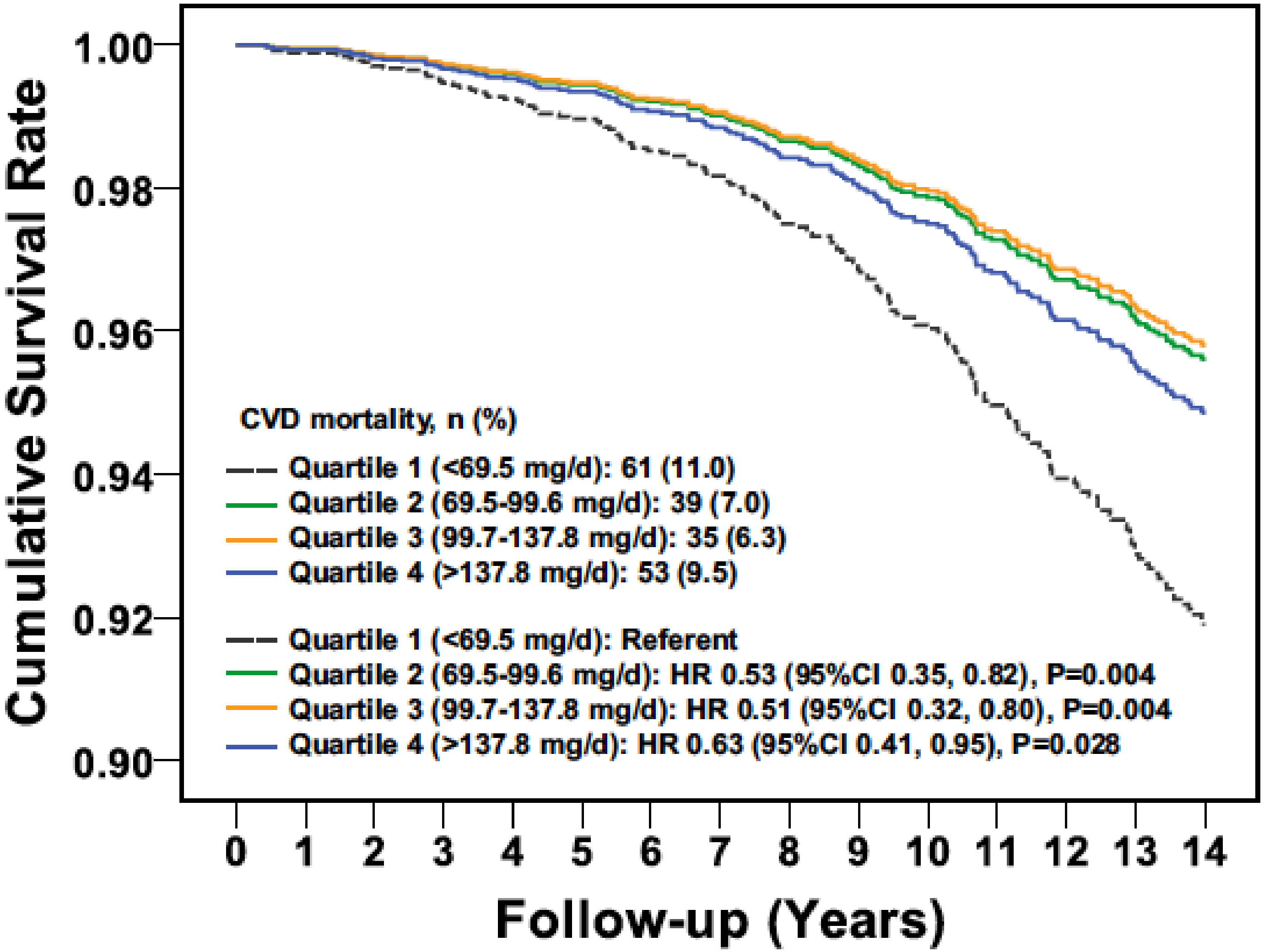
Sweazea KL et al, J Nutr Metab 2018

Nitrate-Rich Fruit and Vegetable Supplement Reduces Blood Pressure in Normotensive Healthy Young Males without Significantly Altering Flow-Mediated Vasodilation: A RCT

Variable	Baseline	Week 1	Week 2	2-week change	*p (Effect size)*
Systolic BP, mmHg					
FVS	116.2 ± 6.5	116.1 ± 9.1	112.1 ± 8.3	−4.1 ± 7.5	0.370
PRU	117.7 ± 10.1	115.2 ± 7.7	115.7 ± 7.1	−2.0 ± 8.5	*(0.020)*
Diastolic BP, mmHg					
FVS	61.7 ± 7.7	61.7 ± 7.7	57.4 ± 6.2	−5.3 ± 7.0	**0.028**
PRU	62.3 ± 8.2	62.3 ± 8.2	62.9 ± 8.0	−2.2 ± 7.7	*(0.112)*
FMD, %peak dilation					
FVS	6.3 ± 2.7	6.5 ± 2.9	6.4 ± 2.6	0.1 ± 2.8	0.145
PRU	5.7 ± 2.6	5.5 ± 2.4	5.2 ± 3.0	−0.5 ± 4.2	*(0.051)*
Plasma nitrates and nitrites, μM					
FVS	27.4 ± 23.5	63.3 ± 67.7	61.5 ± 58.5	34.1 ± 57.6	**0.001**
PRU	38.7 ± 37.0	31.8 ± 30.4	29.1 ± 25.5	−9.7 ± 21.0	*(0.244)*
POMS					
FVS	13.5 ± 19.0	10.7 ± 20.8	9.2 ± 17.3	−4.0 ± 19.1	0.369
PRU	10.1 ± 22.7	1.5 ± 14.7	2.9 ± 21.7	−7.3 ± 9.9	*(0.020)*
PSQI					
FVS	4.3 ± 2.4	4.5 ± 2.4	4.2 ± 2.6	−0.1 ± 1.7	0.970
PRU	4.1 ± 2.3	3.8 ± 2.1	4.0 ± 2.7	−0.2 ± 2.0	*(0.000)*

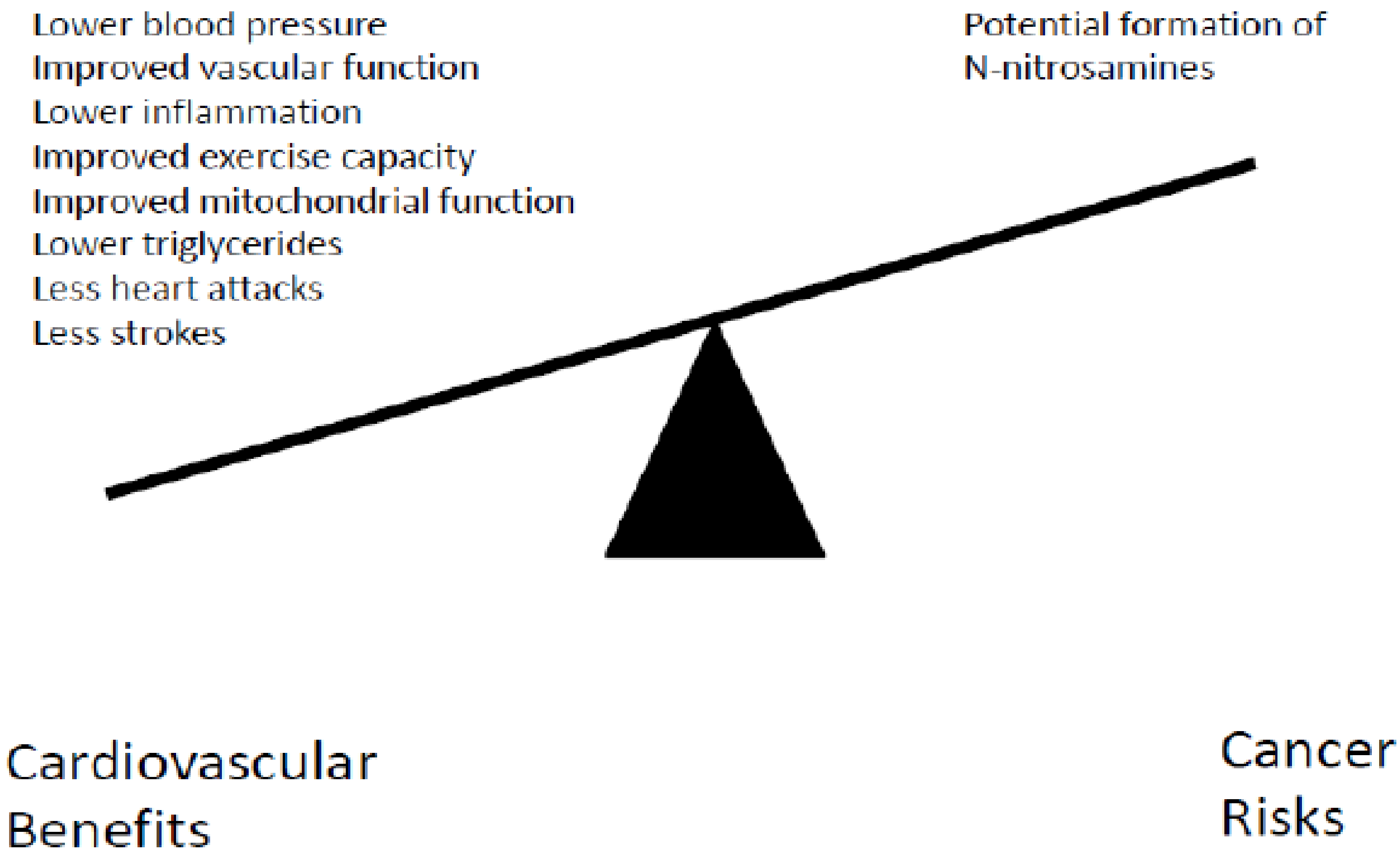
Sweazea KL et al, J Nutr Metab 2018

Dietary nitrate intake from vegetables and CVD mortality: a prospective study in a cohort of older Australians



Liu AH et al, Eur J Nutr 2018

Health effects of dietary Nitrates: CV vs. Cancer



Bryan NS et al, Nutr Res 2015

Relazione tra apporto di nitrati/nitriti e tumori

- A review of data by the World Health Organisation Expert Committee on Food Additives found that there was no evidence that NO_3^- was carcinogenic to humans.
- The International Agency for Research on Cancer reported that "There is inadequate evidence in humans for the carcinogenicity of nitrate in food and in drinking water".
- However, they also reported that "There is limited evidence in humans and animals for the carcinogenicity of NO_2^- in food; NO_2^- in food is associated with an increased incidence of stomach cancer".
- There is sufficient evidence in experimental animals for the carcinogenicity of nitrite in combination with amines or amides" . . . . ..There is limited evidence in experimental animals for the carcinogenicity of NO_2^- per se."
- Large prospective studies do not support the hypothesis of an association between ingestion of NO_3^- or NO_2^- and stomach cancer.
- Thus, in sum while it seems that the risk of cancer with NO_3^- is negligible concerns still remain with respect to NO_2^-.

Rathod KS et al, Mol Nutr Food Res 2015

Long-term consumption of fruits and vegetables and risk of chronic obstructive pulmonary disease: a prospective cohort study of women

Table 3. Hazard ratios (95% CIs) of chronic obstructive pulmonary disease by quintiles of long-term fruit and vegetable consumption in 34 739 Swedish women, follow-up January 2002 to December 2014

	Quintiles of long-term consumption, servings/day (median)[a]					P-trend
	Q1	Q2	Q3	Q4	Q5	
Fruits	<0.8 (0.6)	0.8–1.2 (1.1)	1.3–1.7 (1.5)	1.8–2.4 (2.0)	≥2.5 (2.9)	
No. of cases/person-years	546/78 467	305/80 012	245/80 871	235/81 943	181/81 152	
Age-SIR per 100 000 person-years	721	393	313	292	232	
Age and smoking-adjusted HR	1.00	0.74 (0.65–0.86)	0.65 (0.56–0.76)	0.68 (0.58–0.79)	0.57 (0.48–0.67)	<0.0001
Multivariable HR[b,c]	1.00	0.80 (0.69–0.93)	0.73 (0.62–0.86)	0.78 (0.66–0.92)	0.63 (0.52–0.75)	<0.0001
Vegetables	<1.3 (0.9)	1.3–1.8 (1.5)	1.9–2.3 (2.0)	2.4–3.0 (2.6)	≥3.1 (3.7)	
No. of cases/person-years	453/75 985	296/80 667	277/81 517	243/82 116	243/82 159	
Age-SIR per 100 000 person-years	586	368	354	314	316	
Age and smoking-adjusted HR	1.00	0.74 (0.64–0.85)	0.74 (0.64–0.86)	0.65 (0.56–0.76)	0.67 (0.57–0.79)	<0.0001
Multivariable HR[b,c]	1.00	0.85 (0.73–0.99)	0.95 (0.81–1.11)	0.88 (0.74–1.04)	0.94 (0.79–1.13)	0.65

CI, confidence interval; HR, hazard ratio; SIR, standardized incidence rate.

[a]Long-term consumption was calculated as an average consumption in FFQ 1987 and FFQ 1997.

[b]Adjusted for age (years, continuous), education (less than high school, high school or university), BMI (<18.5, 18.5–24.9, 25–29.9 or ≥30 kg/m^2), total physical activity (MET × h/d, quintiles), smoking status and pack-years of smoking (never; past <20, 20–39 or ≥40 pack-years; or current <20, 20–39 or ≥40 pack-years), dietary supplement use (regular, non-regular or no use), intake of energy (kcal/day, quintiles), alcohol consumption (g/day, quintiles), modified Recommended Food Score (score, continuous) and Non-Recommended Food Score (score, continuous).

[c]Fruits and vegetables were included in the same multivariable model.

Kaluza J et al, Int J Epidemiol 2018

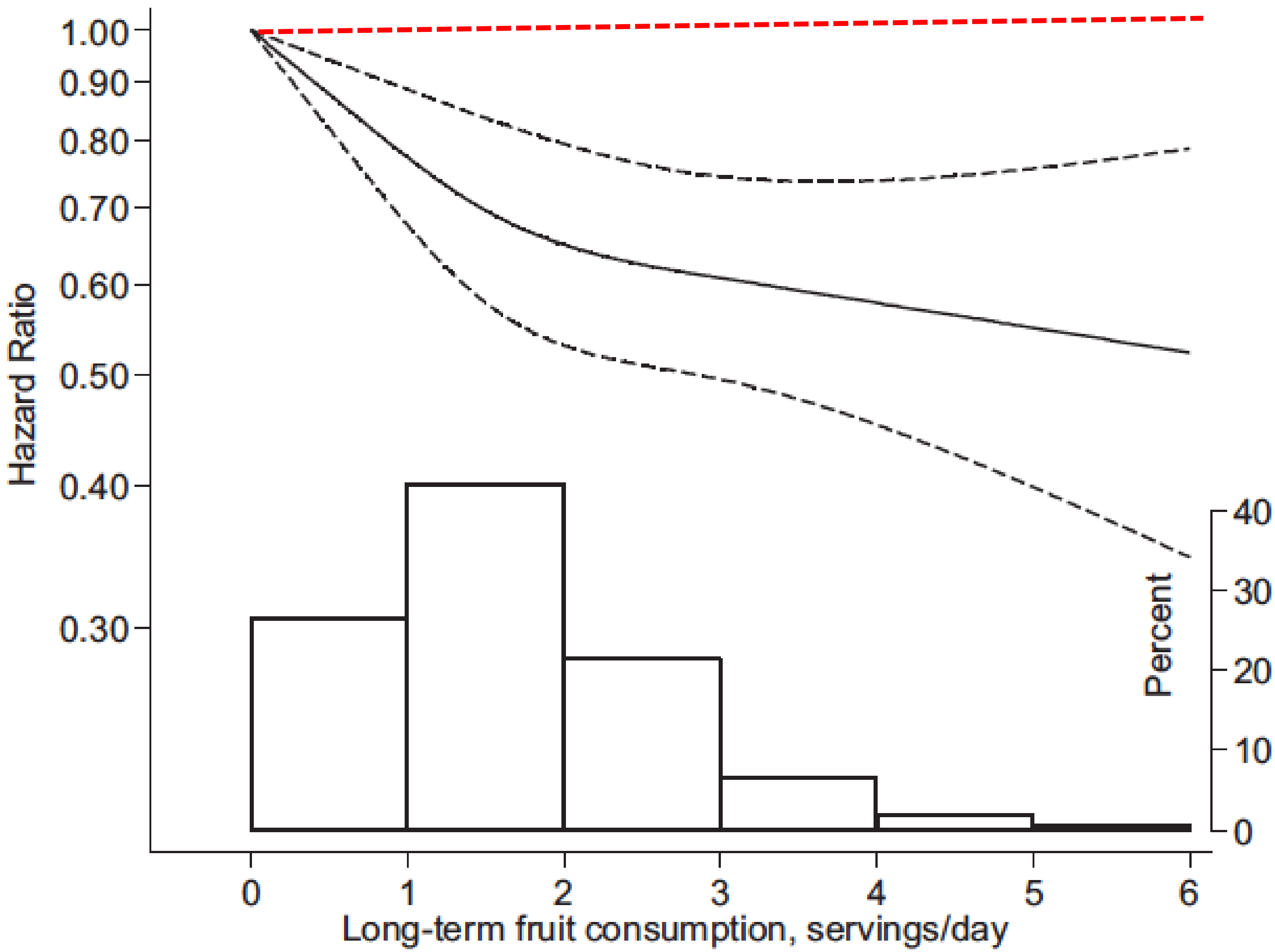
Long-term consumption of fruits and vegetables and risk of chronic obstructive pulmonary disease: a prospective cohort study of women

Table 4. Hazard ratios (95% CIs) of chronic obstructive pulmonary disease by categories of subgroups of long-term fruit and vegetables consumption in 34 739 Swedish women, follow-up January 2002 to December 2014

	Categories of long-term consumption, servings/day (median)[a]			*P*-trend
Fruits				
Apples or pears	0 (0)	0.1–0.9 (0.5)	≥1.0 (1.4)	
No. of cases/no. of women	44/389	1134/25 359	231/7372	
Multivariable HR[b]	1.00	0.75 (0.54–1.05)	0.62 (0.43–0.89)	<0.0001
Bananas	0 (0)	0.1–0.9 (0.3)	≥1.0 (1.0)	
No. of cases/no. of women	60/705	1280/29 864	67/2245	
Multivariable HR[b]	1.00	0.83 (0.63–1.09)	0.65 (0.46–0.94)	0.008
Citrus fruits	0 (0)	0.1–0.9 (0.3)	≥1.0 (1.2)	
No. of cases/no. of women	74/764	1118/26 966	119/3172	
Multivariable HR[b]	1.00	1.02 (0.78–1.32)	1.09 (0.79–1.51)	0.16
Vegetables				
Green leafy vegetables[c]	<0.2 (0.1)	0.2–0.9 (0.5)	≥1.0 (1.2)	
No. of cases/no. of women	398/6492	952/24 156	162/4091	
Multivariable HR[b]	1.00	0.85 (0.73–0.98)	0.91 (0.72–1.15)	0.028

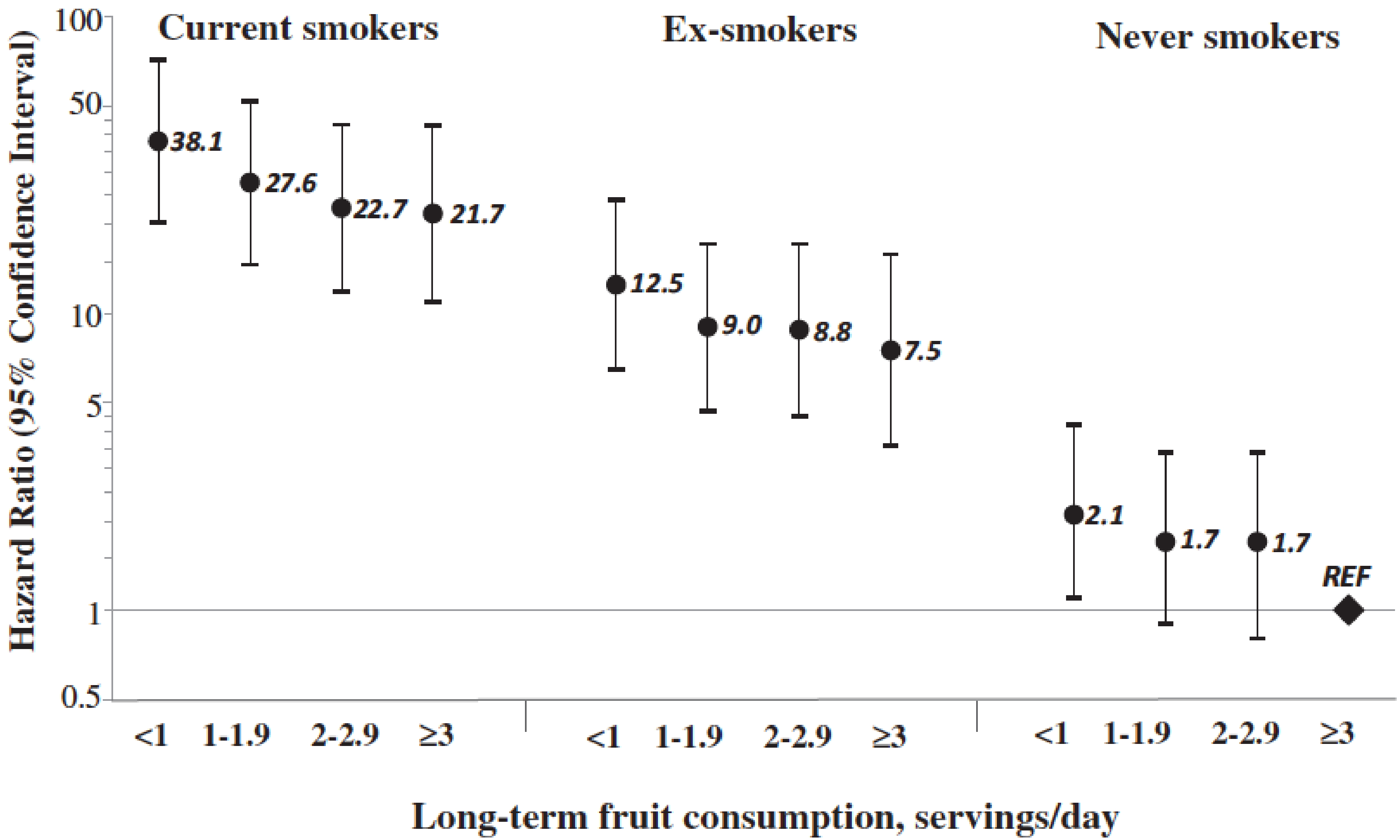
Kaluza J et al, Int J Epidemiol 2018

Long-term consumption of fruits and vegetables and risk of chronic obstructive pulmonary disease: a prospective cohort study of women



Kaluza J et al, Int J Epidemiol 2018

Long-term consumption of fruits and vegetables and risk of chronic obstructive pulmonary disease: a prospective cohort study of women



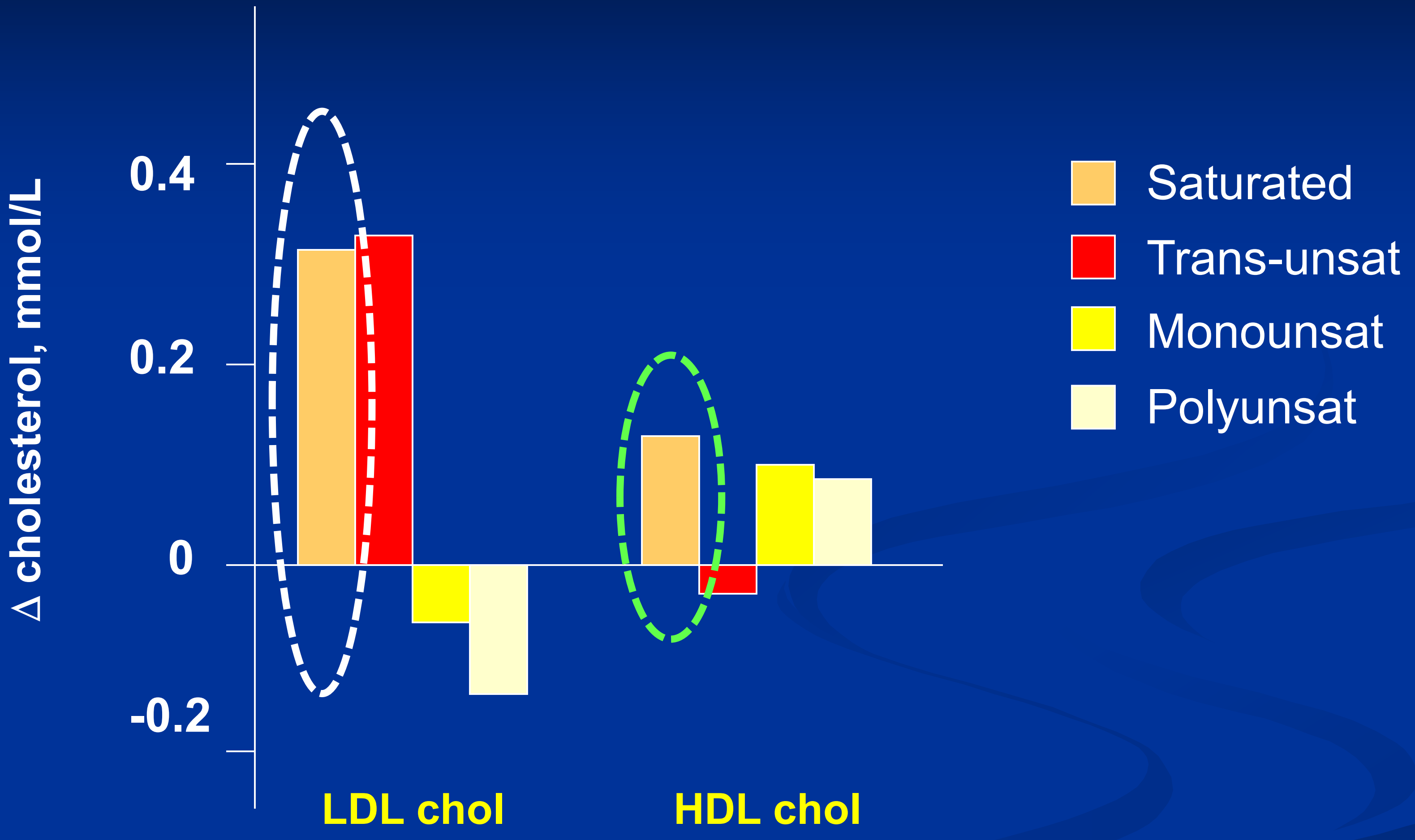
Kaluza J et al, Int J Epidemiol 2018

PURE Healthy Diet Score: Foods

Foods	Least Healthy: Quintile (Number of Servings per Day)	Most Healthy: Quintile 5 (Number of Servings per Day)
Fruits and vegetables	1.8	8.4
Nuts and legumes	0.7	2.5
Dairy	0.6	3.0
Red meat	0.3	1.4
Fish	0.2	0.3

PURE Study group, ESC 2018, unpublished

Effects of SAT, *trans* MONO, *cis* MONO, and *cis* POLY Fatty Acids on LDL and HDL Cholesterol

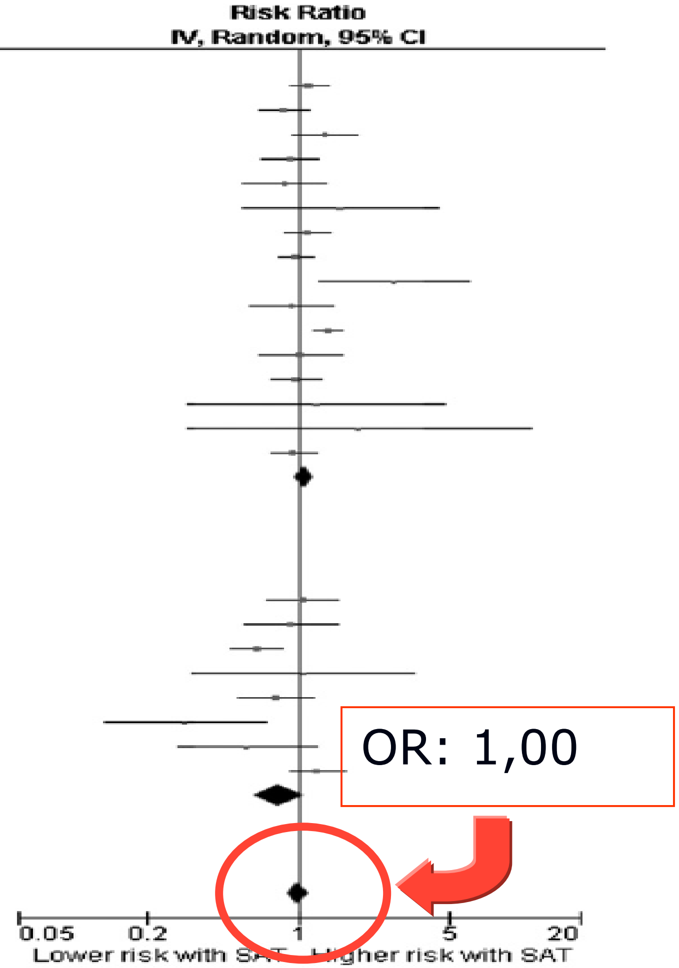


Values obtained by meta-analysis of 32 controlled dietary trials in humans

Zock P et al., Can J Physiol Pharmacol 1997

Saturated fats and CVD: a meta-analysis

Study or Subgroup	Risk Ratio IV, Random, 95% CI	Year
Coronary Heart Disease		
Shekelle et al(17)	1.11 [0.91, 1.36]	1981
McGee et al(9)[1]	0.86 [0.67, 1.12]	1984
Kushi et al(13)	1.33 [0.95, 1.87]	1985
Posner et al(16)	0.92 [0.68, 1.24]	1991
Goldbourt et al(35)[1]	0.86 [0.56, 1.35]	1993
Fehily et al(28)	1.57 [0.56, 4.42]	1994
Ascherio et al(4)[1]	1.11 [0.87, 1.42]	1996
Esrey et al(6)	0.97 [0.80, 1.18]	1996
Mann et al(32)	2.77 [1.25, 6.13]	1997
Pietinen et al(15)	0.93 [0.60, 1.44]	1997
Boniface et al(5)[1]	1.37 [1.17, 1.60]	2002
Jakobsen et al(8)[1]	1.03 [0.66, 1.60]	2004
Oh et al(33)	0.97 [0.74, 1.27]	2005
Tucker et al(18)[1]	1.22 [0.31, 4.77]	2005
Xu et al(10)	1.91 [0.31, 11.84]	2006
Leosdottir et al(14)	0.95 [0.74, 1.21]	2007
Subtotal (95% CI)	**1.07 [0.96, 1.19]**	
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 25.54$, df = 15 (P = 0.04); $I^2 = 41\%$		
Test for overall effect: Z = 1.22 (P = 0.22)		
Stroke		
McGee et al(9)[1]	1.04 [0.72, 1.50]	1984
Goldbourt et al(35)[1]	0.92 [0.56, 1.51]	1993
Gillman et al(11)	0.64 [0.49, 0.84]	1997
Iso et al(31)	1.05 [0.33, 3.39]	2001
He et al(29)[1]	0.79 [0.52, 1.19]	2003
Iso et al(30)	0.30 [0.13, 0.71]	2003
Sauvaget et al(34)	0.58 [0.28, 1.20]	2004
Leosdottir et al(14)	1.22 [0.91, 1.64]	2007
Subtotal (95% CI)	**0.81 [0.62, 1.05]**	
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 18.03$, df = 7 (P = 0.01); $I^2 = 61\%$		
Test for overall effect: Z = 1.58 (P = 0.11)		
Total (95% CI)	**1.00 [0.89, 1.11]**	
Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 52.63$, df = 23 (P = 0.0004); $I^2 = 56\%$		
Test for overall effect: Z = 0.06 (P = 0.95)		

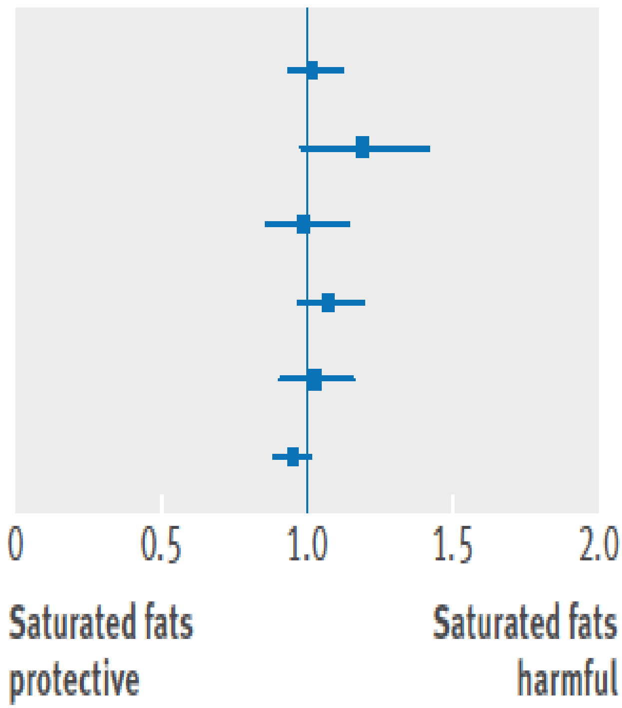


Siri-Tarino PW et al.; Am J Clin Nutr 2010

June 12th, 2014

Intake of saturated and trans unsaturated fatty acids and risk of all cause mortality, cardiovascular disease, and type 2 diabetes: systematic review and meta-analysis of observational studies

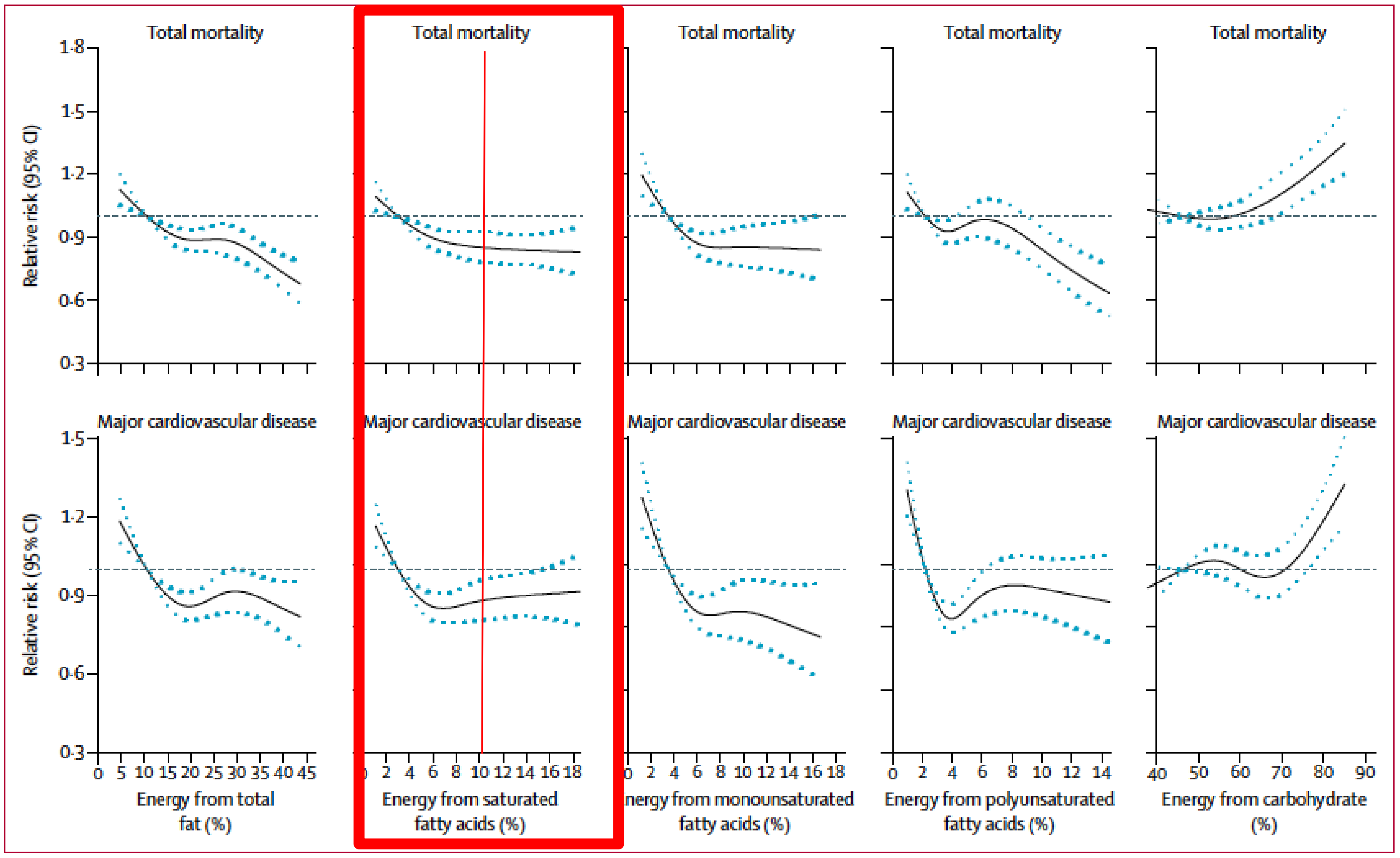
Outcome	No of studies /comparisons	No of events /participants	Risk ratio (95% CI)	Relative risk (95% CI)	P	P_{het}	I^2 (%)
All cause mortality	5/7	14 090/99 906		0.99 (0.91 to 1.09)	0.91	0.17	33
CHD mortality	11/15	2970/101 712		1.15 (0.97 to 1.36)	0.10	<0.001	70
CVD mortality	3/5	3792/90 501		0.97 (0.84 to 1.12)	0.69	0.29	19
CHD total	12/17	6383/267 416		1.06 (0.95 to 1.17)	0.29	0.02	47
Ischemic stroke	12/15	6226/339 090		1.02 (0.90 to 1.15)	0.79	0.002	59
Type 2 diabetes	8/8	8739/237 454		0.95 (0.88 to 1.03)	0.20	0.61	0



Saturated fats

de Souza RJ et al, Brit Med J 2015

Associations of fats with CVD and mortality: the PURE study



135m persons, 35-70 yrs,
18 countries, av. follow-up 7.4 yrs

Dehghan M et al, Lancet 2017

Saturated FA and risk of CHD: data from the EPIC-NL study

Multivariable HRs with 95% CIs for the associations between the intake of total and individual SFAs with incidence of ischemic heart disease in 35,597 subjects from the EPIC-NL cohort[1]

	Median intake, en%	HR expressed per en%	Model 1[2]	Model 2[3]	Model 3[4]	Model 4[5]
Total SFAs	14.9	5	1.14 (1.05, 1.24)	1.02 (0.94, 1.10)	0.94 (0.86, 1.02)	0.83 (0.74, 0.93)
Sum of butyric (4:0) to capric (10:0) acid	0.62	0.27	0.99 (0.94, 1.03)	0.85 (0.81, 0.90)	0.95 (0.90, 1.00)	0.93 (0.89, 0.99)[6]
Lauric acid (12:0)	0.61	0.24	1.04 (1.00, 1.09)	0.88 (0.84, 0.93)	0.96 (0.91, 1.00)	0.97 (0.91, 1.02)[6]
Myristic acid (14:0)	1.44	0.44	1.05 (1.01, 1.10)	0.92 (0.87, 0.96)	0.95 (0.90, 0.99)	0.90 (0.83, 0.97)[6]
Palmitic acid (16:0)	6.5	1.19	1.06 (1.02, 1.11)	1.05 (1.01, 1.10)	0.98 (0.94, 1.03)	1.00 (0.91, 1.10)[6]
Sum pentadecylic (15:0) and margaric (17:0) acids	0.35	0.11	1.03 (0.99, 1.08)	0.91 (0.87, 0.95)	0.96 (0.91, 1.01)	0.91 (0.83, 0.99)[6]
Stearic acid (18:0)	3.2	0.66	1.08 (1.03, 1.13)	1.08 (1.03, 1.12)	1.00 (0.95, 1.04)	1.05 (0.97, 1.14)[6]

Praagman J et al, Am J Clin Nutr 2016

Saturated FA and risk of CHD: data from the EPIC-NL study

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Sum of butyric (4:0) to capric (10:0) acid	0.62	0.27	0.99 (0.94, 1.03)	0.85 (0.81, 0.90)	0.95 (0.90, 1.00)	0.93 (0.89, 0.99)[6]
Lauric acid (12:0)	0.61	0.24	1.04 (1.00, 1.09)	0.88 (0.84, 0.93)	0.96 (0.91, 1.00)	0.97 (0.91, 1.02)[6]
Myristic acid (14:0)	1.44	0.44	1.05 (1.01, 1.10)	0.92 (0.87, 0.96)	0.95 (0.90, 0.99)	0.90 (0.83, 0.97)[6]
Palmitic acid (16:0)	6.5	1.19	1.06 (1.02, 1.11)	1.05 (1.01, 1.10)	0.98 (0.94, 1.03)	1.00 (0.91, 1.10)[6]
Sum pentadecylic (15:0) and margaric (17:0) acids	0.35	0.11	1.03 (0.99, 1.08)	0.91 (0.87, 0.95)	0.96 (0.91, 1.01)	0.91 (0.83, 0.99)[6]
Stearic acid (18:0)	3.2	0.66	1.08 (1.03, 1.13)	1.08 (1.03, 1.12)	1.00 (0.95, 1.04)	1.05 (0.97, 1.14)[6]

Praagman J et al, Am J Clin Nutr 2016

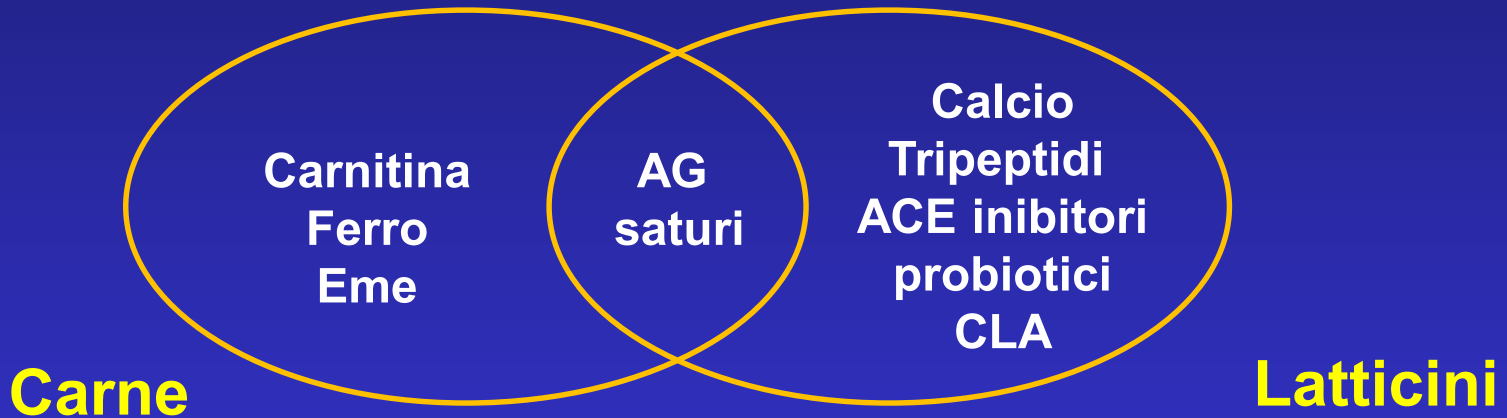
Association of specific dietary fats with total mortality: saturated fats

Table 2. Associations Between Total and Specific Types of Fat Intake and Total Mortality (Comparison Is Isocaloric Substitution for Total Carbohydrates)

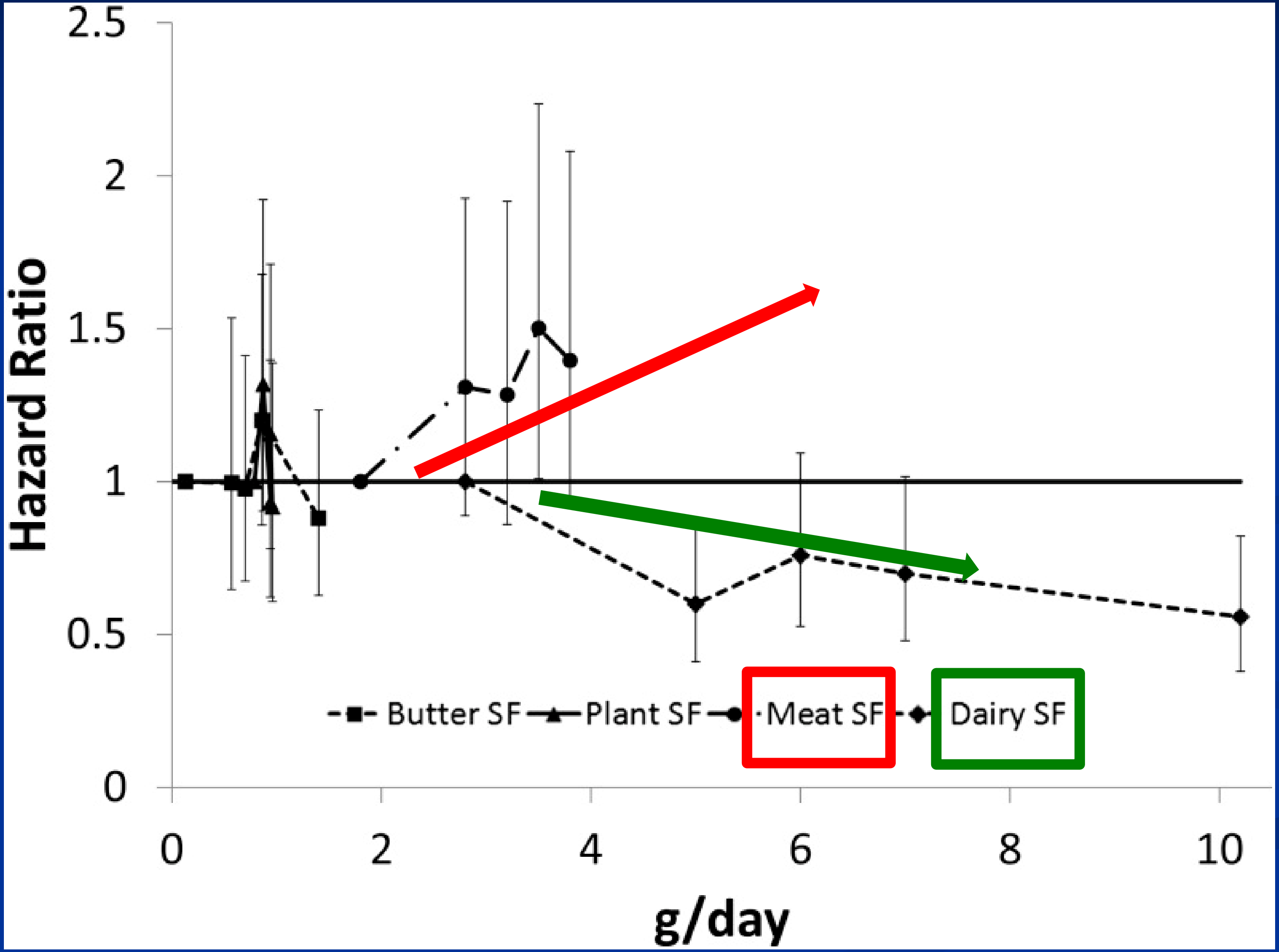
	Quintile of Dietary Fatty Acid Intake					*P* Value for Trend	HR (95% CI)[a]
	1	2	3	4	5		
Saturated fat intake							
NHS							
Median, % of energy	8.2	10.2	11.8	13.5	16.5	NA	NA
No. of deaths	5660	4729	4217	3376	2332	NA	NA
HPFS							
Median, % of energy	7.1	9.0	10.2	11.5	13.5	NA	NA
No. of deaths	2606	2662	2602	2548	2572	NA	NA
Pooled[b]							
Age-adjusted model	1 [Reference]	1.16 (1.12-1.19)	1.32 (1.27-1.36)	1.45 (1.40-1.50)	1.71 (1.65-1.78)	<.001	1.45 (1.42-1.48)
MV-adjusted model[c]	1 [Reference]	1.04 (1.00-1.08)	1.09 (1.05-1.14)	1.09 (1.04-1.14)	1.08 (1.03-1.14)	<.001	1.08 (1.04-1.11)

Wang DD et al, JAMA Int Med 2016

Una possibile spiegazione:



Intake of saturated fat by food source and incident CVD: the MESA study



De Oliveira Otto MC et al, Am J Clin Nutr 2012

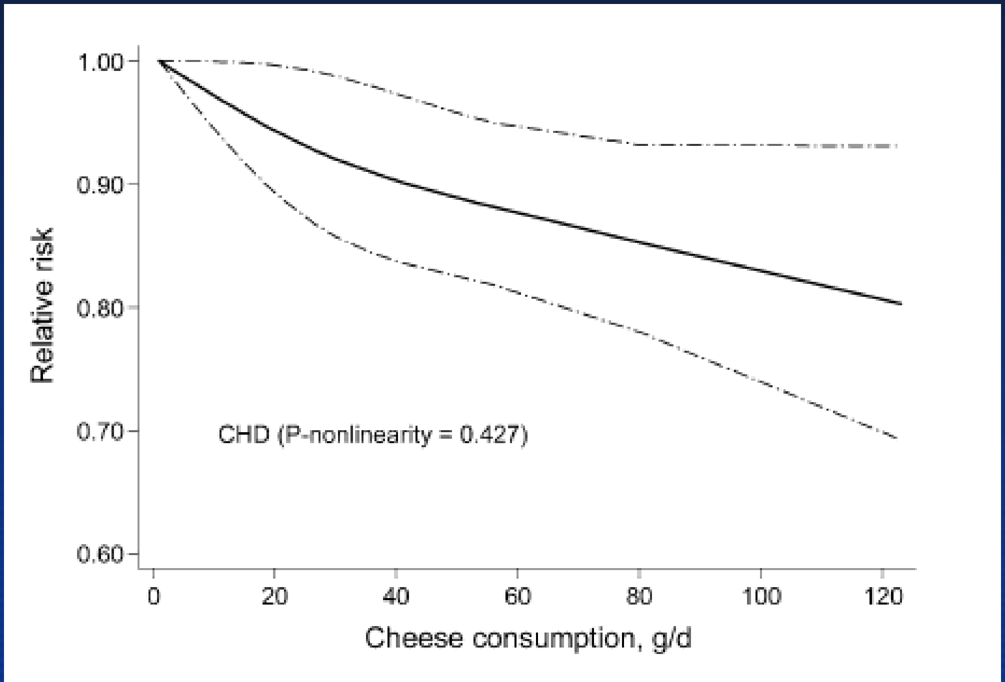
A changing view on SFAs and dairy: from enemy to friend

CONCLUSIONS

The totality of evidence does not support that dairy SFAs increase the risk of coronary artery disease or stroke or CVD mortality. In contrast, lean dairy is clearly associated with decreased risk of type 2 diabetes, and this effect is partly independent of any effect of body fat loss. In addition, lean dairy does not increase body fatness but tends to preserve lean body tissue. There is no evidence left to support the existing public health advice to limit consumption of dairy to prevent CVD and type 2 diabetes. Cheese and other dairy products are, in fact, nutrient-dense foods that give many people pleasure in their daily meals.

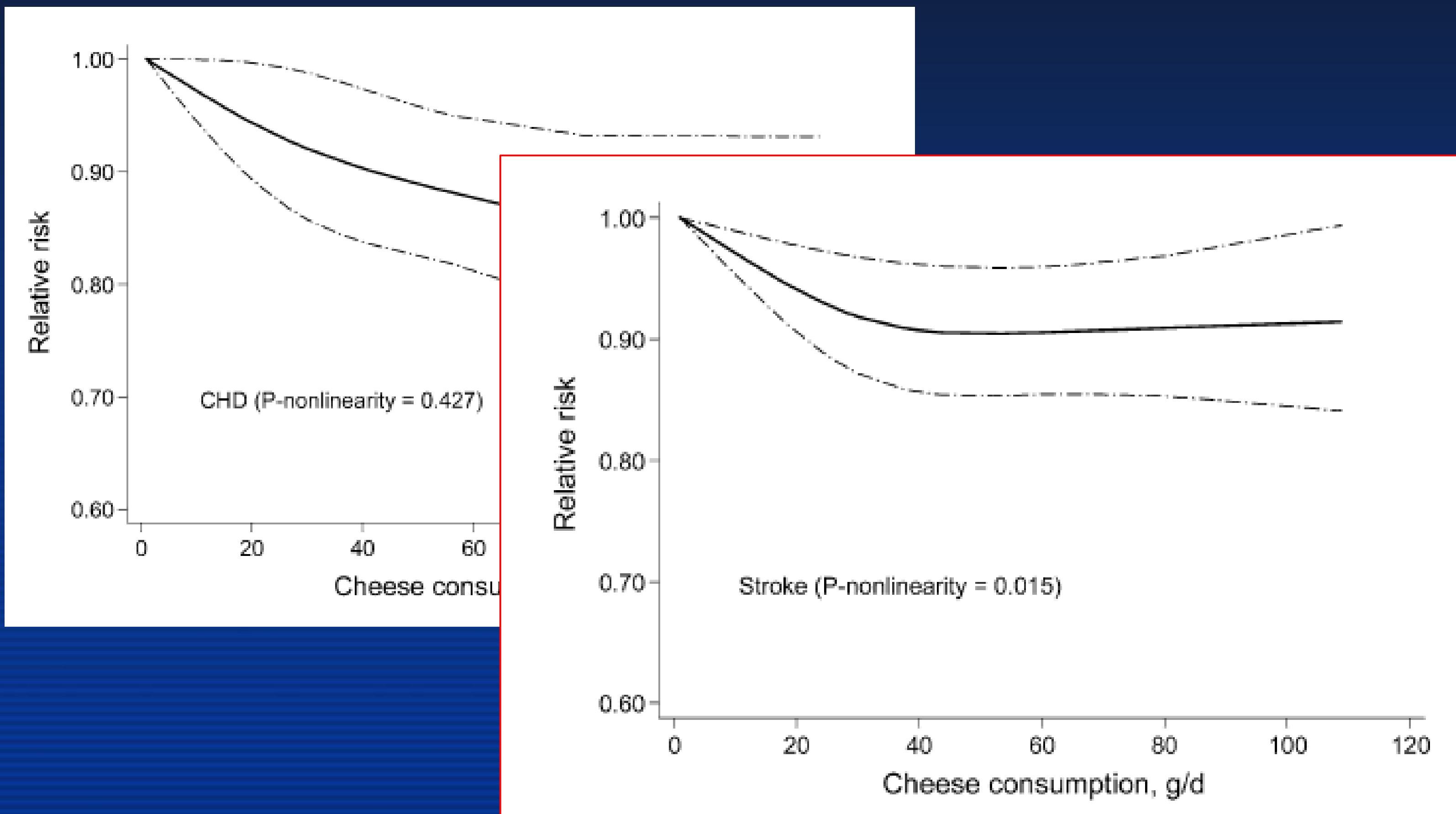
Astrup A, Am J Clin Nutr 2014

Cheese and CV diseases: a metanalysis



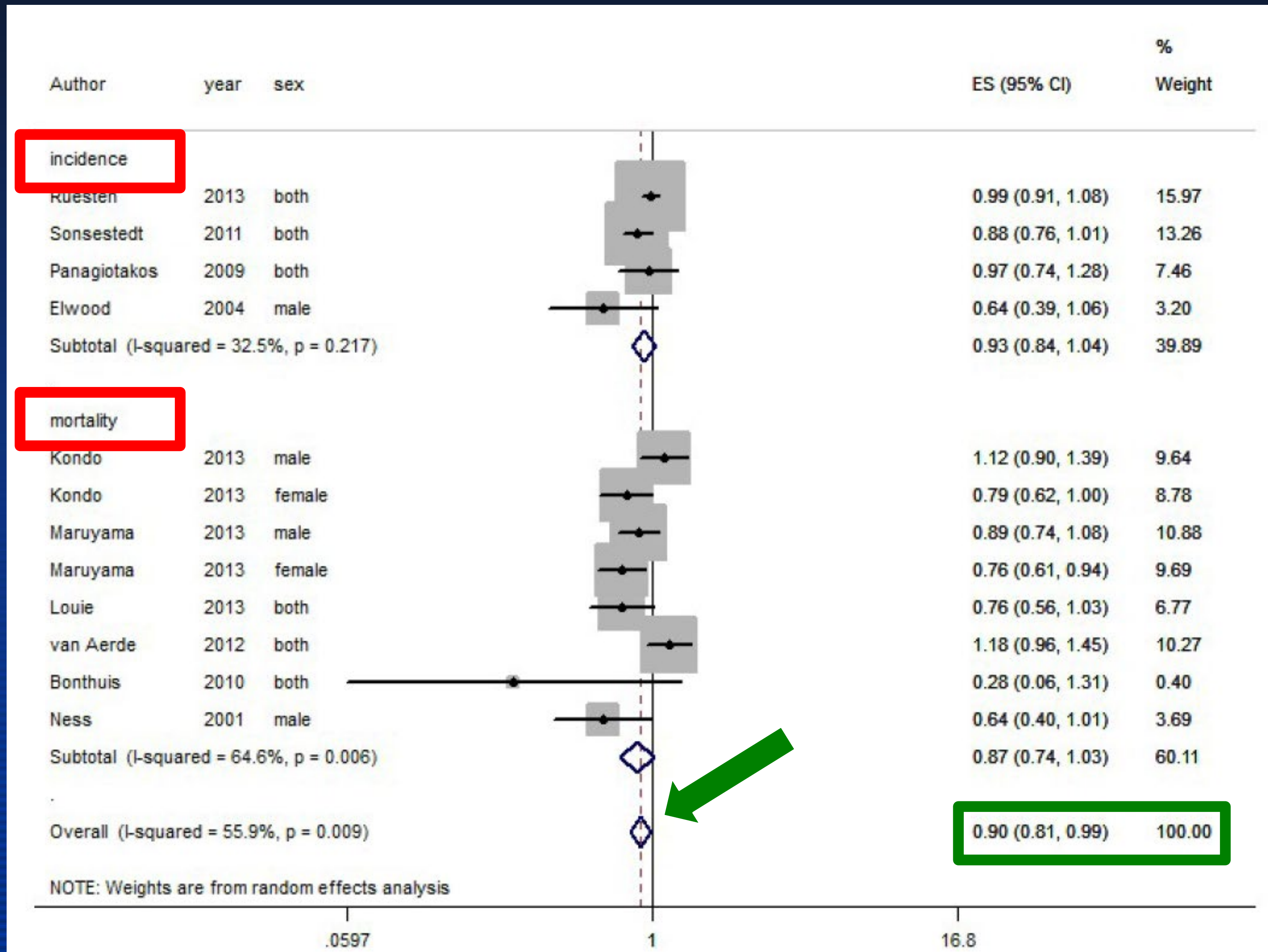
Chen GC et al, Eur J Nutr 2016

Cheese and CV diseases: a metanalysis



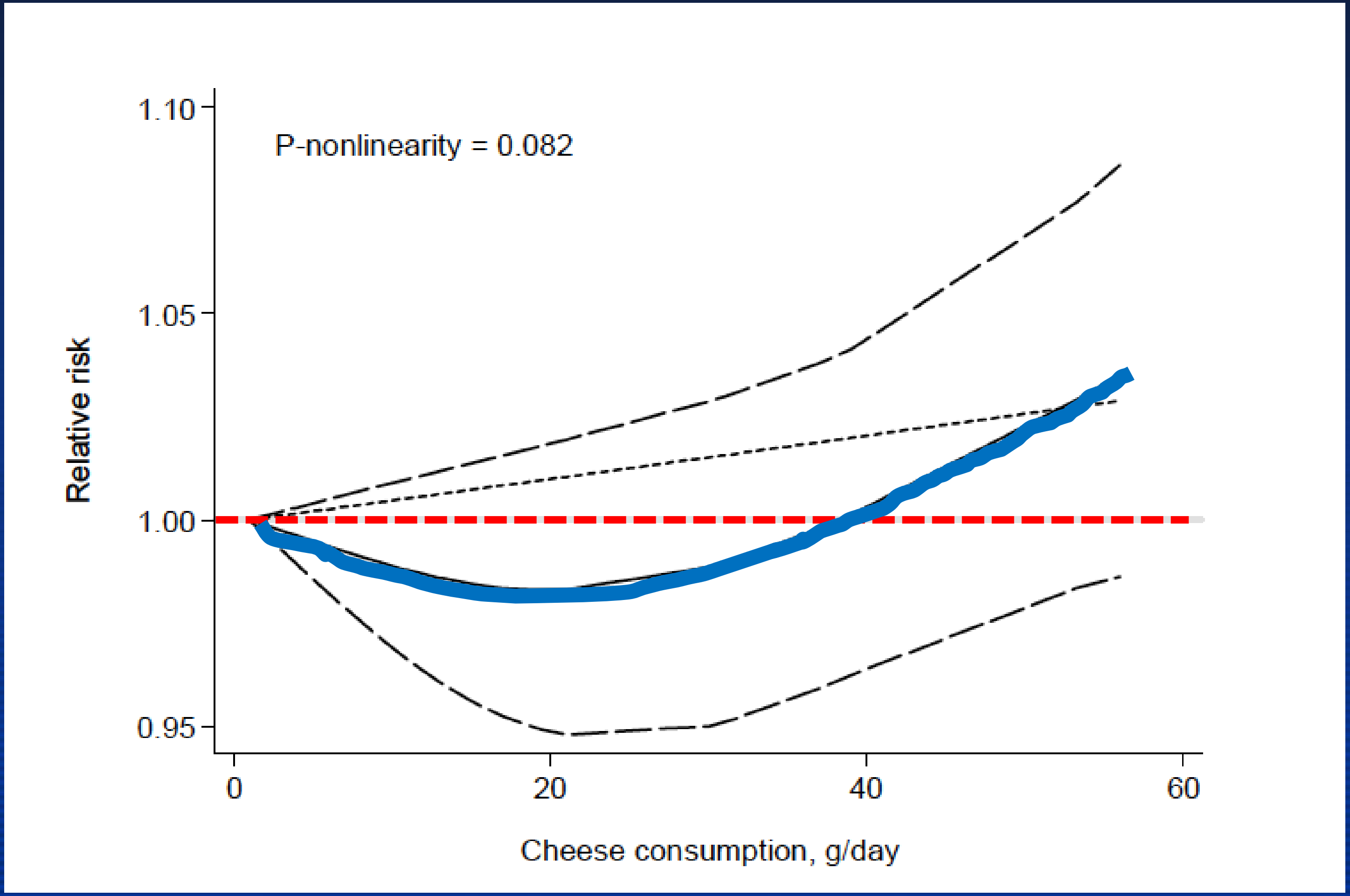
Chen GC et al, Eur J Nutr 2016

Dairy consumption and the prevention of CVD: a meta-analysis of prospective studies



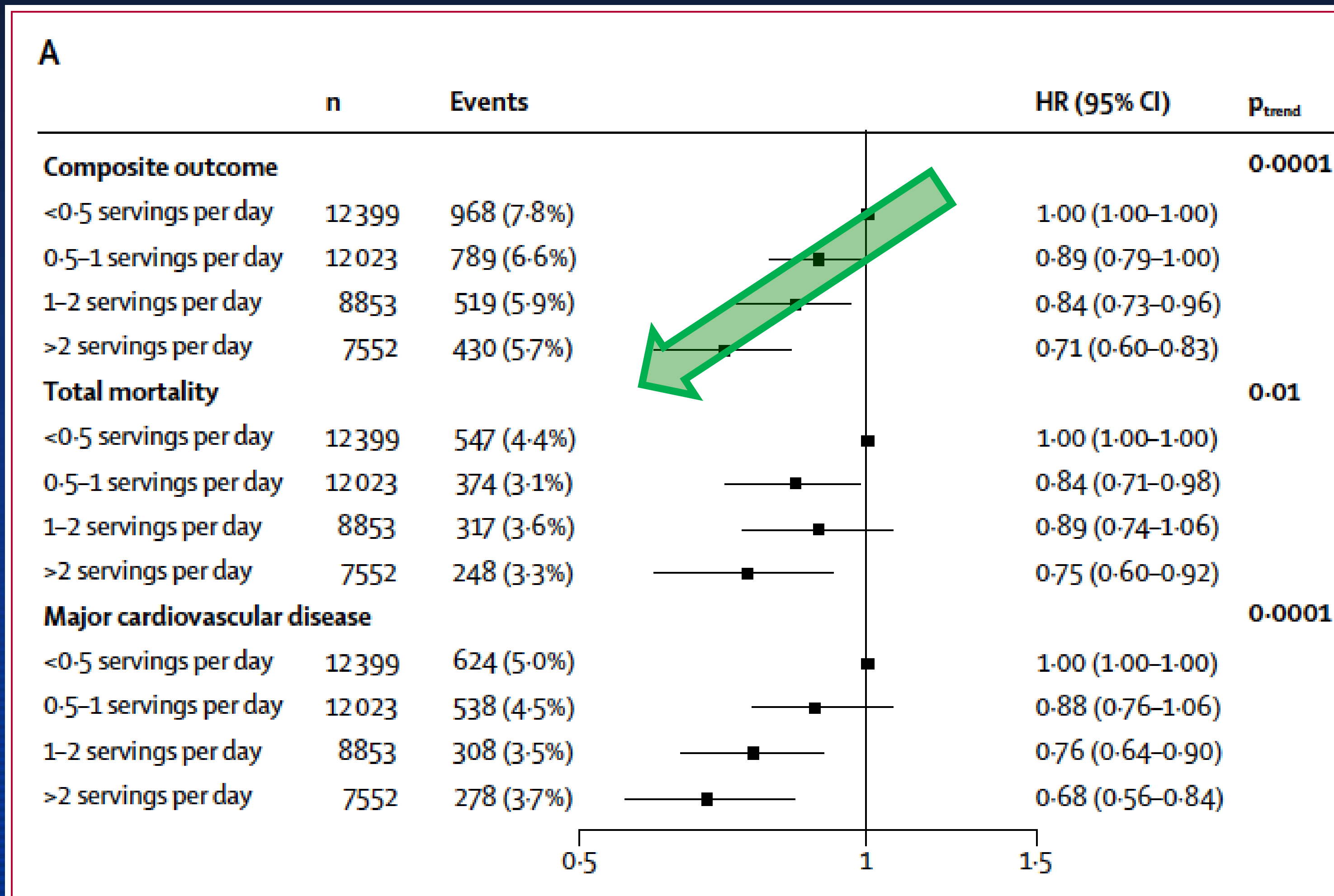
Gholami F et al, J Cardiovasc Thorac Res 2017

Cheese Consumption and Risk of All-Cause Mortality: A Meta-Analysis of Prospective Studies



Tong X et al, Nutrients 2017

Full fat dairy intake, incident CVD and all-cause mortality: the PURE study



Dehghan M et al, Lancet 2018

Il disturbante pensiero di Ioannidis

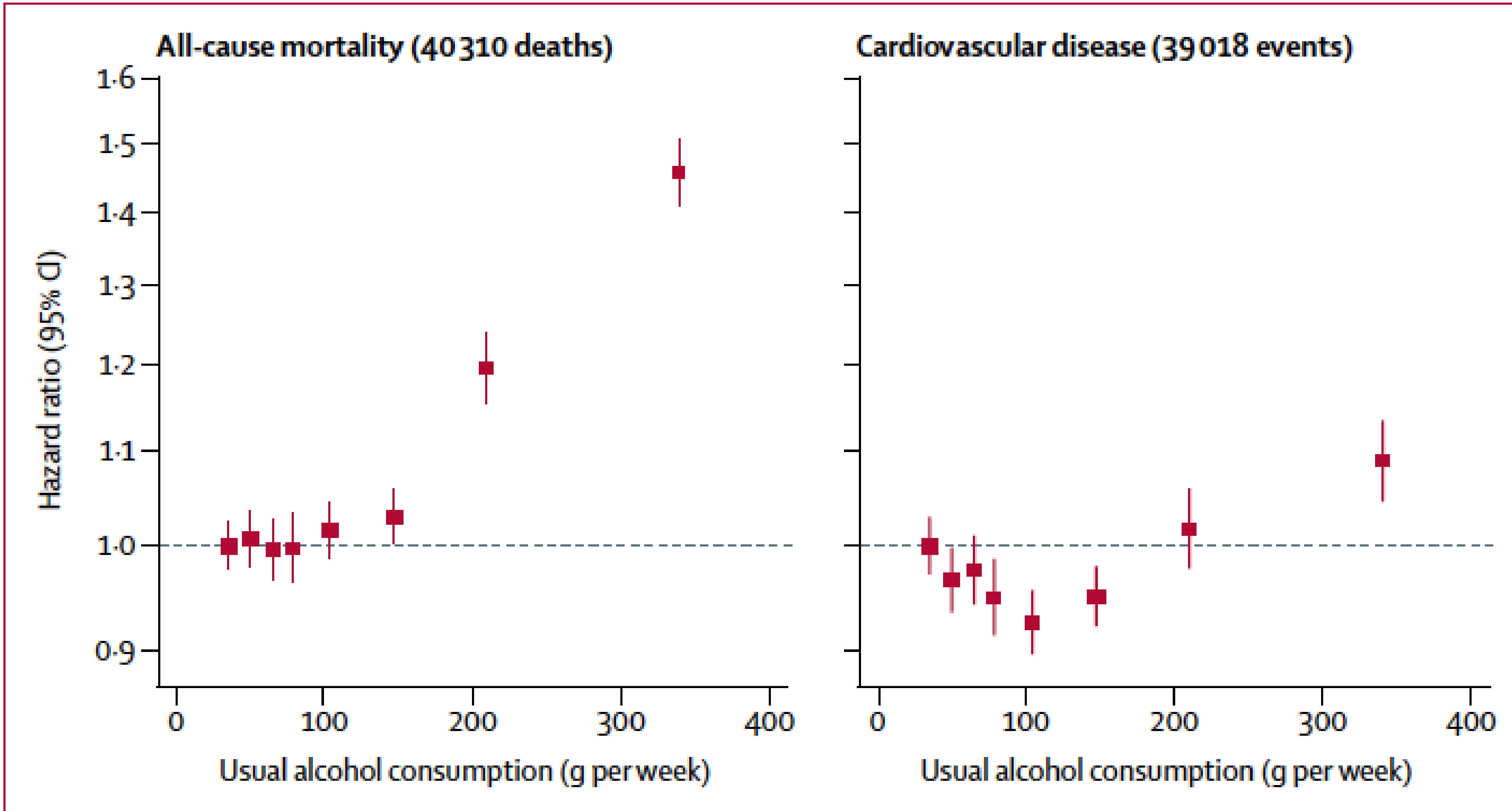
News > Medscape Medical News

Is Nutrition Research Seriously Flawed? Can Hazelnuts Really Add Years to Your Life?

Tara Haelle

September 14, 2018

Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies



Wood AM et al, Lancet 2018

Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies

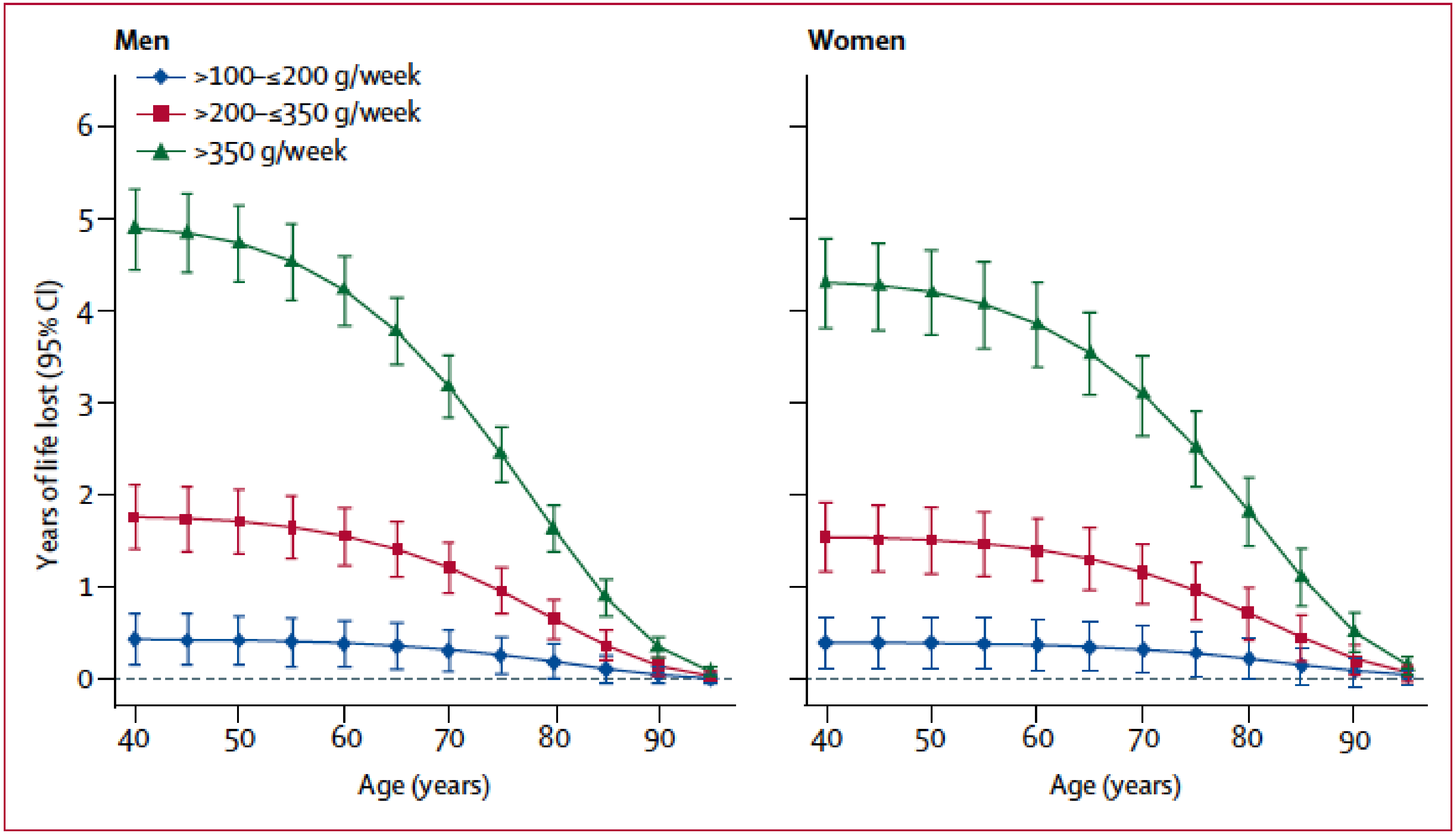


Figure 4: Estimated future years of life lost by extent of reported baseline alcohol consumption compared with those who reported consuming >0–≤100 g per week

Wood AM et al, Lancet 2018

LA RICERCA

Non esiste un livello sicuro di alcol Solo il consumo zero non è pericoloso

Un ampio studio pubblicato su Lancet afferma che l'effetto protettivo su malattie cardiache è superato da altri rischi per la salute. Nel 2016 quasi 3 milioni di morti per l'alcol. I ricercatori: «I due bicchieri al giorno sono solo un mito»

oa OPEN ACCESS CrossMark

Thresholds for safer alcohol use might need lowering

"L'alcol accorcia la vita, 4 anni in meno con 18 bicchieri a settimana"

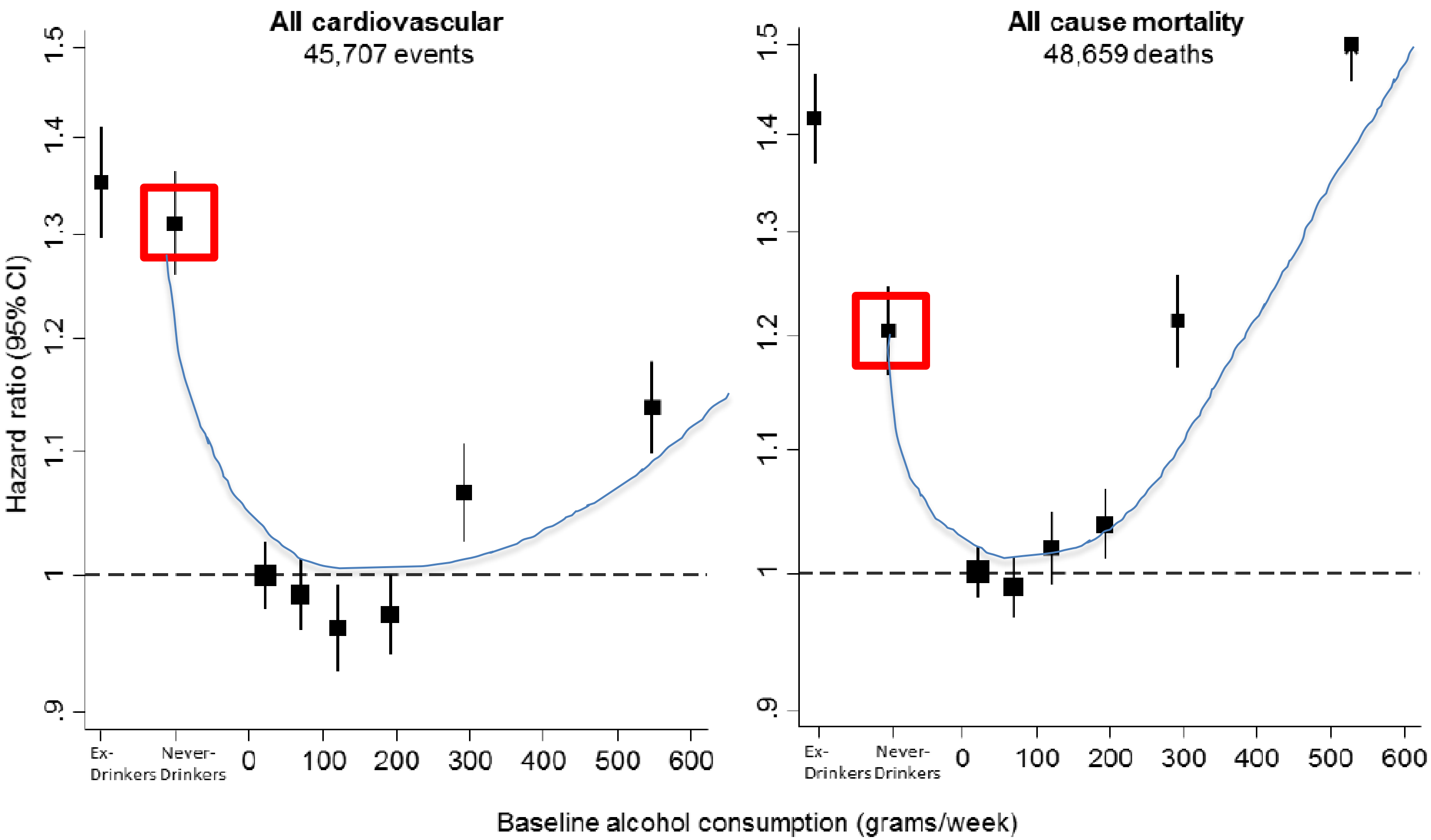
Lo rivela ui conclusioni abbassati"

ANSA.it › Salute&Benessere › Alimentazione › Alcol, con oltre 5-6 bicchieri a settimana sale rischio morte

Alcol, con oltre 5-6 bicchieri a settimana sale rischio morte

Quantità inferiore ai limiti attualmente raccomandati

eFigure 10: Shape of association between baseline alcohol consumption, including ex- and non-drinkers, with all cardiovascular disease and all-cause mortality.



Adjusted for age, smoking and history of diabetes, and stratified by sex and EPIC centre. Alcohol consumption categories amongst current drinkers were >0-≤50 grams/week, >50-≤100 grams/week, >100-≤150 grams/week, >150-≤250 grams/week, >250-≤350 grams/week and >350 grams/week. The reference category is the lowest baseline alcohol consumption category (>0 and ≤50g/week). Studies with fewer than five events of any outcome were excluded from the analysis of that outcome. The sizes of the boxes are proportional to the inverse of the variance of the log-transformed hazard ratios. Vertical lines represent 95% CIs. Individuals for whom we were unable to distinguish as ex- or never- drinkers were excluded from the analysis.

Cosa succede se si confrontano never, ex, e current drinkers

Wood AM et al; Lancet, 2018

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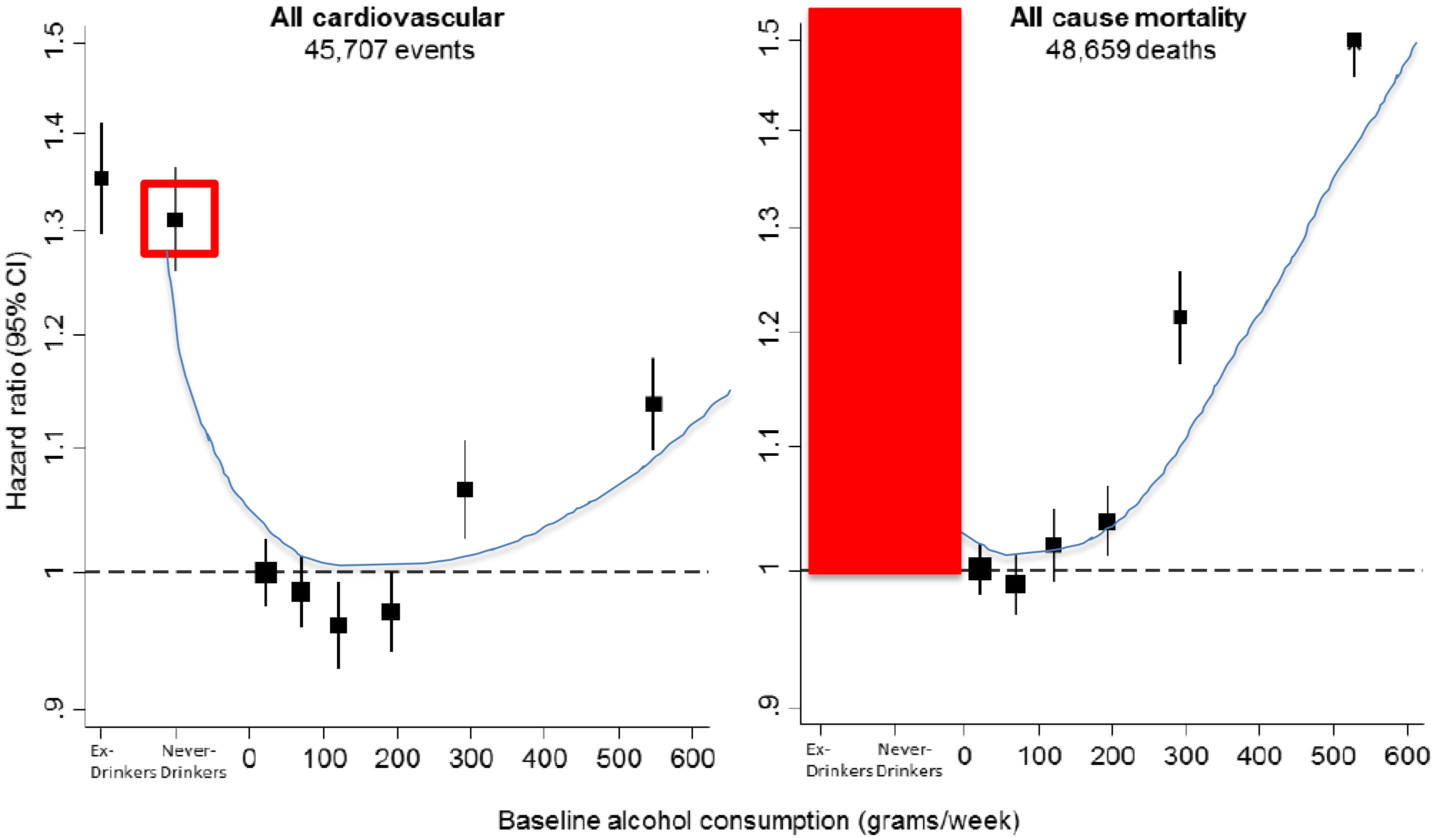

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Cosa succede se si confrontano never, ex, e current drinkers

Wood AM et al; Lancet, 2018

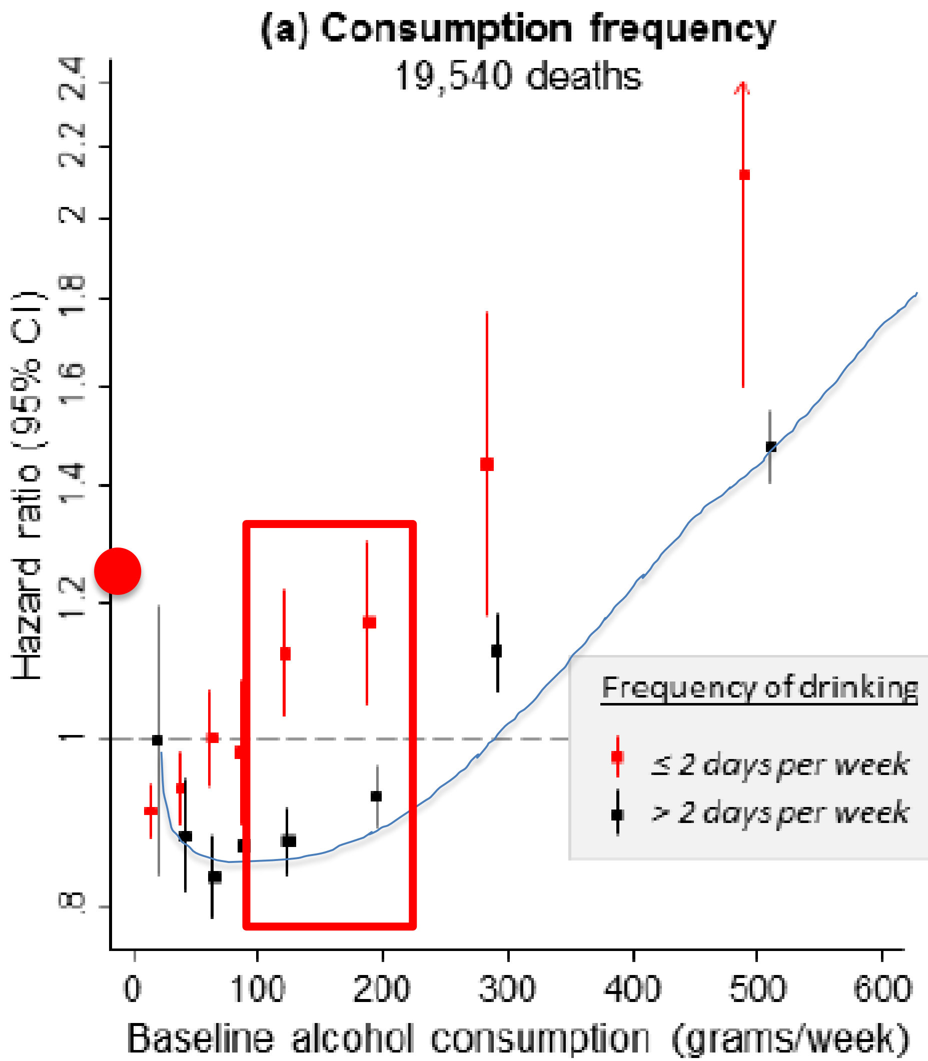
Perché sono stati esclusi gli astemi?

We focused our study on current alcohol drinkers for three main reasons.

1- First, alcohol guidelines provide recommendations about low-risk limits only for drinkers (we are unaware of any guidelines that encourage non-drinkers to consume alcohol).

2- Second, a focus on current drinkers should limit potential biases that are difficult to control in observational studies (eg, reverse causality, residual confounding, and unmeasured effect modification) because ex-drinkers include people who might have abstained from alcohol owing to poor health itself, as well as those who have changed their habits to achieve a healthier lifestyle.

3- Third, never-drinkers might differ systematically from drinkers in ways that are difficult to measure, but which might be relevant to disease causation.



Chi divide il consumo in più di 2 dosi settimanali
ha una riduzione della mortalità fino ai 250 g/settimana

Wood AM et al; Lancet, 2018

Effetto delle modificazioni dietetiche sul profilo lipidico

Nutriente	Effetto su HDL/LDL	Effetto atteso sul colesterolo LDL	Note
Acidi grassi insaturi trans	LDL ⇑ HDL ⇓	-1/1,5% per ogni calo di 1% dell'intake	L'apporto alimentare in Italia è in media basso; l'effetto atteso è modesto.
Acidi grassi saturi	LDL ⇑ HDL ⇑	-1/1,5% per ogni calo di 1% dell'intake	La restrizione del loro apporto non ridurrebbe il rischio CV nonostante il miglioramento della lipidemia
Acidi grassi PUFA omega-6	LDL ⇓	-0,5/1% per ogni aumento di 1% dell'intake	L'apporto alimentare in Italia, in media, non è elevato; l'effetto atteso è di potenziale interesse.
Colesterolo alimentare	LDL ⇑	-1/1,5% per ogni riduzione di 200 mg/die dell'intake	
Fibra solubile	LDL ⇓	-1,5/2,5% per ogni aumento di 5 g/die dell'intake	L'apporto alimentare in Italia, in media, non è elevato; l'effetto atteso è di potenziale interesse.
Effetto complessivo	LDL ⇓	-1,5/5%	L'adesione nel tempo dei pazienti è variabile, ma in genere bassa

Cochrane, 2003

Poli A et al, in preparation, 2018

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EFSA Journal

SCIENTIFIC OPINION

ADOPTED: 25 June 2018

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Scientific opinion on the safety of monacolins in red yeast rice

EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS),
Maged Younes, Peter Aggett, Fernando Aguilar, Riccardo Crebelli, Birgit Dusemund,
Metka Filipič, Maria Jose Frutos, Pierre Galtier, David Gott, Ursula Gundert-Remy,
Gunter Georg Kuhnle, Claude Lambré, Jean-Charles Leblanc, Inger Therese Lillegaard,
Peter Moldeus, Alicja Mortensen, Agneta Oskarsson, Ivan Stankovic, Ine Waalkens-Berendsen,
Rudolf Antonius Woutersen, Raul J. Andrade, Cristina Fortes, Pasquale Mosesso,
Patrizia Restani, Fabiola Pizzo, Camilla Smeraldi and Matthew Wright

Abstract

… The Panel considered that ***monacolin K in lactone form is identical to lovastatin***, the active ingredient of several medicinal products authorised for the treatment of hypercholesterolaemia in the EU.

… The Panel considered that the available information on the adverse effects reported in humans were judged to be sufficient to conclude that ***monacolins from RYR when used as food supplements were of significant safety concern at the use level of 10 mg/day***.

… The Panel further considered that individual cases of severe adverse reactions have been reported ***for monacolins from RYR at intake levels as low as 3 mg/day.***

Abstract – continued

… The Panel concluded that exposure to ***monacolin K from RYR could lead to severe adverse effects on musculoskeletal system, including rhabdomyolysis, and on the liver***. In the reported cases, the product contained other ingredients in addition to RYR.

… On the basis of the information available and several uncertainties highlighted in this opinion***, the Panel was unable to identify a dietary intake of monacolins from RYR that does not give rise to concerns about harmful effects to health, for the general population, and … for vulnerable subgroups of the population.***

EFSA sta forse cercando di dirci qualcosa?

"The Panel noted that there is a large variability and discrepancy in both the content of monacolin K and the ratio between monacolin K lactone and its hydroxyacid form in the 10 commercial products considered (Table 4). Some samples *showed a clear predominance of monacolin K lactone, which seems not usual in natural RYR products*."

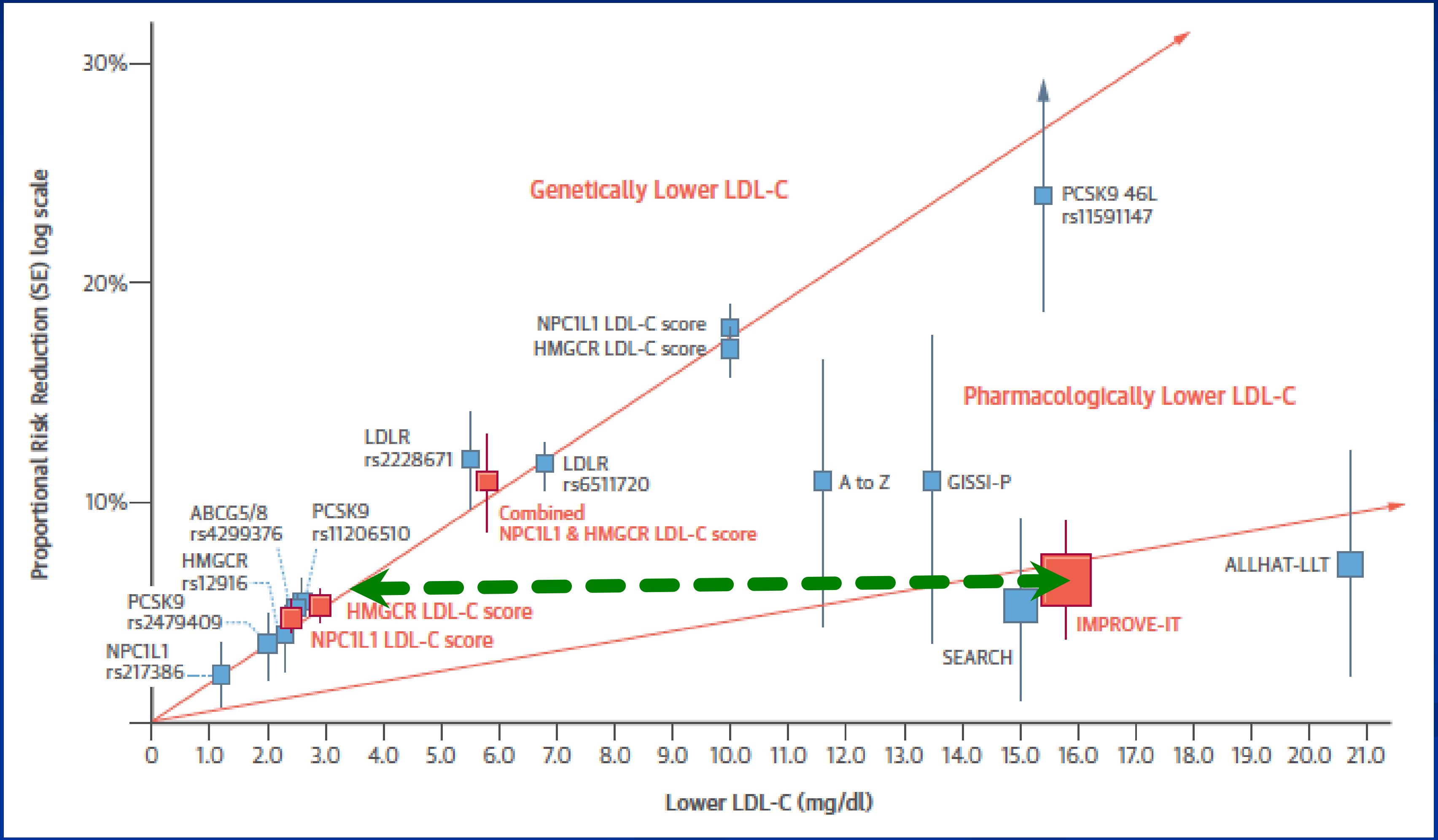
Table 4: Level of monacolins in 10 commercial products (Li et al., 2004)

Product	Reference	Total monacolins	MK	MKA	MKA/ MK	MJ	MJA	MX	MXA	ML	MLA	MM	MMA	DMK	PI
RYRP	μg/g	622.65	362.37	103.23	0.28	12.64	7.08	4.74	3.64	23.32	15.36	5.19	0.72	72.22	12.14
CP1	μg/capsule	307.08	302.48	3.57	0.01	ND	ND	ND	ND	ND	ND	ND	ND	1.03	ND
CP2	μg/capsule	98.20	93.65	2.81	0.03	ND	ND	ND	ND	ND	ND	ND	ND	1.74	ND
CP3	μg/capsule	142.34	112.76	6.9	0.06	ND	ND	ND	ND	ND	ND	ND	ND	22.98	ND
CP4	μg/capsule	135.68	126.61	3.44	0.03	ND	ND	ND	ND	ND	ND	ND	ND	5.63	ND
CP5	μg/tablet	17.27	10.52	6.75	0.64	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
CP6	μg/tablet	13.91	ND	12.8	ND	ND	1.11	ND	ND	ND	ND	ND	ND	ND	ND
CP7	μg/tablet	155.68	112.00	19.60	0.18	ND	ND	ND	ND	4.48	ND	0.91	ND	15.05	1.75
CP8	μg/capsule	18.69	34.19	11.55	0.34	ND	ND	ND	ND	ND	ND	ND	ND	7.14	ND
CP9	μg/capsule	357.76	198.65	63.48	0.32	7.22	4.33	2.75	2.08	13.47	8.86	3.01	0.44	46.5	6.97
CP10	μg/tablet	461.56	259.32	82.66	0.32	8.56	3.62	2.94	3.12	18.46	9.23	3.22	0.52	59.68	8.23
Average[(a)]	μg/unit	170.82	138.91	21.36	0.15									15.98	ND
St Dev[(a)]		155.25	97.39	28.10										21.11	ND
Median[(a)]	μg/unit	139.01	119.68	9.23										6.39	ND

RYRP: RYR powder; CP: Commercial product: MK: monacolin K; MKA: monacolin K acid form; MJA: monacolin J acid form; MJ: monacolin J; MXA: monacolin X acid form; MLA: monacolin L acid form; MX: monacolin X; ML: monacolin L; MMA: monacolin M acid form; MM: monacolin M; DMK: dehydroxymonacolin K; PI: compactin, ND: not detectable.
Products C1–C6 were from US store market; C7 and C8 from Taiwan; and C9 and C10 from China marketing.
(a): Calculated by the Panel on CP values, where ND was considered 0.01.

EFSA ANS panel, EFSA Journal 2018

Effect of a genetically or pharmacologically mediated LDL-C reduction on CHD risk

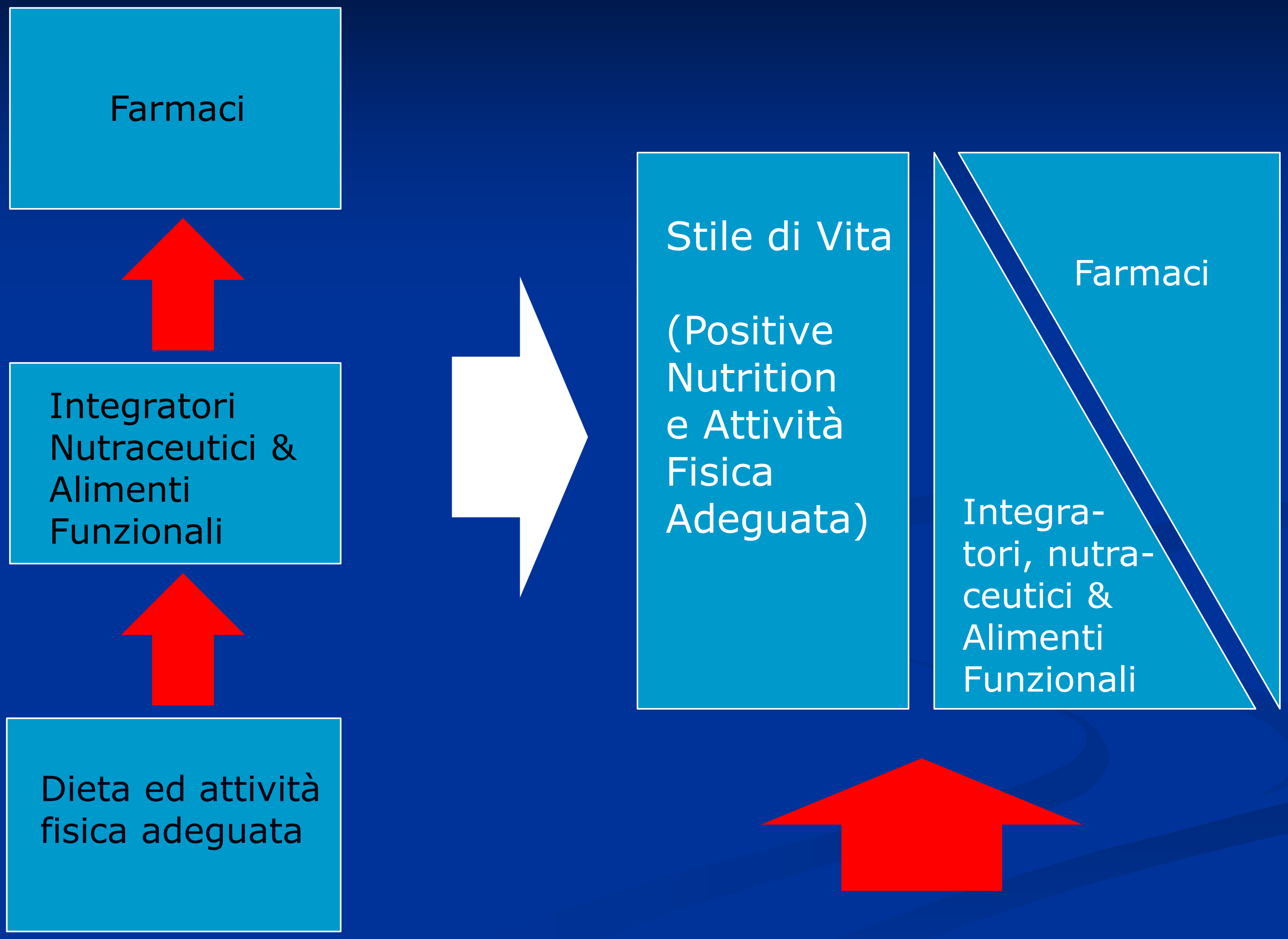


Ference BA et al, JACC 2015

Strategie di prevenzione CV

Poli A et al, Pharm Res, 2018

Strategie di prevenzione CV



Poli A et al, Pharm Res, 2018