Dietary bioactives, polyphenols and potential health effects: facts, fiction and the future…

Daniele Del Rio

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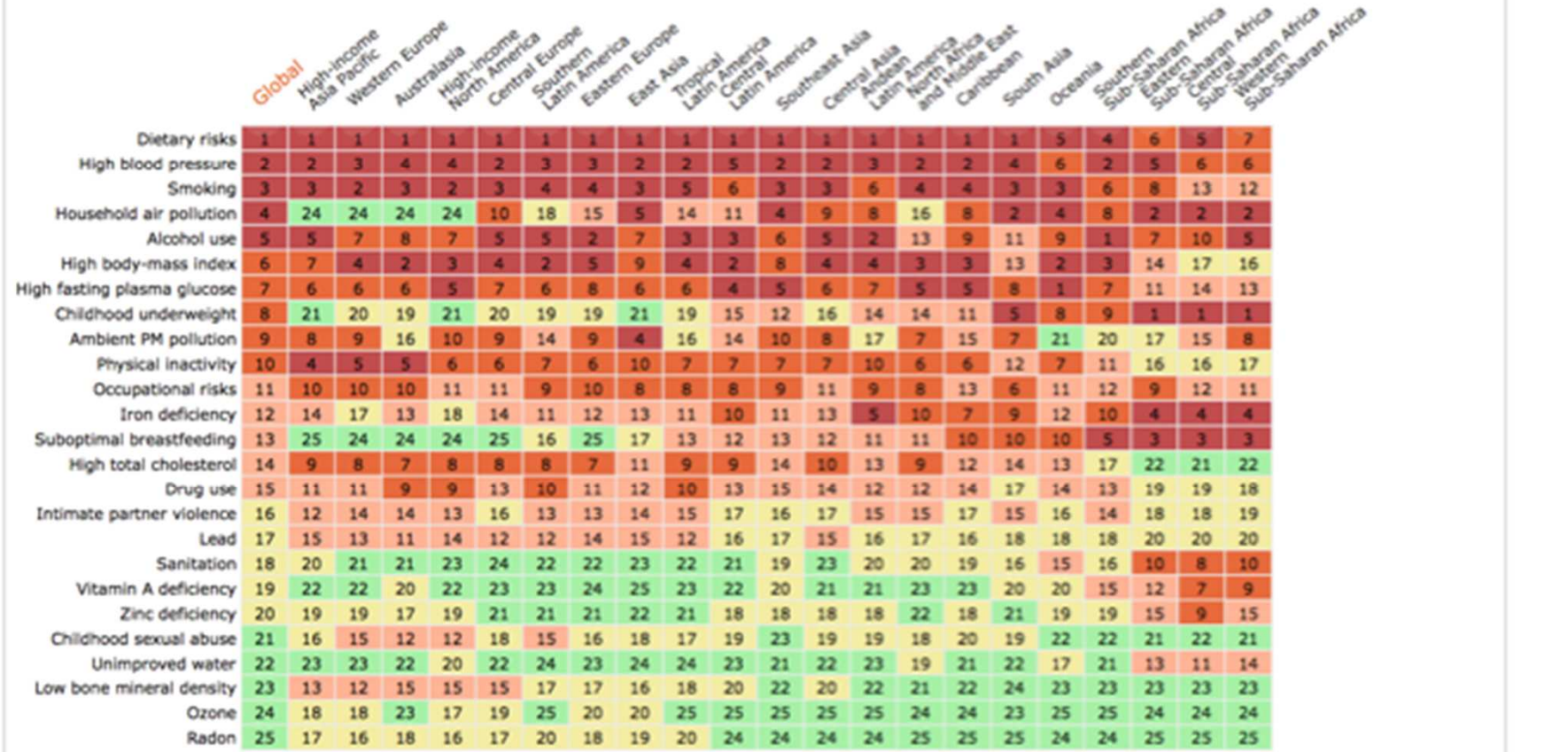
The Need for Nutrition Education/Innovation Programme (NNEdPro)

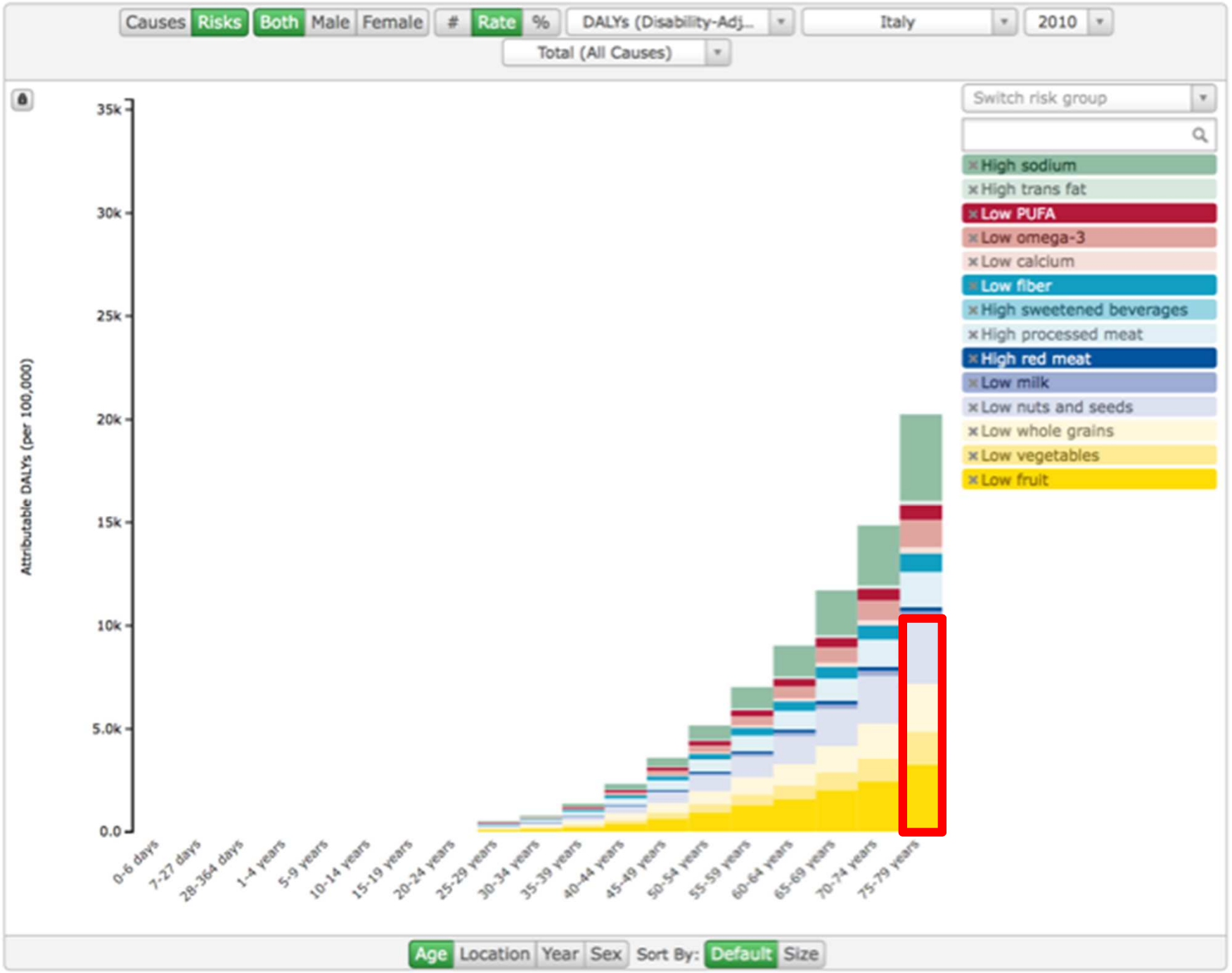
University of Parma
Department of Food Science
Food for thought

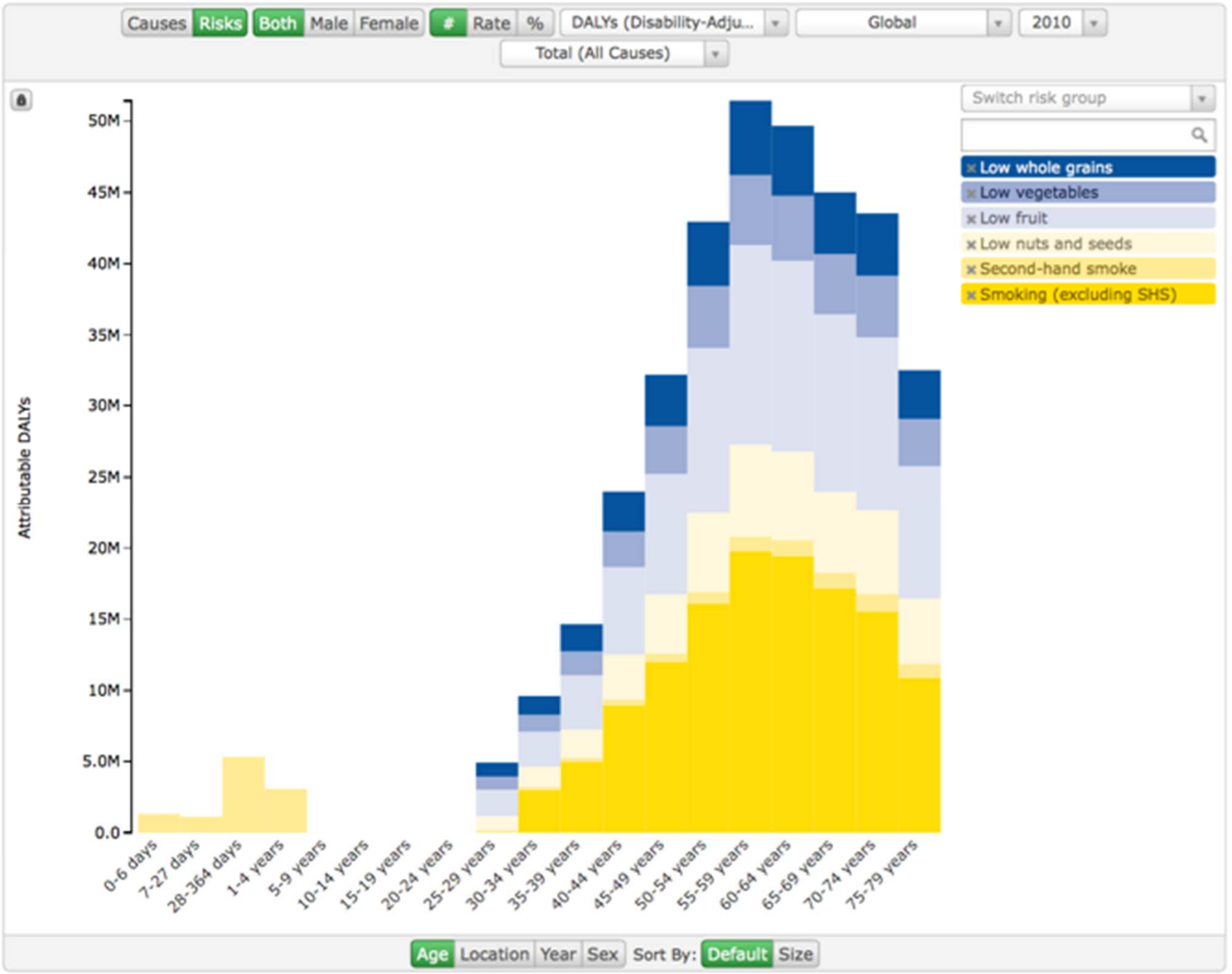
WOLF5ON

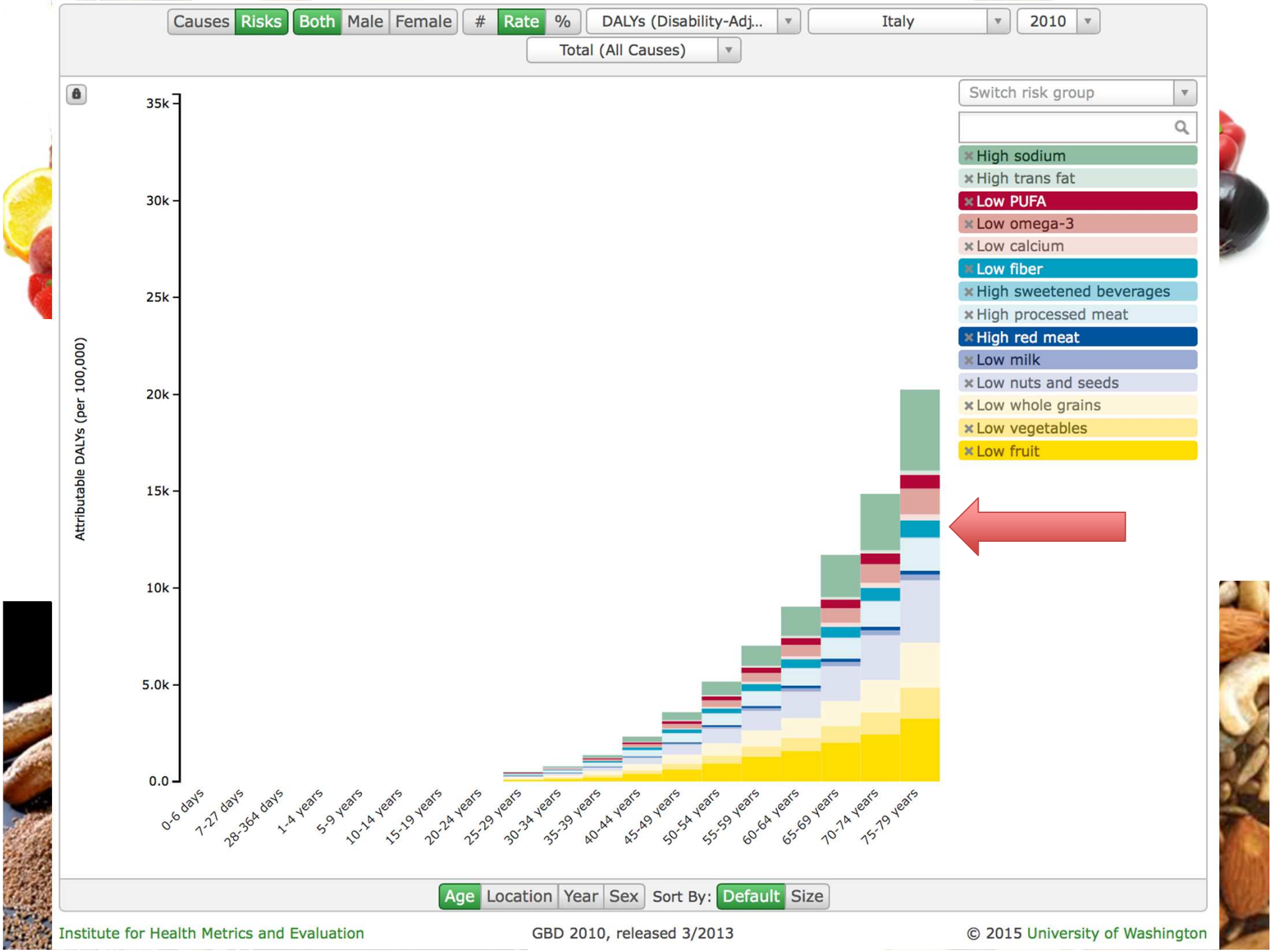
Top 25 | Causes | Risks | Both | Male | Female | DALY (Disability-Adjusted Li... | All ages | 1990 | 2010

GBD Regions | Add or Remove Location








Causes
Risks
Both
Male
Female
#
Rate
%
DALYs (Disability-Adj...
Italy
2010
Total (All Causes)
Switch risk group
High sodium
High trans fat
Low PUFA
Low omega-3
Low calcium
Low fiber
High sweetened beverages
High processed meat
High red meat
Low milk
Low nuts and seeds
Low whole grains
Low vegetables
Low fruit
Attributable DALYs (per 100,000)
35k
30k
25k
20k
15k
10k
5.0k
0.0
0-6 days
7-27 days
28-364 days
1-4 years
5-9 years
10-14 years
15-19 years
20-24 years
25-29 years
30-34 years
35-39 years
40-44 years
45-49 years
50-54 years
55-59 years
60-64 years
65-69 years
70-74 years
75-79 years
Age
Location
Year
Sex
Sort By:
Default
Size
Institute for Health Metrics and Evaluation
GBD 2010, released 3/2013
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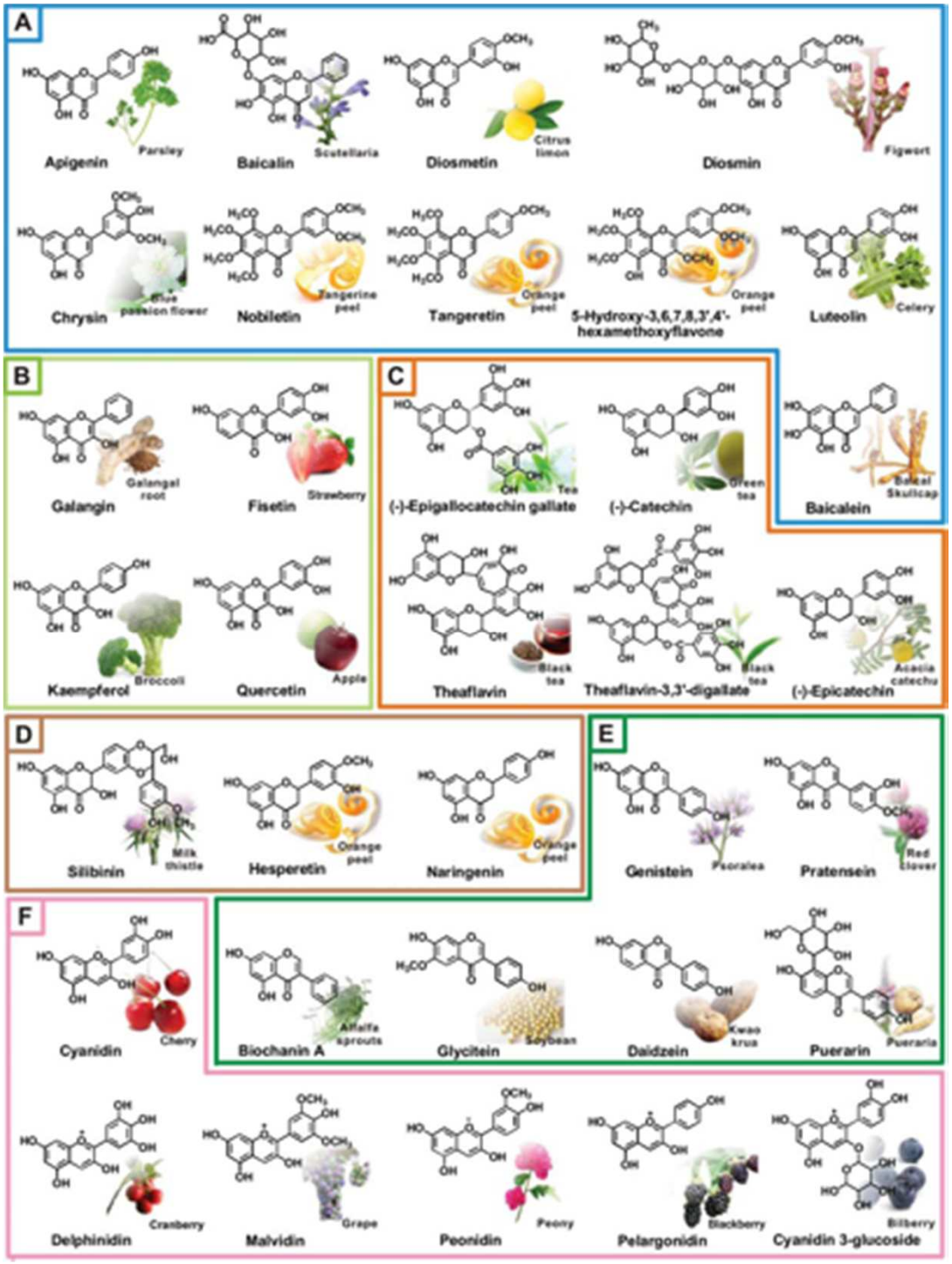

A
Apigenin
Parsley
Baicalin
Scutellaria
Diosmetin
Citrus limon
Diosmin
Figwort
Chrysin
Blue passion flower
Nobiletin
Tangerine peel
Tangeretin
Orange peel
5-Hydroxy-3,6,7,8,3',4'-hexamethoxyflavone
Orange peel
Luteolin
Celery
B
Galangin
Galangal root
Fisetin
Strawberry
Kaempferol
Broccoli
Quercetin
Apple
C
(-)-Epigallocatechin gallate
Tea
(-)-Catechin
Green tea
Baicalein
Baical Skullcap
Theaflavin
Black tea
Theaflavin-3,3'-digallate
Black tea
(-)-Epicatechin
Acacia catechu
D
Silibinin
Milk thistle
Hesperetin
Orange peel
Naringenin
Orange peel
E
Genistein
Psoralea
Pratensein
Red clover
F
Cyanidin
Cherry
Biochanin A
Alfalfa sprouts
Glycitein
Soybean
Daidzein
Kwao krua
Puerarin
Pueraria
Delphinidin
Cranberry
Malvidin
Grape
Peonidin
Peony
Pelargonidin
Blackberry
Cyanidin 3-glucoside
Bilberry

Main sources?

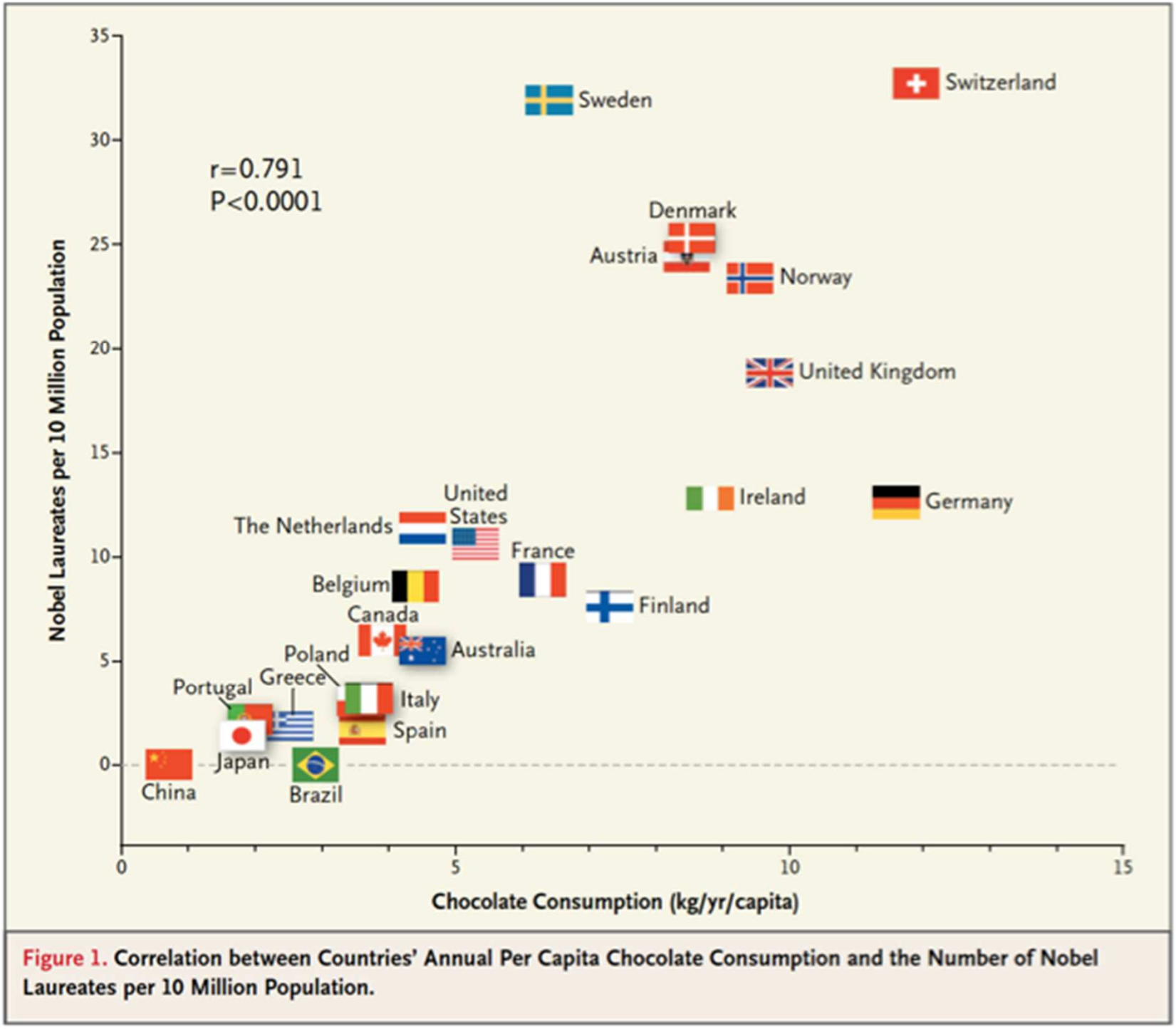
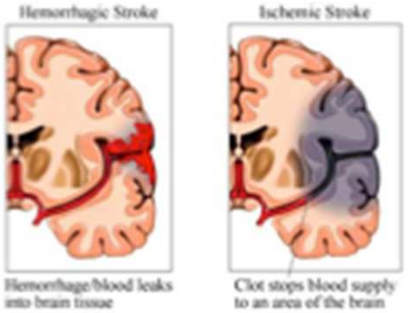
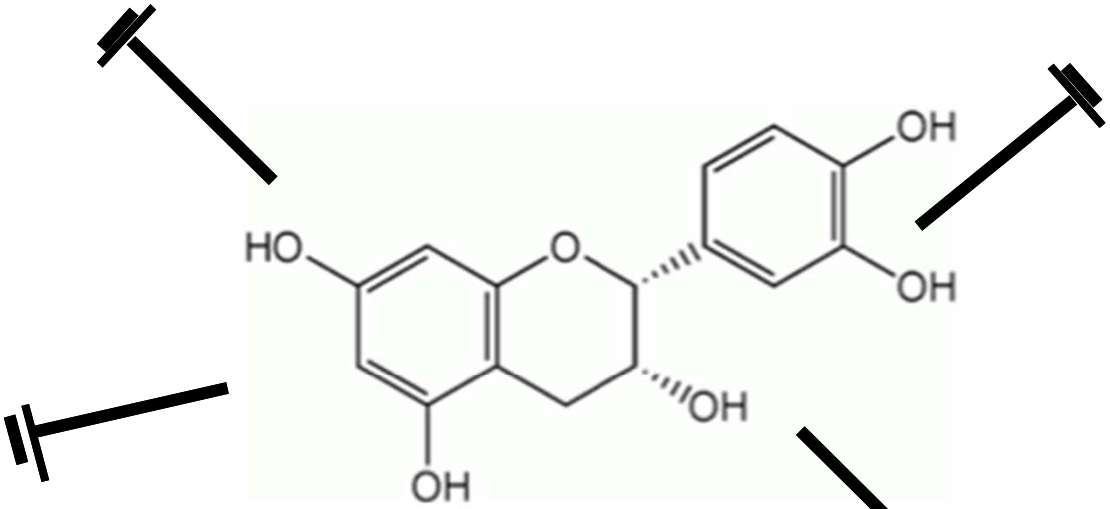
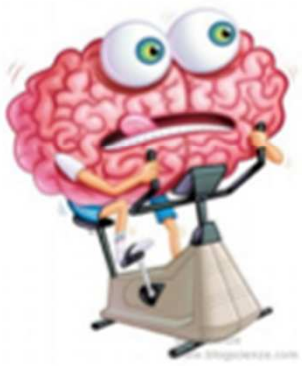


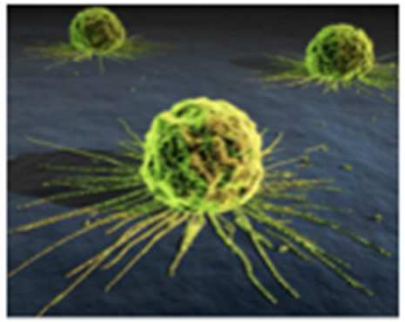
Figure 1. Correlation between Countries' Annual Per Capita Chocolate Consumption and the Number of Nobel Laureates per 10 Million Population.

They prevent!!?







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- TV's Culinary Genius
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MIND
IMMUNE SYSTEM
Welch's
100%
Welch's To health
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They prevent!

	Daily flavonoid intake (mg)			p for trend
	0–19·0	19·1–29·9	>29·9	
Mortality from coronary heart disease (n=804)				
Number of men	268	268	268	
Deaths	39	30	21	
Mortality rate (per 1000 person-years)	20·4	14·5	9·9	
Crude relative risk (95% CI)	1·00	0·71 (0·44–1·14)	0·49 (0·29–0·83)	0·007
Relative risk adjusted for age, diet, and risk factors*†	1·00	0·58 (0·35–0·95)	0·47 (0·27–0·82)	0·006
Incidence of fatal and non-fatal first myocardial infarction (n=692)‡				
Number of men	230	231	231	
Deaths	37	32	23	
Incidence rate (per 1000 person-years)	17·6	14·8	10·4	
Crude relative risk (95% CI)	1·00	0·84 (0·53–1·35)	0·59 (0·35–1·00)	0·049
Relative risk adjusted for age, diet, and risk factors*	1·00	0·89 (0·55–1·44)	0·62 (0·236–1·05)	0·078

*Intake of total energy, saturated fatty acids, physical activity, body-mass index, smoking, serum total and high-density-lipoprotein cholesterol, and systolic blood pressure. †History of myocardial infarction in 1985 included as additoinal covariate. ‡Only men with no history of myocardial infarction at baseline.

Relative risk of mortality from coronary heart disease and occurrence of myocardial infarction during 10 years of follow-up by tertile of flavonoid intake (Zutphen Elderly Study)

THE LANCET

Vol 349 • March 8, 1997

Ann Intern Med. 1996;125:384-389.

No they don't!

Relation between Intake of Flavonoids and Risk for Coronary Heart Disease in Male Health Professionals

Eric B. Rimm, ScD; Martijn B. Katan, PhD; Alberto Ascherio, MD; Meir J. Stampfer, MD; and Walter C. Willett, MD

In summary, our data do not support an important inverse association between the flavonoids studied and the incidence of coronary heart disease. We did find that flavonols may be inversely associated with death from coronary heart disease among men with prevalent coronary heart disease. Alternatively, such an association might be explained by bias or confounding attributable to the severity of prevalent disease and recent changes in lifestyle. Currently, intake of flavonoids at the levels typically consumed in the United States cannot be considered an established protective factor for coronary heart disease.

Or maybe yes!

Dietary Flavonol Intake May Lower Stroke Risk in Men and Women[1,2]

Peter C. H. Hollman,[3,4]* Anouk Geelen,[3] and Daan Kromhout[3]

[3]Wageningen University, Division of Human Nutrition, 6700 EV Wageningen, The Netherlands; and [4]RIKILT-Institute of Food Safety, 6700 AE, Wageningen, The Netherlands

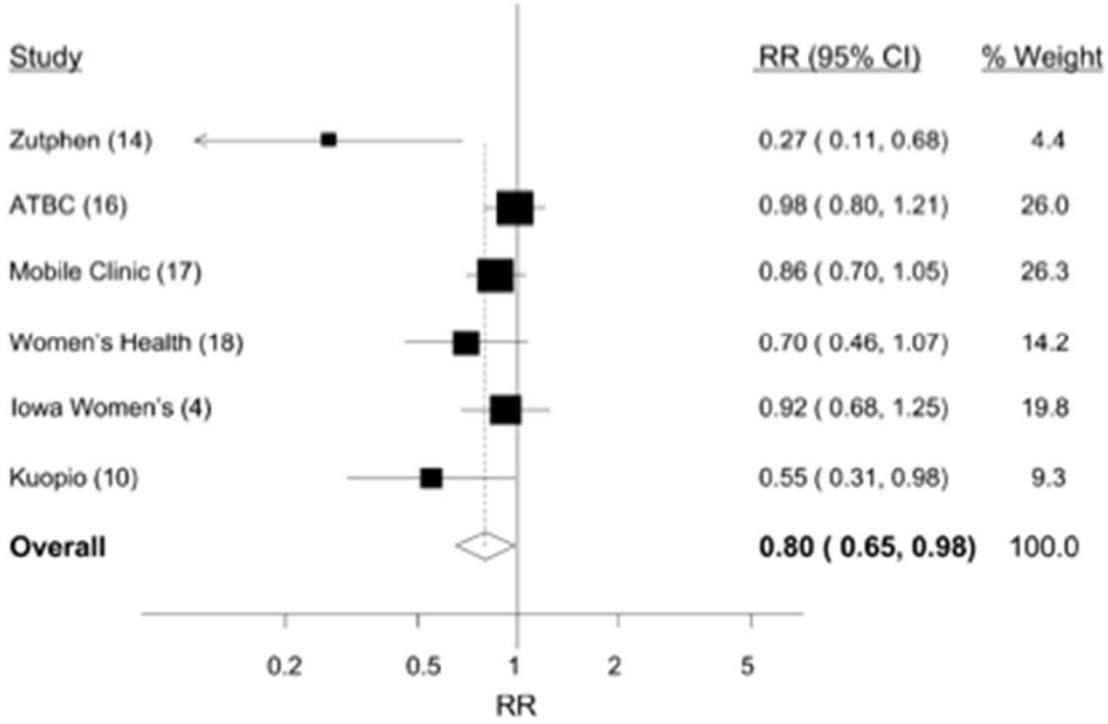


FIGURE 1 Forest plot of the RR of fatal and nonfatal stroke and flavonol consumption (highest compared with lowest category of intake) for 6 independent estimates from 6 cohort studies. The contribution of each estimate to the metaanalysis (its weight) is represented by the size of the black box. Heterogeneity $I^2 = 54\%$ ($P = 0.05$). M, Male; F, female.

J. Nutr. 140: 600–604, 2010.

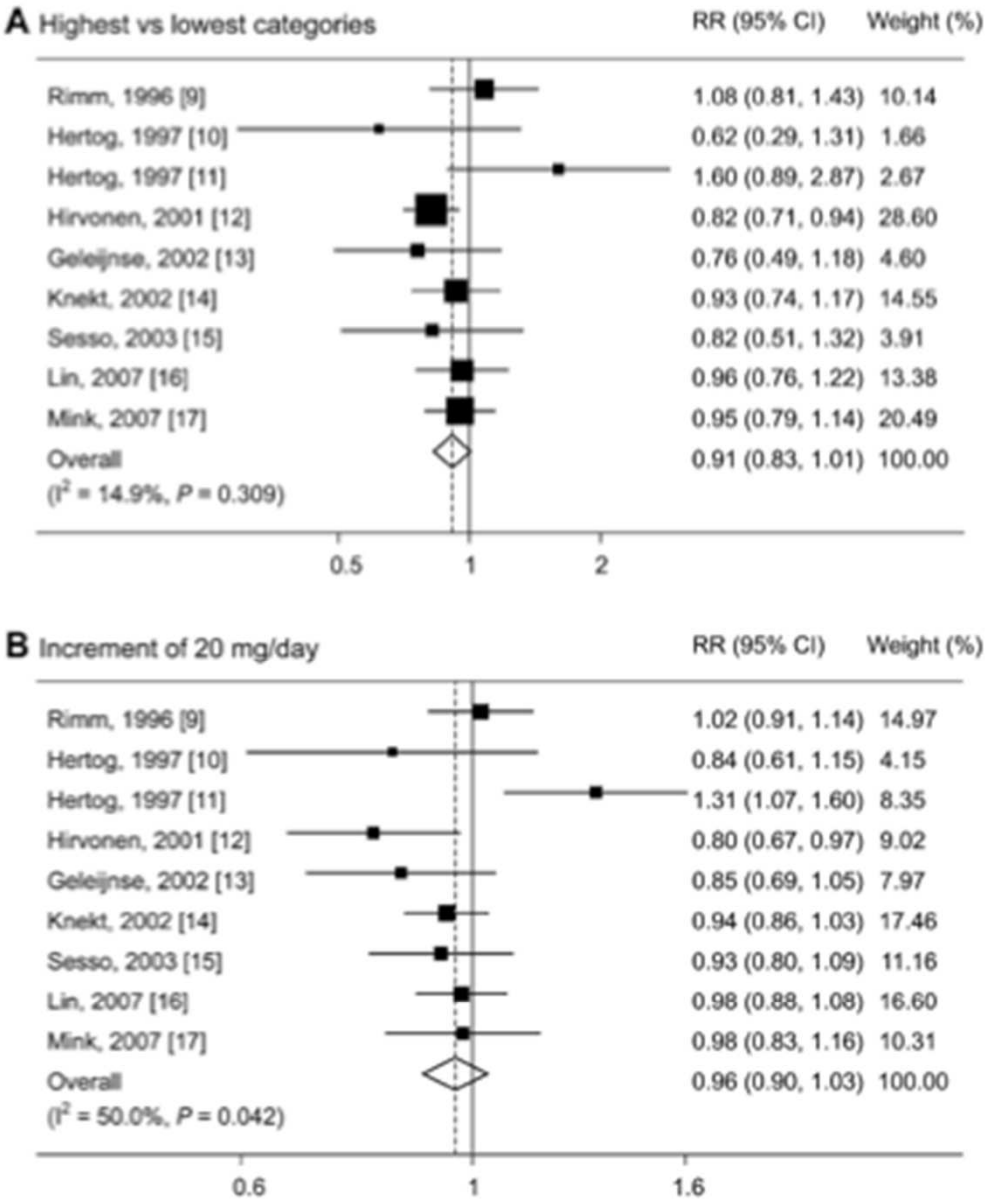
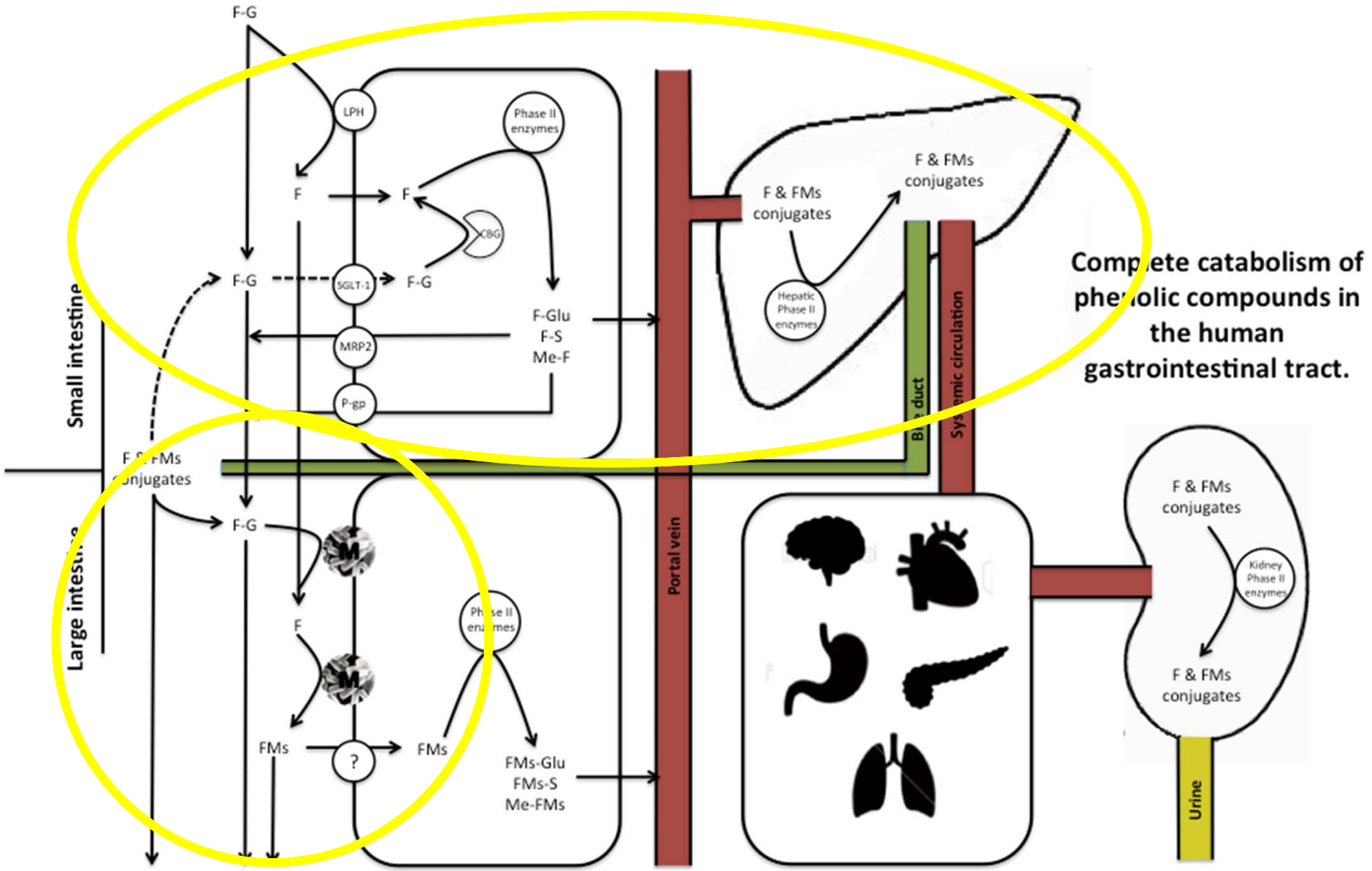


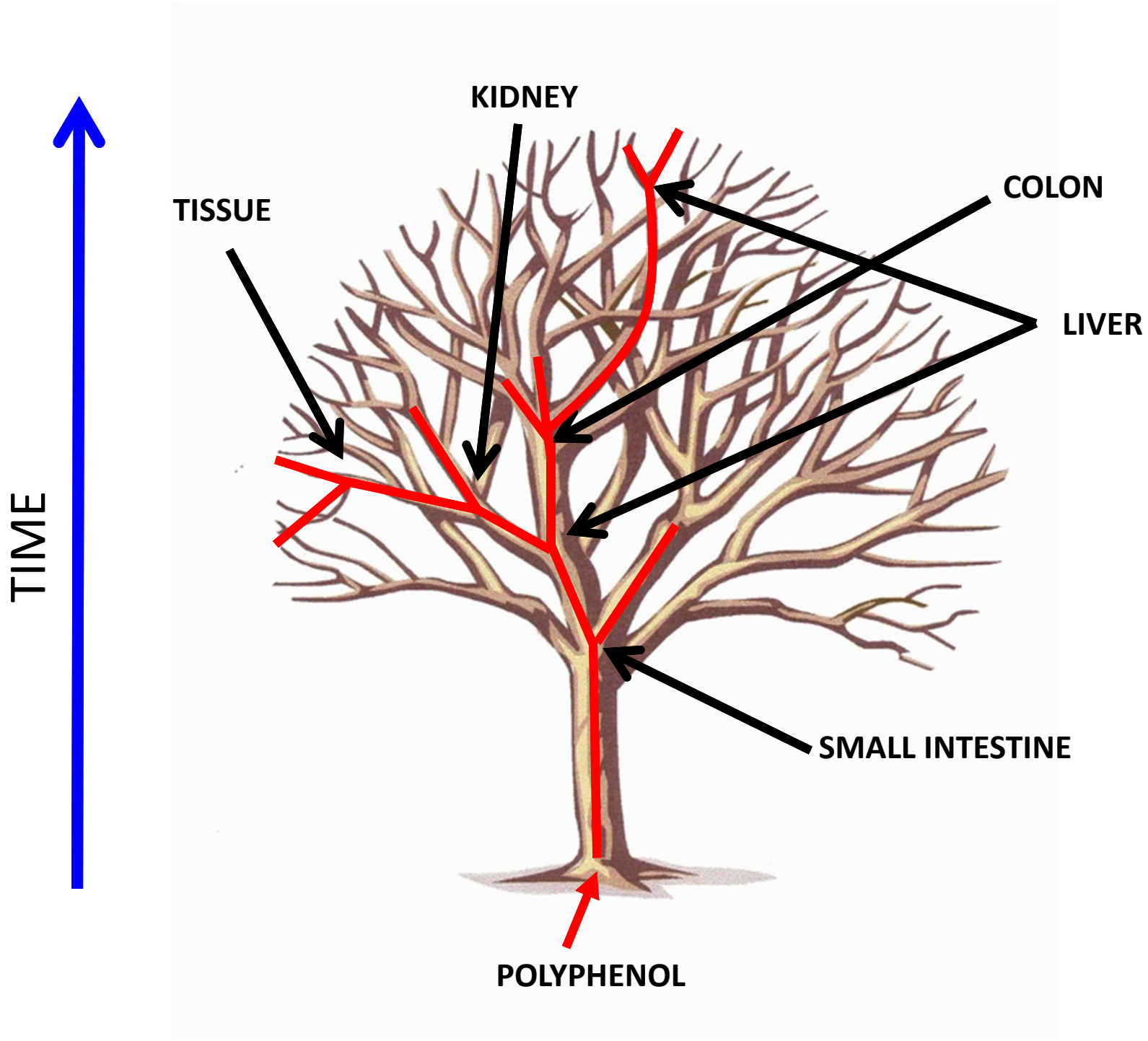
Fig. 1. Relationship between flavonols intake and the risk of CHD. (A) showed summary RRs of CHD comparing highest with lowest flavonols intake. (B) showed summary RRs of CHD for an increase in flavonols intake of 20 mg/day. Squares indicate study-specific risk estimates (size of square reflects the study's statistical weight); horizontal lines indicate 95% confidence intervals; diamond indicates summary relative risk estimate with its corresponding 95% confidence interval. RR, relative risk; CI, confidence interval.

Z.-M. Wang et al. / Atherosclerosis 222 (2012) 270–273

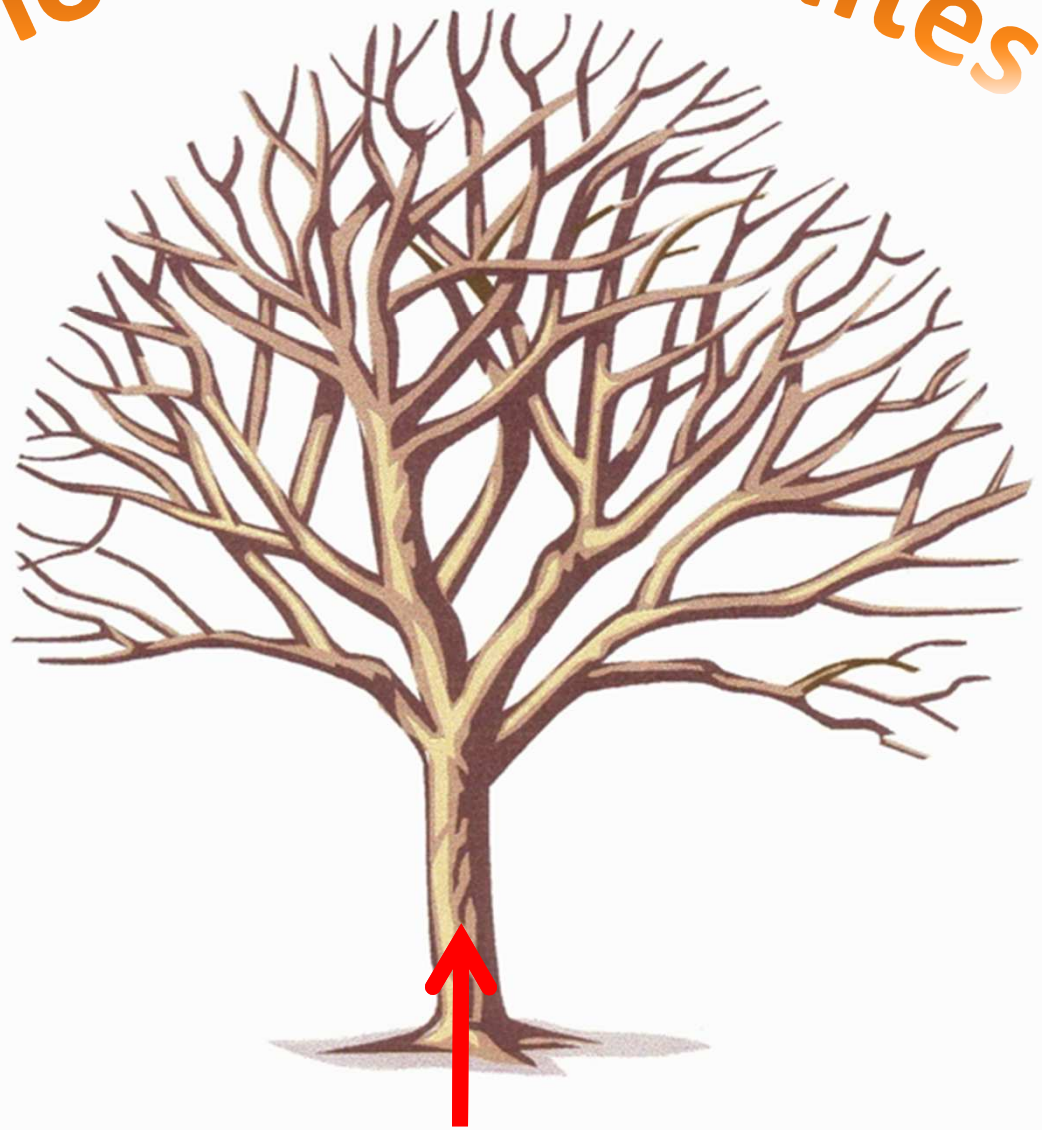
No, no, they don't!

BIOAVAILABILITY & METABOLISM




TIME
KIDNEY
TISSUE
COLON
LIVER
SMALL INTESTINE
POLYPHENOL

A lot of metabolites



A FEW PLANT POLYPHENOLS

Ellagitannins

Ellagic acid

Urolithin D

Urolithin C

Urolithin A

Urolithin B

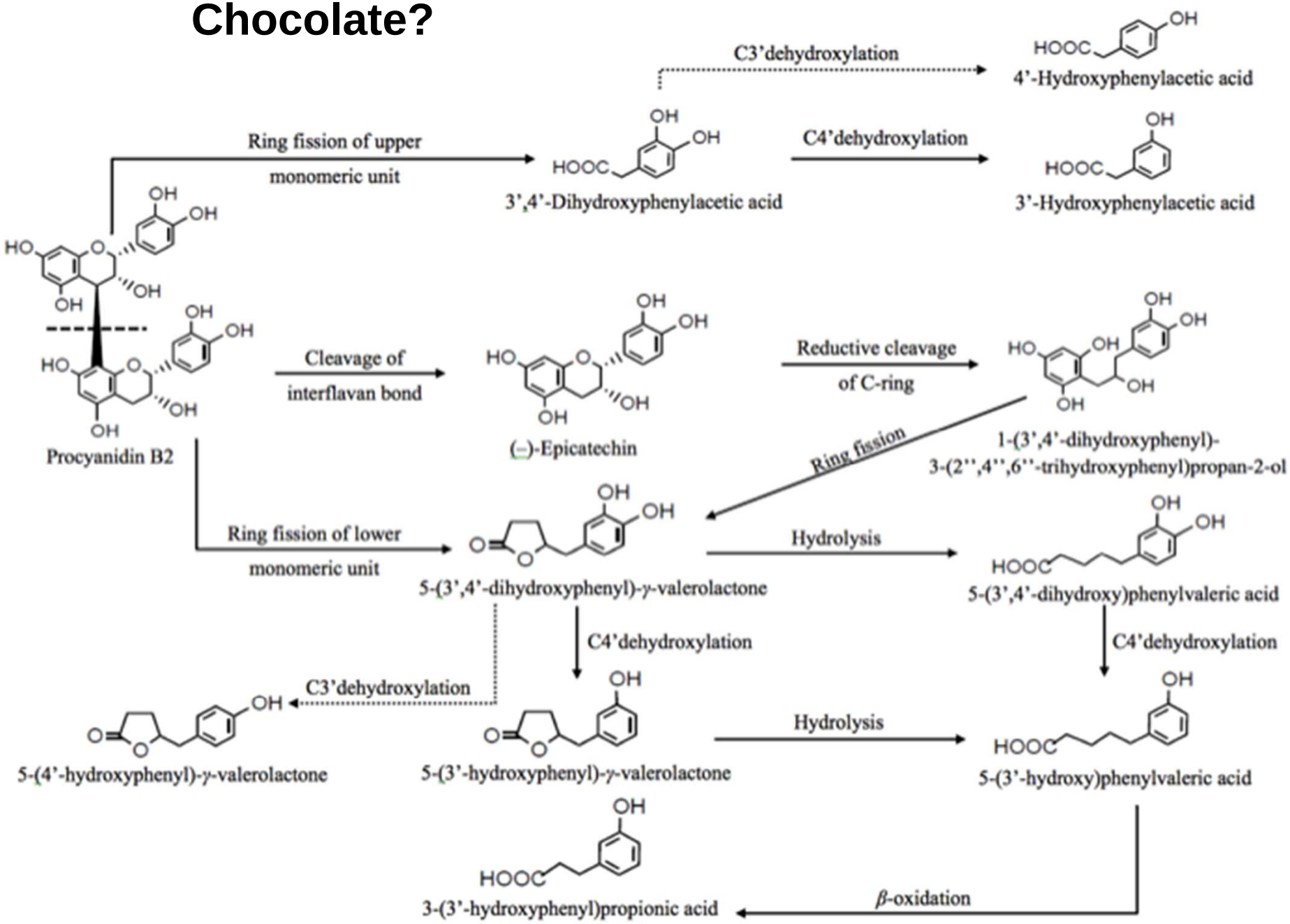
Isourolithin A

Urolithin B-3-O-glucuronide

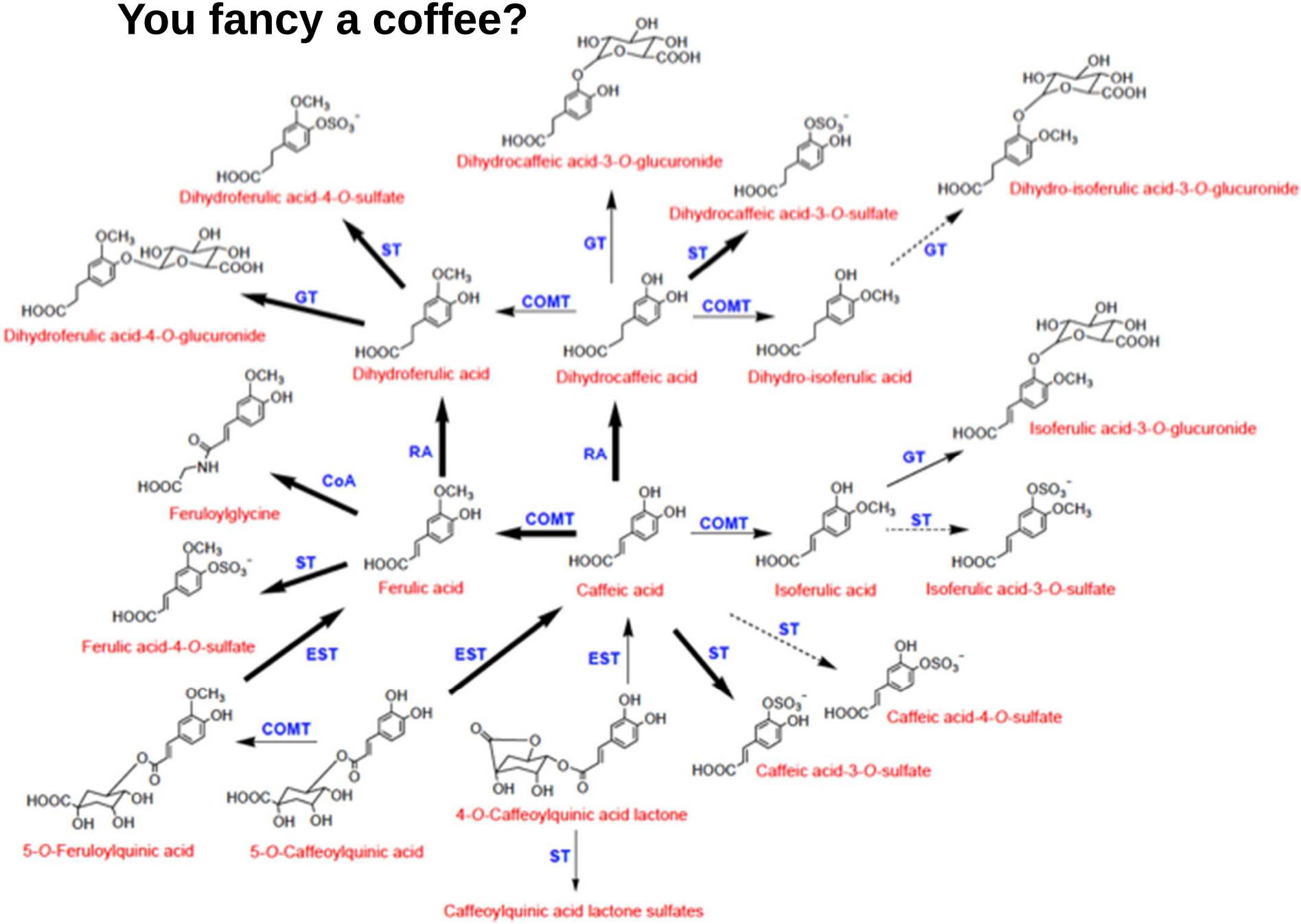
3,8-O-Dimethylellagic acid-2-O-glucuronide

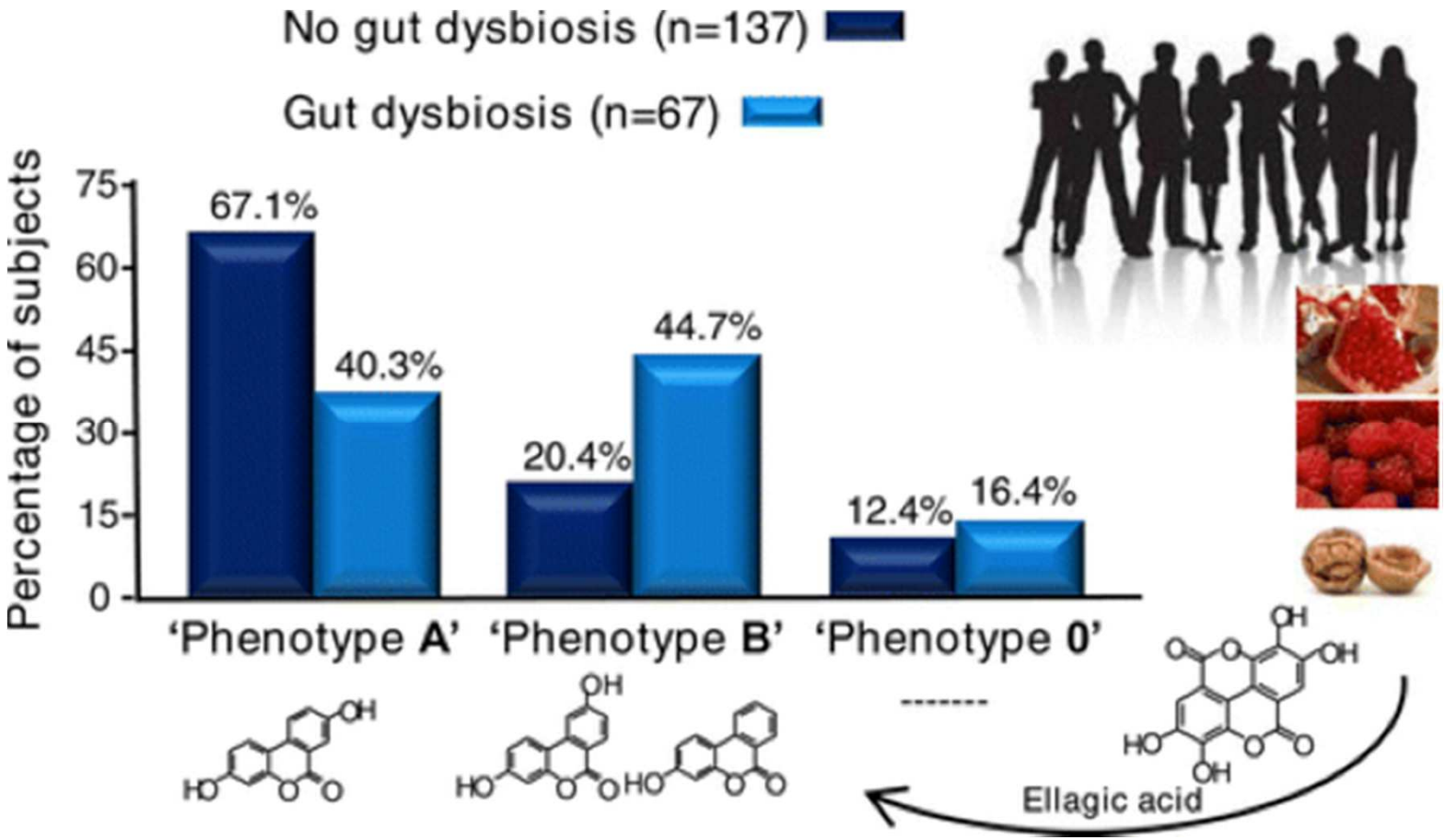
Urolithin A-3-O-glucuronide

Chocolate?


C3'dehydroxylation
4'-Hydroxyphenylacetic acid
Ring fission of upper
monomeric unit
3',4'-Dihydroxyphenylacetic acid
C4'dehydroxylation
3'-Hydroxyphenylacetic acid
Procyanidin B2
Cleavage of
interflavan bond
(–)-Epicatechin
Reductive cleavage
of C-ring
1-(3',4'-dihydroxyphenyl)-
3-(2'',4'',6''-trihydroxyphenyl)propan-2-ol
Ring fission
Ring fission of lower
monomeric unit
5-(3',4'-dihydroxyphenyl)-γ-valerolactone
Hydrolysis
5-(3',4'-dihydroxy)phenylvaleric acid
C4'dehydroxylation
C4'dehydroxylation
C3'dehydroxylation
5-(4'-hydroxyphenyl)-γ-valerolactone
5-(3'-hydroxyphenyl)-γ-valerolactone
Hydrolysis
5-(3'-hydroxy)phenylvaleric acid
3-(3'-hydroxyphenyl)propionic acid
β-oxidation

You fancy a coffee?



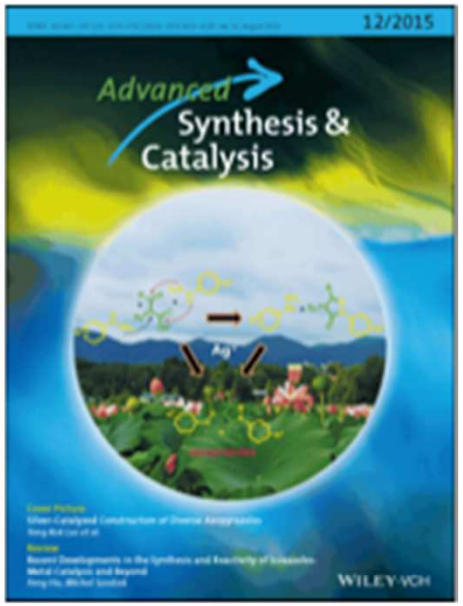


J. Agric. Food Chem., **2014**, *62* (28), pp 6535–6538 **DOI:** 10.1021/jf5024615

We are trying to change the paradigm!

Work out more physiological models!

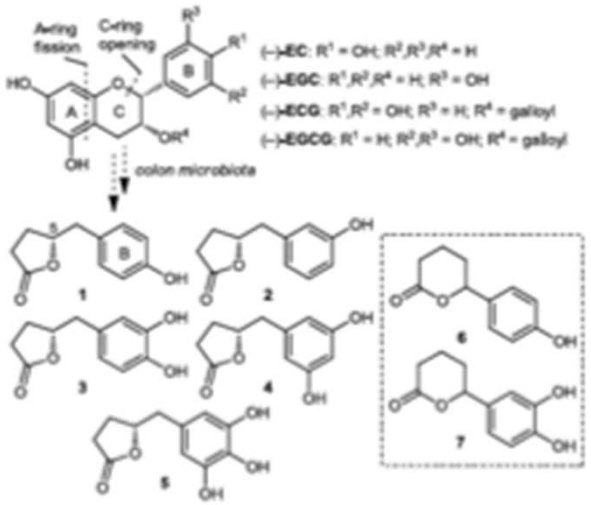
Synthesising metabolites that are not commercially available!

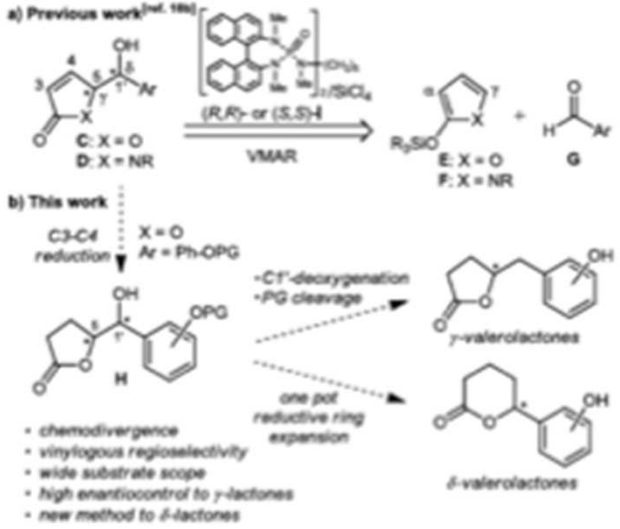


Catalytic, Enantioselective, Vinylogous Mukaiyama Aldol Reaction of Furan-Based Dienoxy Silanes: A Chemodivergent Approach to γ-Valerolactone Flavan-3-ol Metabolites and δ-Lactone Analogues

Claudio Curti[a,*] Nicoletta Brindani,[a,b] Lucia Battistini,[a] Andrea Sartori,[a] Giorgio Pelosi,[c] Pedro Mena,[b] Furio Brighenti,[b] Franca Zanardi,[a] Daniele Del Rio[b,d]

[a] Dipartimento di Farmacia, Università degli Studi di Parma, Parco Area delle Scienze 27/A, 43124 Parma, Italy
Fax: (+39)-0521-905006; phone: (+39)-0521-905079; e-mail: claudio.curti@unipr.it
[b] Dipartimento di Scienze degli Alimenti, Università degli Studi di Parma, Via Volturno 39, 43125 Parma, Italy
[c] Dipartimento di Chimica, Università degli Studi di Parma, Parco Area delle Scienze 17/A, 43124 Parma, Italy
[d] The Need for Nutrition Education/Innovation Programme (NNEdPro), University of Cambridge, UK

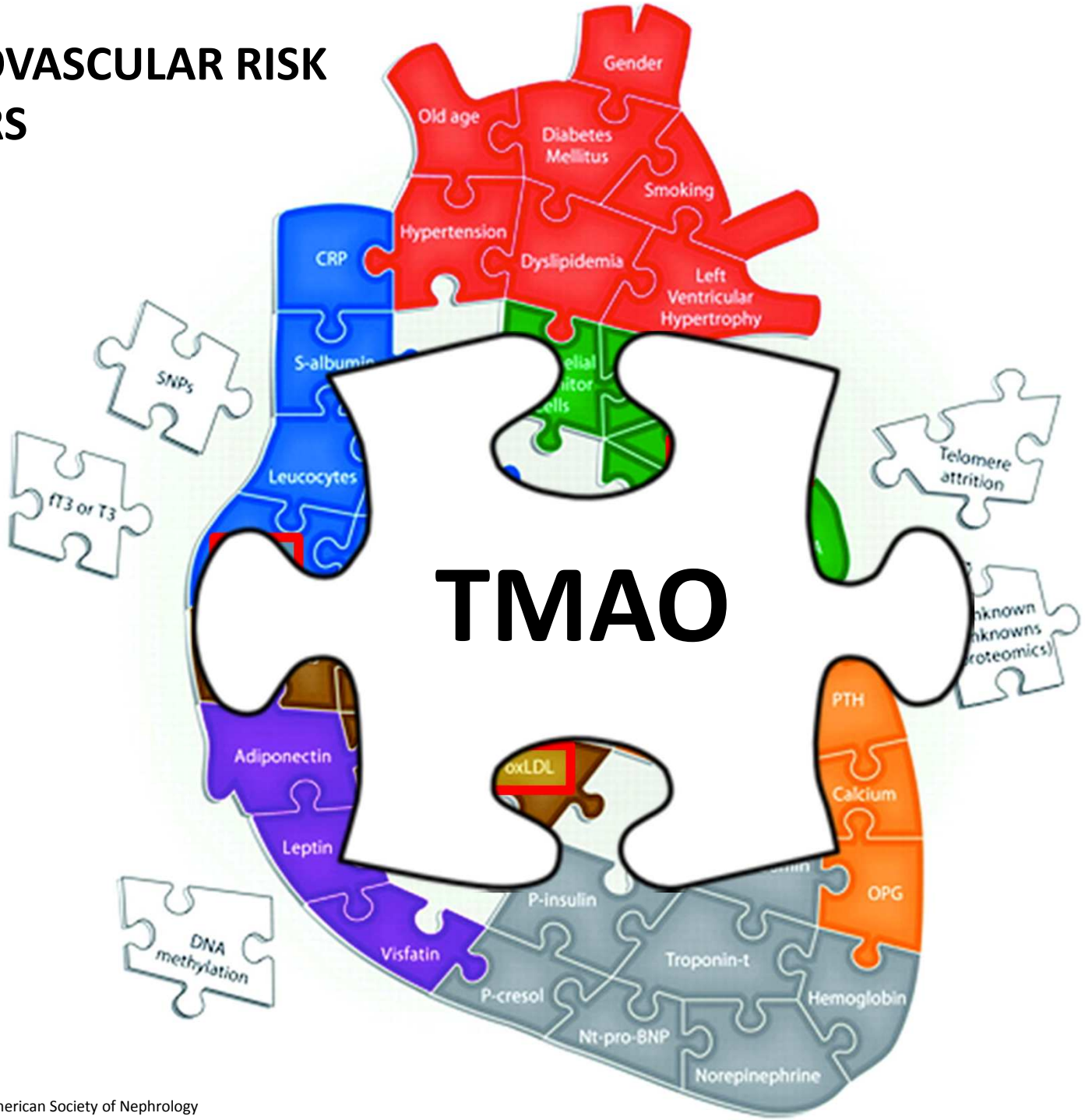


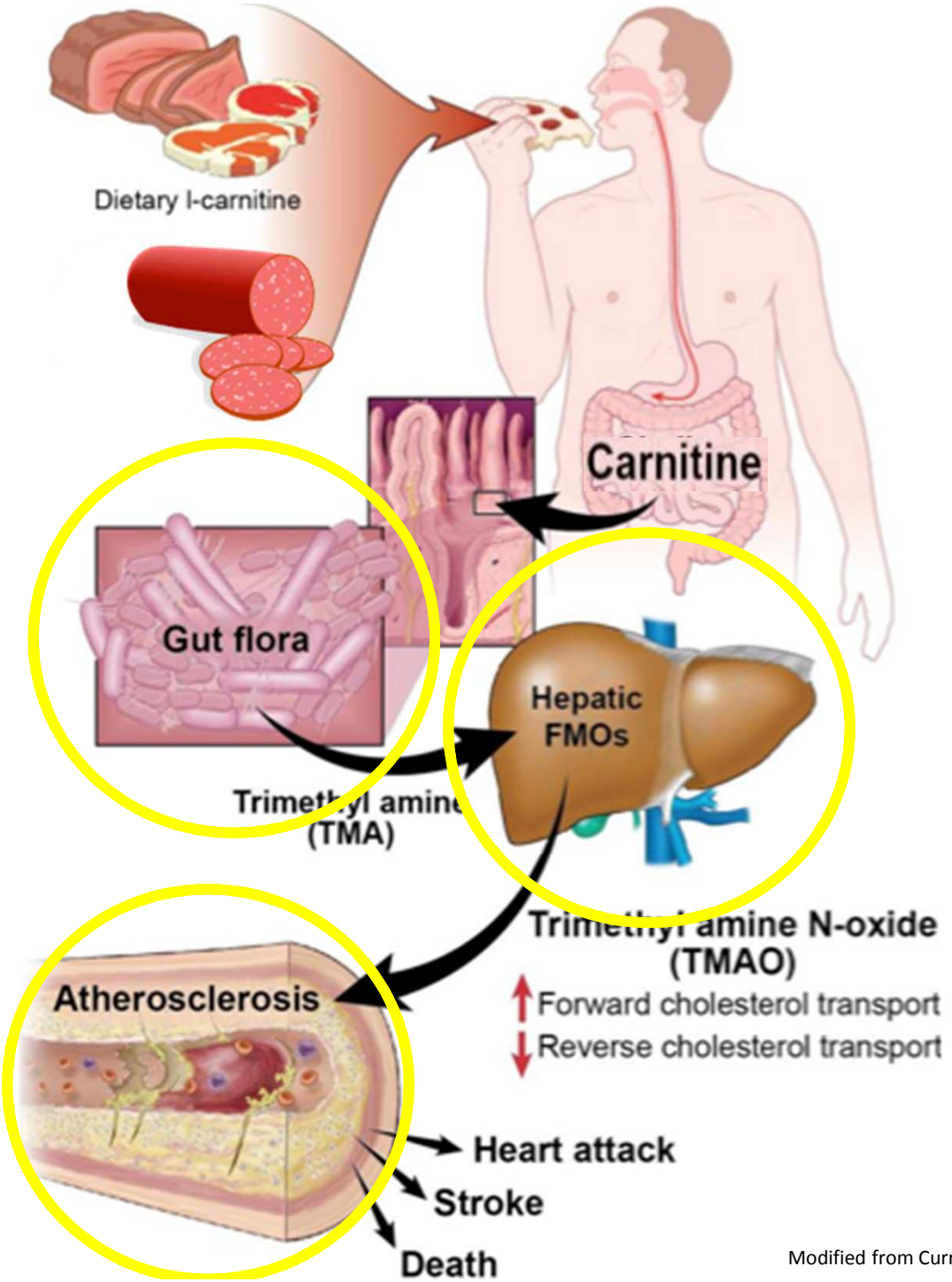


Study the interactions of phenolic metabolites with drugs!

Identify new and emerging targets!

CARDIOVASCULAR RISK FACTORS





Modified from Curr Opin Lipidol. 2014 Feb; 25(1): 48–53.

Volume 6 | Number 1 | January 2015 | Pages 1–332

Food & Function

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REVIEW

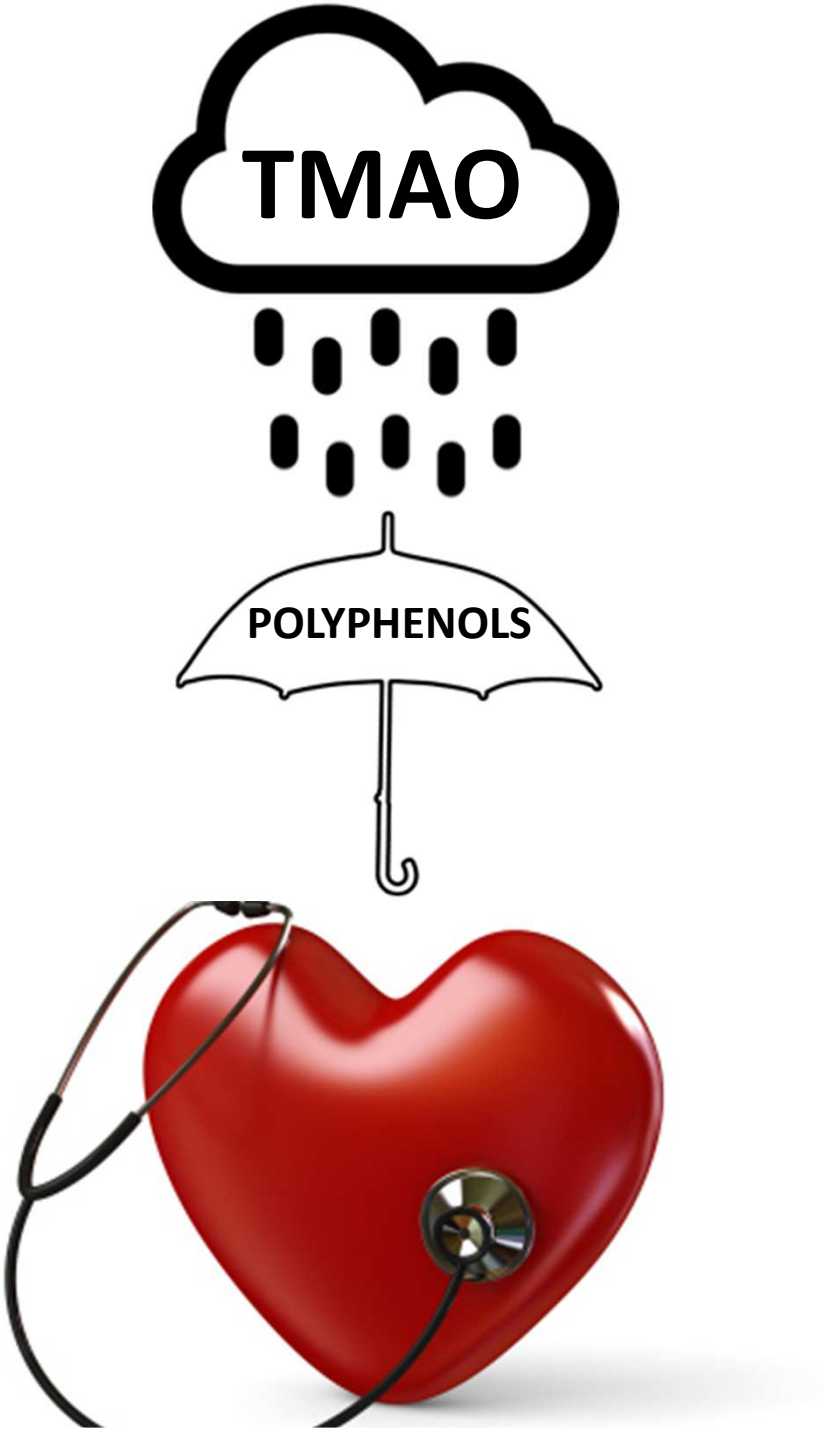
Ilaria Zanotti, Daniele Del Rio *et al.*

Atheroprotective effects of (poly)phenols: a focus on cell cholesterol metabolism

ISSN 2042-6496

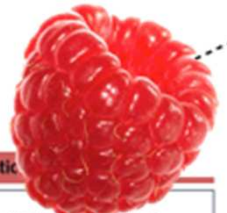
ROYAL SOCIETY OF CHEMISTRY

REVIEW
Ilaria Zanotti, Daniele Del Rio *et al.*
Atheroprotective effects of (poly)phenols: a focus on cell cholesterol metabolism


TMAO
POLYPHENOLS

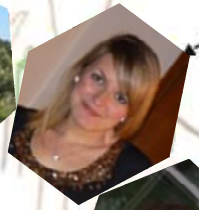
We are working in humans, with a multiplicity of approaches….

Bioavailability of Ellagitannins in Healthy Humans



Time 0 - Ingestic

300 g of strawberries or 100 ml of pomegranate juice allow the administration of approx 140 μmol of ellagic acid and ellagitannins.



After 1 Hour

Ellagic acid, obtained by basic hydrolysis of ET downline of gastric passage, is detected in plasma at Cmax 0.06 μM, AUC 0.17 μmol*h/L

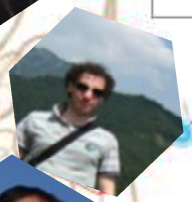
After 5 Hours

Ellagic acid disappears from plasma. The amount unabsorbed in the small intestine enters the large intestine where is biotransformed by resident colonic microflora.

Large Intestine

Urolithin M5. First step of microbial rearrangement of ellagic acid.

Urolithin D



Large Intestine

The colonic microflora produces four different urolithins by a fixed order. Urolithin D appears first, is modified to Urolithin C, then to A and finally to Urolithin B.

Urolithin C

Urolithin A

Urolithin B

Liver

Urolithins can be glucuronidated, sulphated or methylated by Phase II enzymes in the liver.

Urolithin B 3-O-Glucuronide

Variability

All reports highlight a great interindividual variability, likely due to different microfloras. Total urinary excretion of ET-metabolites may range from 1 to 53%.

MRC Human Nutrition Research

THE NEED FOR NUTRITION EDUCATION/INNOVATION PROGRAMME