Caféine et HTA: bon ou mauvais?

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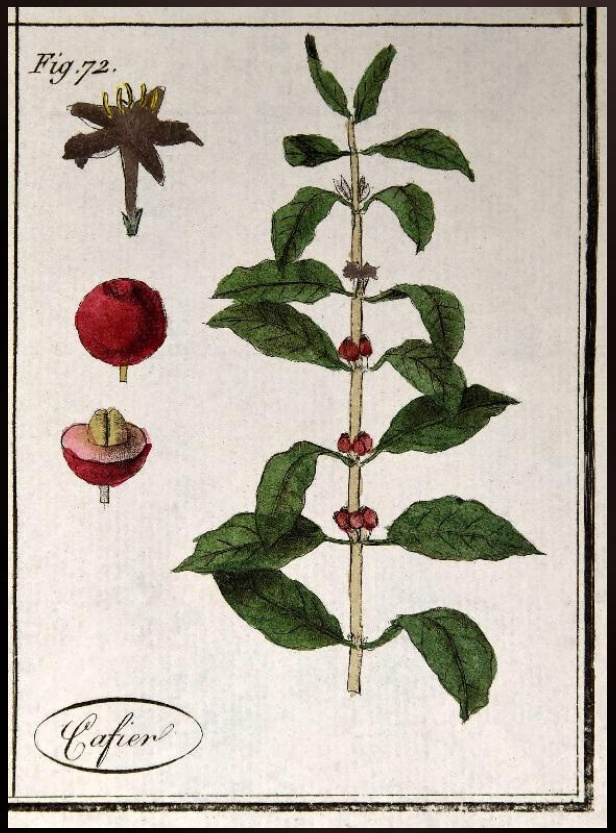
PLAN

- Un peu d'histoire et d'épidémiologie
- Caféine: métabolisme
- Caféine et santé?
- Caféine et HTA ?
- Conclusions



Caféine: Histoire et description

Histoire du café commence déjà 800 AD….

- 1819: Isolation de la caféine par physicien allemand (Friedlieb Ferdinand Runge)
- 1821: description de la caféine (Pelletier et Robiquet)
- 1827: Isolation théine du thé (Oudry)
- 1838: démonstration que théine = même substance que caféine.
- Fin du XIXème siècle, élucidation de la structure de la caféine (Hermann Emil Fischer) .

TEA, COFFEE, AND COCOA.

ON Wednesday Mr. Ernest Hart, Chairman of the Council of the National Health Society, delivered an address on this subject at the rooms of the Society, 53, Berners Street, in which he aimed at dispelling many common errors, and discussing the matter in hand practically as well as from the scientific point of view. The lecturer began by referring to the overwhelming argument in favour of these beverages deducible from the principle *quod ubique, quod ab omnibus*. A universal, discriminating, and all-powerful instinct had led first all the nations of the East and the South to use as their beverage, and subsequently all the Western nations, to adopt from them beverages derived from tea, coffee, Paraguay tea, cocoa, Guarana chocolate, or the kola nut. These were all extremely different in their flavour, and altogether different in their sources of origin. The tea was the dried leaf of a camellia; coffee the dried seed of a species of cinchona; the Paraguay tea, drunk by millions of people in Southern America, was derived from the leaves of a holly; guarana from the seed of paullinia; kola from the nut of sterculia. Modern chemical processes had succeeded in discovering that the whole of these beverages were characterised, however different in flavour or source, by the presence of a single and practically identical alkaloid or active principle known as theine or caffeine. Taking tea and coffee as the two typical beverages of the kind prevalent throughout the East and in Western Europe, Mr. Ernest Hart proceeded to discuss what were the important matters known or unknown about them, and to compare the methods of preparation and of infusion which prevailed in the West and in the East. Describing in comparative detail the processes of plucking and preparing China tea and the teas of India and Ceylon, he pointed out that however different in detail, they were essentially alike in principle. After plucking from the shrub the leaf was subjected to the softening and wrinkling process known as withering; the leaves were then, in India, China, and Ceylon, fermented in a wet mass, rolled and crushed under heavy pressure, re-roasted and packed for the market. In Japan the practice differed especially for teas intended for home consumption. The leaf was moistened by steam, roasted at a very mild heat or basket fired, rolled, and for the purposes of the finest tea reduced to powder, which was the most highly esteemed and the only kind of tea used in the tea ceremonies of Japan. It will be observed that the essential point in all these modes of preparation is the *softening* of the tealeaf and the *crushing* it so as to set free within the substance of the leaf the theine and essential oils which it contains, so as to render them more easily diffused when infused in hot water as a beverage. In all cases the leaf most highly valued was the small top leaf of the twig and the bud. There was no reason whatever, however, to believe that this was either finer in quality, richer in content, or intrinsically better in flavour than the leaves next in succession, but being more tender and softer in structure, it yielded more completely to the crushing process and gave better and more flavoured liquor.

Setting aside for the moment the various obscure and untrustworthy varieties of preparation and selection of China tea, as to which there was much mystery and some misrepresentation, and dealing only with Indian, Ceylon, and Japan teas, where everything was open and above board, Mr. Hart pointed out that the common and prevalent impression that the trade names Orange Pekoe, Pekoe, Suchong, Congou, represented different products having some generic distinction, was altogether unfounded and contrary to the fact. They were all the same in respect of origin; they were picked at the same time from the same plant and from the same bush. The bud and the top leaf constituted Orange Pekoe, the two or three larger leaves growing on the same twig a little lower down were Suchong, and below that the leaves became Congou, a name, however, not much recognised either in Indian or Ceylon teas.

After describing the mode of growth and of selection of the leaf, the lecturer paid a warm compliment to the Ceylon teas and the Indian teas, pointing out, however, that the great favour with which Ceylon teas were now regarded was no doubt due to the fact that, while equally rich in theine, they had a less proportion of tannin than the Indian teas. In 1880 the total export of tea from Ceylon was under 120,000 lbs.; this year it had reached 80,000,000 lbs. The housewife, in selecting a fine tea, should not be guided by any trade name, but should obtain Orange Pekoe of whatever growth, whether from Ceylon, Assam, or Darjeeling, and should then determine by pouring a little boiling water over the leaves, and examining them that the leaf was a whole leaf, and not cut into small pieces from the larger leaf, as was commonly the practice. The larger the leaf the weaker the infusion and the less the value. Green tea from China was for the most part tea fermented and made bitter like black tea, and then faced with Prussian blue or indigo to simulate green tea. Nearly all the Indian and Ceylon teas were also fermented and were all black teas.

The only true natural green tea produced in quantity by any country now was the green tea of Japan as drunk by the natives and largely consumed in America. This tea was neither so bitter nor so strong as to require to be doctored with an albuminoid fluid such as milk to make it drinkable, or with sugar to further hide its bitterness. It needed to be infused only for a short time, never more than five minutes, and the water used should be just off the boiling point, so as not to dissipate the delicate aroma of the tea. Japanese "green," or unfermented and unfaced tea, so drunk was, in the lecturer's opinion, the very perfection of the beverage. Our European tastes, however, had so long been vitiated by the habit of drinking the strong, bitter, fermented tea, that he had no great anticipation that any but the more delicate and cultivated palate would appreciate and habitually prefer this exquisitely aromatic and harmless beverage, which was the staple drink of the far East. He showed the mode of preparing tea after the fashion of the Japanese from a series of specimens, some of his own importation, and some procured from a Japanese resident in London.

Referring then to the question of tannin in tea, Mr. Hart gave the result of a series of experiment, which threw much doubt upon the current views on the subject. It was supposed generally that letting the hot water stand upon the leaves more than fifteen minutes extracted a considerable additional amount of tannin from the tea, and was very deleterious. This was hardly the fact. After fifteen minutes very little more tannin could be extracted from the tea by the ordinary methods of infusion. What came over was an unpleasant disagreeably flavoured bitter extractive, which had lost all delicacy of flavour, and was unpleasant to the palate, but it did not contain the excess of tannin popularly attributed to it. Tannin was so highly soluble that it was dissolved in the water from the very first instant of contact, and the three minutes' infusion of pale tea contained a very large proportion of tannin. He agreed with Sir William Roberts in believing that the alleged ill-effects of the tannin in the tea were probably very much exaggerated, and that the ill-effect of drinking too much tea and too strong tea were due to the theine and volatile extractives of the tea, and not to the tannin. It was quite a fallacy to suppose, although he often saw it stated, that common teas contained more tannin than the choicer varieties. In many cases the opposite was the fact. Varieties of tea, however, such as the "digestive" tea, might be had in which the tannin of the tea was so altered by electrical treatment that it did not precipitate gelatine, and interfered but little with the digestion of starch; of these Mr. Hart showed specimens which he considered deserving of notice.

The most essential point of all for making good tea of the finest quality, and with the least waste, was the thorough crushing of the leaf, and its subdivision in such a manner that the largest possible surface was rapidly exposed to the boiling water in infusing it. Hence the traditional preference by the Japanese, who in this matter had shown their customary intelligence and refinement of taste, for their carefully prepared and selected "tea powder," which produced the finest tea in the world. Hence, too, probably, the superiority of the thoroughly crushed tea bricks of the best quality formerly sent from China to Russia. This matter had been greatly overlooked in the West, but undoubtedly it was the key to any further progress in the art and economics of tea drinking. The difficulties and disadvantages of tea powder obtainable in Europe at present were its liability to adulteration, its uncertain mixture, and the discomforts attending

Café-ine consommation

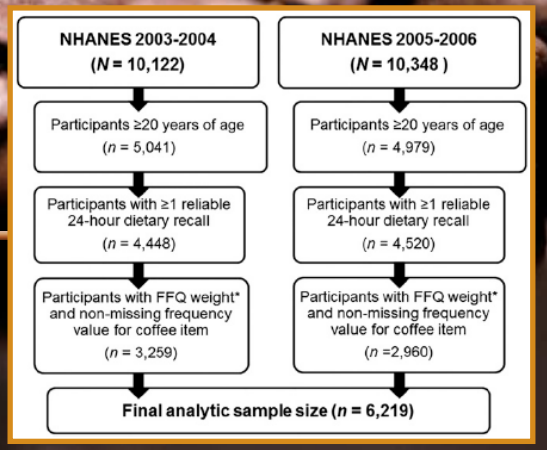
USA

- 75% adultes boivent café
- 50% quotidiennement
- 2011: 4.24kg/an par tête
- Consommation moyenne =200-300mg/h

CH

- 7.85kg/an par tête

Café-ine consommation



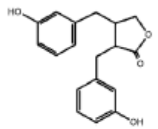
	Adjusted mean coffee intake, fluid ounces/d					
		NHANES survey cycle				
Subgroup	Overall (2003–2012)	2003–2004	2005–2006	2007–2008	2009–2010	2011–2012
Overall	11.4 ± 0.3	11.8 ± 0.6	11.8 ± 0.4	11.1 ± 0.5	11.6 ± 0.5	10.8 ± 0.4
Sex						
Female	10.0 ± 0.2	10.1 ± 0.4	10.2 ± 0.5	9.8 ± 0.5	10.2 ± 0.4	9.6 ± 0.4
Male	12.9 ± 0.4	13.7 ± 0.9	13.6 ± 0.5	12.4 ± 0.7	13.0 ± 0.8	12.1 ± 0.8
Age						
20 to <30 y	4.8 ± 0.3	4.5 ± 0.5	4.0 ± 0.6	4.9 ± 0.7	5.8 ± 0.6	4.7 ± 0.7
30 to <40 y	9.5 ± 0.4	10.0 ± 0.7	10.0 ± 0.7	8.7 ± 0.9	9.9 ± 1.0	9.1 ± 0.5
40 to <50 y	13.4 ± 0.5	14.9 ± 1.3	14.5 ± 0.9	12.5 ± 0.7	13.1 ± 0.9	12.0 ± 1.1
50 to <60 y	15.0 ± 0.6	15.2 ± 1.4	16.6 ± 1.2	15.1 ± 1.6	15.6 ± 0.8	13.0 ± 0.6
≥60 y	13.6 ± 0.4	13.9 ± 0.6	13.6 ± 0.6	13.5 ± 0.9	13.0 ± 0.5	14.1 ± 1.0
Race/ethnicity						
Non-Hispanic black	4.9 ± 0.2	5.3 ± 0.5	5.3 ± 0.5	4.4 ± 0.4	4.6 ± 0.3	4.8 ± 0.4
Hispanic or other race	8.5 ± 0.3	8.9 ± 0.5	9.8 ± 0.5	8.0 ± 0.5	7.8 ± 0.5	8.3 ± 0.5
Non-Hispanic white	13.2 ± 0.3	13.6 ± 0.6	13.5 ± 0.5	12.9 ± 0.6	13.7 ± 0.6	12.4 ± 0.5

Lotfield: JNutr2016

Autres substances dans le café

- ✓ Magnesium
- ✓ Polyphenols
  flavanoides….
- ✓ Diterpenes
- ✓ melanoidins

LIGNANI



↓TC and LDL-C levels [161,162]; ↓incidence of diabetes[7]; ↓inflammatory molecules [163]; ↑FMD[165]; decrease in atrial fibrillation in patients at high risk for CVD[169].

OTHERS POLYPHENOLS

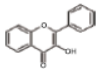
Curcumin: ↓ TC, LDL-C, TG and ↑ HDL-C[178].

Sylimarin: ↓TC, LDL-C and TG[176-177].

Triterpenes: Improve the lipoprotein particle subclasses distribution and their associated atherogenic ratios[171]; HDL-C efflux capacity significantly improved[172]; ↑HDL size, promoted a greater HDL stability and enhanced the HDL oxidative status[173,174]; ↓cIMT[179].

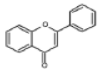
FLAVONOIDS

FLAVONOLS



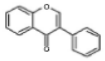
Significant ↓TC, LDL-C, TG, ↑HDL-C[95,96,98,100]; significant ↓LDL oxidizability [99]; ↓insulin[96]; lowers BP[95-96]; ↓WC and hip circumference[100]; weak risk reduction for CHD death with a higher intake[52]; LDL lipid hydroperoxide content was not increased by myricetin, nor did it promote the depletion of the endogenous antioxidant alpha-tocopherol in the LDL[50]; protects against lipid peroxidation, reduces VCAM-1 and E-selectin[45]; positive effect on hypertension[44-47]; reverse endothelial vasomotor dysfunction[34,48,49].

FLAVONES



Beneficial effect on plaque progression[74], inhibited collagen- and arachidonic acid-induced platelet aggregation in washed human platelets, inhibited the phosphorylation of PLCγ2, PKC, MAPKs in collagen-activated human platelets, and markedly ↓intracellular calcium mobilization and OH formation[55]; did not affect either phorbol-12,13-dibutyrate-stimulated PKC activation or platelet aggregation, neither SQ22536, an adenylate cyclase inhibitor nor 1H-[1,2,4]oxadiazole[4,3-a]quinoxalin-1-one significantly reversed[55], inhibits the platelet-derived growth factor-induced proliferation and migration of smooth muscle cells [54].

ISOFLAVONES

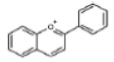


↓LDL-C[57], ↓DBP[76] and improve postprandial microvascular endothelial reactivity[77], ↓cIMT progression[58,59,129]; ↓cIMT progression[58,59,129], ↓TC, LDL-C and TG[61-63]; ↓risk of ischaemic stroke and risk of MI[64].

FLAVANONES

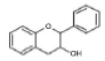
Beneficial effect on plaque progression[74], significantly modified lipids, LDL subclasses and cIMT[68].

ANTHOCYANIDINS



↓TC, TG and LDL-C[81,82,111,112,125]; ↑HDL-C concentrations[83,84]; ↓ CETP[85]; ↑ blood glucose[84,124]; ↓insulin[117]; ↓serum malondialdehyde, urinary 8-OHdG and isoprostanes levels[82,87,88]; ↓oxidative stress[82,86,112]; blocking anti-death signaling mediated via JNK-1 and c-JUN[109]; ↓SBP and DBP[87,111,116,117,118,121]; ↓BMI[86,114]; ↓platelet aggregation, increase platelet-derived NO release and decrease superoxide production[92, 110,126,127]; ↓cIMT[125,128]; improved brachial artery FMD and digital pulse amplitude tonometry[88,112,114,116,117,118]; not associated with MI or total stroke risk[90,91].

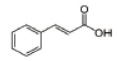
FLAVANOLS



Significant ↓TC, LDL-C, TG, ↑HDL-C[95,96,98,100], significant ↓LDL oxidizability [99]; ↓insulin[96]; lowers BP[95-96]; ↓WC and hip circumference[100].

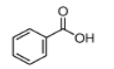
PHENOLIC ACIDS

CINNAMIC ACID



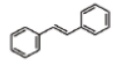
↓fasting glucose[139,142], ↓TC, TG, LDL-C, non HDL-C[139,140]; lower risk of diabetes [142]; ↓SBP and arterial elasticity[143], ↓BMI and abdominal fat[143]; lower risk of CVD[141,142]; inhibition of LDL oxidative modification[144]; ↑IL-6[145].

BENZOIC ACID



Improved brachial artery FMD[133]; acute glycemic control actions[134,135].

STILBENES



Improvement of FMD[147], ↓lipid profile (LDL-C, ApoB, oxLDL and oxLDL/ApoB ratio), ↑non-HDL-C (total atherogenic cholesterol load/ApoB ratio)[148], significant ↓markers of inflammation (TNF-α, PAI-1, IL-6/IL-10 ratio, and sICAM), and ↑IL-10 and adiponectin ↓oxidative stress [140,158,158,159] ↓fibrinolytic biomarkers [148]; ↑anti-inflammatory serum adiponectin and ↓thrombogenic PAI-1[155]; positive effect on inflammatory markers [150], protection against cardiovascular or cerebrovascular disease[151,157]; enhance FMD acutely[153]; miRNAs regulation [156].

Giglio. CurrentPharmaDesign2018

Caféine contenue dans…

Estimated caffeine content of commonly consumed beverages.

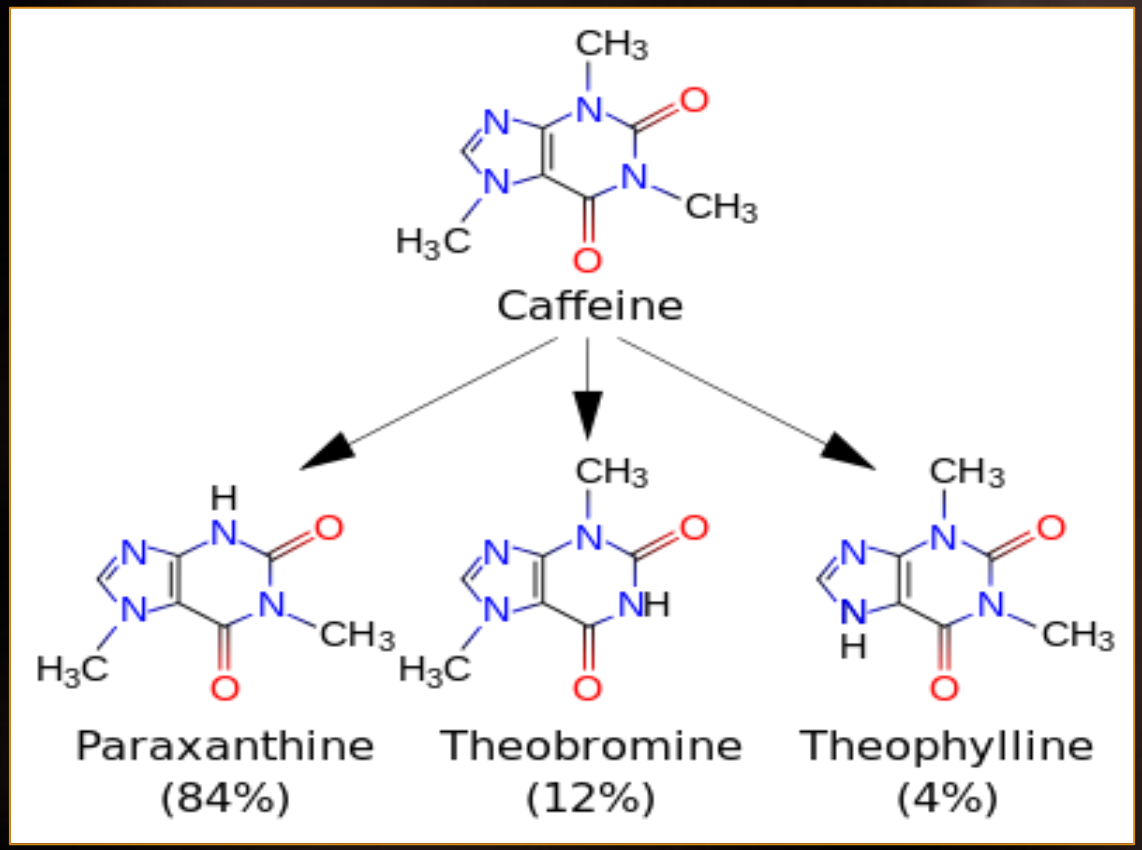
Beverage	Caffeine (g)	Volume (mL)
Cup of hot chocolate	10 mg	250 mL
Arizona green iced tea	15 mg	470 mL
Arizona black iced tea	32 mg	470 mL
Can of Coca Cola	32 mg	375 mL
Cup of Lipton green tea	35 mg	150 mL
Cup of Lipton black tea	55 mg	150 mL
Starbucks Café Latte – short	75 mg	236 mL
Red Bull Energy drink	80 mg	250 mL
Iced coffee	99 mg	500 mL
Espresso shot	106 mg	25 mL
Starbucks Café Latte – grande	150 mg	473 mL
Monster Energy drink	160 mg	473 mL
Wired X344 Energy drink	344 mg	473 mL
Fixx Energy drink	500 mg	591 mL

Voskoboinik. Trends CV Medicine 2018

Caféine: métabolisme

« 1, 3, 7 – trimethyxanthine » = purine alkaloid

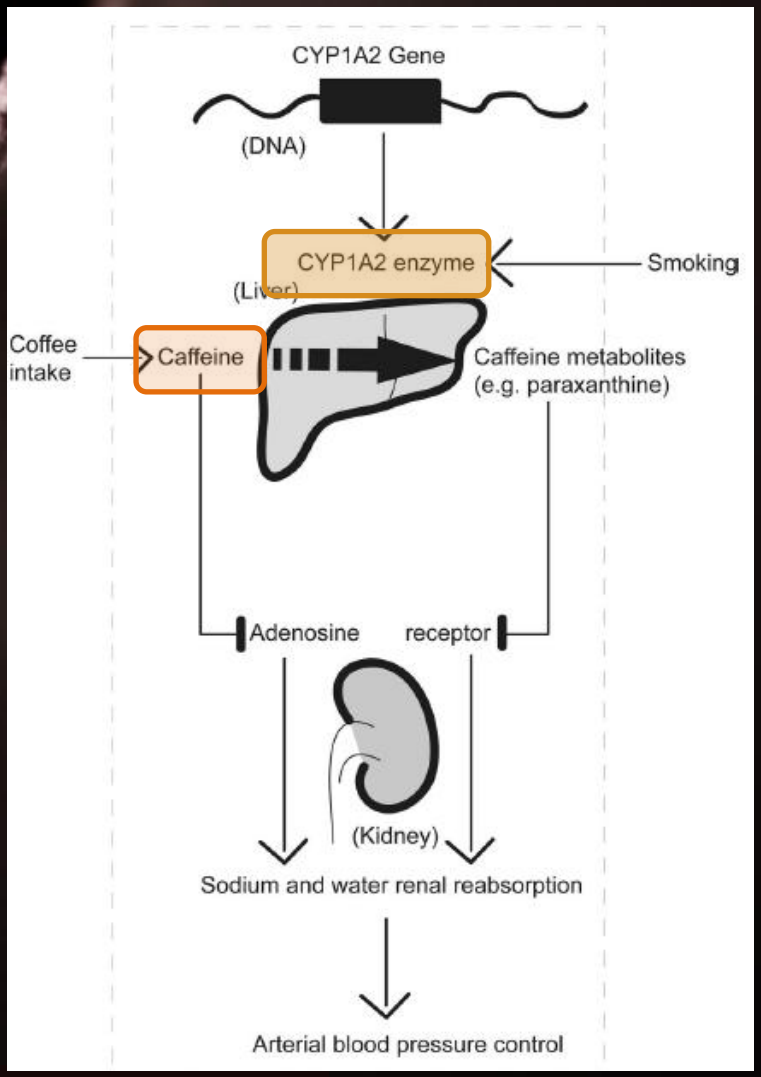
- Métabolisme hépatique : 95% CYP1A2



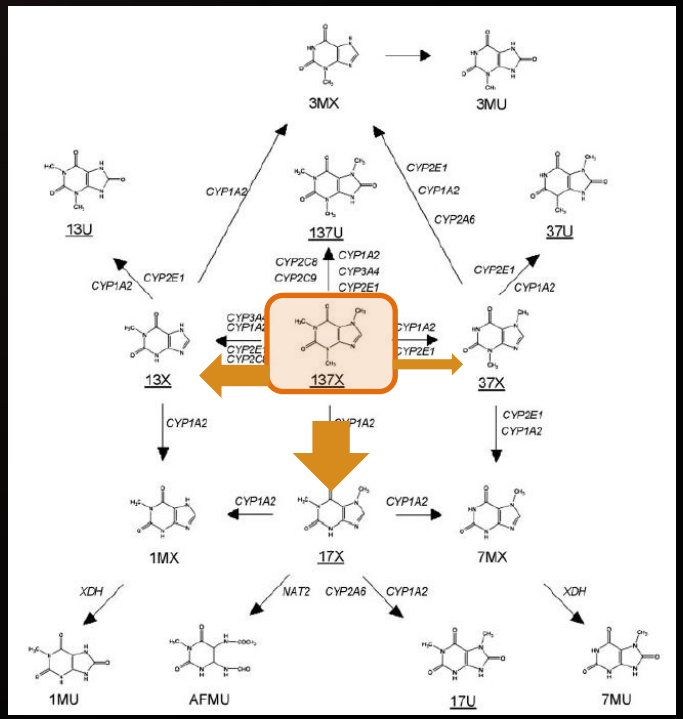
Ratio paraxanthine/caféine informe sur activité CYP1A2

Guessous. CurrHypertReport2014

Caféine: métabolisme



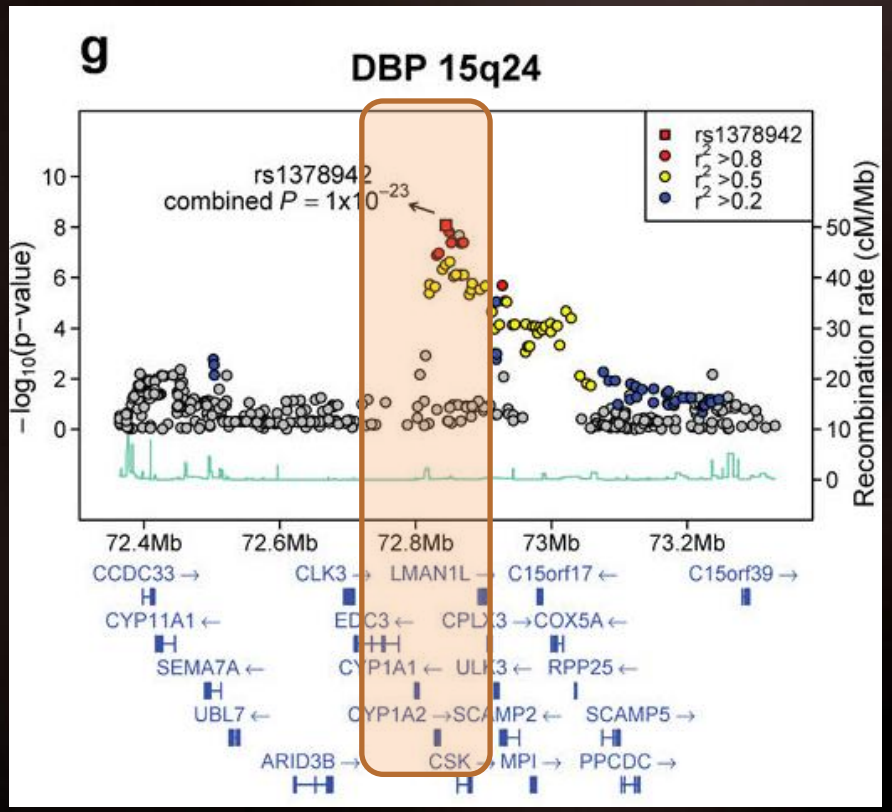
↑ : omeprazole, carbamazépine
↓ : contraception orale, fluvoxamine



Guessous. CurrHypertRepo2014
Cornelis. HumanMolGenetics2016

CYP1A2: métabolisme et génétique

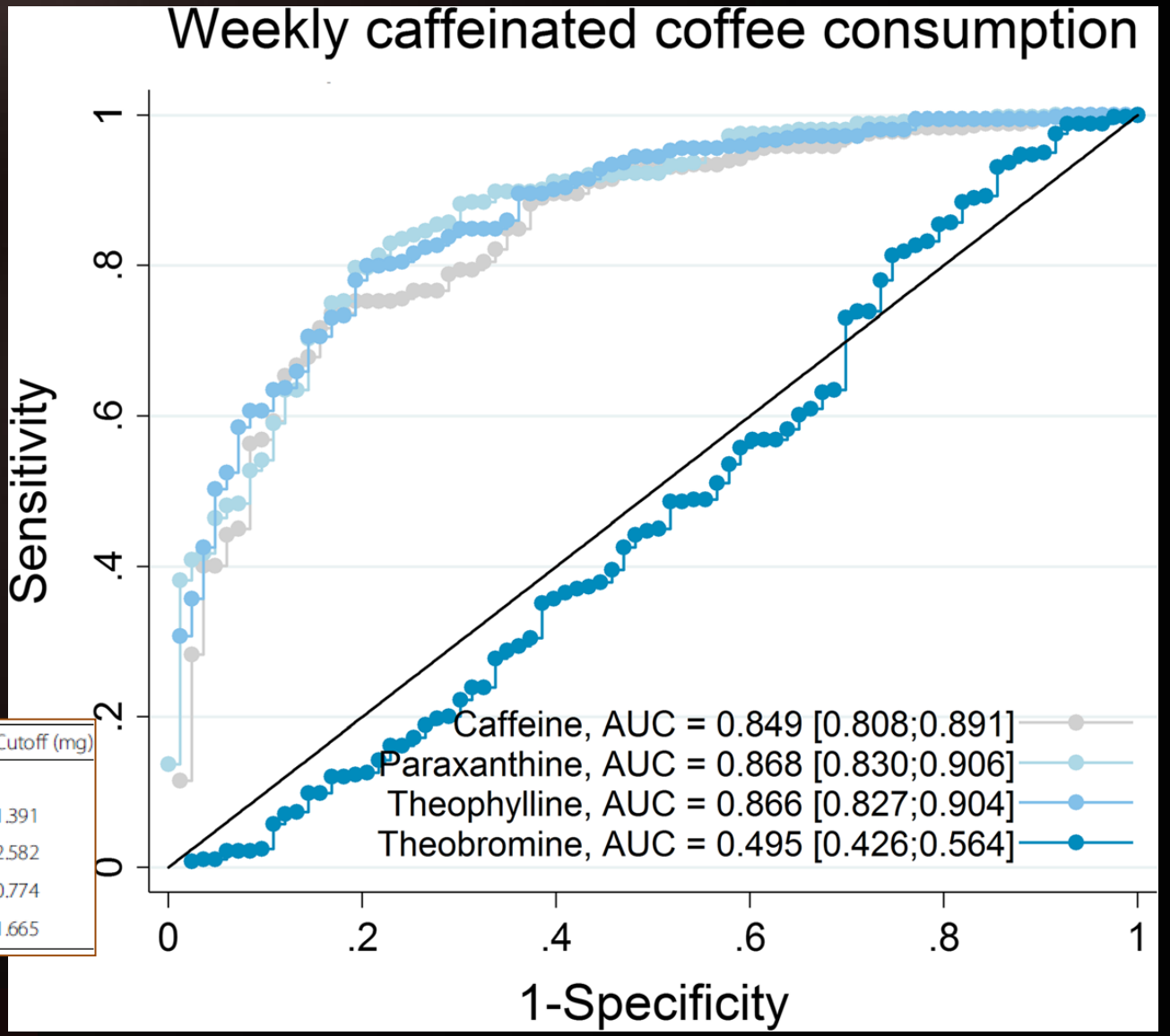
- Facteurs génétiques expliquent variation métabolisme caffeine
- CYP1A2 variants → ↓ PA non fumeurs
  → ↑ prise caffeine
- CYP1A2 activity → ↓ PA



Guessous. Hum Mol Gen 2012
Newton-Cheh. Nat Gen2009

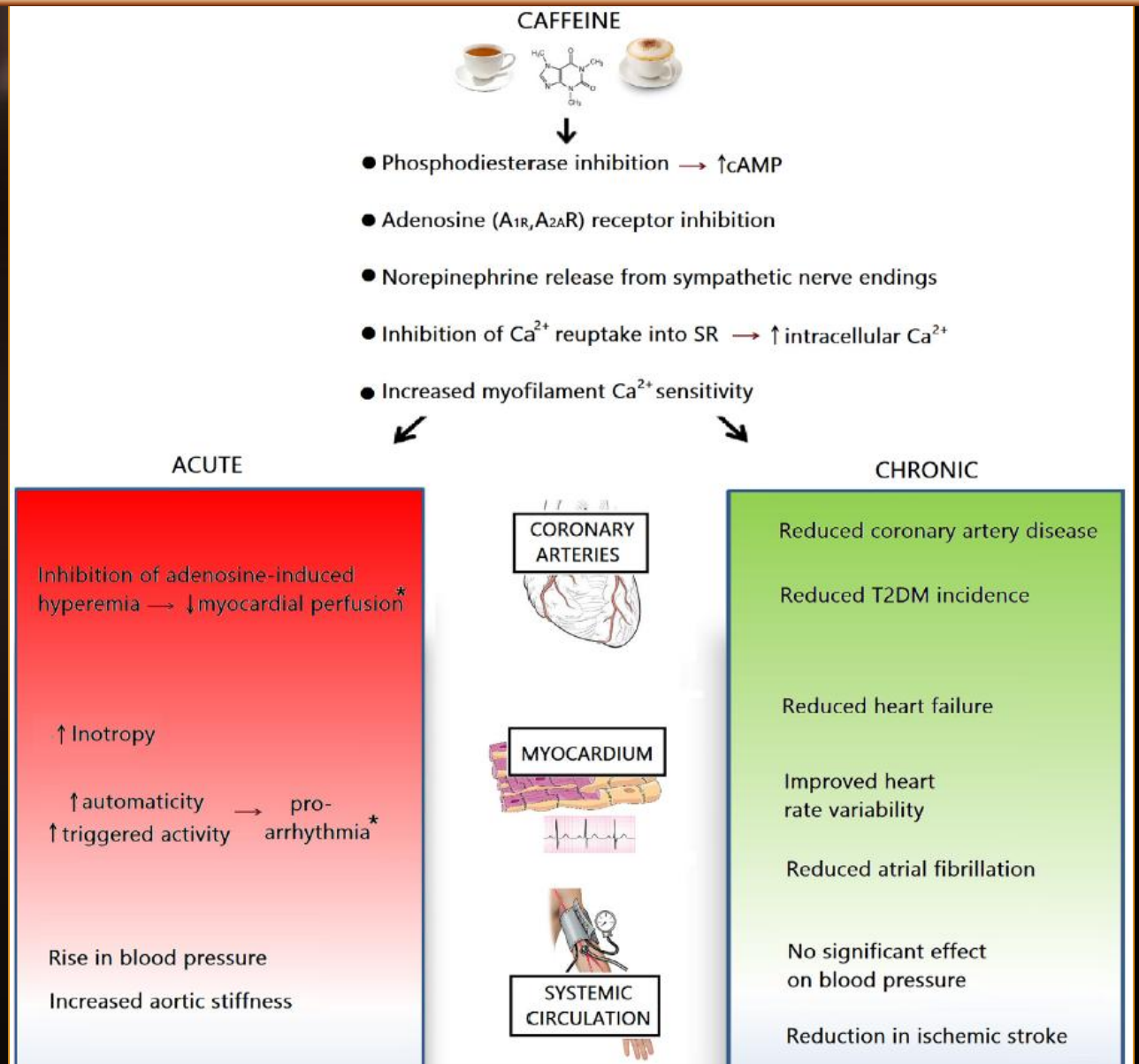
Mesure: Questionnaire café vs dosage

	Sensitivity	Specificity	Cutoff (mg)
24-h urinary metabolite			
24-h urinary caffeine	0.723	0.840	1.391
24-h urinary paraxanthine	0.801	0.790	2.582
24-h urinary theophylline	0.787	0.800	0.774
24-h urinary theobromine	0.938	0.160	1.665

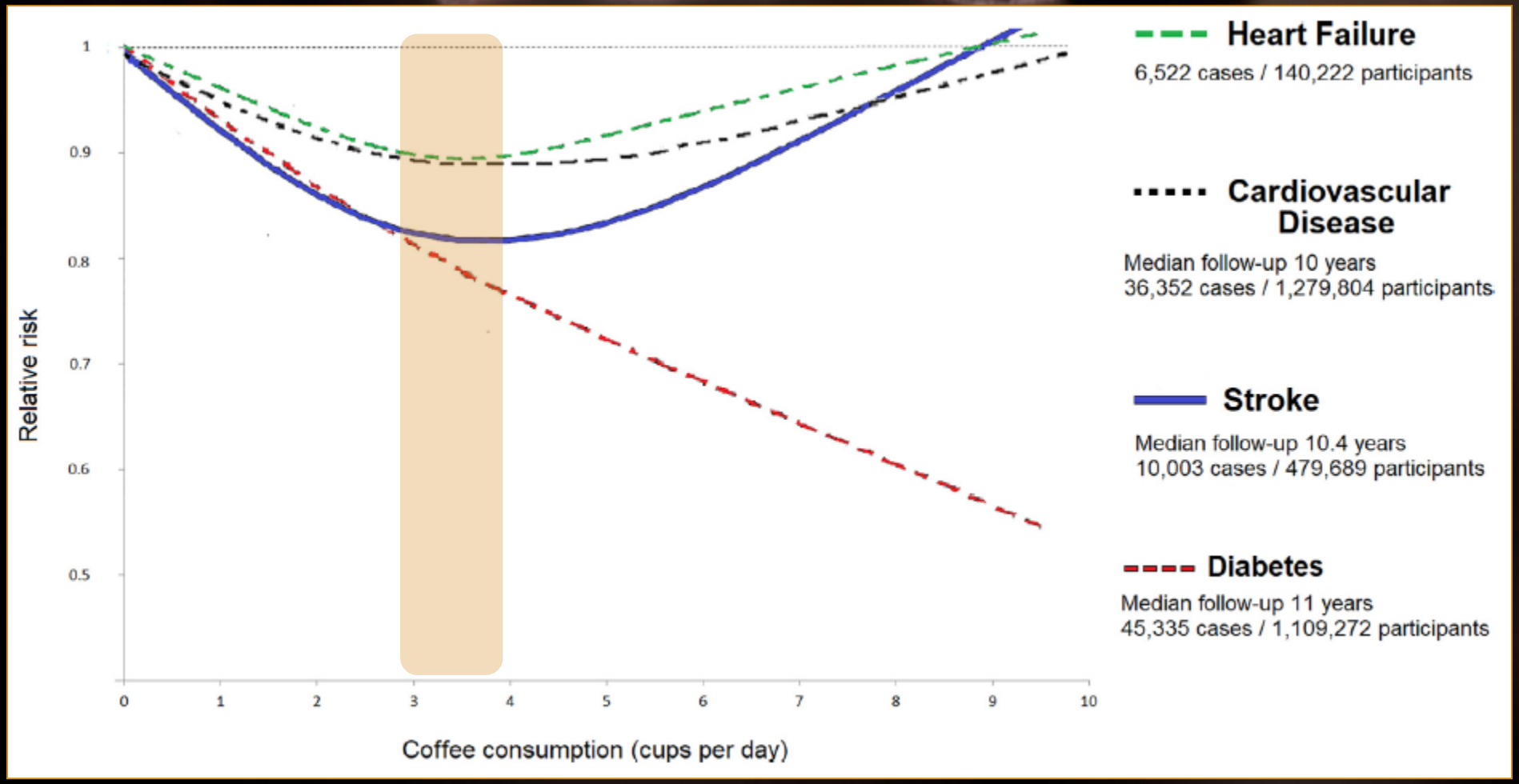


Petrovic. Nutrition&MEtabolism2016

Café-ine: Effets sur la santé ?

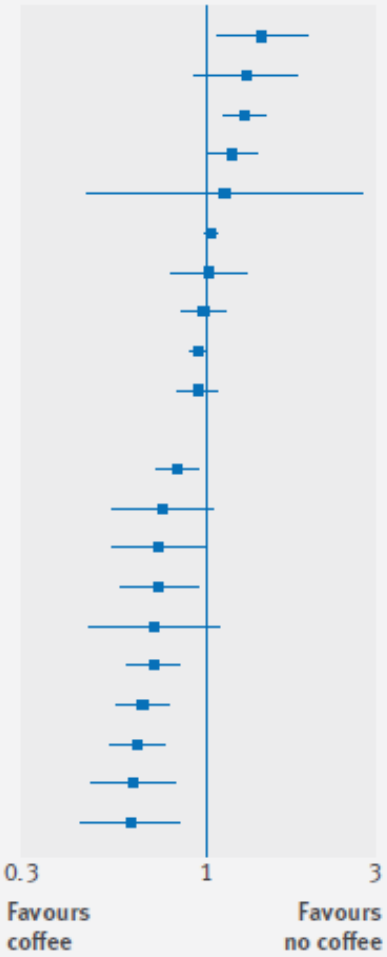


Trends in CV Medicine 2018



Voskoboinik. Trends in CV Medicine 2018

Outcome	No of events /total	Follow-up range (years)	Risk estimate (95% CI)	Estimate (95% CI)	Total studies	Cohort	Case-control	τ^2	I^2 (%)	Egger's P value	AMSTAR
10 most harmful											
Acute leukaemia in childhood[88 89]	NP	NA		1.44*† (1.07 to 1.92)	3	0	3	NP	42	0.33	4
Lymphoma[60]	219/124 131	NP		1.29 (0.92 to 1.80)	3	3	0	0.04	18	ND	7
Lung cancer[47]	11 145/NP	NP		1.28 (1.12 to 1.47)	8	8	0	0.02	87	ND	5
Urinary tract cancer[49]	NP	NP		1.18* (1.01 to 1.38)	14	0	14	NP	NP	0.51	6
Endometriosis[81]	387/385	NP		1.13 (0.46 to 2.76)	3	1	2	0.43	70	ND	5
Hypertension[35]	36 178/1 246 388	6-33		1.03 (0.98 to 1.08)	4	4	0	0.00	73	ND	6
Gastric cancer[50]	1535/255 112	2-25		1.02 (0.79 to 1.31)	8	8	0	0.07	58	ND	7
Rectal cancer[52]	4594/NP	NA		0.98* (0.85 to 1.13)	10	0	10	NP	71	NP	4
Breast cancer[38]	NP‡	8-24		0.95 (0.90 to 1.01)	11	11	0	0.00	20	0.58	5
Venous thromboembolism[33]	4215/65 951	12-19		0.94 (0.82 to 1.07)	2	2	0	0	0	ND	3
10 most beneficial											
Colorectal cancer[52]	9568/NP	NA		0.83* (0.73 to 0.95)	13	0	13	NP	80	NP	4
Urinary incontinence[68]	7284/47 518	NP		0.75* (0.54 to 1.04)	3§	1	0	0.08	93	ND	6
Alzheimer's disease[127]	454/5497	NP		0.73 (0.54 to 0.99)	2	2	0	0.00	0	ND	3
Liver fibrosis[63]	1414/3738	NP		0.73* (0.56 to 0.94)	7	7	0	0.08	81	ND	7
Chronic kidney disease[69]	NP/14 898	NA		0.71 (0.47 to 1.08)	4§	0	0	0.11	66	ND	7
NAFLD[62]	NP/2407	NP		0.71 (0.60 to 0.85)	3§	1	1	0	0	ND	7
Liver cancer[43]	3414/2 267 143	10-44		0.66 (0.55 to 0.78)	12	12	0	0.06	80	0.24	6
Parkinson's disease[77]	1940/719 187	10-27		0.64 (0.53 to 0.77)	6	6	0	0.02	29	ND	7
Chronic liver disease[43]	1463/437 355	6-19		0.62 (0.47 to 0.82)	6	6	0	0.07	80	ND	6
Liver cirrhosis[63]	1880/130 496	NP		0.61* (0.45 to 0.84)	3	3	0	0	0	ND	7



NP=not published; NA=not appropriate; ND=not done; NAFLD=non-alcoholic fatty liver disease
*Summary measure expressed as odds ratio in original meta-analysis article
†Fixed effects model
‡Could not be separated from other outcomes
§Included cross sectional studies

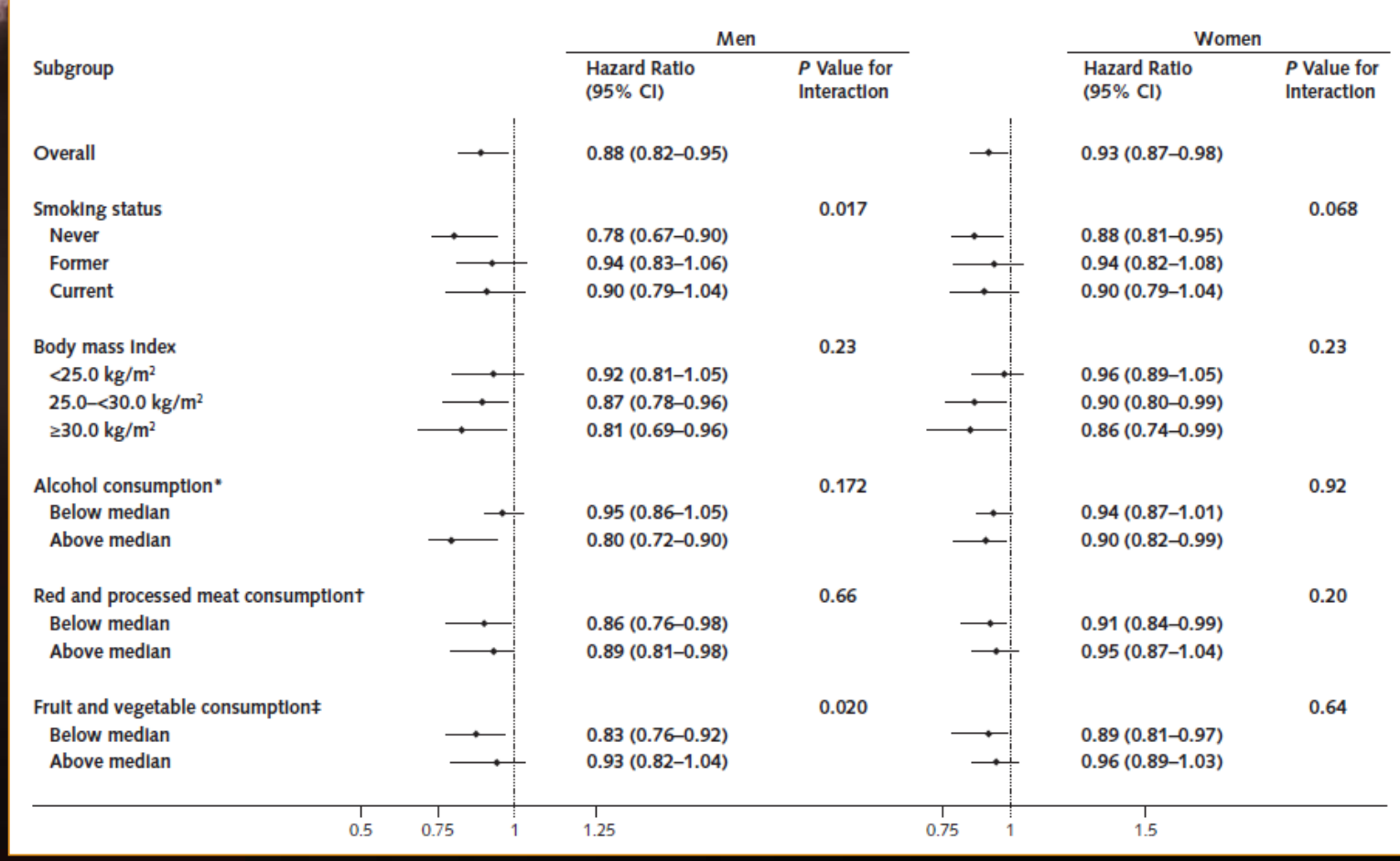
Any vs no coffee consumption

Poole. BMJ 2017

Café et mortalité

European Prospective Investigation into Cancer and Nutrition (EPIC)
N=521 330 (10 pays d'EU)

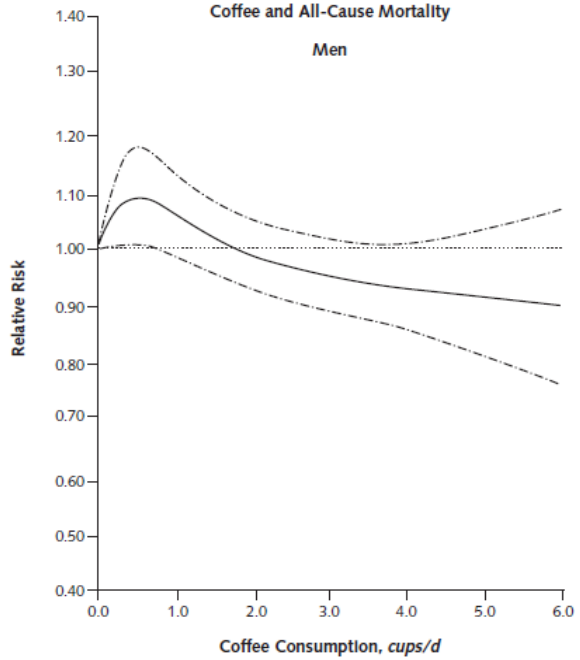
Figure. Subgroup analysis of association between daily coffee consumption and all-cause mortality among men and women.

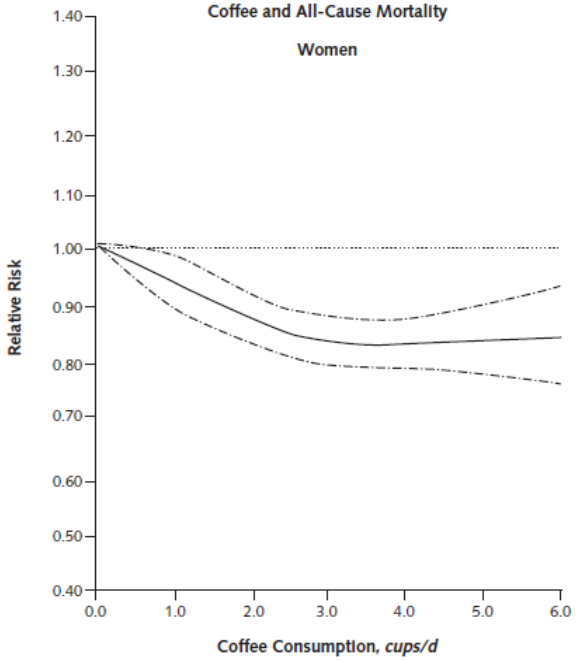


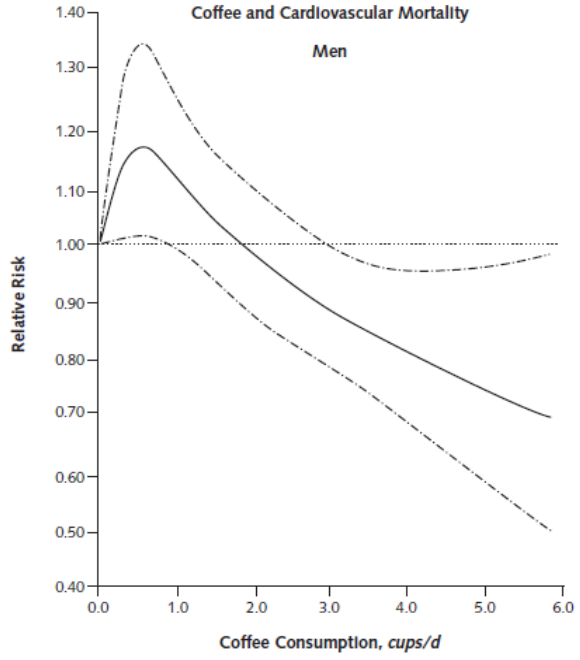
Subgroup	Men		Women	
	Hazard Ratio (95% CI)	*P* Value for Interaction	Hazard Ratio (95% CI)	*P* Value for Interaction
Overall	0.88 (0.82–0.95)		0.93 (0.87–0.98)	
Smoking status		0.017		0.068
Never	0.78 (0.67–0.90)		0.88 (0.81–0.95)	
Former	0.94 (0.83–1.06)		0.94 (0.82–1.08)	
Current	0.90 (0.79–1.04)		0.90 (0.79–1.04)	
Body mass index		0.23		0.23
<25.0 kg/m²	0.92 (0.81–1.05)		0.96 (0.89–1.05)	
25.0–<30.0 kg/m²	0.87 (0.78–0.96)		0.90 (0.80–0.99)	
≥30.0 kg/m²	0.81 (0.69–0.96)		0.86 (0.74–0.99)	
Alcohol consumption*		0.172		0.92
Below median	0.95 (0.86–1.05)		0.94 (0.87–1.01)	
Above median	0.80 (0.72–0.90)		0.90 (0.82–0.99)	
Red and processed meat consumption†		0.66		0.20
Below median	0.86 (0.76–0.98)		0.91 (0.84–0.99)	
Above median	0.89 (0.81–0.98)		0.95 (0.87–1.04)	
Fruit and vegetable consumption‡		0.020		0.64
Below median	0.83 (0.76–0.92)		0.89 (0.81–0.97)	
Above median	0.93 (0.82–1.04)		0.96 (0.89–1.03)	

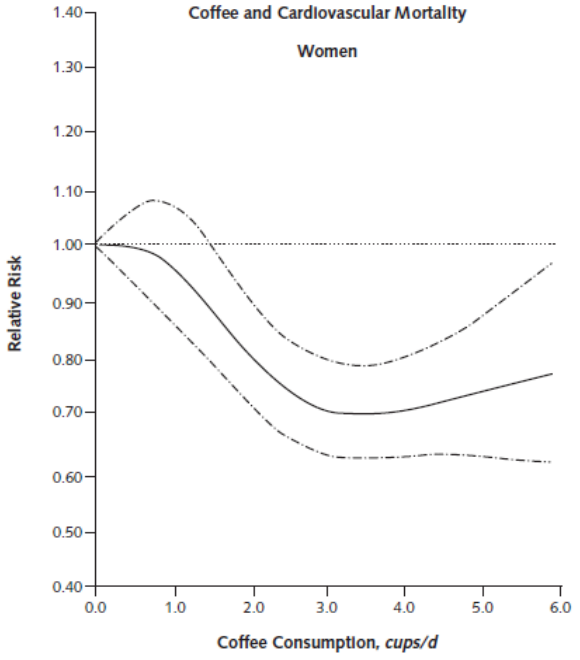
Gunter. Annals of Internal Medicine2017

USA HPFS and NHS
41 736 H
86 214 F









Lopez-Garcia. AnAlsInterMed2008

Café-ine et Pression Artérielle

Source	N	Age, y/Characteristics of Subjects	Type of Study*	Caffeine Dose, mg/d	Effect on Blood Pressure
Robertson et al[6]	9	21-30/caffeine-naive	DB, R, P, crossover, acute	250	Increase
Robertson et al[7]	18	21-52/caffeine-naive	DB, R, P, parallel, acute/long-term	250	Acute, increase; long-term, no change
Ammon et al[8]	10	20-30/7 d off caffeine	DB, R, P (DC), crossover, acute/long-term	504	Acute, increase; long-term, no change
Izzo et al[9]	20	27 ± 1 (n = 12), 62 ± 2 (n = 8)/ caffeine-naive (n = 10), caffeine users (n = 10)	DB, P (n = 8 only), crossover, acute	250	Caffeine-naive, increase; caffeine users, no change
Whitsett et al[10]	54	22-47/off caffeine 24 h	Open-label, R, crossover, acute	2.2 mg/kg	Increase
Van Nguyen and Myers[11]	10	24-42/caffeine-naive	DB, R, P, crossover, acute	300	Increase
Pincomb et al[12]	15	20-35/caffeine abstainers	DB, R, P	3.3 mg/kg	Increase
Smits et al[13]	8	21-25/caffeine users (1-2 d off caffeine)	Open-label, crossover, acute	250-350 (estimated)	Increase
Myers et al[14]	70	36-75/7 d off caffeine after myocardial infarction	DB, R, P, crossover, acute	300	Increase
Smits et al[15]	12	17-38/caffeine users	DB, R, no P, acute	350 (estimated)	Increase
Lang et al[16]	1491	15-70/users and abstainers	Cross-sectional survey, long-term	. . .	Increase (diastolic only)
Lang et al[17]	6321	18-60/users and abstainers	Cross-sectional survey, long-term	. . .	Increase (systolic only)
Klatsky et al[18]	80 000	. . .	Cross-sectional survey, long-term	. . .	Negatively correlated with caffeine use
Prineas et al[19]	7311	37-57/male only	Cross-sectional survey, long-term	. . .	Negatively correlated with caffeine use
Periti et al[20]	500	18-62	Cross-sectional survey, long-term	. . .	Negatively correlated with caffeine use
Charney et al[21]	11	Mean, 37/caffeine users	Open-label, crossover	10 mg/kg	No change
Piters et al[25]	17	40-74/angina patients, caffeine-users	DB, R, P (DC), crossover, acute	100-200 (estimated)	No change

Myers. Arch intern med 1988

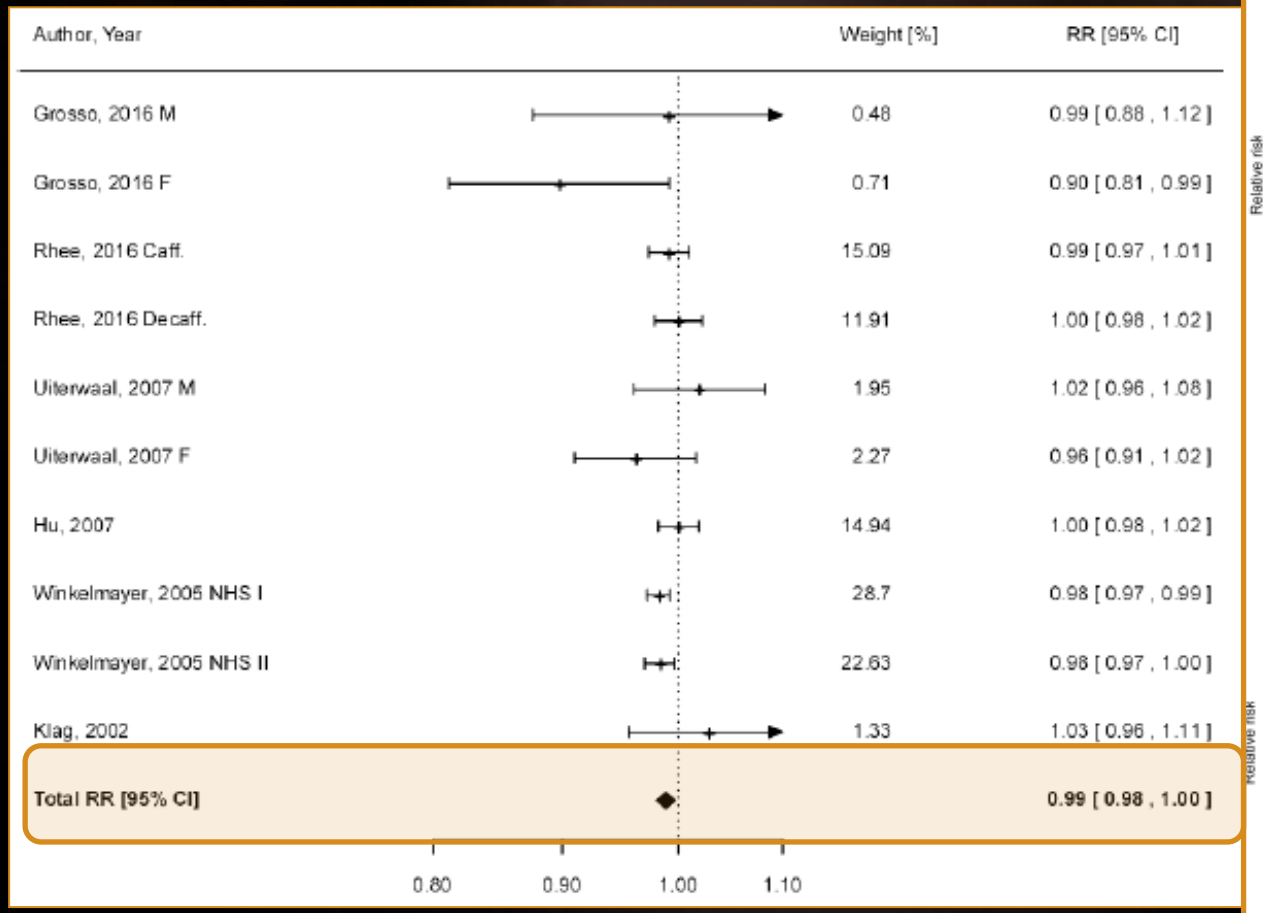
Caféine et pression artérielle: Méta-analyses

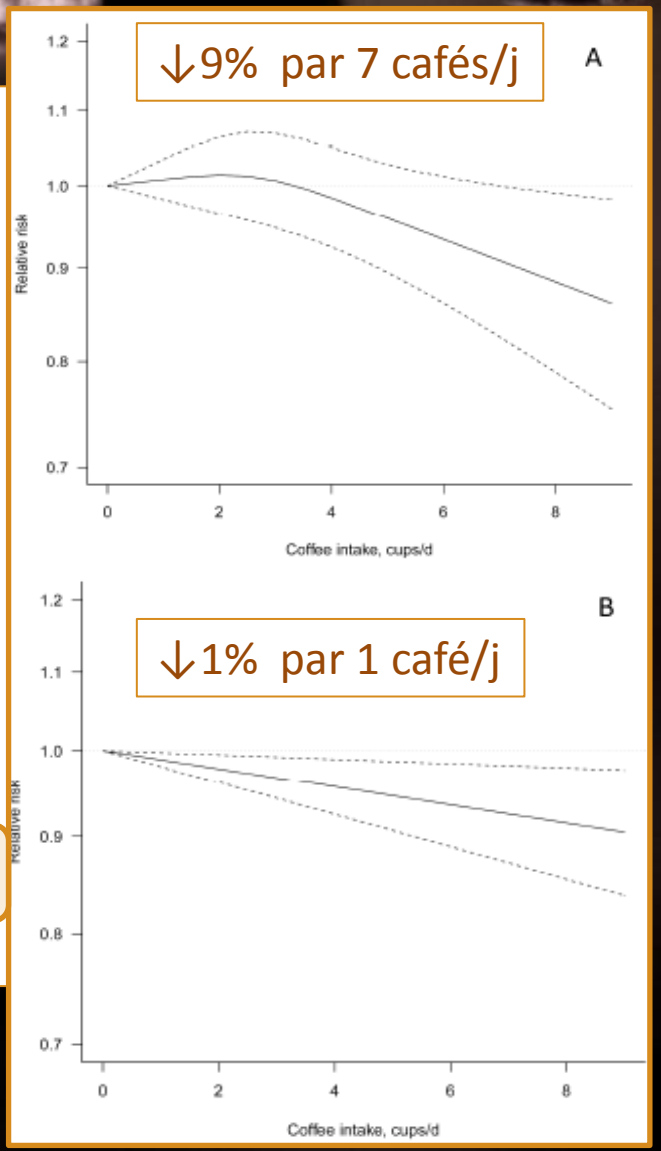
Publication year	Study design included	Number of strata pooled	Number of participants included (% normotensive)	Intervention (caffeine content range) / Exposure	Duration range	Outcome	Overall associations (95% CI)
2012	RCT	10	913 (97%)	Coffee dose (not reported)	6–16 weeks	Change in systolic BP	Coffee dose *vs.* no coffee dose: -0.55 mmHg (-2.46, 1.36)
						Change in diastolic BP	Coffee dose *vs.* no coffee dose: -0.45 mmHg (-1.52, 0.61)
1999	RCT	11	522 (96%)	Coffee dose (504–887 mg)	4–79 days	Change in systolic BP	**Coffee dose *vs.* no coffee dose: 2.4 mmHg (1.0, 3.7)**
						Change in diastolic BP	**Coffee dose *vs.* no coffee dose: 1.2 mmHg (0.4, 2.1)**
2005	RCT	18	1,010 (NS)	Coffee dose (225–798 mg)	9–79 days	Change in systolic BP	Coffee dose *vs.* no coffee or decaffeinated dose: 1.22 mmHg (0.52, 1.92)
						Change in diastolic BP	Coffee dose *vs.* no coffee or decaffeinated dose: 0.49 mmHg (-0.06, 1.04)
2005	RCT	7	159 (NS)	Caffeine-only dose (295–750 mg)	7–84 days	Change in systolic BP	**Caffeine dose *vs.* no caffeine dose: 4.16 mmHg (2.13, 6.2)**
						Change in diastolic BP	Caffeine dose *vs.* no caffeine dose: 2.41 mmHg (0.98, 3.84)
2012	Cohort	4	1,467,130 (100%)	Self-reported coffee intake	6.4–33 years	Risk of HTN	Higher intake *vs.* lower intake: 1.03 (0.98, 1.08)
2011	Cohort	6	172,567 (100%)	Self-reported coffee intake	6.4–33 years	Risk of HTN	**1–3 cups/day *vs.* <1 cup/day: 1.09 (1.01, 1.18)** 3–5 cups /day *vs.* <1 cup/day: 1.07 (0.96, 1.20) >5 cups /day vs. <1 cup/day: 1.08 (0.96, 1.21)

Guessous. CurrHypertReport2014

Caféine et risque HTA: Méta-analyses

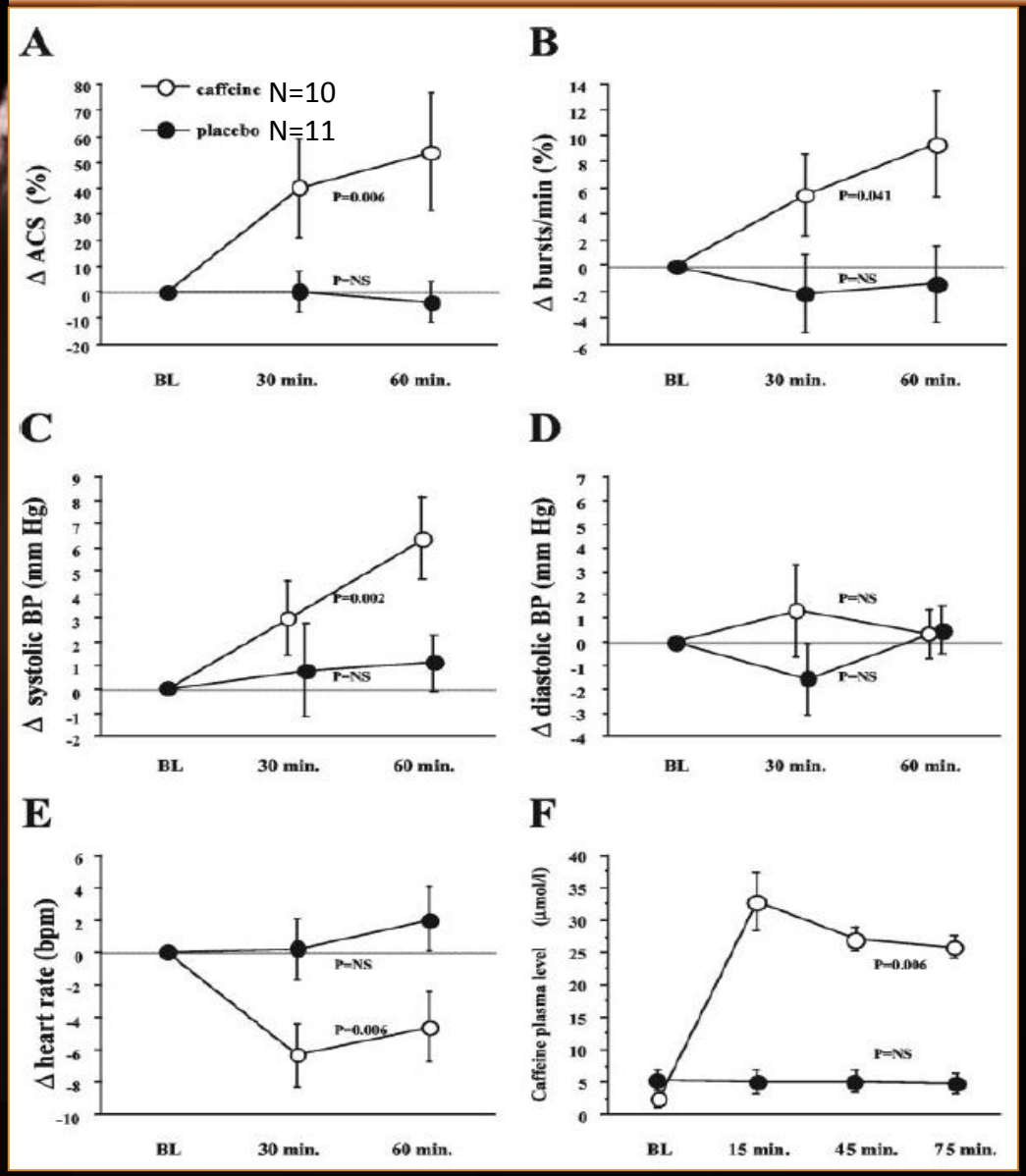
Risque HTA pour 1 café/J dans études de cohortes



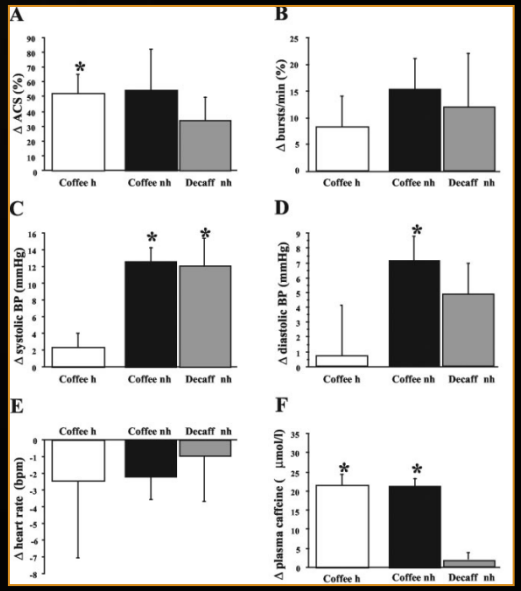


Grosso. Nutrients2017

Caféine: Effets aigus

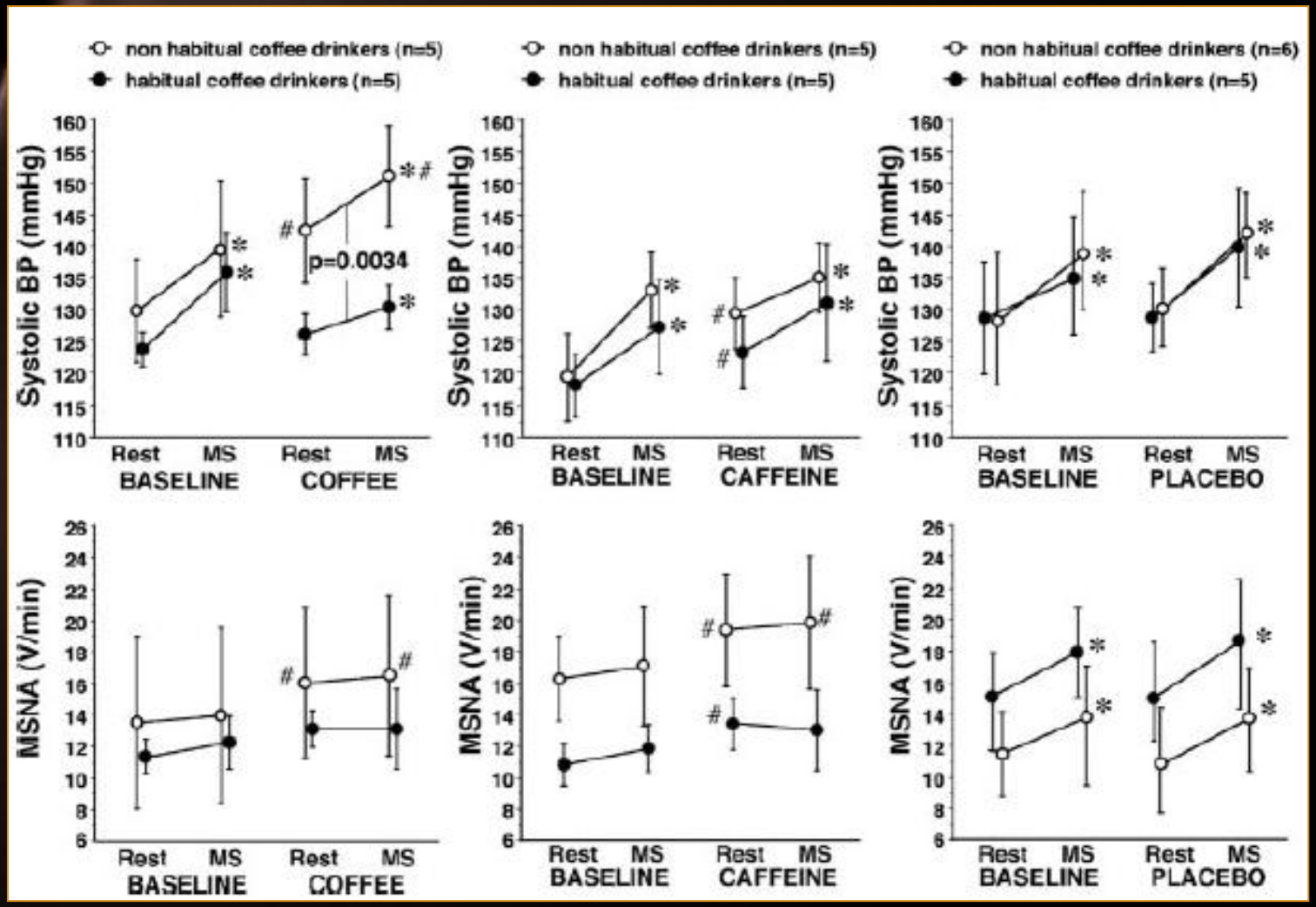


Caféine iv (250mg):
↑Activité sympathique
↑ PA, ↑ FC



Corti. Circulation 2002

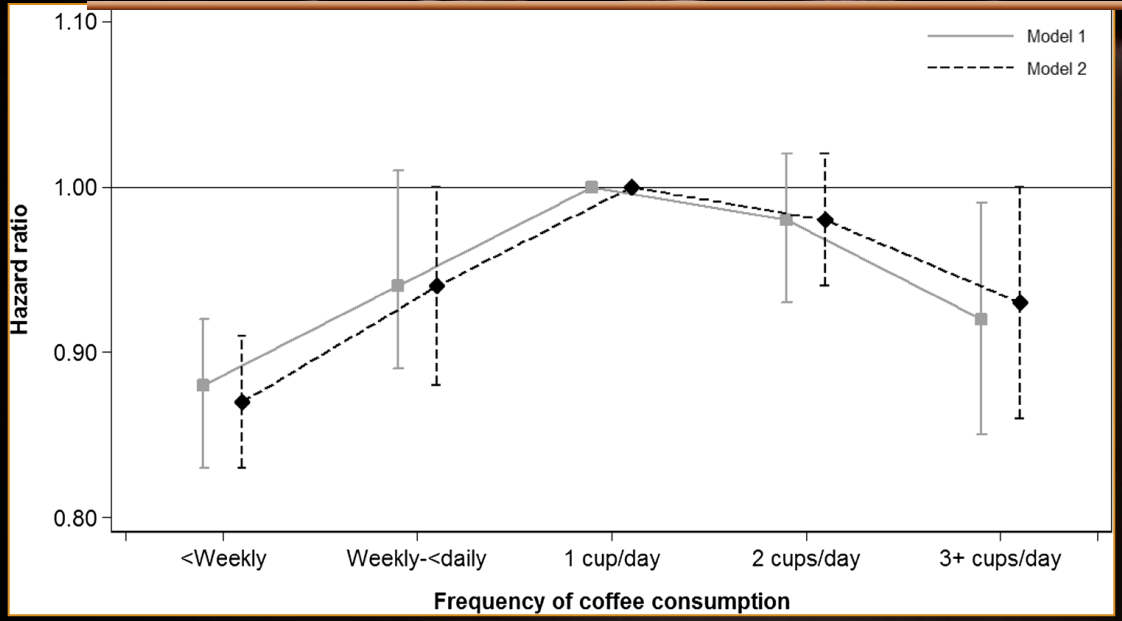
Changement PA selon habitudes



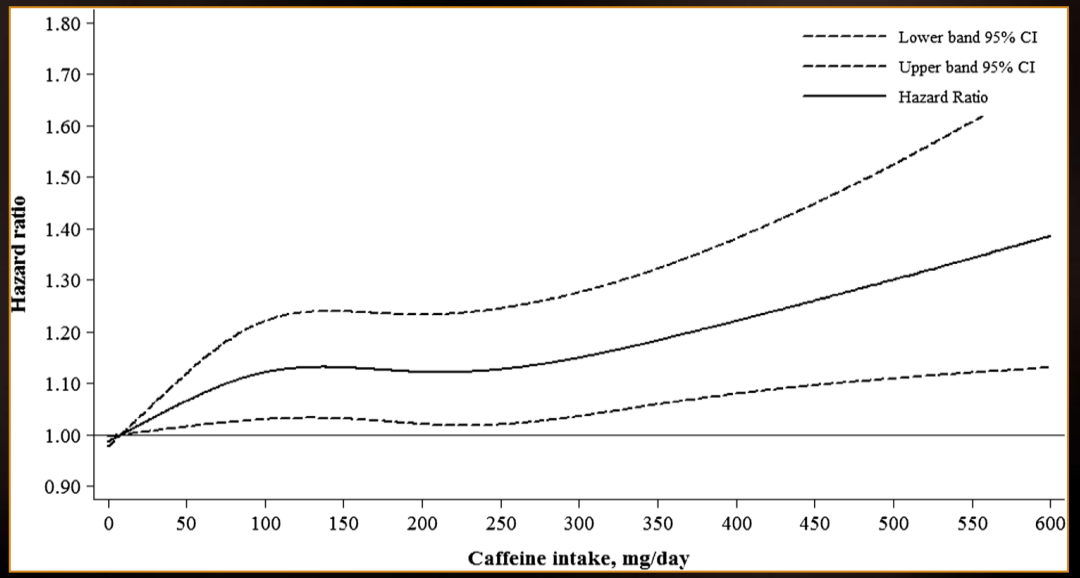
Effet de stress mental (MS) sur PA et activité sympatihque (MSNA)

Sudano. Hypertension 2005

Café chronique et HTA - Singapour



Singapore Health Study:
n=63’257 chinois 45-74 ans



Chei. EurJNutr2018

Café chronique et HTA - SUN

Seguimiento Universidad Navarra
N= 13 374 sans HTA Follow-up 9.1 an

Hazard ratios (95% CI) of hypertension according to baseline regular coffee consumption stratified by sex.

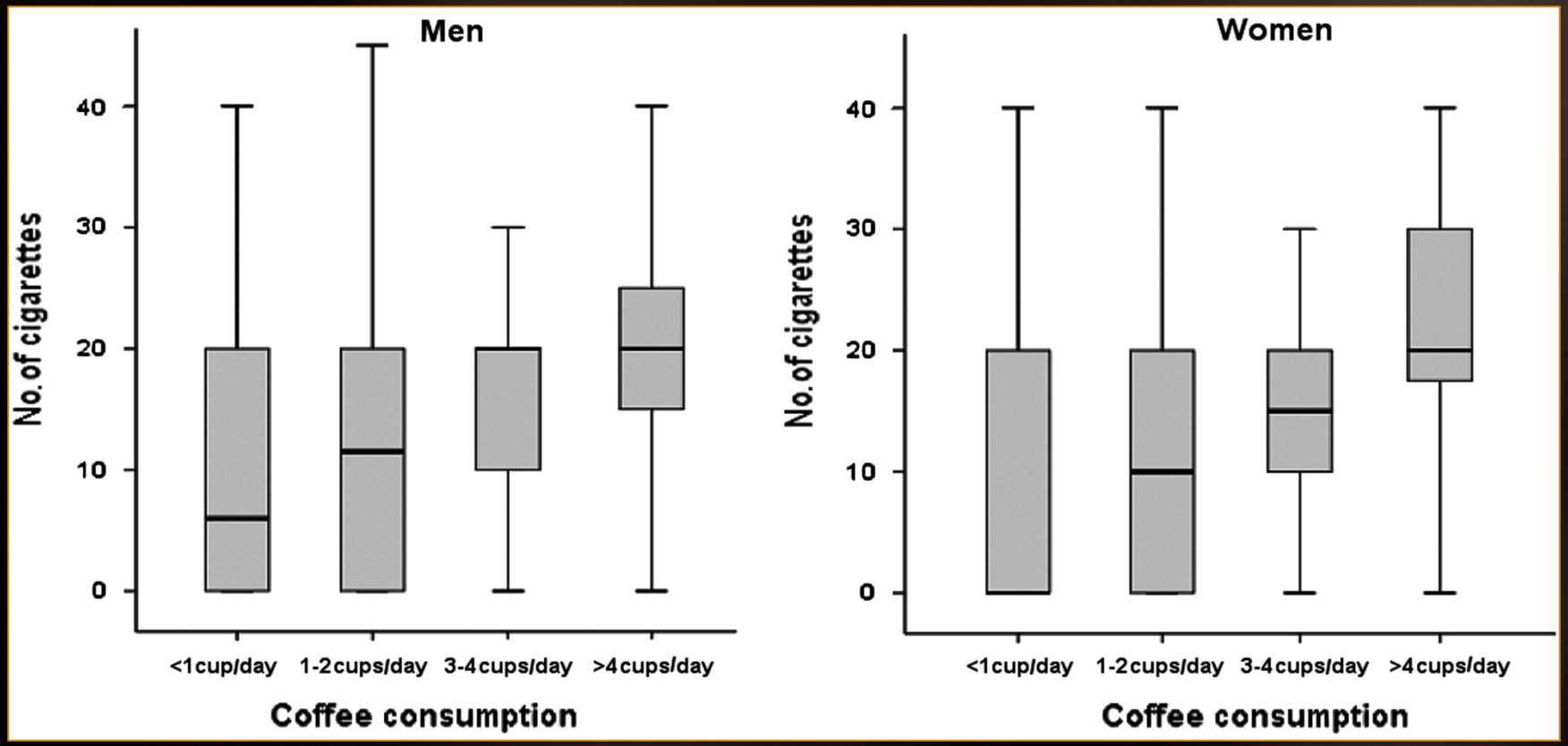
	Regular coffee consumption (cups per day)				
	Never	<1	1	≥2	P for trend
	Men				
n	1005	1048	1103	1668	
Person/years	8718	9284	9711	15219	
Crude model	1 Ref.	1.09 (0.89–1.33)	1.17 (0.97–1.41)	1.04 (0.87–1.24)	0.855
Age, and period adj.	1 Ref.	1.09 (0.90–1.33)	1.15 (0.96–1.40)	1.04 (0.87–1.25)	0.884
Multivariable adj[a]	1 Ref.	1.05 (0.86–1.29)	1.11 (0.92–1.35)	0.97 (0.81.1.17)	0.389
	Women				
n	2053	1552	2105	2840	
Person/year	18174	14148	19221	26923	
Crude model	1 Ref.	0.75 (0.59–0.94)	0.73 (0.59–0.90)	0.77 (0.64–0.93)	0.079
Age, and period adj.	1. Ref.	0.73 (0.58–0.93)	0.72 (0.59–0.89)	0.78 (0.65–0.94)	0.110
Multivariable adj[a]	1 Ref.	0.72 (0.57–0.92)	0.74 (0.60–0.92)	0.74 (0.61–0.91)	0.039

26% réduction risque HTA seulement chez femmes

Chei. EurJNutr2018

Café chronique et HTA -HAPIEE

Health, Alcool and Psychosocial factors in Eastern Europe
N= 2725 sans HTA. Follow-up 5 ans



Consommation de 3-4 café ↓ risque HTA chez non –fumeurs surtout

Chei. EurJNutr2018

Café chronique et HTA -WHIOS

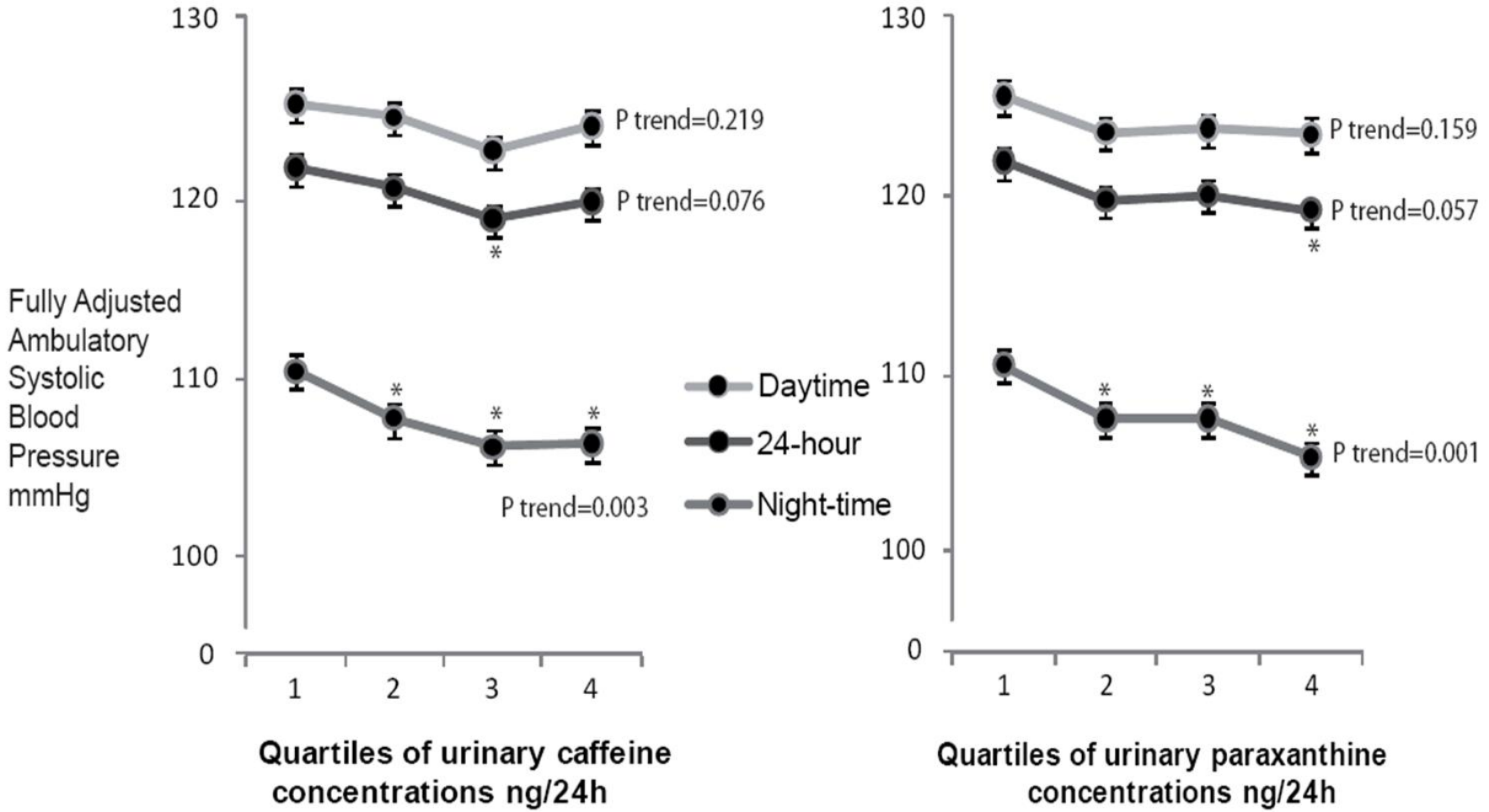
Women Health Initiative Observational Study
N= 29 985 femme ménauposées sans HTA.

	Intake of caffeinated coffee					Intake of decaffeinated coffee				
	0 cups/d (n = 6150)	1 cup/d (n = 6865)	2–3 cups/d (n = 12,473)	≥4 cups/d (n = 4497)	P-trend	0 cups/d (n = 16,634)	1 cup/d (n = 6331)	2–3 cups/d (n = 5555)	≥4 cups/d (n = 1465)	P-trend
Systolic blood pressure										
Model 1[2]										
Mean	119.8	120.1	120.5	119.9	0.60	120.5	119.8	119.8	119.4	<0.001
95% CI	(119.5, 120.2)	(119.8, 120.5)	(120.2, 120.7)	(119.5, 120.3)		(120.3, 120.7)	(119.4, 120.1)	(119.4, 120.2)	(118.7, 120.2)	
Model 2[3]										
Mean	120.9	120.9	121.2	121.0	0.45	121.1	121.0	120.9	120.9	0.06
95% CI	(120.5, 121.4)	(120.5, 121.4)	(120.8, 121.6)	(120.5, 121.5)		(120.7, 121.5)	(120.5, 121.4)	(120.5, 121.4)	(120.1, 121.6)	
Diastolic blood pressure										
Model 1[2]										
Mean	71.2	71.6	71.8	71.3	0.40	71.8	71.2	71.1	70.9	<0.001
95% CI	(71.0, 71.4)	(71.4, 71.8)	(71.7, 72.0)	(71.1, 71.6)		(71.7, 71.9)	(71.2, 71.6)	(71.1, 71.5)	(70.6, 71.5)	
Model 2[3]										
Mean	71.5	71.8	72.0	71.4	0.13	71.9	71.7	71.7	71.5	0.01
95% CI	(71.2, 71.8)	(71.6, 72.1)	(71.7, 72.2)	(71.4, 72.0)		(71.7, 72.1)	(71.5, 72.0)	(71.4, 71.9)	(71.1, 72.0)	

Légère diminution PAD moy lors de prise décaféiné
Pas d'augmentation de risque d'HTA

Rhee. AmJClinNutrition 2016

Caféine / metabolites et pression artérielle



N=836

*P value <0.05 compared to (lowest) quartile 1 (reference)

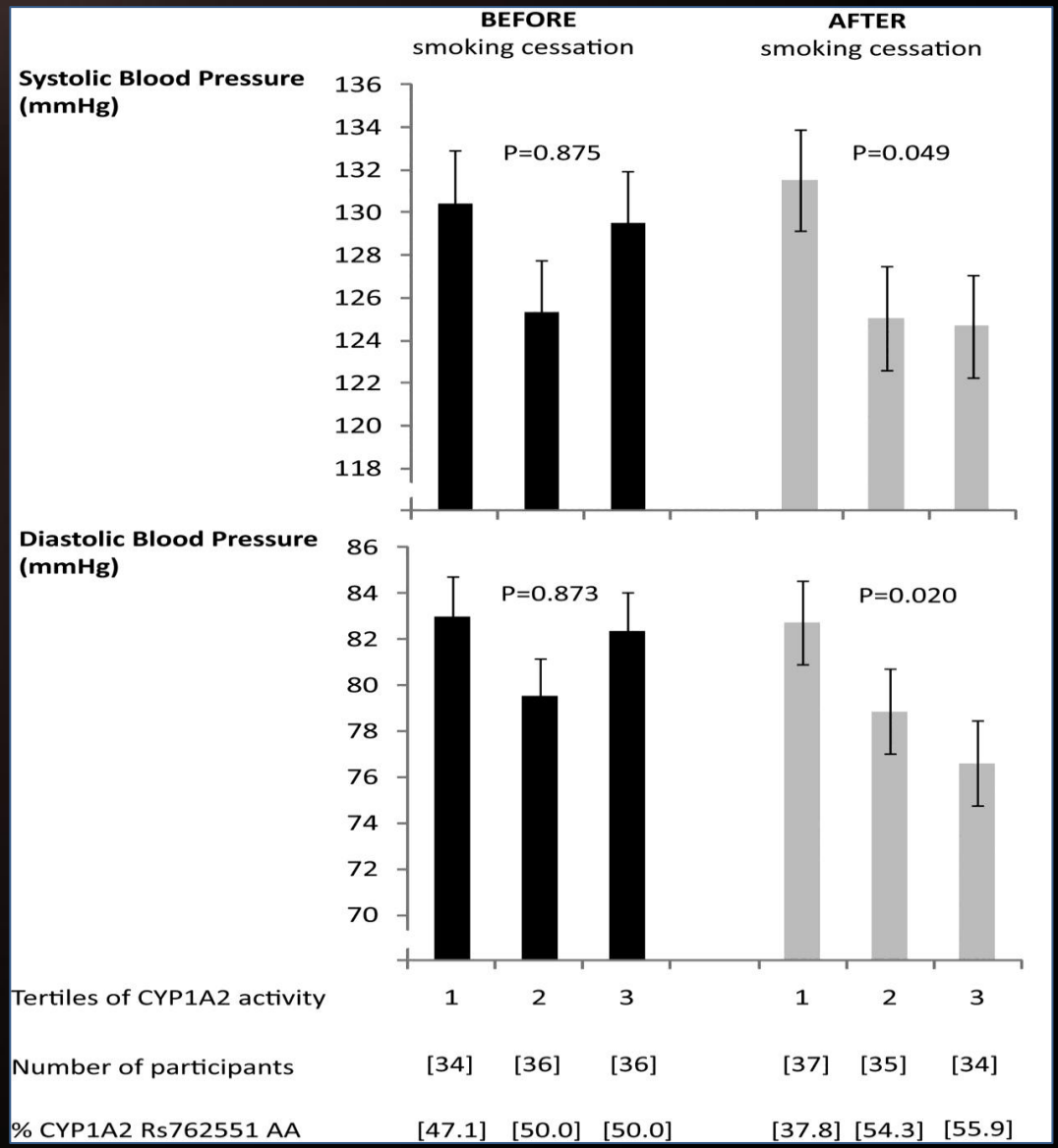
Guessous. Hypertension 2015

Métabolites caféine et pression artérielle

	Systolic BP		Diastolic BP	
Methylxanthine	Beta, SE	*P* Value	Beta, SE	*P* Value
Caffeine*				
24 h	–0.642, 0.296	**0.030**	0.252, 0.182	0.166
Day	–0.505, 0.313	0.107	0.342, 0.202	0.091
Night	–1.107, 0.315	**<0.001**	–0.074, 0.183	0.686
Paraxanthine*				
24 h	–0.718, 0.343	**0.036**	0.353, 0.211	0.094
Day	–0.545, 0.362	0.132	0.442, 0.234	0.059
Night	–1.376, 0.364	**<0.001**	–0.039, 0.212	0.851
Theophylline*				
24 h	–0.633, 0.341	0.064	0.391, 0.209	0.062
Day	–0.458, 0.360	0.204	0.530, 0.232	**0.022**
Night	–1.183, 0.363	**0.001**	–0.032, 0.211	0.881
Theobromine*				
24 h	0.302, 0.338	0.372	0.237, 0.208	0.254
Day	0.325, 0.357	0.363	0.263, 0.230	0.254
Night	0.003, 0.361	0.993	–0.015, 0.209	0.942

Guessous. Hypertension 2015

Effet selon CYP1A2 et tabagisme



Guessous. Hum Mol Gen 2012

Mecanismes potentiels baisse PA

- ✓ Effet natriurétique, diurétique

- ✓ Effets sympathomimetiques
- ✓ Relaxation musculaire
- ✓ Inhibition phosphodiesterase

- ✓ Influence sur la rigidité artérielle ?

Mecanismes potentiels baisse PA

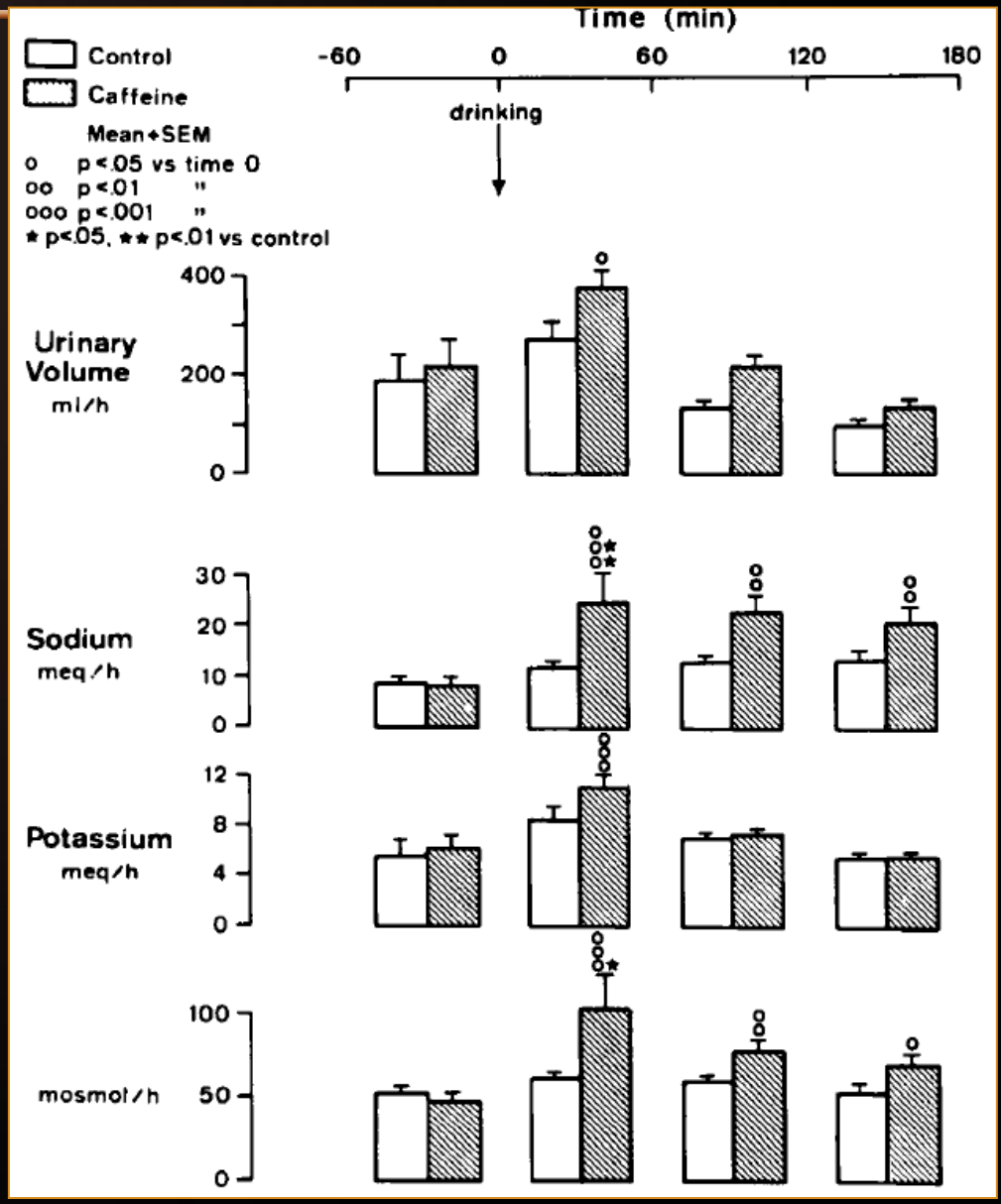
- ✓ Effet natriurétique, diurétique

- ✓ Effets sympathomimetiques
- ✓ Relaxation musculaire
- ✓ Inhibition phosphodiesterase

- ✓ Influence sur la rigidité artérielle ?

Effets natriurétiques-diurétiques

Etude randomisée cross-over
Caféine 250mg po
8 H volontaires sains



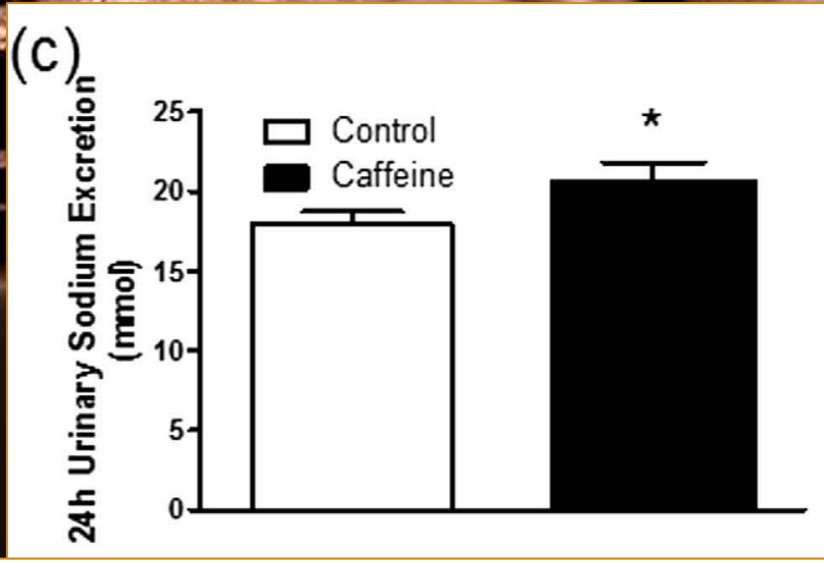
Nussberger. J CArdiovasc1990
Passmore. Clin Scie 1987

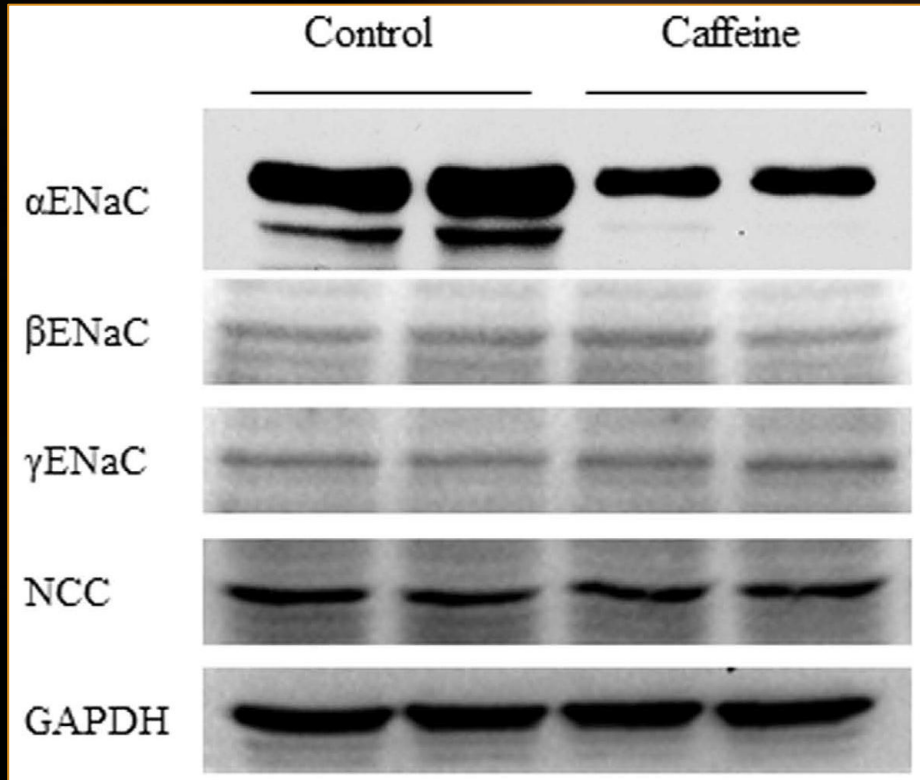
Caféine chronique atténue HTA liée à sel

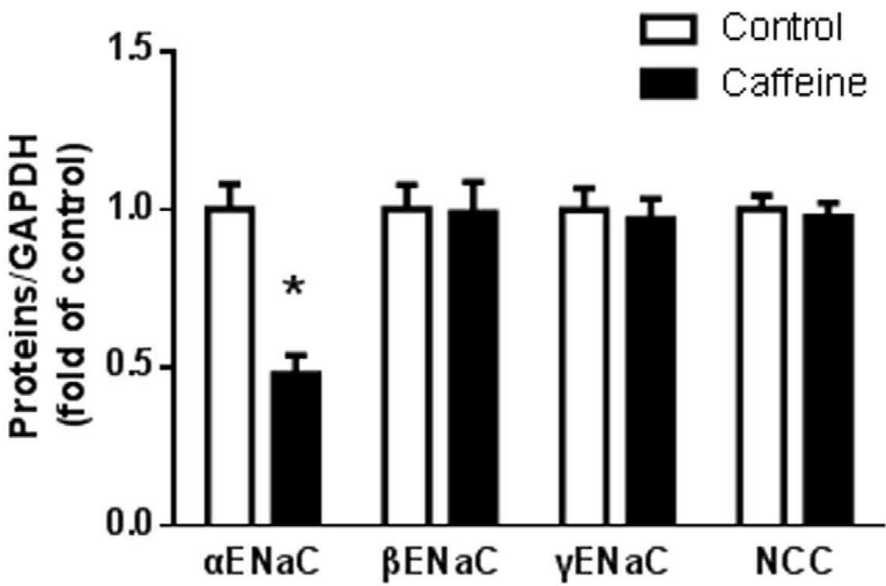
✓Augmente excrétion urinaire Na+

✓Semble médiée par αENax

✓↓ expression Enac médiée par ↑ P-AMPK



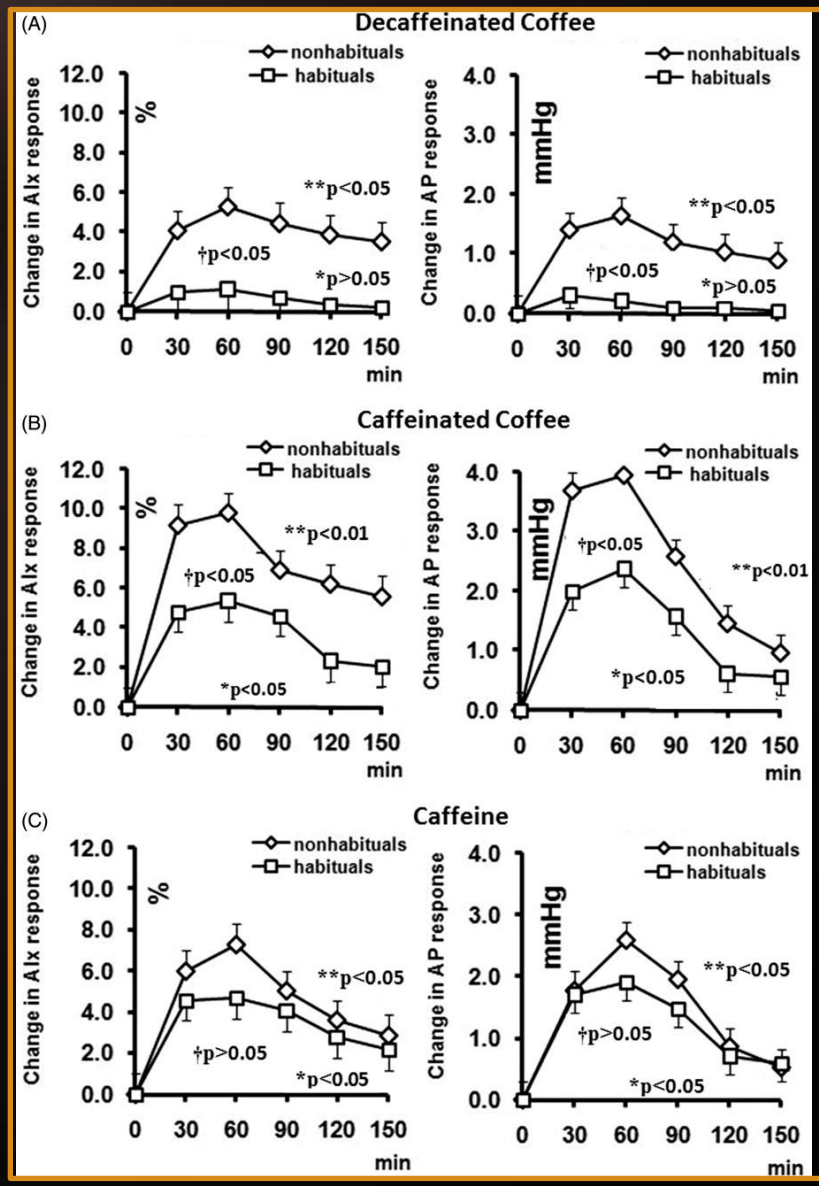


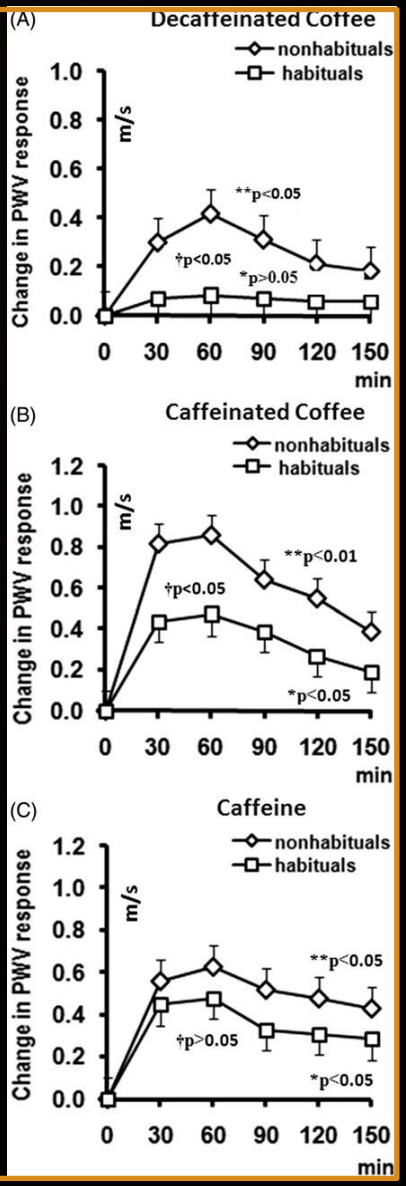


Yu. Scientific rep 2016

Café et rigidité artérielle

Effet aigus sur rigidité artérielle





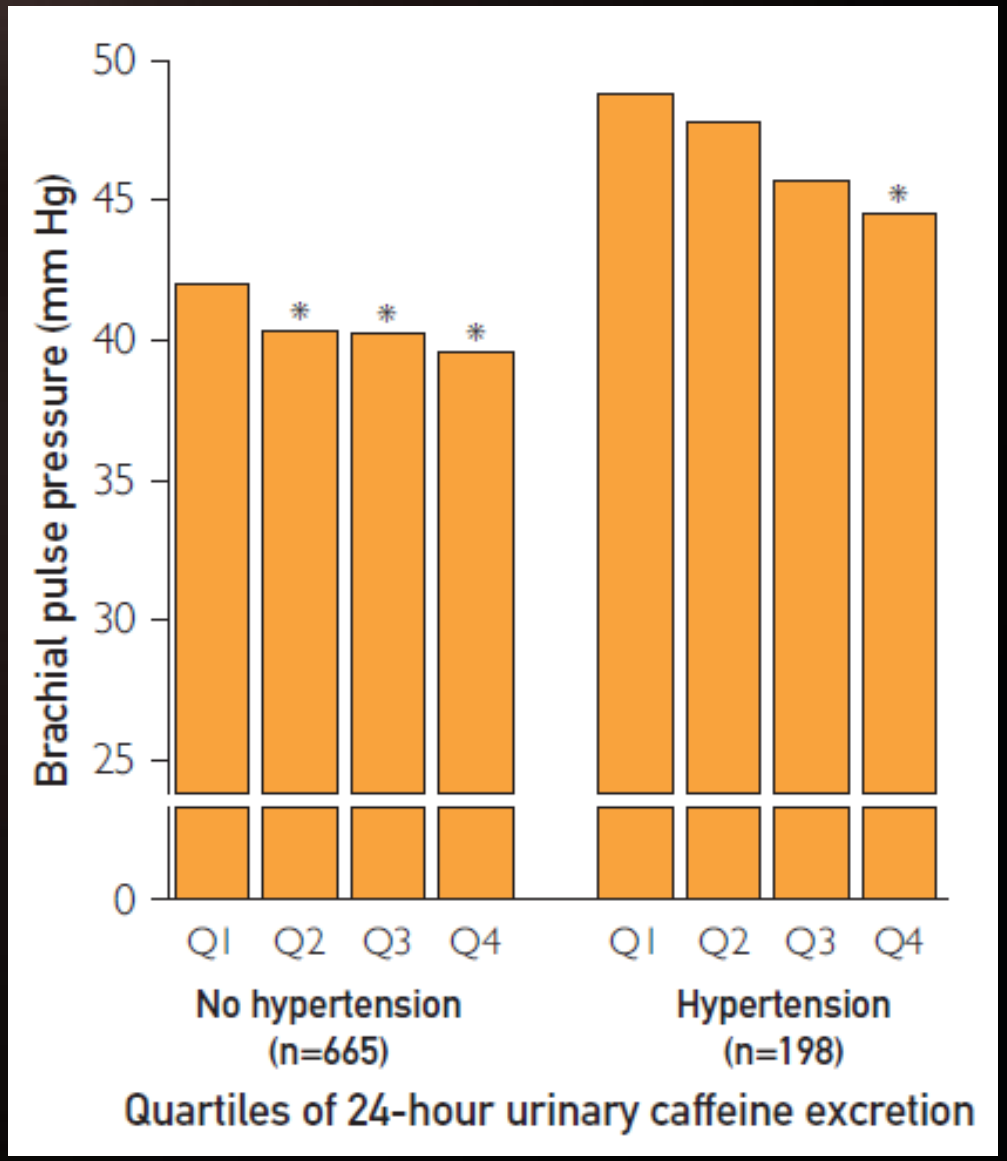
Iokeimidis.
Int J Food Sciences Nutrition 2018
Feely. Hypertension 2001

Caféine et rigidité artérielle

Variable	Brachial pulse pressure (mm Hg)					Pulse wave velocity (m/s)				
	Quartile 1 (lowest)	Quartile 2	Quartile 3	Quartile 4 (highest)	*P* value for linear trend[b]	Quartile 1 (lowest)	Quartile 2	Quartile 3	Quartile 4 (highest)	*P* value for linear trend[b]
Caffeine										
Age-, sex-, center-adjusted	43.9 (0.6)	42.5 (0.6)	40.9 (0.6)[c]	40.4 (0.7)[c]	<.001	8.1 (0.1)	8.1 (0.1)	8.0 (0.1)	7.7 (0.1)[c]	.005
Model 1	43.6 (0.6)	42.4 (0.6)	41.0 (0.6)[c]	40.7 (0.7)[c]	<.001	8.1 (0.1)	8.0 (0.1)	8.0 (0.1)	7.8 (0.1)[c]	.04
Model 2	43.5 (0.5)	42.4 (0.5)	41.2 (0.5)[c]	40.5 (0.6)[c]	<.001	8.1 (0.1)	8.0 (0.1)	8.0 (0.1)	7.8 (0.1)[c]	.03
Paraxanthine										
Age-, sex-, center-adjusted	43.8 (0.6)	42.7 (0.6)	41.1 (0.6)[c]	40.2 (0.6)[c]	<.001	8.1 (0.1)	8.2 (0.1)	7.9 (0.1)	7.7 (0.1)[c]	—
Model 1	43.3 (0.6)	42.8 (0.6)	41.4 (0.6)[c]	40.3 (0.6)[c]	<.001	8.0 (0.1)	8.2 (0.1)	7.9 (0.1)	7.8 (0.1)	—
Model 2	43.3 (0.5)	42.9 (0.5)	41.3 (0.5)[c]	40.2 (0.5)[c]	<.001	8.0 (0.1)	8.2 (0.1)	7.9 (0.1)	7.8 (0.1)	—
Theophylline										
Age-, sex-, center-adjusted	43.6 (0.6)	42.7 (0.6)	41.3 (0.6)[c]	40.1 (0.6)[c]	<.001	8.1 (0.1)	8.1 (0.1)	8.0 (0.1)	7.7 (0.1)[c]	—
Model 1	43.1 (0.6)	43.0 (0.6)	41.2 (0.6)[c]	40.4 (0.6)[c]	.001	8.0 (0.1)	8.1 (0.1)	8.0 (0.1)	7.8 (0.1)[c]	—
Model 2	43.1 (0.5)	42.9 (0.5)	41.6 (0.5)[c]	40.1 (0.5)[c]	<.001	8.0 (0.1)	8.1 (0.1)	8.0 (0.1)	7.7 (0.1)[c]	—
Theobromine										
Age-, sex-, center-adjusted	43.1 (0.6)	41.4 (0.6)[c]	41.2 (0.6)[c]	42.0 (0.6)	—	8.1 (0.1)	8.0 (0.1)	7.9 (0.1)	8.0 (0.1)	—
Model 1	42.8 (0.6)	41.5 (0.6)	41.4 (0.6)	42.1 (0.6)	—	8.0 (0.1)	7.9 (0.1)	7.9 (0.1)	8.0 (0.1)	—
Model 2	42.9 (0.5)	41.5 (0.5)[c]	41.3 (0.5)[c]	42.0 (0.5)	—	8.0 (0.1)	7.9 (0.1)	7.9 (0.1)	8.0 (0.1)	—

Ponte. Mayo Clin Proc 2018

Caféine et Pression Pulsée



Ponte. Mayo Clin Proc 2018

Caféine et Index de résistance rénaux

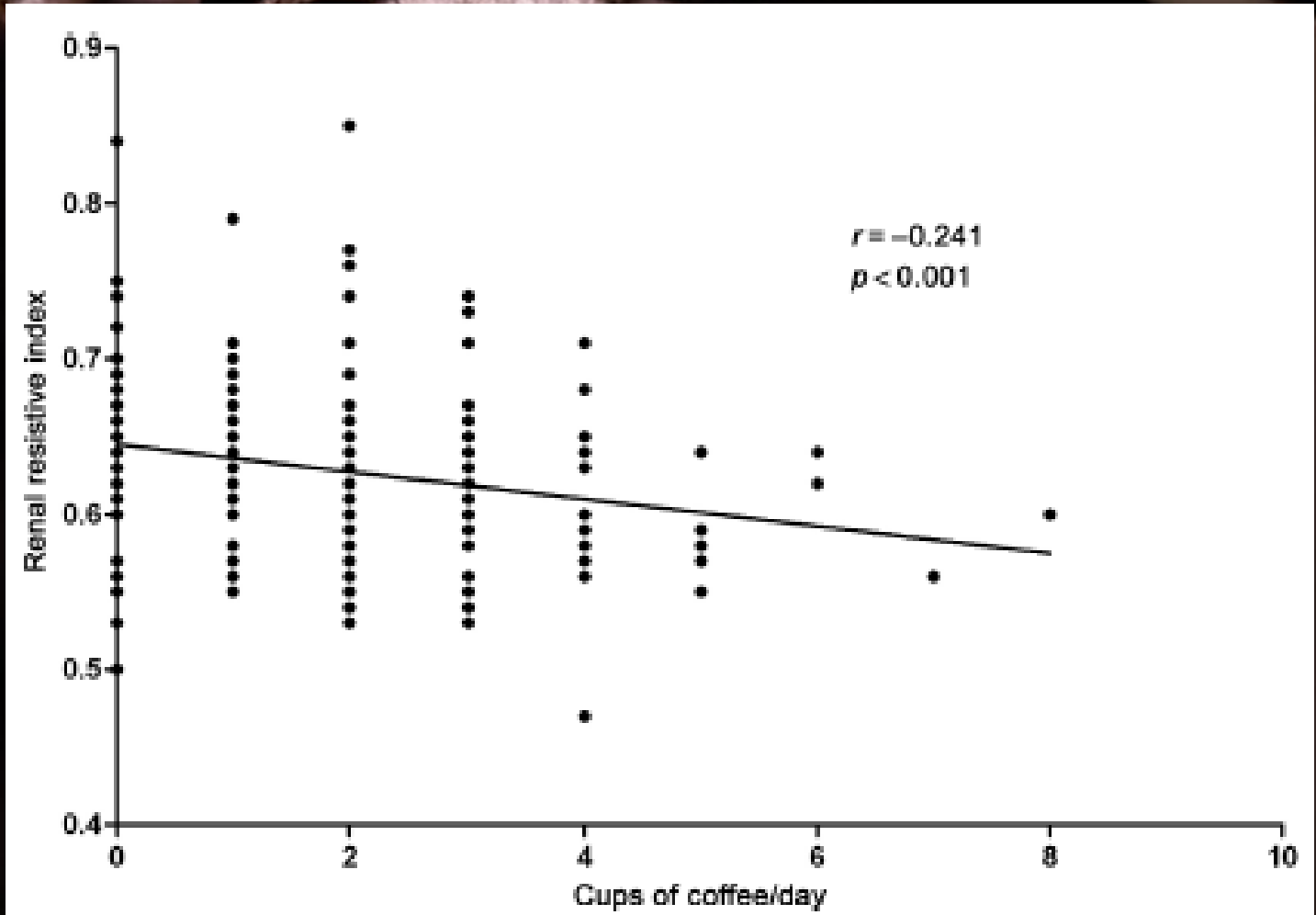


Figure 2. Relationship of renal resistive index versus number of coffee cups/day.

Trovato. Renal Failure 2010

CONCLUSIONS

- Distinguer effets du café et de la caféine

- Effets différents en aigu et chronique
- Effets différents chez consommateur habitué
- Modification effet par: tabagisme
- Rôle de la génétique et du CYP1A2

CONCLUSIONS

- Effet aigu semble ↑ PA
- Effet chronique semble plutôt ↓ PA et risque HTA
  - ✓Liés à natriurèse, diurèse
  - ✓Effets sur rigidité artérielle
- Effets favorables sur mortalité à confirmer

PAS de recommendations dans Sociétés HTA ?

What else.....

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