Sodium et risque CV

G du Cailar

DIU HTA-Risque CV
Novembre 2018

-Estimation de l'apport sodé

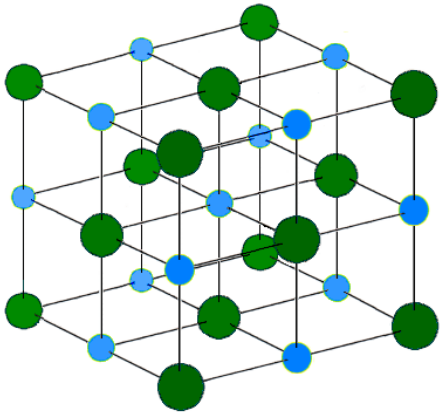
-Sodium et PA

-Sodium et organes cibles de l'HTA

-Le sodium un facteur de risque CV ?

-En pratique: les recommandations

Chaque **gramme** de sel (NaCL) contient **17 mmol** de sodium



La structure d'un cristal de chlorure de sodium.
Légende :
- ***Bleu : = Na^+***
- ***Vert = Cl^-***

Le sel est un assemblage d'ions Na^+ et Cl^- de maille cubique.

Le sel est un cristal, car ses atomes forment une structure périodique et symétrique.

-Cation essentiellement extracellulaire
-Principal déterminant du vol extracel
-Augmentation du pool sodé
=hyperhydratation extracellulaire
-Régulation par le tubule

Test:

-Apport sodé moyen à Montpellier

-Recommendations chez l’hypertendu ?

-Apport sodé à Montpellier

Languedoc : UnaV 150 et 170 mmol/24h

respectivement chez la femme et chez l'homme (10 g)

40% des hommes plus de 11g NaCl /j
40% des femmes plus de 8g NaCl/j

Prise en charge de l'HTA
1ère étape

- Mesures hygiéno-diététiques:
  - Limitation de la consommation en sel 6-8 g/j **(100 mmol à 150 mmol)**
  - Réduction de la surcharge pondérale: IMC < 25 kg/m², ou ↓ poids 10%
  - Activité physique: 30 min, 3x/semaine
  - Alcool: H: < 3 vdv; F < 2 vdv
  - Arrêt du tabac
  - Régime riche en légumes, en fruits et pauvre en graisses saturées

ESTIMATION OF DIETARY SODIUM INTAKE

-Dietary Recall	No
-Na/Creat ratio in first morning urine	No
-24-h urine collection	Yes

Where is Salt ?

Table salt added	**10%**
Cooking	**5%**
Food salt	**85%**

Roquefort	**3g/100g**
Emmental	**1.5g/100g**
Parmesan	**2.5g/100g**
Jambon de Parme	**6.2g/100g**
Corn Flakes	**3g/100g**
Bacon	**4.6g/100g**
Pain	**1.5g/100g**

Sodium content of Fast Foods
(in mmoles of sodium)

• French dip sandwich	76
• Chicken dinner	66
• Taco salad	48
• Chili	48
• Pepperoni pizza	47
• Double hamburger	43
• Turkey sandwich	41
• Fish sandwich	35

DETERMINANTS DE LA CONSOMMATION DE SEL

Correlations univariées de UNaV avec:

Sexe masculin		**Positive**
IMC		**Positive**
	2.52 imc+64.9	**Femme**
	4.25 imc+56.5	**Homme**

Sexe et IMC expliquent 20 % de la variance

Sodium requis vs appetit pour sodium?

Sodium et risque cardiovasculaire

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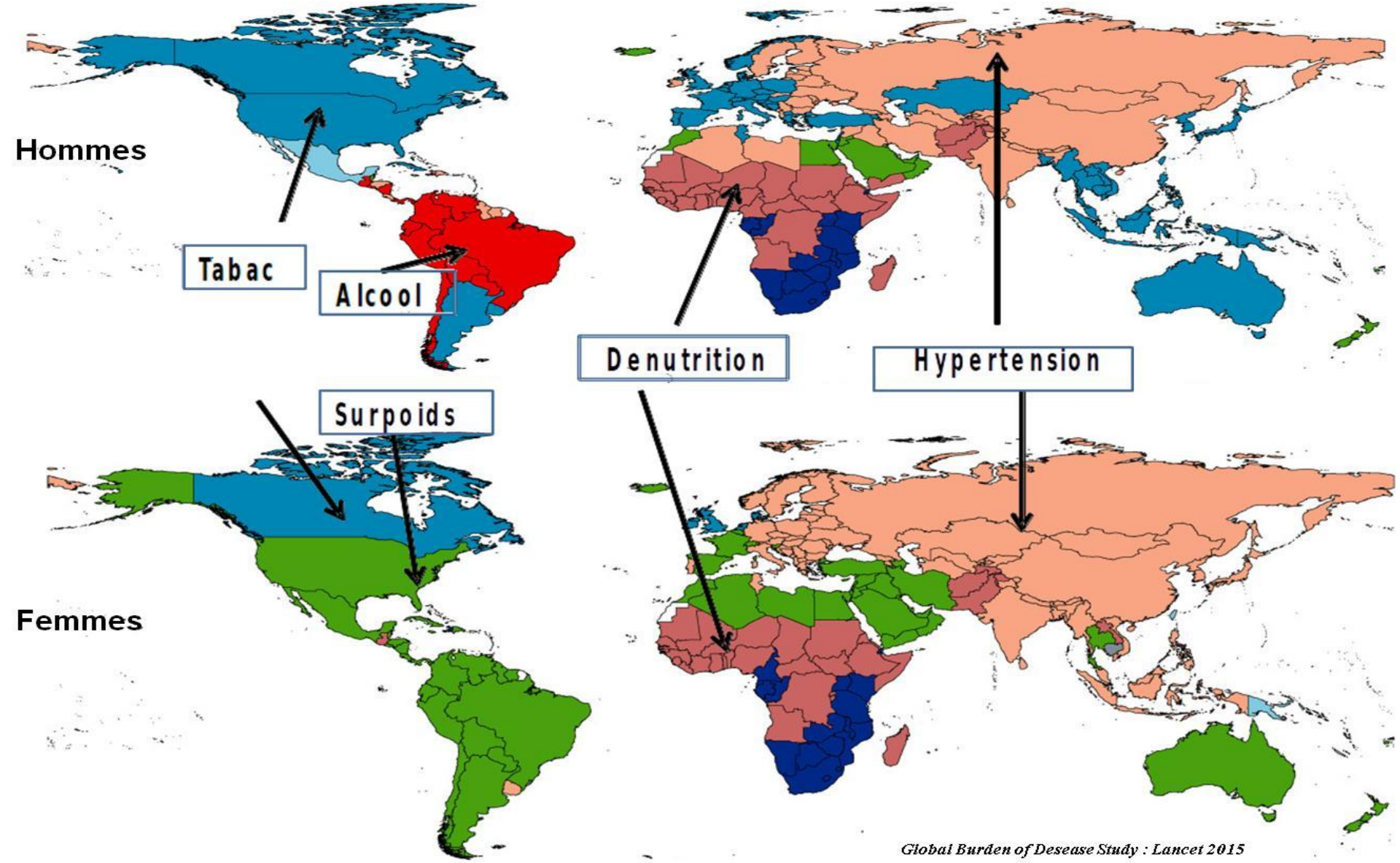
HTA première cause mondiale de réduction de l'espérance de vie en bonne santé



Global Burden of Desease Study : Lancet 2015

Sodium et pression artérielle

Questions ?

- **Relation sodium et PA ?**
- **Facteurs pouvant influencer cette relation**
- **Restriction sodée et PA ?**

INDIENS YANOMAMO

PA: 90/60 mmHg

La plus petite consommation de sel:

Forets équatoriale d'Amazonie: Bresil nord et Venezuela sud

24-h urine: 1-4mmoles/j Sodium
152 mmoles/j Potassium

Nourriture habituelle: Bananes cuites, poisson,legumes sauvages

Poids moyen: 48.4kg (controles 72kg)

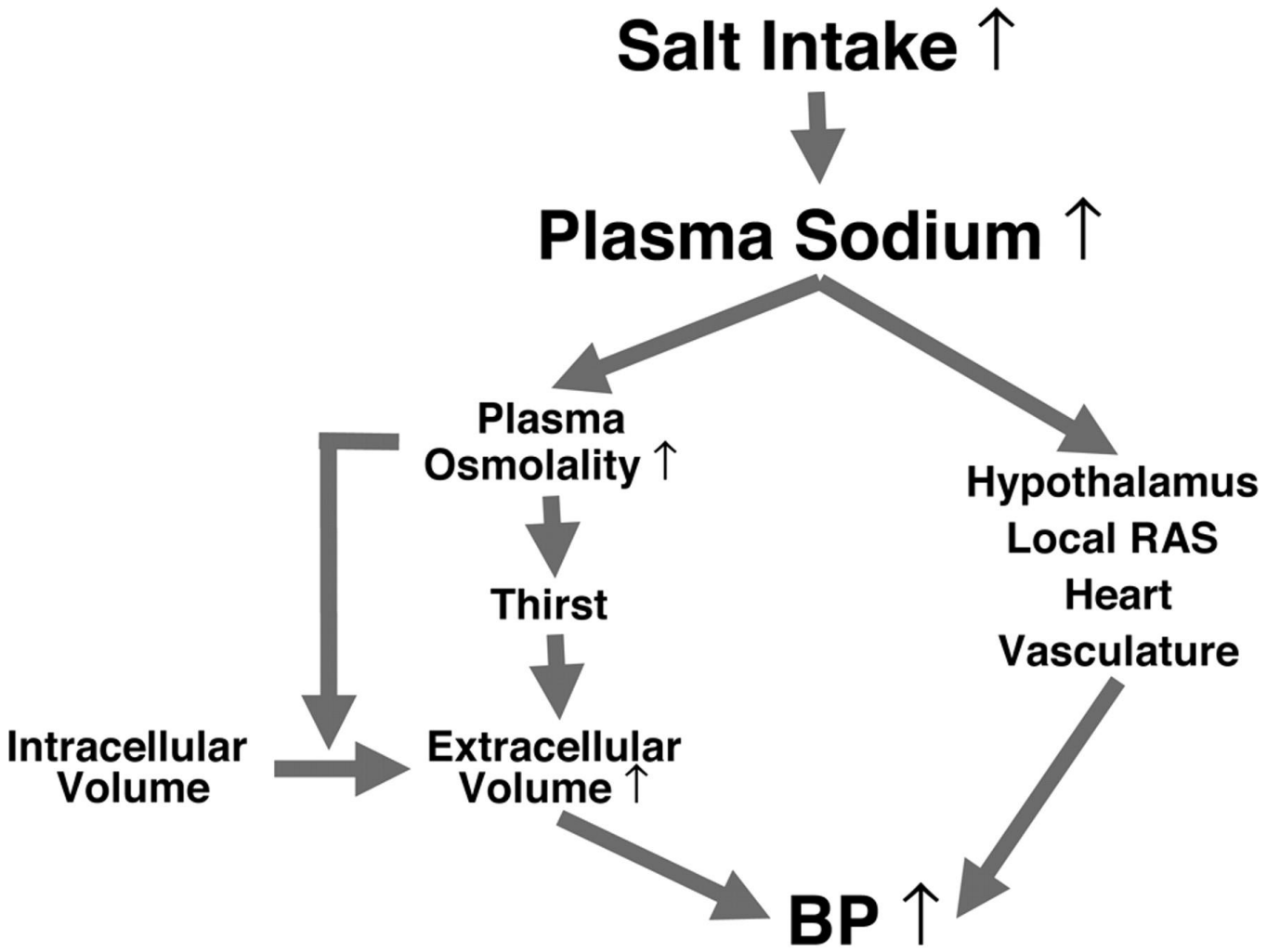
Creatininurie: 8.5mmoles/j

Renine et aldosterone élevées

La PA augmente pendant 1ere and 2^{ieme} decade puis reste constante ulterieurement

Esperance de vie de 42ans (Brésil 67ans)
Taux de Mortalité 2 fois le reste du Bresil: Tuberculose ++

Hypothesis on the possible links between salt intake, plasma sodium, and blood pressure



He, F. J. et al. Hypertension 2005;45:98-102

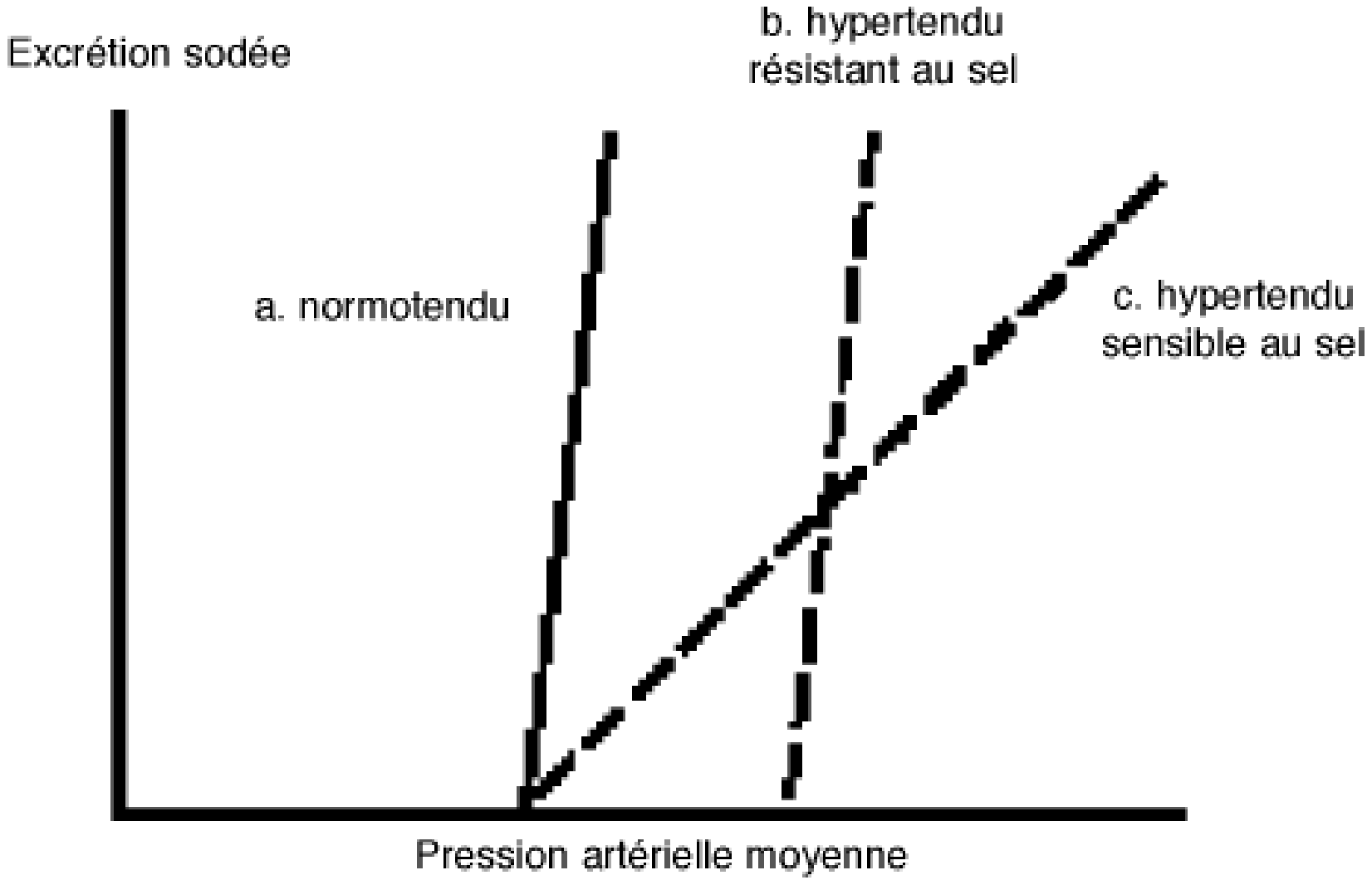
-Facteurs pouvant influencer la relation PA et apport sodé

-Relation pression-natriurèse
-Determinants génétiques
-Age
-Sensibilité au sel
……

Relation pression natriurèse

Guyton et al 1972

Augmentation de la consommation en sel et PA



Sodium sensitivity

Incidence of Sodium sensitivity (Sullivan et al Hypertension 1987,9:398)

20% in Normotensive subjects

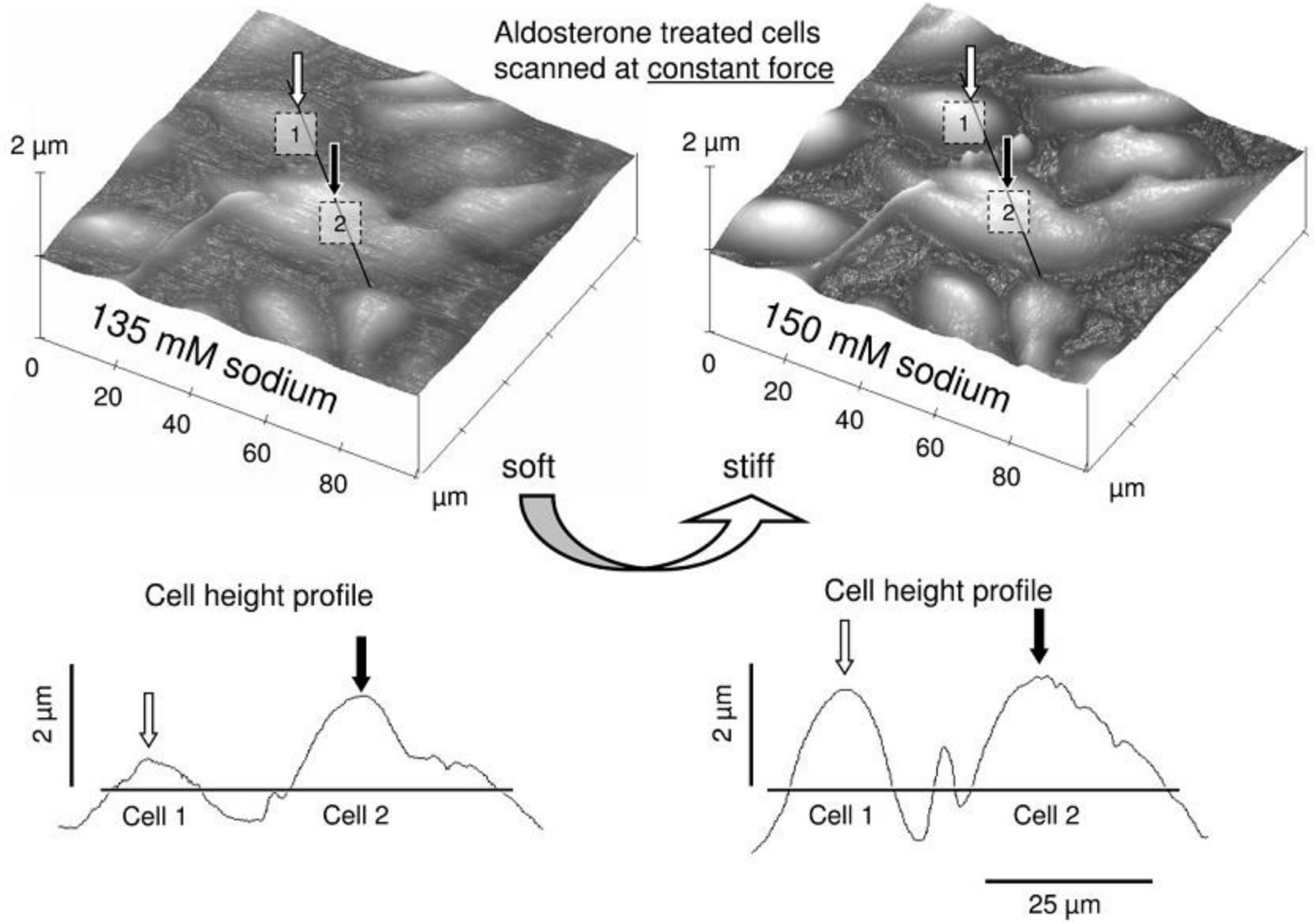
35 to 50% in Hypertensive subjects

Determinants of sensitivity of BP to dietary Sodium

- Older age
- Black race
- Overweight
- Type 2 Diabetes
-Lower Plasma Renin concentration
-Menopause chirurgicale

Uric acid and MA

Plasma sodium stiffens vascular endothelium and reduces nitric oxide release.



Oberleithner et al PNAS 2007;104:16281

Amplification of sodium intake on the risk of developing hypertension

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Association Between Sodium Intake and Change in Uric Acid, Urine Albumin Excretion, and the Risk of Developing Hypertension

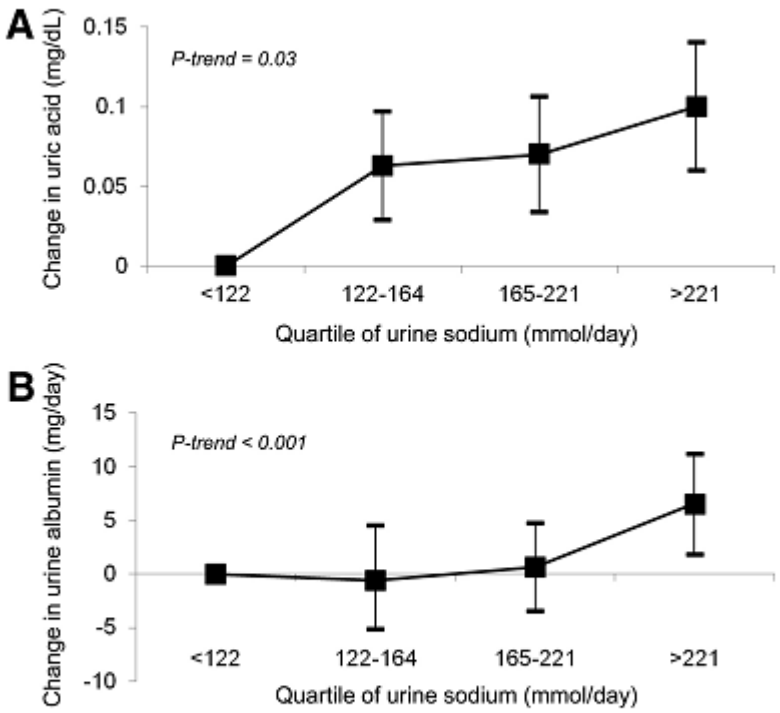
John P. Forman, Lieneke Scheven, Paul E. de Jong, Stephan J.L. Bakker, Gary C. Curhan and Ron T. Gansevoort

Circulation. 2012;125:3108-3116; originally published online June 18, 2012;

Endothelial dysfunction ?

Sodium intake as a marker of endothelial dysfonction

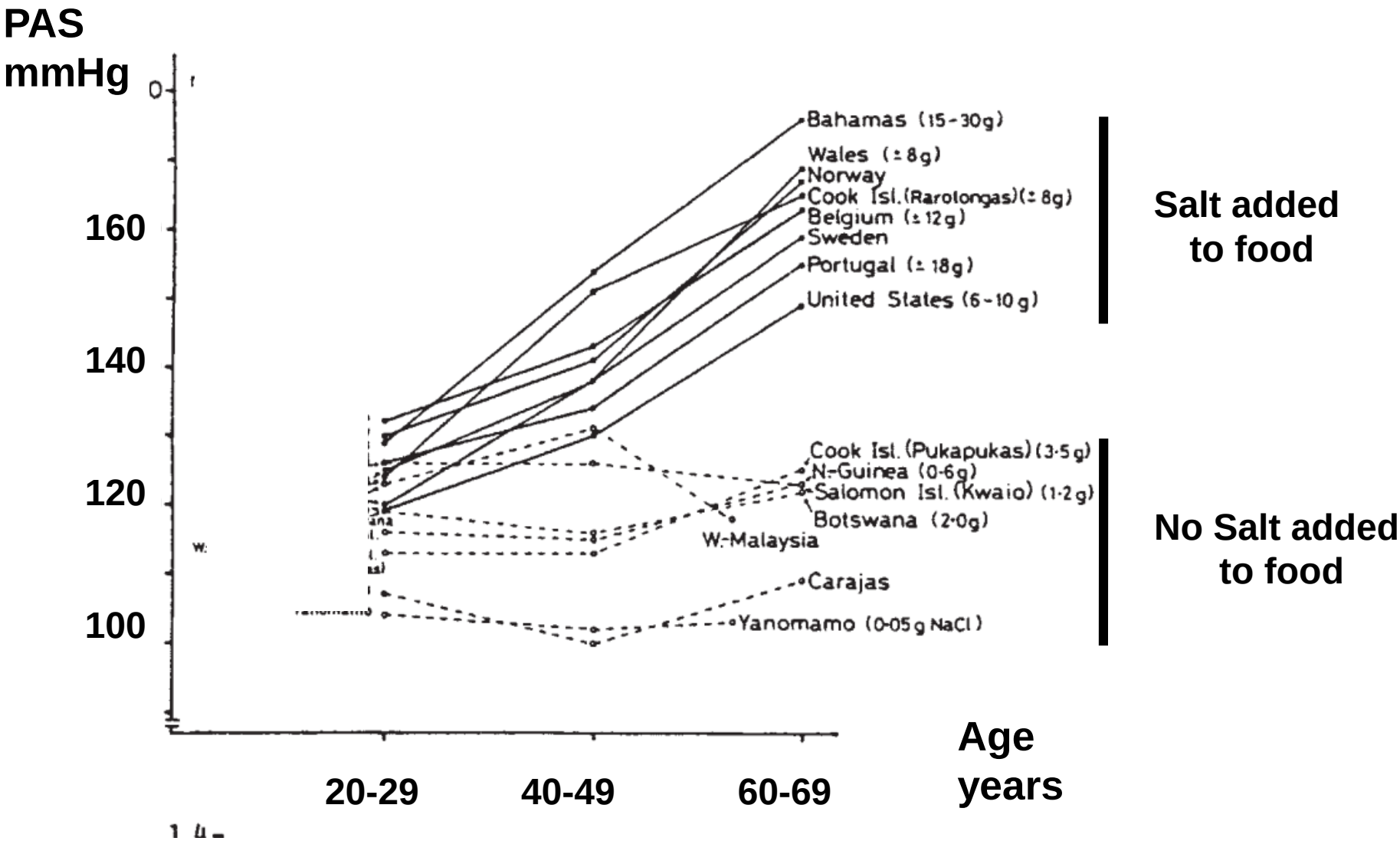
Forman et al : Circulation 2012



Quartile of UNaV

Change in UAE an UA during follow-up according to sodium intake

Influence of Age and Salt on BP



Skin Sodium and Hypertension: a Paradigm Shift?

Curr Hypertens Rep (2018) 20: 94

Viknesh Selvarajah [1] · Kathleen Connolly [1] · Carmel McEniery [1] · Ian Wilkinson [1]

A ‘Three-Compartment Model’ of Body Sodium

The Skin as a ‘Third Compartment’ of Body Sodium and Relevance to BP

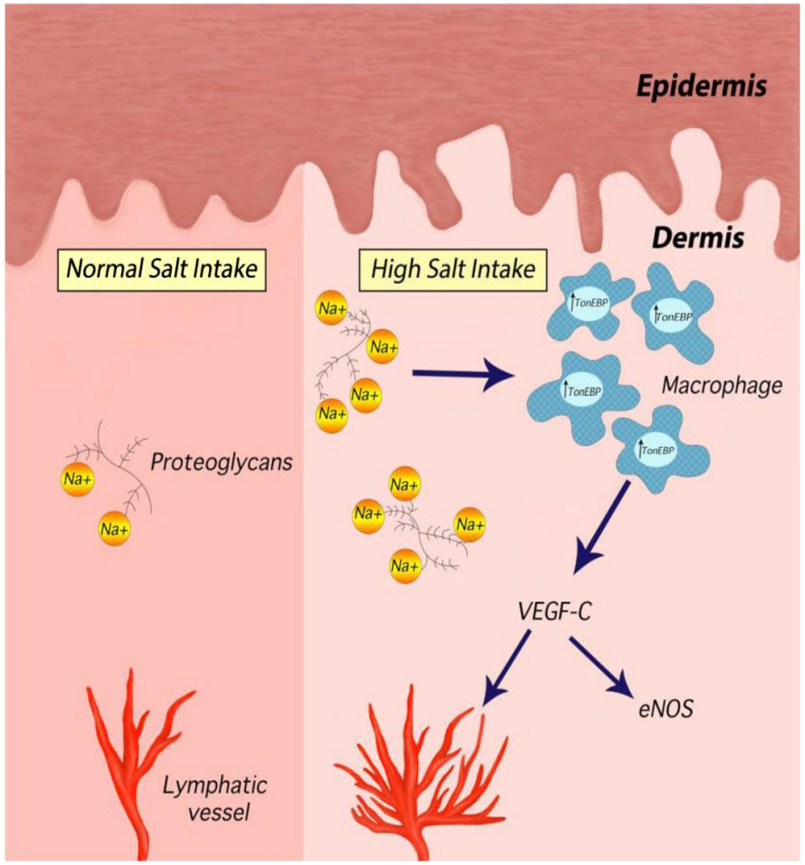
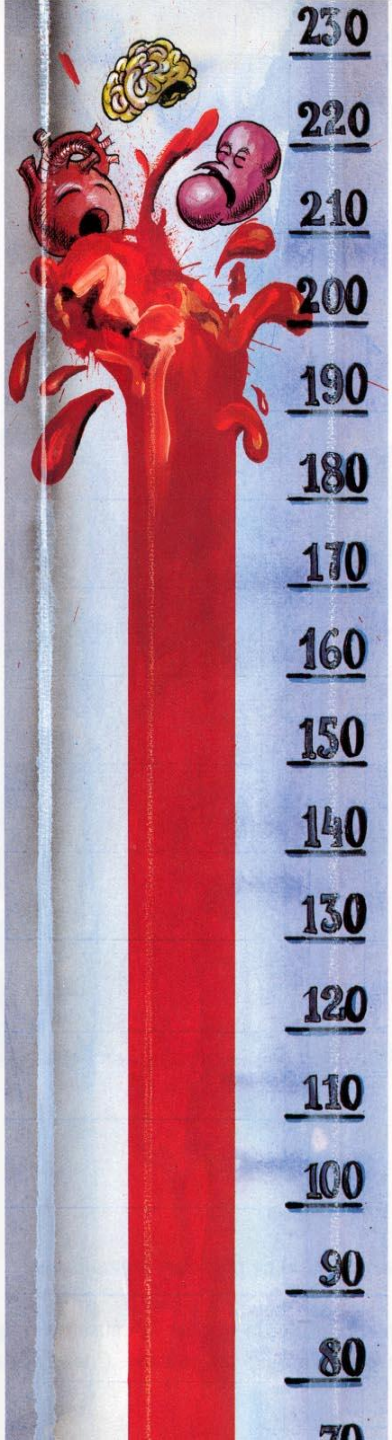


Fig. 1 A novel extra-renal mechanism for buffering dietary salt.



Sodium et pression artérielle

Questions ?

-**Relation sodium et PA ? oui**

-**Facteurs pouvant influencer cette relation**

-**Restriction sodée et PA ?**

Question: peut on diminuer la PA en diminuant l'apport sodé ?

DASH: Dietary Approaches to Stop HT

NEJM 200

120/88
160/95
150-100-50 mmol/24h
30 days
n=412

SAP
mmHg

135
130
125
120

Control Diet
Dash Diet

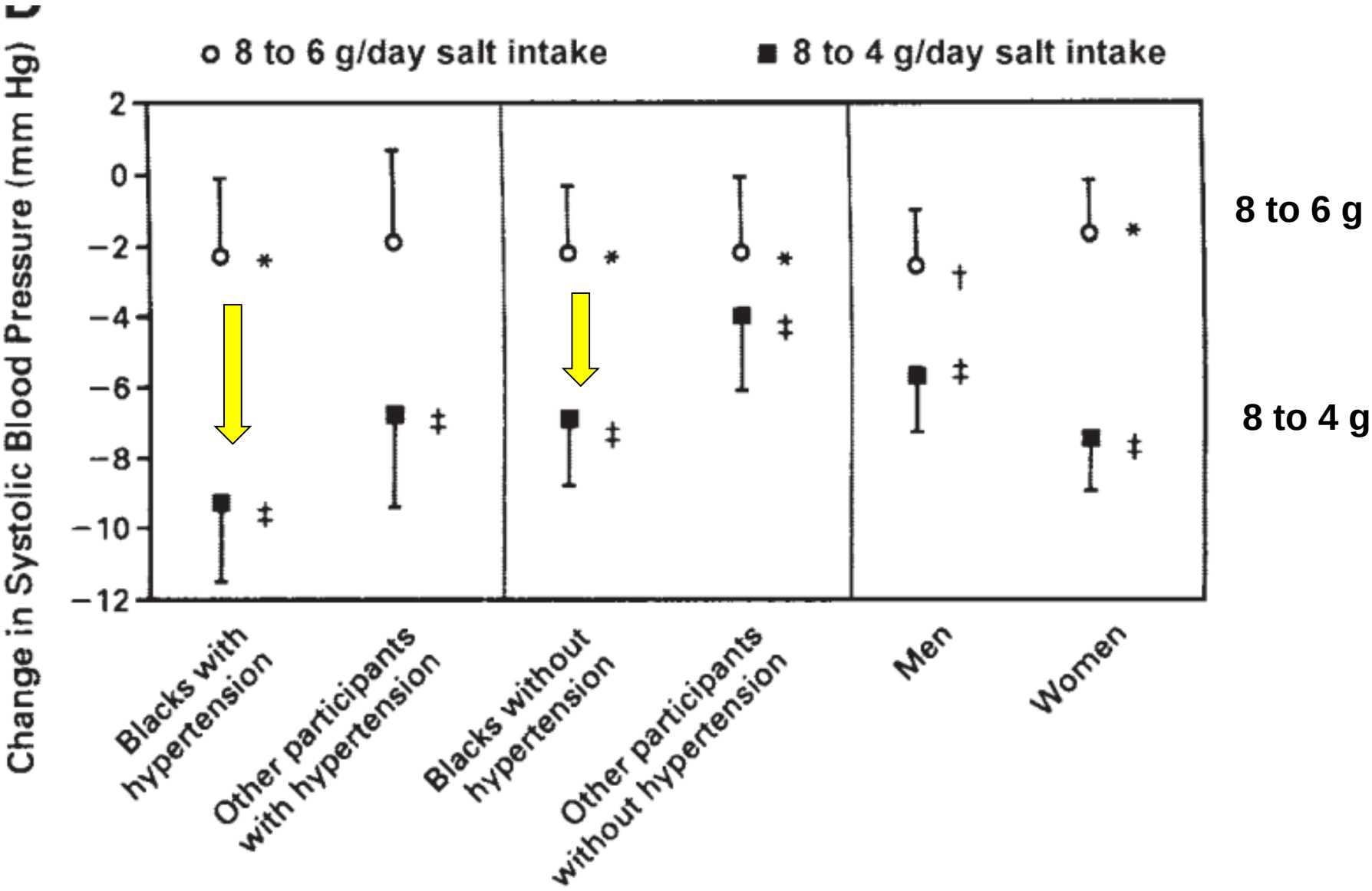
6.7
9

Delta PAS :mmHg

High 150 (9)
Intermediate 100 (6)
Low 50 (3)

Sodium intake
mmol/24h
grammes NaCl

DASH: BP according population



Sodium et risque cardiovasculaire

DIU HTA-Risque CV
Novembre 2018

-Estimation de l'apport sodé

-Sodium et PA

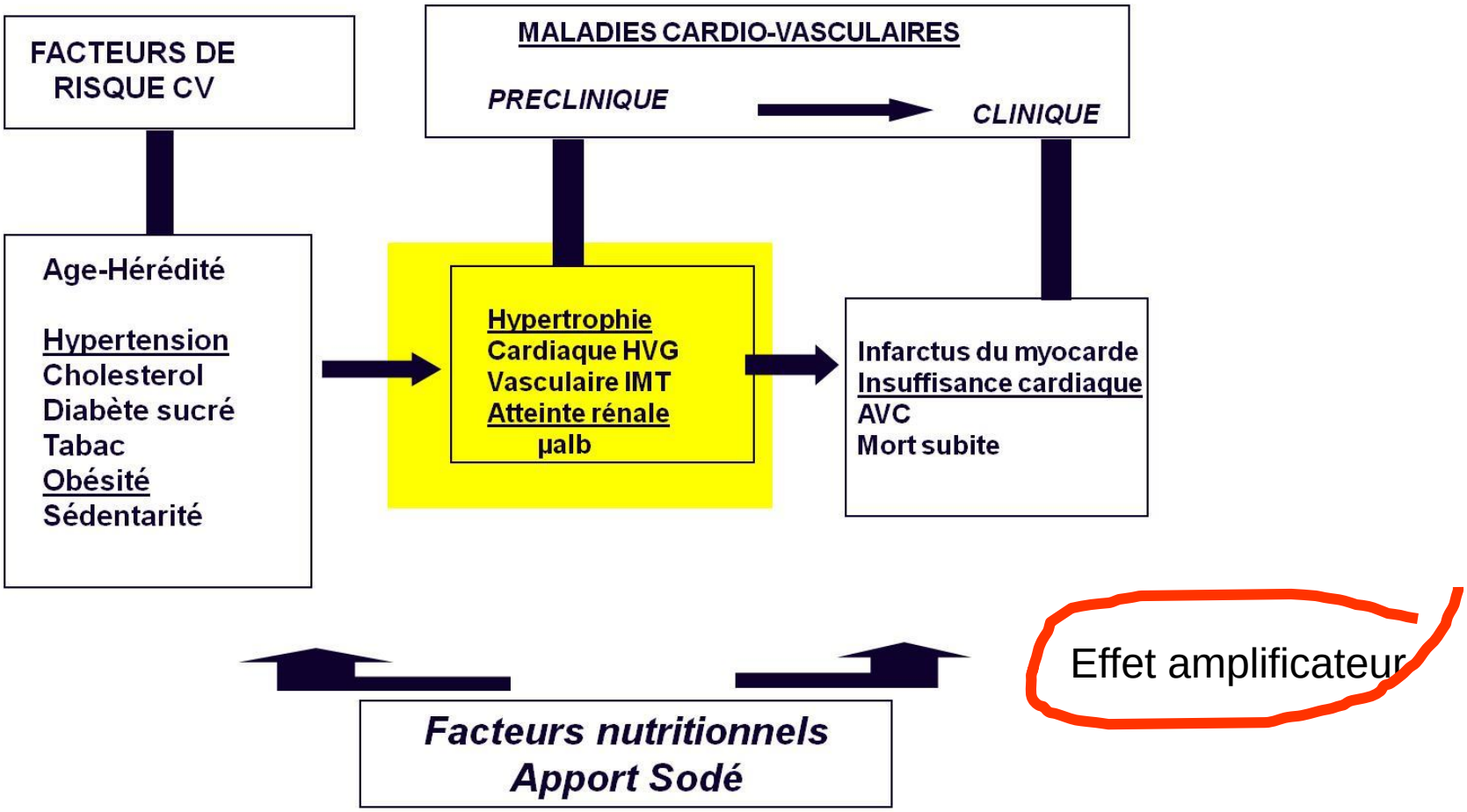
-Sodium et organes cibles de l'HTA

-Le sodium un facteur de risque CV ?

-En pratique: les recommandations

Existe-t-il d'autres arguments que la seule diminution de la PA pour recommander une limitation de l'apport sodé ?

Effet « pleiotrope » de l'apport sodé: PA , Organes cibles…..



La réponse immunitaire et inflammatoire à l'élévation de l'apport sodé

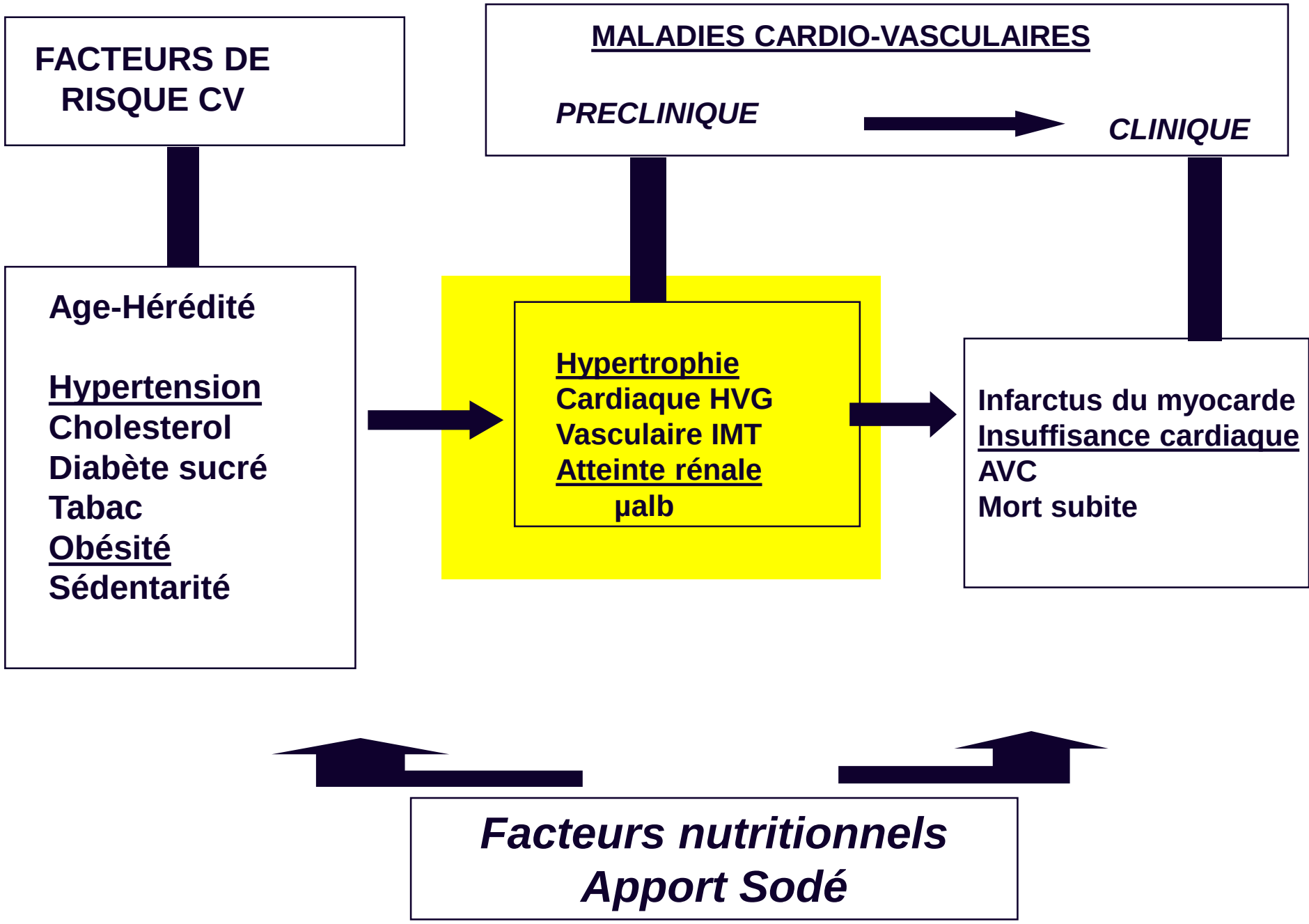
.Le sodium alimentaire est associé à la génération de lymphocytes T "Helper" 17 et en diminuant les T régulateurs.

.Les lymphocytes Th17 sécrètent de l'IL 17 et jouent un rôle important dans la régulation de l'auto-immunité et de l'inflammation.

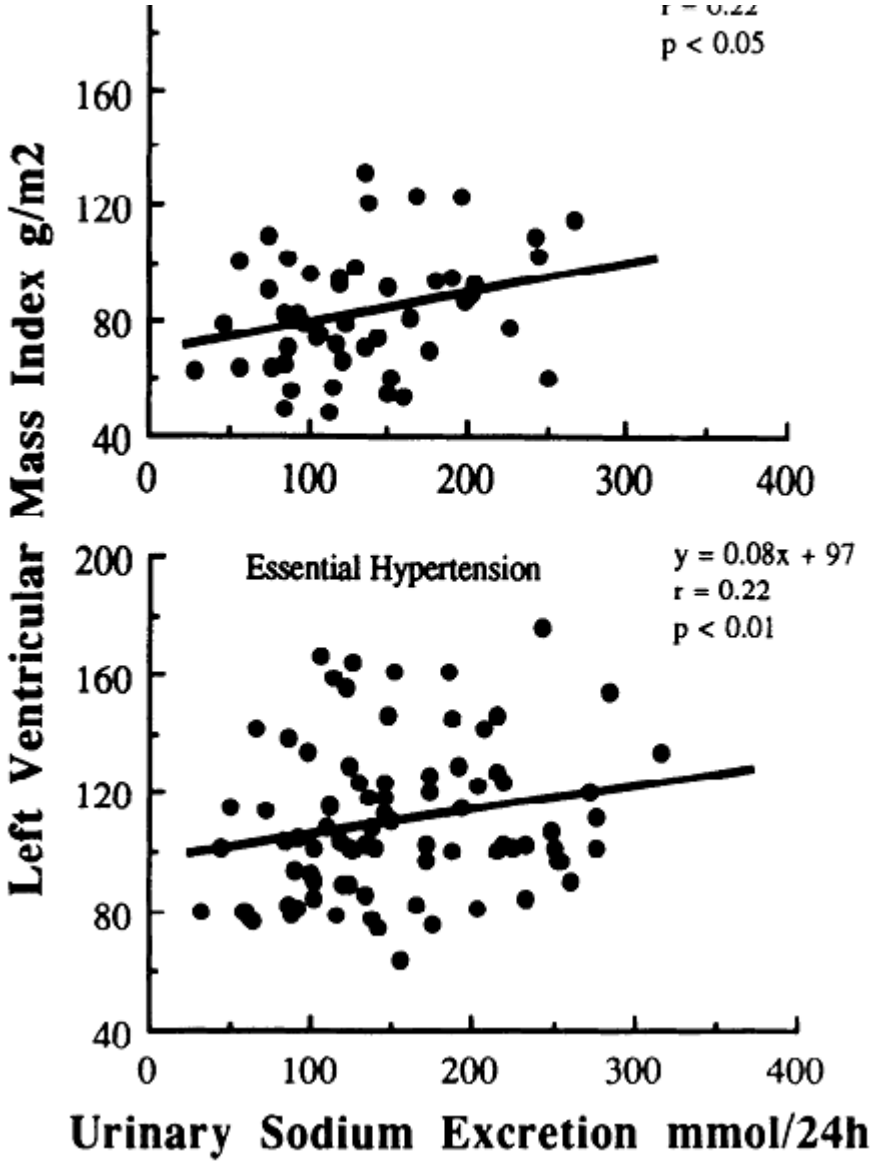
Sodium chloride drives autoimmune disease by the induction of pathogenic T_H17 cells

Markus Kleinewietfeld[1,2], Arndt Manzel[3,4], Jens Titze[5,6], Heda Kvakan[7,8], Nir Yosef[2], Ralf A. Linker[3], Dominik N. Muller[7,9]* & David A. Hafler[1,2]*

Nature 2013


FACTEURS DE RISQUE CV
MALADIES CARDIO-VASCULAIRES
PRECLINIQUE
CLINIQUE
Age-Hérédité
Hypertension
Cholesterol
Diabète sucré
Tabac
Obésité
Sédentarité
Hypertrophie
Cardiaque HVG
Vasculaire IMT
Atteinte rénale
µalb
Infarctus du myocarde
Insuffisance cardiaque
AVC
Mort subite
Facteurs nutritionnels
Apport Sodé

Sodium and left ventricular mass in untreated hypertensive and normotensive subjects

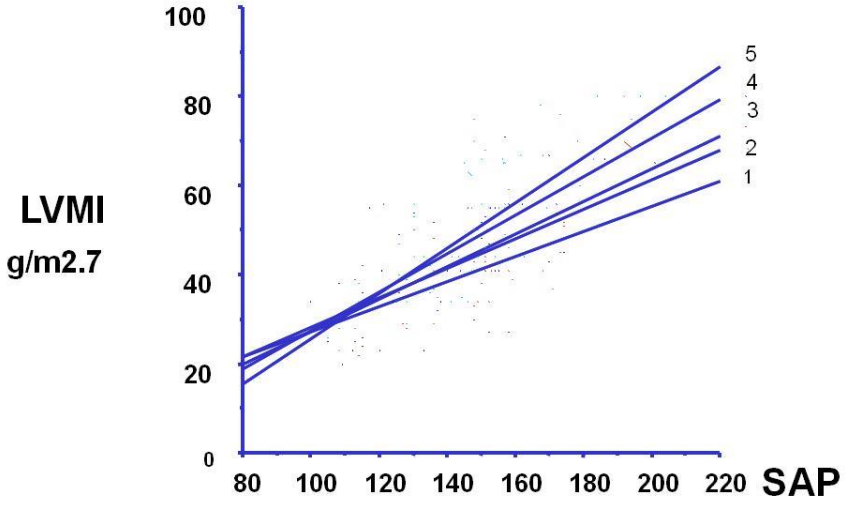


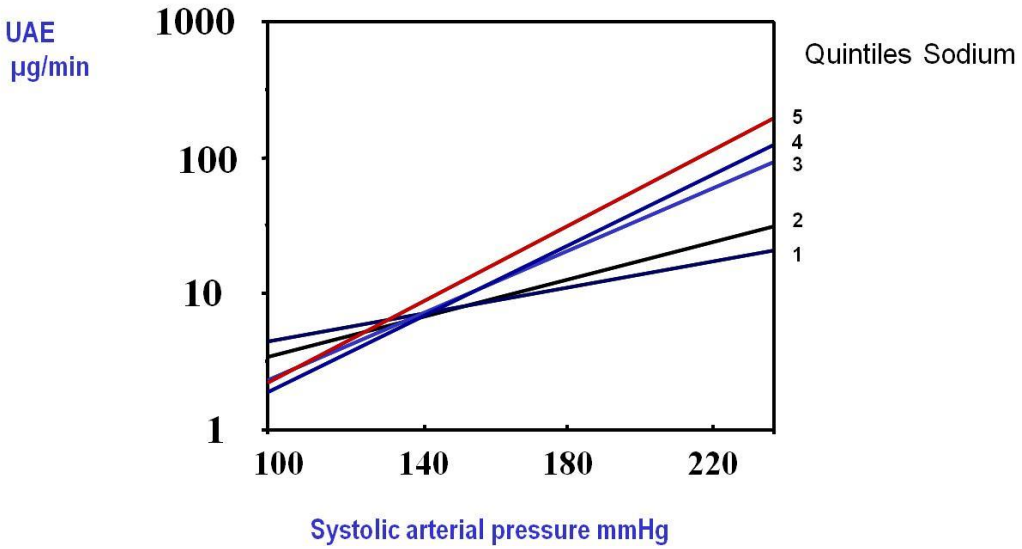
61 never-treated HT
50 NT subjects

Relationship independent of
- age
- gender
- SAP

du Cailar Mimran
Am J Physiol 1992

Effet amplificateur du sodium sur la relation PA –HVG -MA





du Cailar, Mimran Am J Hypertens 2002

Left Ventricular Mass Changes After Renal Transplantation: Influence of Dietary Sodium and Change in Serum Uric Acid

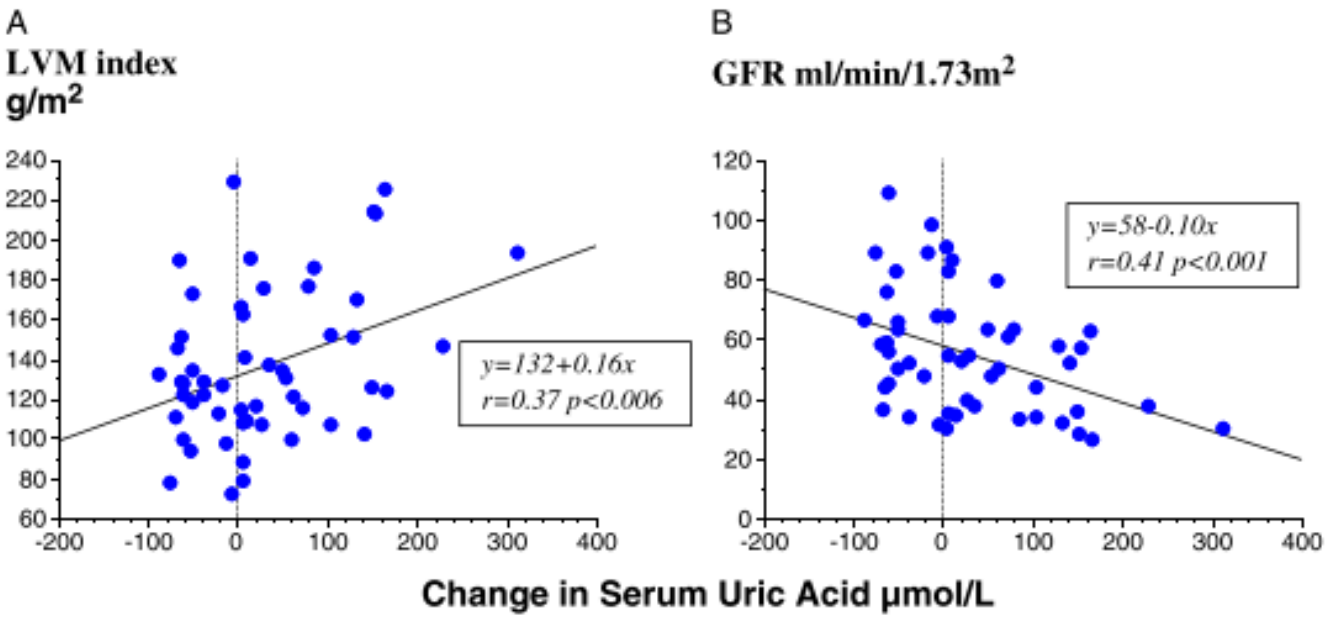


FIGURE 1. Relationship between change in serum uric acid during follow-up and final left ventricular mass (LVM) index and final DTPA-glomerular filtration rate (GFR) in patients on the highest tertile of 24-hr urinary sodium excretion.

du Cailar et al Transplantation 2014;98: 202Y207

Association of Sodium and Potassium Intake With Left Ventricular Mass

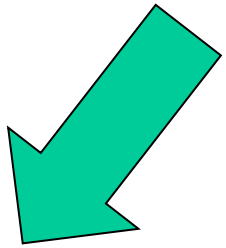
Coronary Artery Risk Development in Young Adults

Carlos J. Rodriguez, Kirsten Bibbins-Domingo, Zhezhen Jin, Martha L. Daviglus, David C. Goff, Jr, David R. Jacobs, Jr

Hypertension 2011

Table 4. Race-Specific and Sex-Specific Relationships of UNa Excretion, UK Excretion, and UNa/K Ratio With LVM

Characteristic/ Model Used	Whites, n=468		
	β	SE	*P*
Y 5 LVM			
UNa	0.510	0.280	0.07
UK	0.295	0.272	0.28
UNa/K	0.729	0.487	0.15
	Whites, n=214		
Y 10 LVM			
UNa	0.235	0.223	0.30
UK	0.129	0.221	0.56
UNa/K	1.4	0.588	0.02

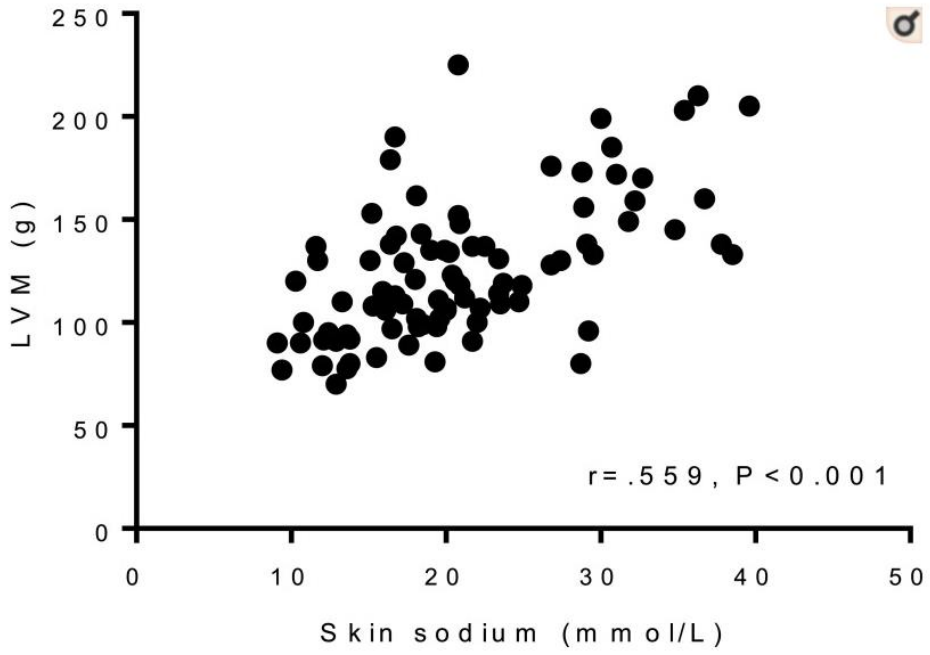


JASN

PMC full text: J Am Soc Nephrol. 2017 Jun; 28(6): 1867–1876.
Published online 2017 Feb 2. doi: [10.1681/ASN.2016060662]

<< Prev Figure 4. Next >>

Figure 4.



Relationship between skin sodium content and LVM.

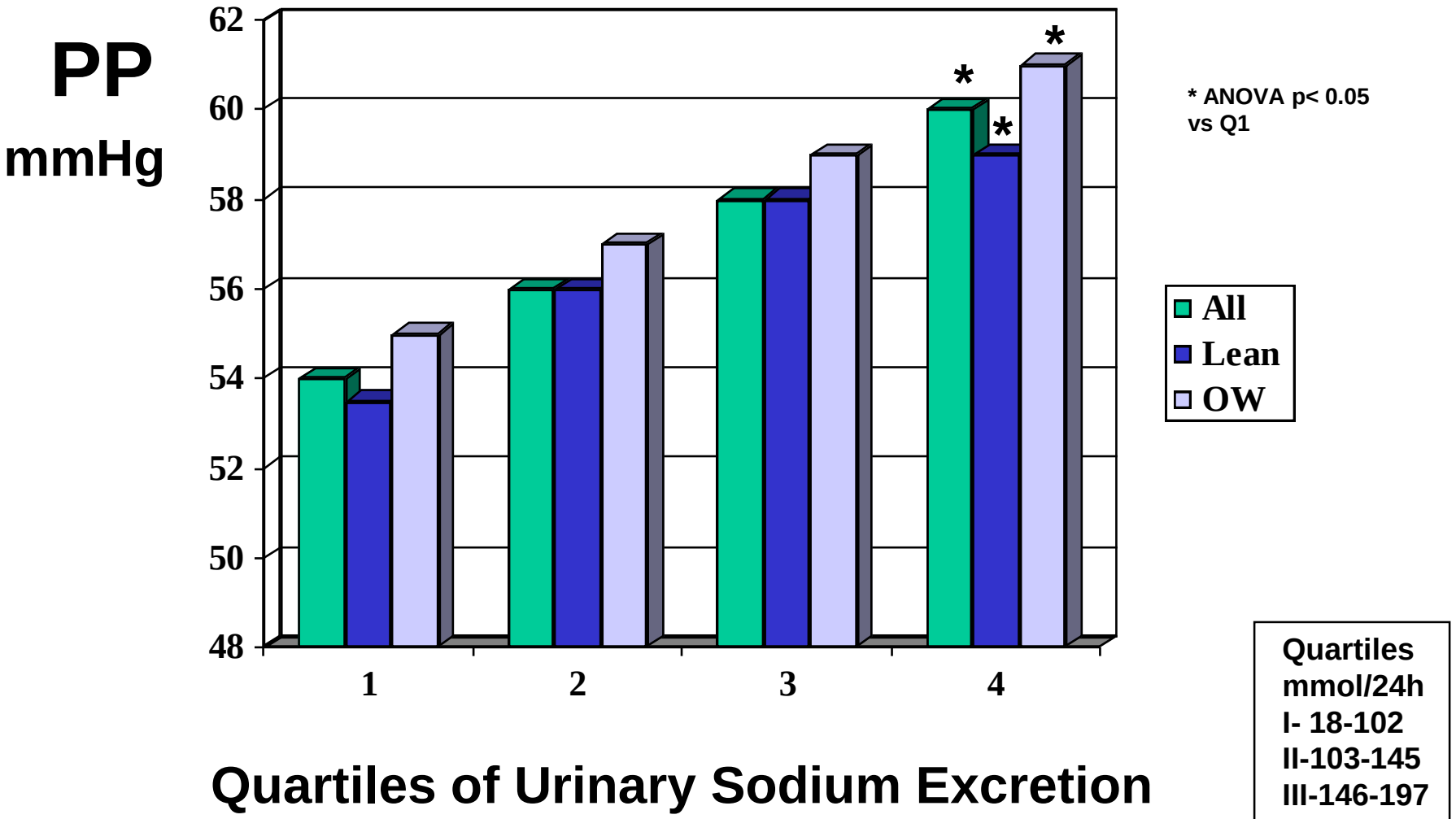
Format: Abstract Send to

Eur Heart J Cardiovasc Imaging. 2018 Oct 10. doi: 10.1093/ehjci/jey134. [Epub ahead of print]

Increased myocardial sodium signal intensity in Conn's syndrome detected by 23Na magnetic resonance imaging.

Christa M[1,2], Weng AM[3], Geier B[1], Wörmann C[1], Scheffler A[4], Lehmann L[4], Oberberger J[1,2], Kraus BJ[1,2], Hahner S[2], Störk S[1,2], Klink T[3], Bauer WR[1,2], Hammer F[1,5], Köstler H[1,3].

PP and sodium intake



du Cailar, Mimran J Hypertens 2004;22:697

Relationship Between Urinary Salt Excretion and Pulse Pressure and Central Aortic Hemodynamics Independent of Steady State Pressure in the General Population

Michelle Redelinghuys, Gavin R. Norton, Leon Scott, Muzi J. Maseko, Richard Brooksbank, Olebogeng H.I. Majane, Pinhas Sareli, Angela J. Woodiwiss

. (*Hypertension*. 2010;56:584-590.)

Table 3. Multivariate Adjusted Relationships Between the Ratio of Urinary Na^+/K^+ and Central Hemodynamics

Urinary Na^+/K^+ vs	Partial *r**	CI	*P*†
With adjustments for MAP			
Forward wave (P1) (n=635)	0.10	0.02 to 0.17	0.005

speed of wave conduction. Consequently, we assume that the relationship between urinary Na^+/K^+ and central PP and the augmented pressure wave is in part mediated by the magnitude of wave reflection, possibly by altering vascular smooth muscle tone in medium-sized arteries, a mechanism proposed recently as mediating age-induced changes in central PP.[21] This has important clinical implications because, unlike age,

Réversibilité de l’atteinte des organes cibles avec la restriction sodée ?

Moderate Sodium restriction and LVH in untreated patients with essential hypertension

Jula et al Circulation 1994, 89: 1023

---

76 patients, Duration 12mos

- **38 No treatment**
- **38 Treatment group: sodium restriction**

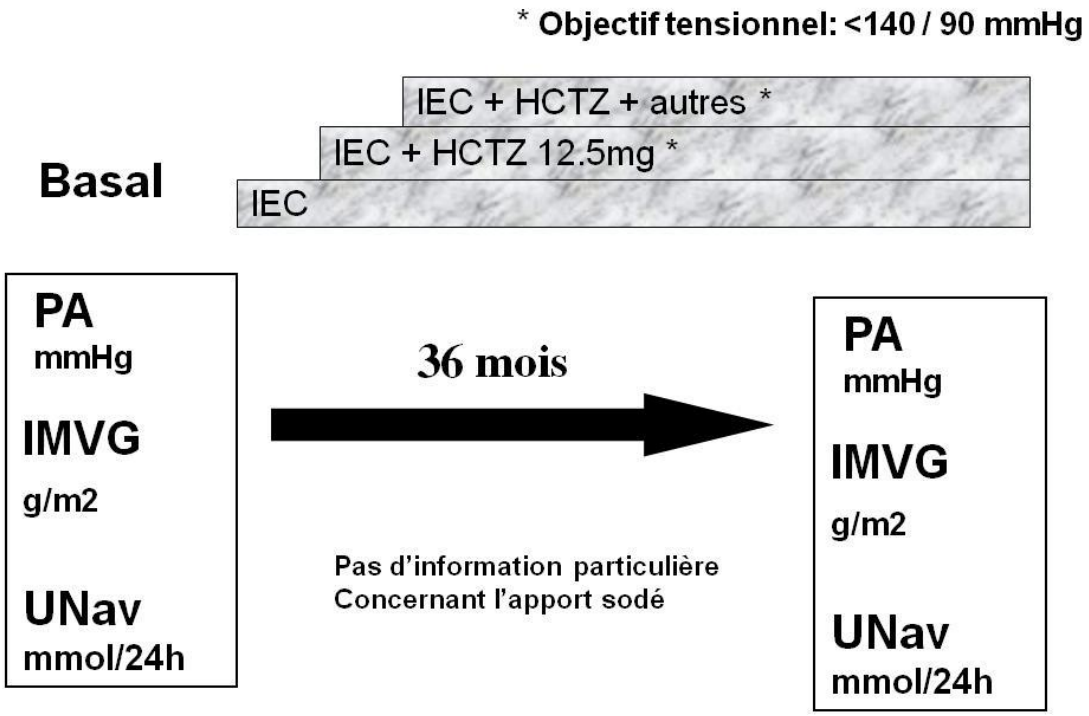
REDUCTION NATRIURESIS FROM 195 to 109

a decrease in LVMI by 7.1% was observed only in the group with LVH at baseline, despite similar final BP values

---

Dietary Sodium, Aldosterone, and Left Ventricular Mass Changes During Long-Term Inhibition of the Renin-Angiotensin System

Guilhem du Cailar, Pierre Fesler, Jean Ribstein, Albert Mimran



Hypertension 2010

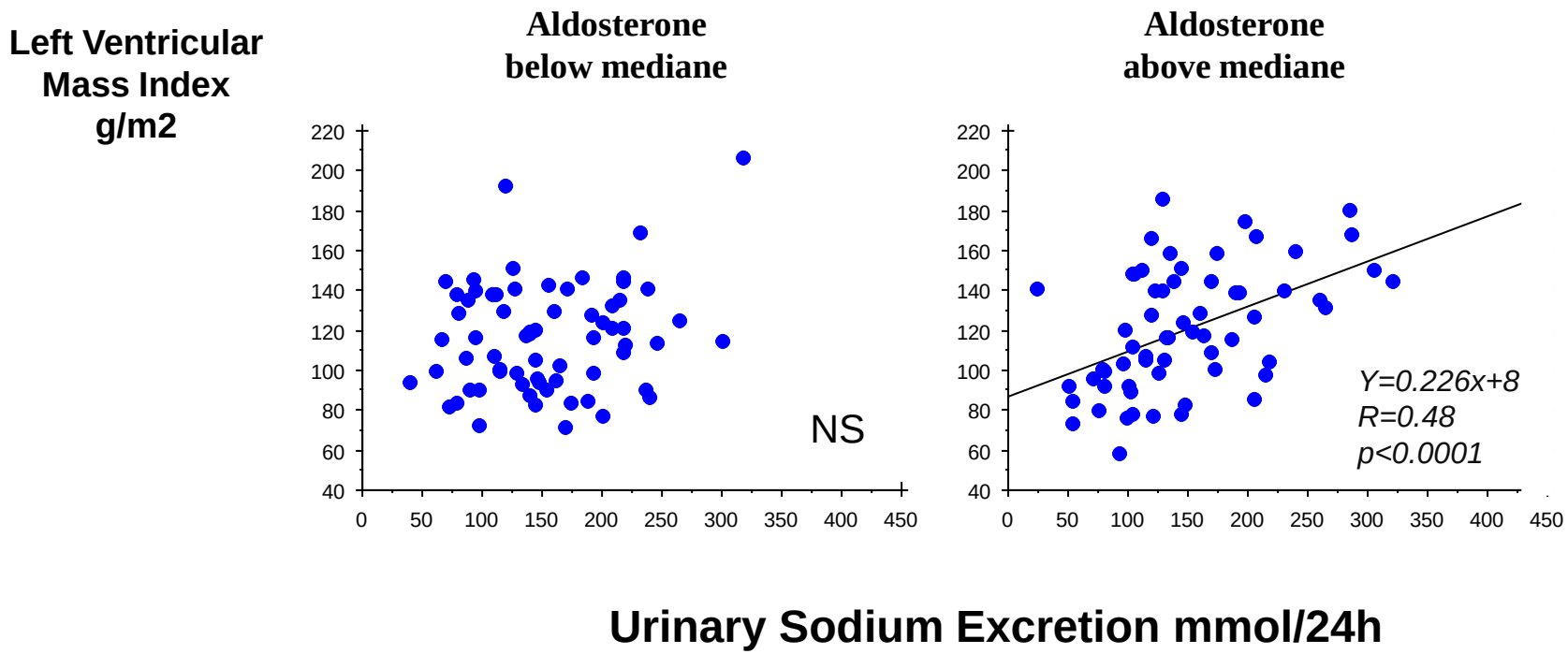
Dietary Sodium, Aldosterone, and Left Ventricular Mass Changes During Long-Term Inhibition of the Renin-Angiotensin System

	Univariate Relationship		Multivariate Analysis		
Dependent Variable	*r*	β	SE	*t*	*P*
Percentage change from baseline LVMI					
Male sex	NS				
Age, y	NS				
Basal LVMI, g/m	−0.56*	−0.22	0.03	−8	<0.0001
Change systolic BP, %	0.46*	0.50	0.09	5.1	<0.0001
Change in urinary sodium, mmol/24 h	0.21*	0.05	0.016	3.4	0.01
Change in plasma aldosterone, ng/dL	0.32*	0.38	0.15	2.4	0.01

NS indicates not significant.
*$P<0.05$.

du Cailar Hypertension 2010

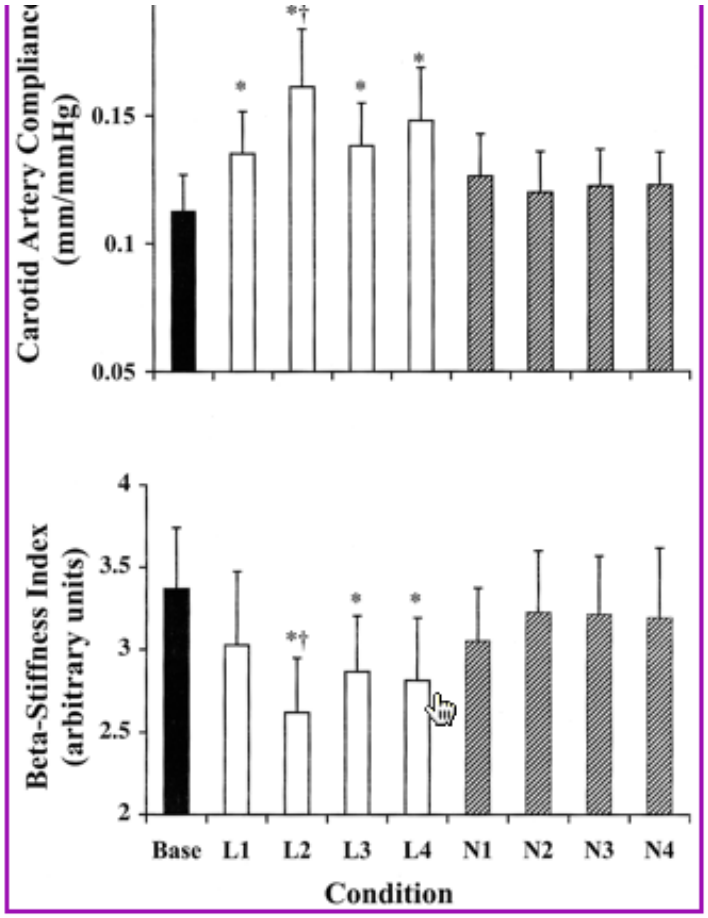
High sodium intake and aldosterone during therapy with RAS blockers adversely affect LVH regression in HT patients



du Cailar Hypertension 2010

Dietary Sodium Restriction Rapidly Improves Large Elastic Artery Compliance in Older Adults With Systolic Hypertension

Phillip E. Gates, Hirofumi Tanaka, William R. Hiatt, Douglas R. Seals



Na reduction from 135 to 54 mmol/day for 2wks in elderly ISH

Basal Low Sodium Normal Sodium

Hypertension 2004;44:35

Nutricoeur :

Visites	V1		V2	V3		V4
Semaines	2	***Sodium 85mmol/j vs PL***	8	9	***Sodium 85mmol/j vs PL***	15

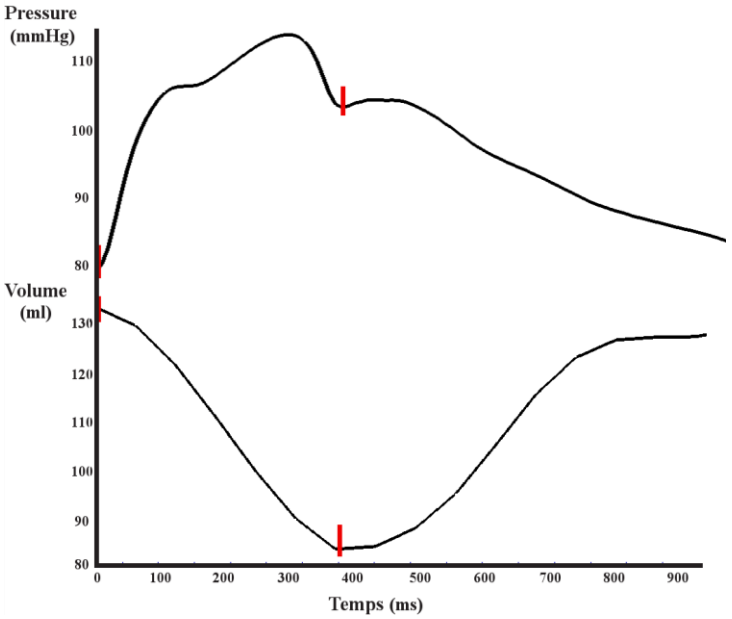
Limitation de l'apport sodée

Random — Wash-out — Cross-Over

Restriction Sodée (Sodium 85 mmol/j) pendant toute la durée de l'étude

Tonomètre

Echo 3D



Effets secondaires digestifs

Nausées+++++

Cancer gastrique

Conclusion: Sodium et organes cibles

Hypertension September 2011

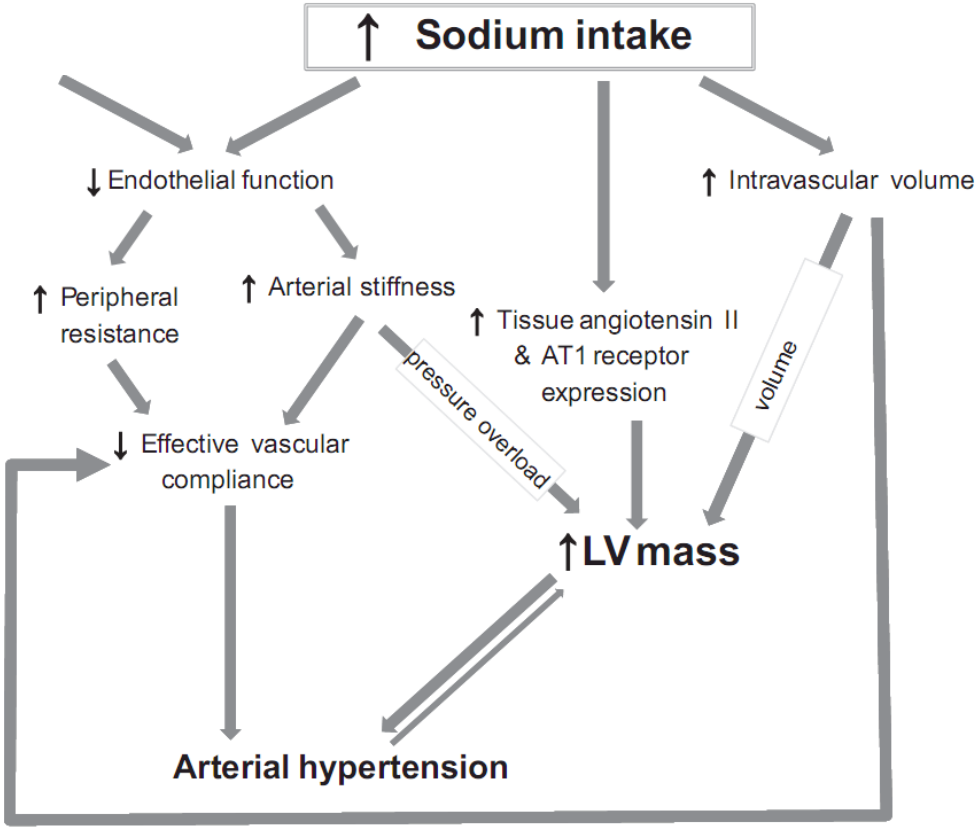


Figure. Possible interrelations among unbalanced electrolyte intake, high LV mass, and arterial hypertension.

Sodium et risque cardiovasculaire

DIU HTA-Risque CV
Novembre 2016

Un récolteur de sel au lac Rose au Senegal

-Estimation de l'apport sodé

-Sodium et PA

-Sodium et organes cibles de l'HTA

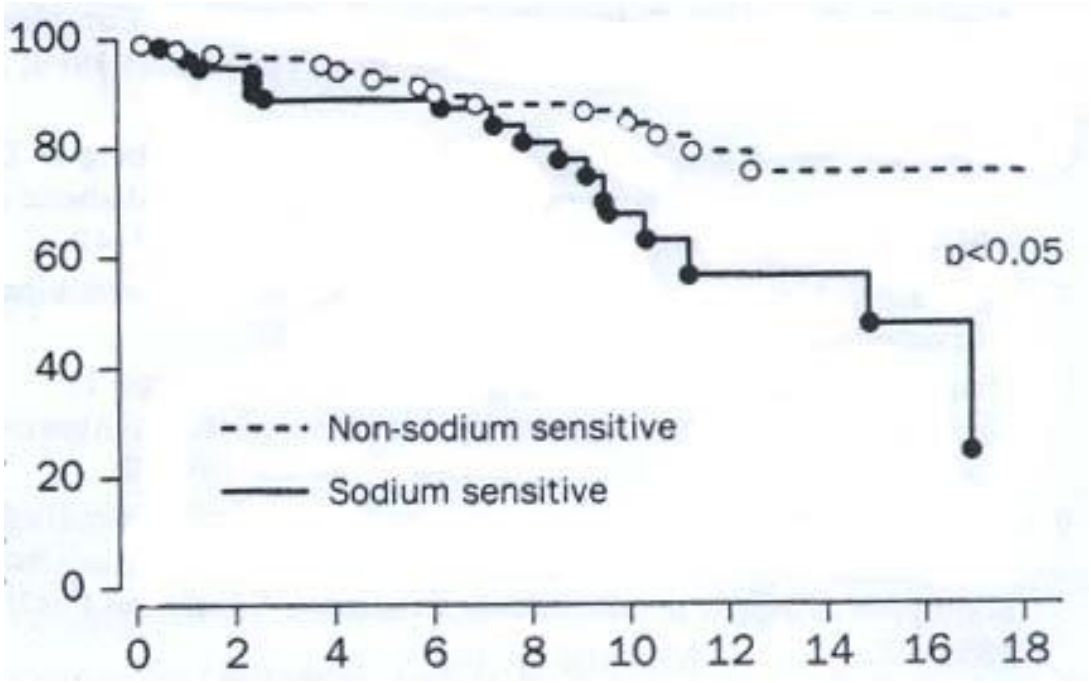
-Le sodium un facteur de risque CV ?

-En pratique: les recommandations

Sodium Sensitivity and Cardiovascular events

Morimoto: 1997;350:1734 Lancet

% of pt Free of Events



Time Years

Cox 's model

Mean AP

Smoking

Sodium sensitivity

The First National Health And Nutrition Examination. Epidemiologic Follow-up Study

He et al. JAMA 1999; 282: 2027

Single 24-h dietary recall

2688 0W + 6797 non OW

19 yrs follow-up

Quartiles of Sodium-to-Energy Ratio (mmol / 1452 kJ)

For a 100 mmol increase in Na intake and only in OVERWEIGHT SUBJECTS

(BMI > 27.8 M & 27.3 F)

Progressive increase in

- **Stroke incidence (by 32%) and mortality (by 89%)**
- **Coronary mortality (by 44%) but not incidence**
- **Cardiovascular mortality (by 61%)**

Cardiovascular mortality in Finland: Influence of Sodium

Tuhomilehto et al Lancet 2001; 357: 848-851

1173 men and 1263 women, age 26-64, baseline data collected in1982 and 1987

Median Natriuresis 205 in men (25% less than 159)
154 in women (25% less than 119)
No influence of Na on BP

For a 100mmol increase in natriuresis

RR	**coronary heart disease**	**1.51**
	cardiovascular disease	**1.45**
	all cause mortality	**1.26**

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Urinary Sodium and Potassium Excretion, Mortality, and Cardiovascular Events

Martin O'Donnell, M.B., Ph.D., Andrew Mente, Ph.D., Sumathy Rangarajan, M.Sc.,

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ABSTRACT

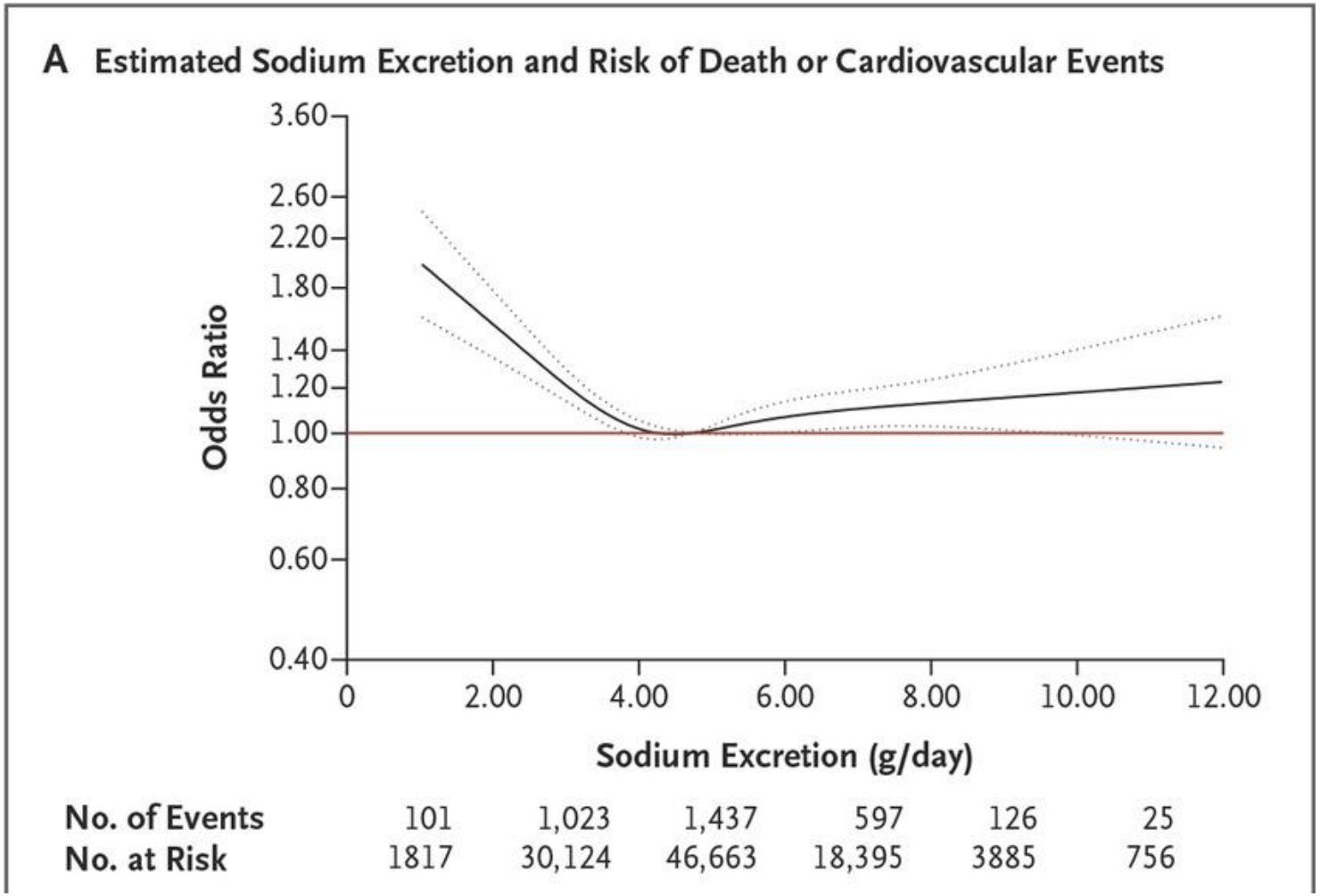
BACKGROUND

The optimal range of sodium intake for cardiovascular health is controversial.

METHODS

We obtained morning fasting urine samples from 101,945 persons in 17 countries and estimated 24-hour sodium and potassium excretion (used as a surrogate for intake). We examined the association between estimated urinary sodium and potassium excretion and the composite outcome of death and major cardiovascular events.

Association of Estimated 24-Hour Urinary Sodium Excretion with Risk of Death and Major Cardiovascular Events.



Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies

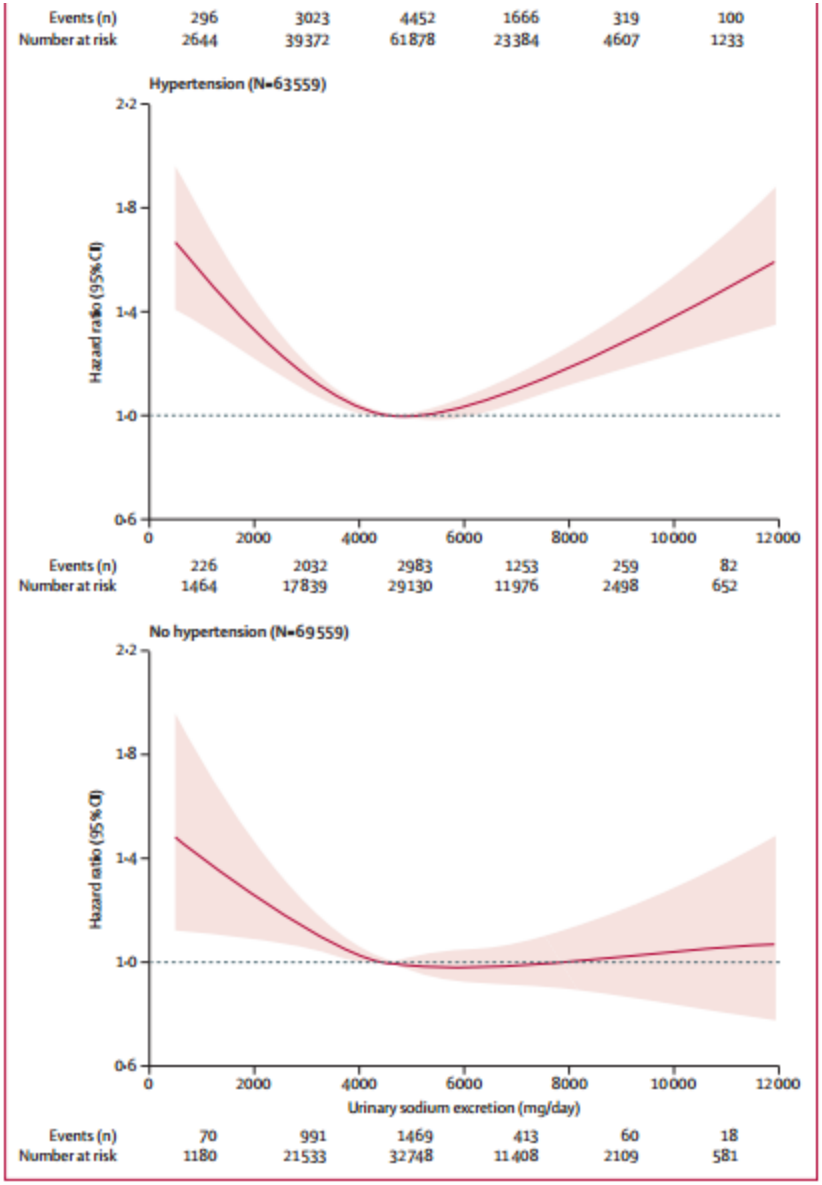
Andrew Mente, Martin O'Donnell, Sumathy Rangarajan, Gilles Dagenais, Scott Lear, Matthew McQueen, Rafael Diaz, Alvaro Avezum, Patricio Lopez-Jaramillo, Fernando Lanas, Wei Li, Yin Lu, Sun Yi, Lei Rensheng, Romaina Iqbal, Prem Mony, Rita Yusuf, Khalid Yusoff, Andrzej Szuba, Aytekin Oguz, Annika Rosengren, Ahmad Bahonar, Afzalhussein Yusufali, Aletta Elisabeth Schutte, Jephat Chifamba, Johannes F E Mann, Sonia S Anand, Koon Teo, S Yusuf, for the PURE, EPIDREAM, and ONTARGET/TRANSCEND Investigators

Methods In this pooled analysis, we studied 133118 individuals (63559 with hypertension and 69559 without hypertension), median age of 55 years (IQR 45–63), from 49 countries in four large prospective studies and estimated 24-h urinary sodium excretion (as group-level measure of intake). We related this to the composite outcome of death and major cardiovascular disease events over a median of 4·2 years (IQR 3·0–5·0) and blood pressure.

Lancet 2016; 388:465-75

Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension:

EVENTS



Hypertension

No Hypertension

Sodium Intake and All-Cause Mortality Over 20 Years in the Trials of Hypertension Prevention

Prehypertensive adults

Nancy R. Cook, ScD,[a] Lawrence J. Appel, MD,[b] Paul K. Whelton, MD[c]

ABSTRACT

BACKGROUND The relationship between lower sodium intake and total mortality remains controversial.

OBJECTIVES This study examined the relationship between well-characterized measures of sodium intake estimated from urinary sodium excretion and long-term mortality.

METHODS Two trials, phase I (1987 to 1990), over 18 months, and phase II (1990 to 1995), over 36 months, were undertaken in TOHP (Trials of Hypertension Prevention), which implemented sodium reduction interventions. The studies included multiple 24-h urine samples collected from pre-hypertensive adults 30 to 54 years of age during the trials. Post-trial deaths were ascertained over a median 24 years, using the National Death Index. The associations between mortality and the randomized interventions as well as with average sodium intake were examined.

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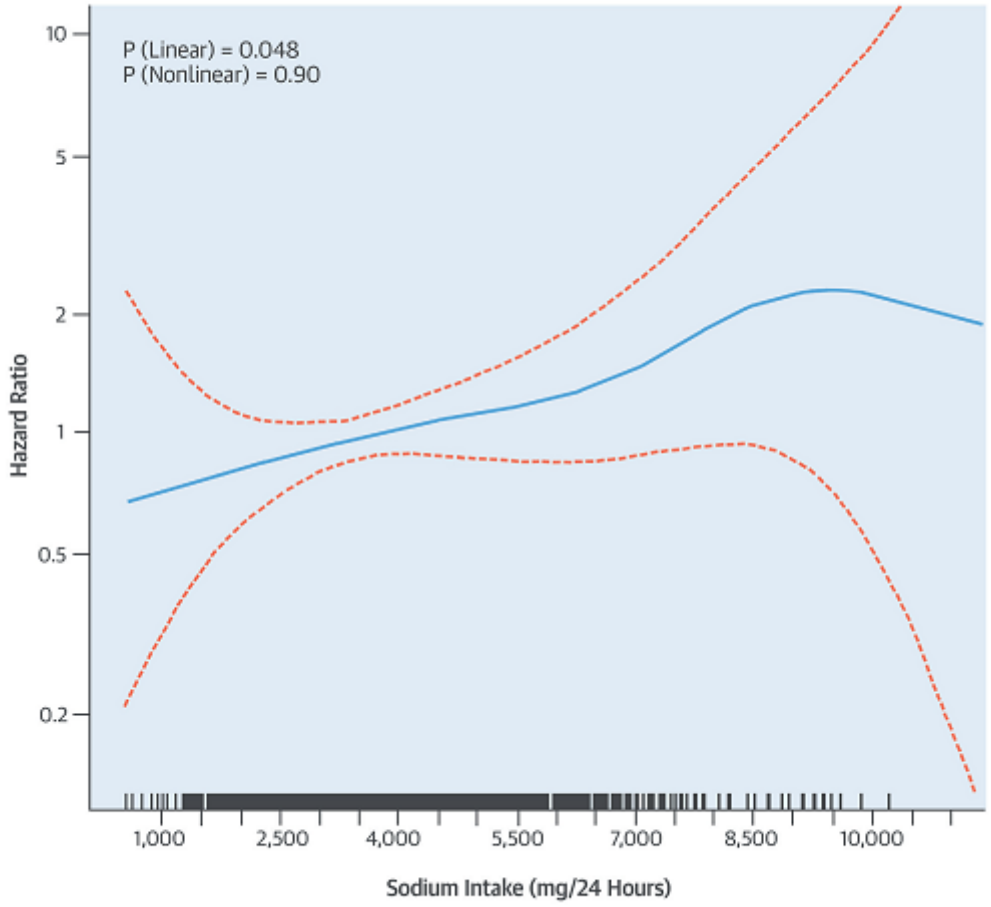
Sodium Intake and All-Cause Mortality Over 20 Years in the Trials of Hypertension Prevention

Nancy R. Cook, ScD,[a] Lawrence J. Appel, MD,[b] Paul K. Whelton, MD[c]

CENTRAL ILLUSTRATION Sodium and All-Cause Mortality Over 20 Years



Cook, N.R. et al. J Am Coll Cardiol. 2016;68(15):1609-17.

Epidemiologie : Résumé

-**Une augmentation de l'apport sodé de 5g/24h pourrait être associée à une majoration du RR de survenue d'un AVC de 23%.**

-Sur la base du bénéfice « tensionnel » associé à une limitation de l'apport sodé de 6 g/jour, il est extrapolé à l'échelle de la population mondiale, une diminution de 2.5 million des décès de cause CV.

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Modélisation:
Projected effect of dietary salt reductions on future cardiovascular disease

-étude de modélisation à partir d'une large méta-analyse

-le bénéfice CV de la réduction de l'apport sodé à l'échelle d'une population serait équivalent à une réduction de 50% de la consommation de tabac ou de l'utilisation d'une statine en prévention primaire.

Goldman L.. N Engl J Med. 2010 :18;590-9.

C’est la raison pour laquelle, cet excès chronique de sel (9-12 g/jour) est devenu dans de nombreux pays un enjeu majeur de politique de santé publique.

En France, le Haut Conseil de Santé Publique a fixé en 2011 un objectif de réduction de l’apport sodé à 5 à 6 g/jour sur 5 ans.

Pour la pratique

Prise en charge de l'HTA
1ère étape (HAS)

- Mesures hygiéno-diététiques:
  - Limitation de la consommation en sel < 6-8 g/j **(100 à 150 m mol de sodium) mmol)**
  - Réduction de la surcharge pondérale: IMC < 25 kg/m², ou ↓ poids 10%
  - Activité physique: 30 min, 3x/semaine
  - Alcool: H: < 3 vdv; F < 2 vdv
  - Arrêt du tabac
  - Régime riche en légumes, en fruits et pauvre en graisses saturées

Is a reduction in Sodium succeptible to

reduce the need or number of antihypertensive agents

Reduction of Sodium intake is similar to addition of a diuretic in Captopril-treated patients

Singer et al Hypertension 1995, 25:1042

Patients on Captopril 25mg bd for at least 1 month
addition of either hydrochlorothiazide
or reduction of Na from 206 to109 mmol

	Captopril	Capto+LS	Capto+HCTZ
SAP	151	137	137
DAP	95	90	87
Serum K	3.9	4.1	3.7

CONCLUSION

-Estimation de l'apport sodé: natriurèse des 24h

-Sodium et PA: un lien étroit avec une modulation de l'effet des médicament

-Sodium et organes cibles de l'HTA:
influence sur l'HVG , la rigidité artérielle et la MA

-Le sodium un facteur de risque CV ? oui

-Les recommandations
Limitation et non restriction
de l'apport sodé (objectif à 6 à8 g)