Sodium and potassium intake: facts, issues and controversies. nutritional and public health perspectives

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Disclosures: *Technical Advisor to the World Health Organization, the Pan American Health Organization, Member of C.A.S.H., W.A.S.H., UK Health Forum and Trustee of the Student Heart Health Trust – all unpaid.*

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Outline

- What is normal salt consumption?
- Is eating too much salt harmful?
- Will salt reduction protect?
- How big is the problem?
- How large might the benefits be?
- Can we do it and how?
- Is it feasible for populations to reduce salt intake?
- What are the next steps?
- How about potassium intake?

Evolutionary diet

- Profound changes in the composition of human diet with the introduction of agriculture and animal husbandry ~10,000 years ago
- Salt: necessity for life – first international commodity of trade – great symbolic importance and economic value – first state monopoly – property of preserving foods from decay – enhancing flavors fulfilling hedonic reward
- Evolutionary diet: estimated intake for sodium ~10mmol/d and for potassium ~200mmol/d (ratio ~0.05)
- Modern diet: measured intake for sodium ~170mmol/d and for potassium ~60mmol/d (ratio ~2.5)

Eaton SB et al. Am J Med 1988; 84: 739-49
Cordain L et al. Am J Clin Nutr 2005; 81: 341-54

No one has 'normal' salt consumption

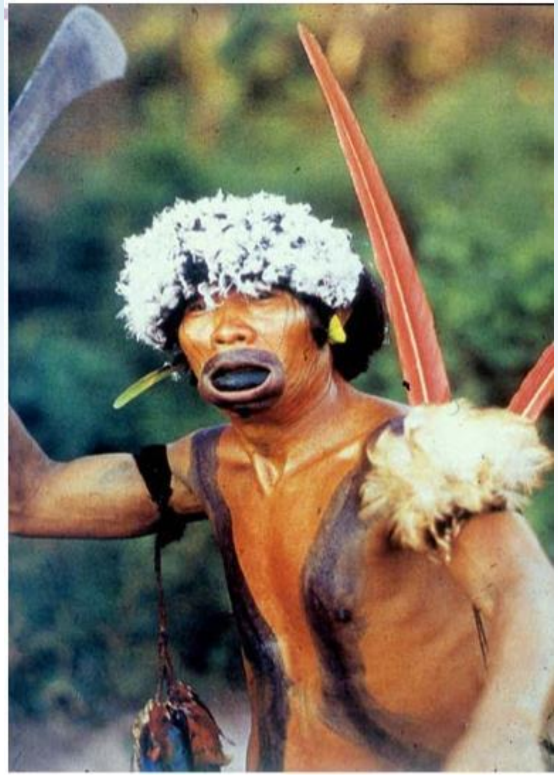
- Salt was scarce for most hominid evolution
- First manufactured 6,000 years ago
- Mass produced for only a few hundred years

Yanomamo Indian

On 'evolutionary' diet (i.e. almost no salt [<1 g/day], very little fat, no refined carbohydrate, fruits & vegetables ↑↑, but aggressive fit, stress ↑↑↑)

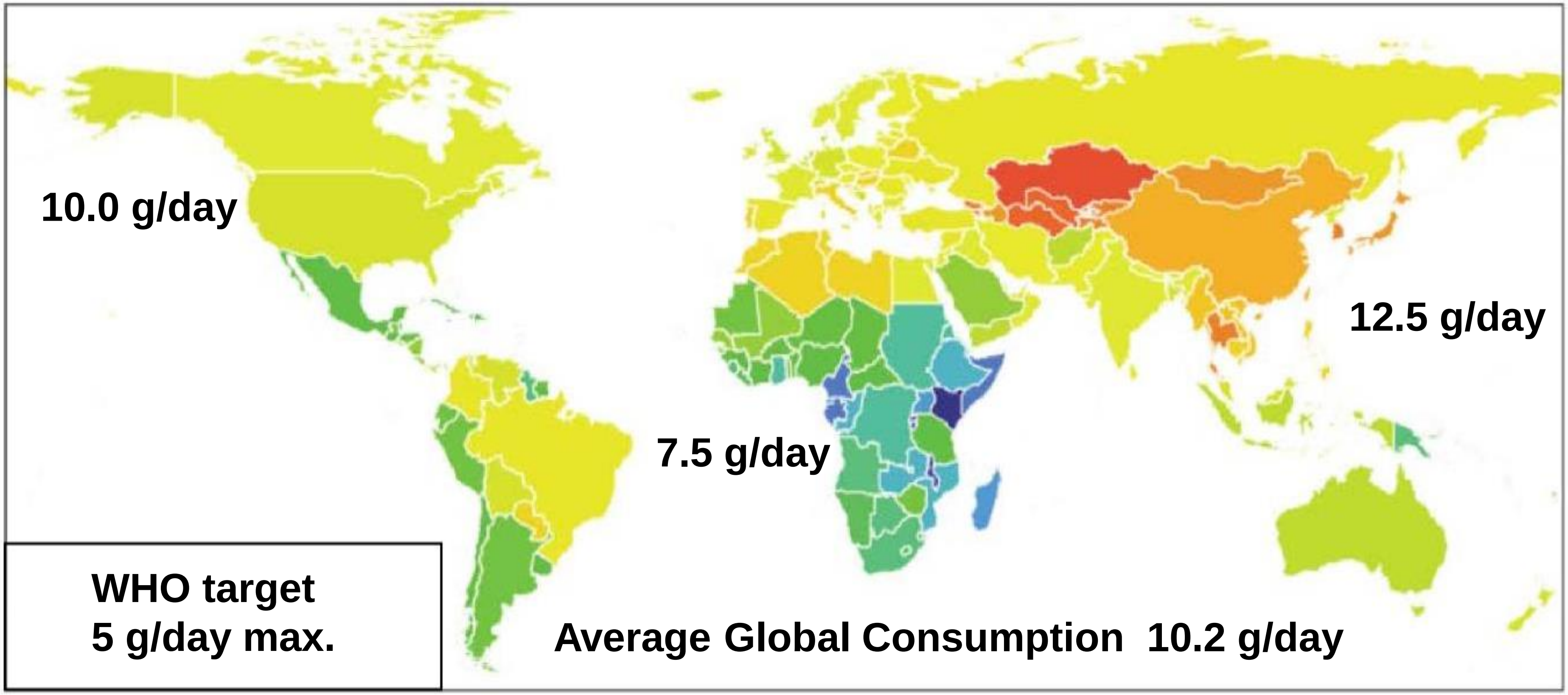
No high BP, no rise in BP with age, no adverse health consequences, no vascular disease

Male adults:	BP:	96 / 61 mmHg
	Cholesterol:	3.1 mmol/L



from **Cappuccio FP & Capewell S. Functional Food Rev 2015; in press**

High salt consumption all around the world



Powles J et al. BMJ Open 2013;3:e003733

Global Sodium Consumption and Death from Cardiovascular Causes

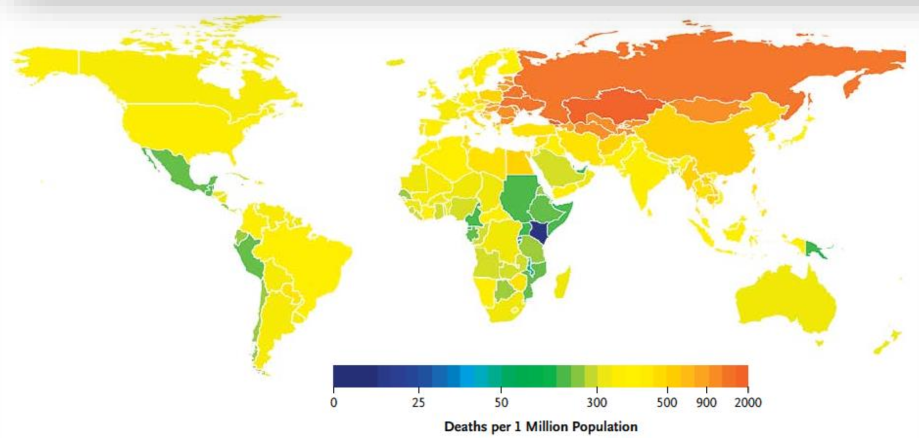


Figure 3. Absolute Cardiovascular Mortality Attributed to Sodium Consumption of More than 2.0 g per Day in 2010, According to Nation.
The scale is based on the number of deaths from cardiovascular causes (per 1 million persons) in 2010 that were attributed to sodium consumption of more than 2.0 g per day.

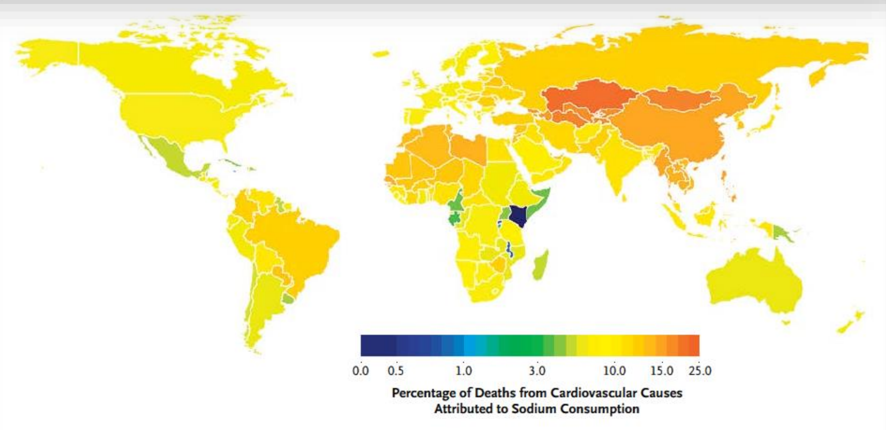


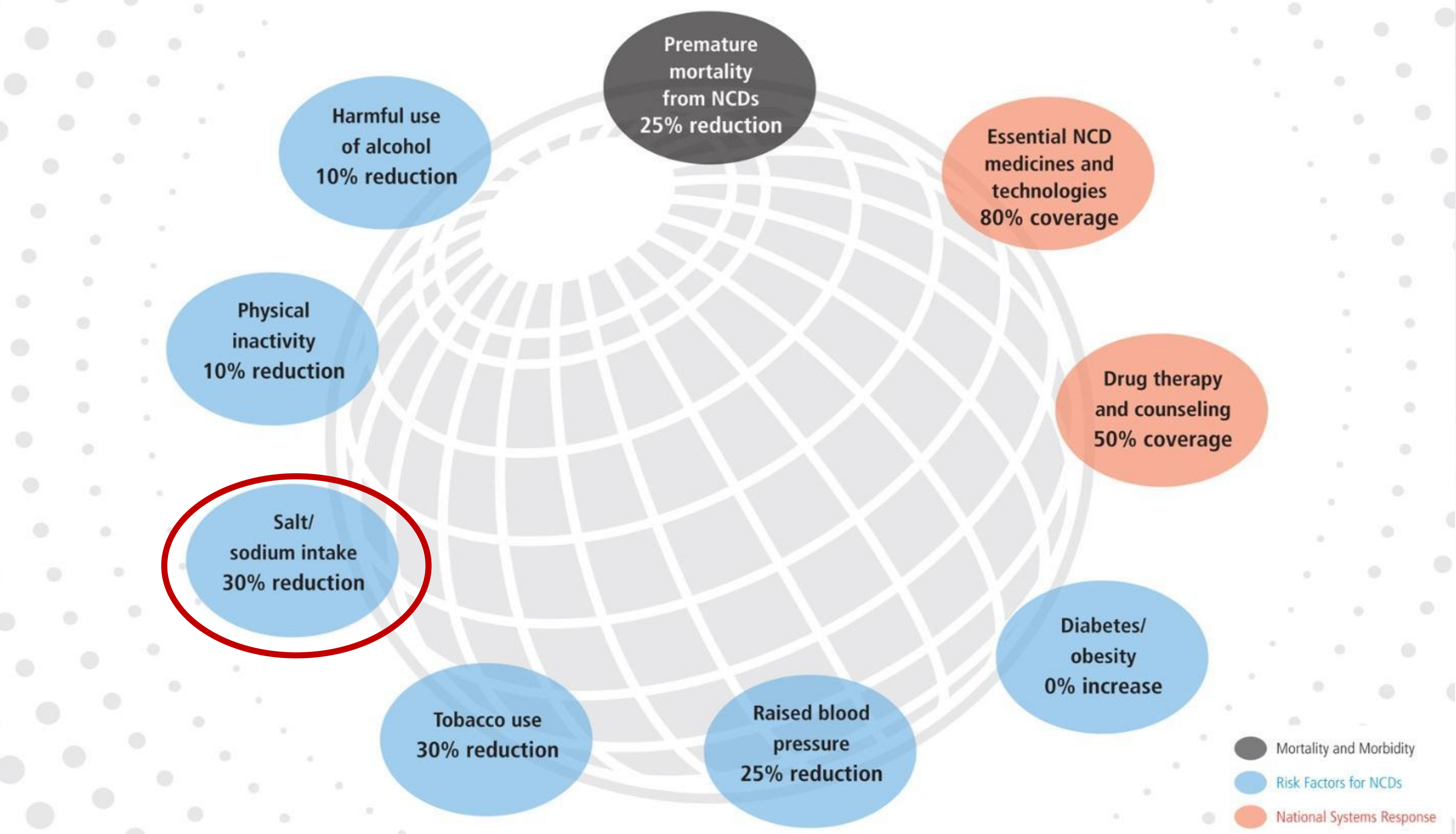
Figure 4. Proportion of Deaths from Cardiovascular Disease Attributed to Sodium Consumption of More than 2.0 g per Day in 2010, According to Nation.
The scale is based on the percentage of all deaths from cardiovascular causes in 2010 that were attributed to sodium consumption of more than 2.0 g per day.

- In 2010, global sodium consumption estimated at 3.95g per day (9.875g salt per day)
- Globally, 1.65m annual CV deaths attributed to sodium intake >2g per day (>5g salt per day)
- These deaths accounted for nearly 10% of CV deaths
- 85% of these deaths occurred in LMICs and 40% were premature (<70 years)

Mozaffarian D et al. NEJM 2014:371:624-34

Formal Meeting of Member States to conclude the work on the comprehensive global monitoring framework including indicators and a set of voluntary targets for the prevention and control of NCDs

Set of 9 voluntary global NCD targets for 2025



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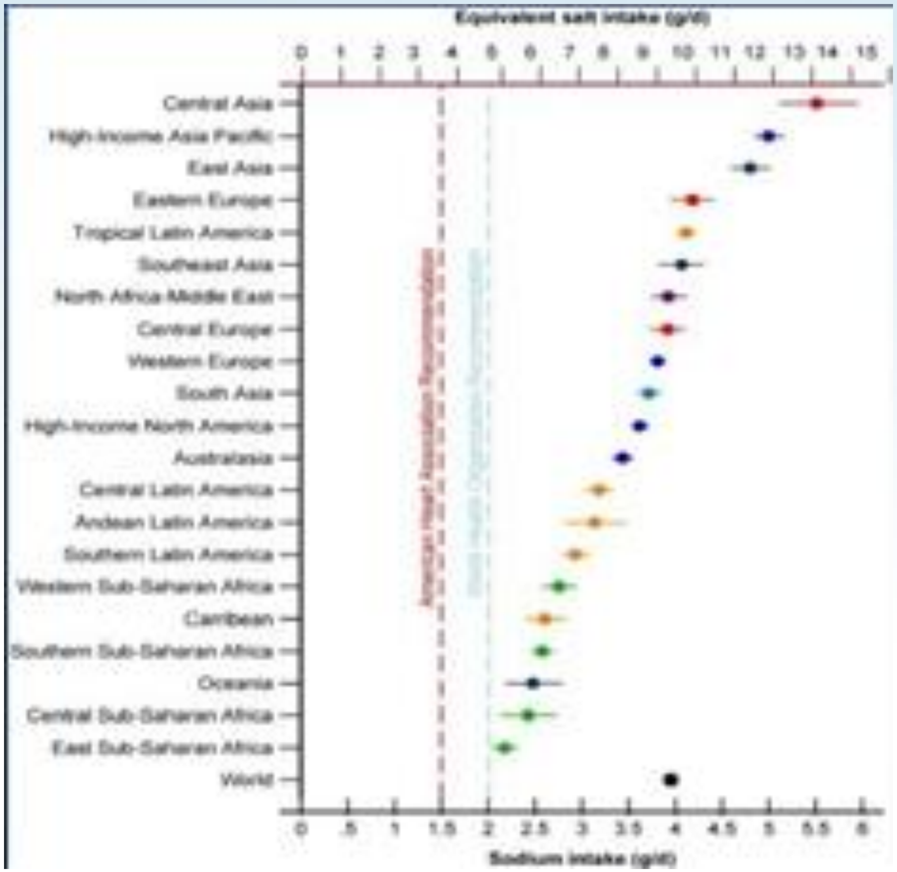
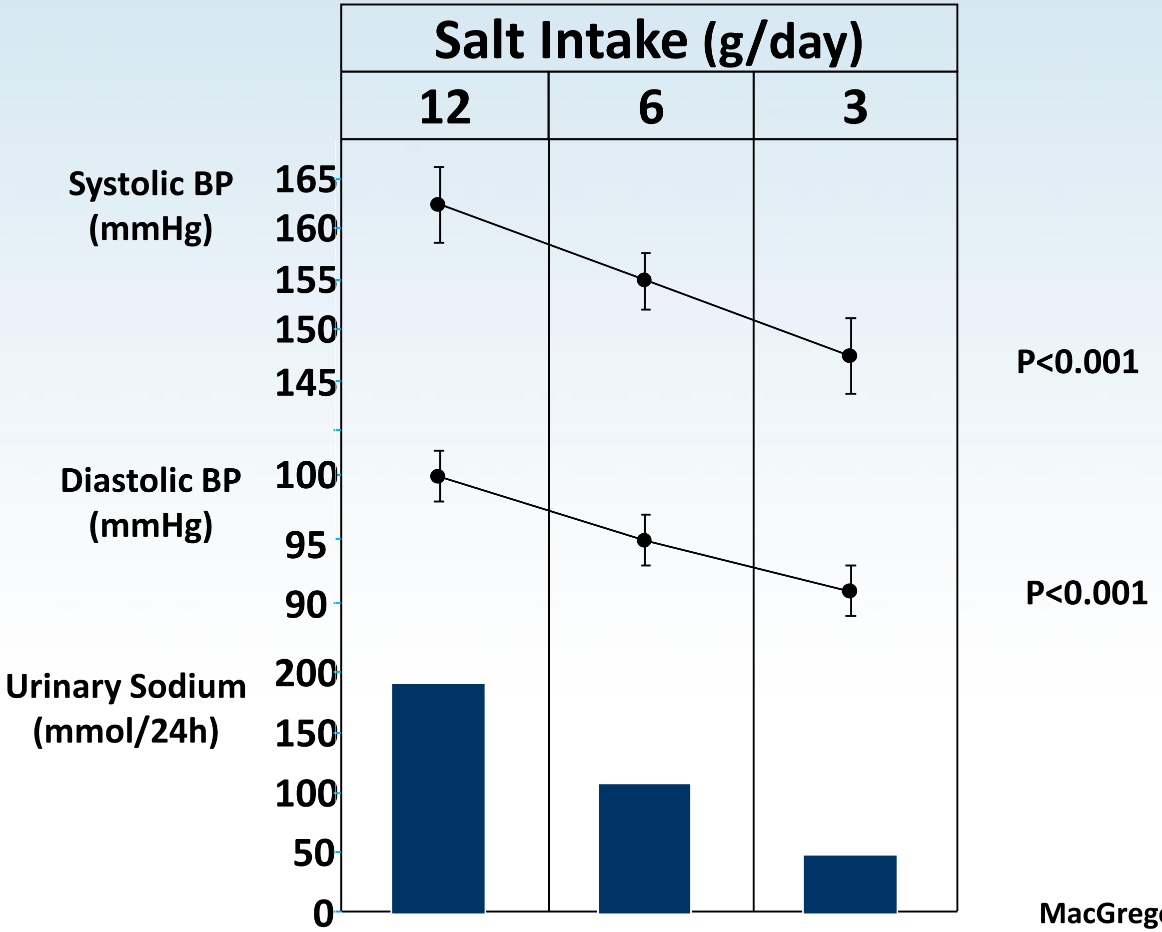
Salt intake is at least twice the maximum recommended level in most countries of the world



8.5M deaths in LMICs could be prevented over 10 years if sodium intake were reduced by 15%

Powles J et al. BMJ Open 2013;3:e003733

DIETARY SALT INTAKE AND BLOOD PRESSURE:
a dose-dependent effect in a randomised crossover trial (n=20)



MacGregor GA et al. Lancet 1989; ii:1244-7

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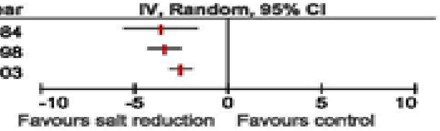
A reduction in dietary salt intake reduces blood pressure in adults …

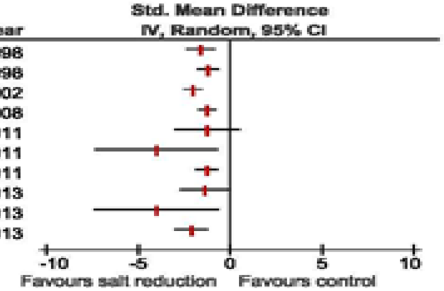
All participants

Study or Subgroup	Std. Mean Difference	SE	Studies Total	Participants Total	Std. Mean Difference IV, Random, 95% CI	Year
Grobbee 1984	-3.6	1	13	584	-3.60 [-5.56, -1.64]	1984
Midgley 1998	-3.4	0.4592	56	3021	-3.40 [-4.30, -2.50]	1998
Geleijnse 2003	-2.54	0.3163	40	0	-2.54 [-3.16, -1.92]	2003



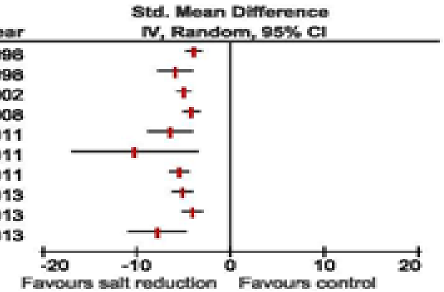
Normotensive participants

Study or Subgroup	Std. Mean Difference	SE	Studies Total	Participants Total	Std. Mean Difference IV, Random, 95% CI	Year
Midgley 1998	-1.6	0.4133	28	2035	-1.60 [-2.41, -0.79]	1998
Graudal 1998	-1.2	0.3061	56	2581	-1.20 [-1.80, -0.60]	1998
He 2002	-2.03	0.2704	17	734	-2.03 [-2.56, -1.50]	2002
Graudal (W) 2003-8	-1.27	0.25	57	5096	-1.27 [-1.76, -0.78]	2008
Graudal (A) 2011	-1.27	0.9184	3	393	-1.27 [-3.07, 0.53]	2011
Graudal (B) 2011	-4.02	1.7092	7	506	-4.02 [-7.37, -0.67]	2011
Graudal (W) 2011	-1.27	0.3112	71	7299	-1.27 [-1.88, -0.66]	2011
Aburto 2013	-1.38	0.6939	7	3067	-1.38 [-2.74, -0.02]	2013
He (B) 2013	-4.02	1.7449	3	412	-4.02 [-7.44, -0.60]	2013
He (W) 2013	-2.11	0.4694	12	1901	-2.11 [-3.03, -1.19]	2013



Hypertensive participants

Study or Subgroup	Std. Mean Difference	SE	Studies Total	Participants Total	Std. Mean Difference IV, Random, 95% CI	Year
Graudal 1998	-3.9	0.4592	58	2161	-3.90 [-4.80, -3.00]	1998
Midgley 1998	-5.9	0.9541	28	966	-5.90 [-7.77, -4.03]	1998
He 2002	-4.96	0.4031	11	2220	-4.96 [-5.75, -4.17]	2002
Graudal (W) 2003-8	-4.18	0.4592	58	3391	-4.18 [-5.08, -3.28]	2008
Graudal (B) 2011	-6.44	1.2296	9	674	-6.44 [-8.85, -4.03]	2011
Graudal (A) 2011	-10.21	3.4541	8	477	-10.21 [-16.98, -3.44]	2011
Graudal (W) 2011	-5.48	0.5357	76	4903	-5.48 [-6.53, -4.43]	2011
He (W) 2013	-5.12	0.5867	17	623	-5.12 [-6.27, -3.97]	2013
Aburto 2013	-4.06	0.5612	24	2273	-4.06 [-5.16, -2.96]	2013
He (B) 2013	-7.83	1.597	5	0	-7.83 [-10.96, -4.70]	2013



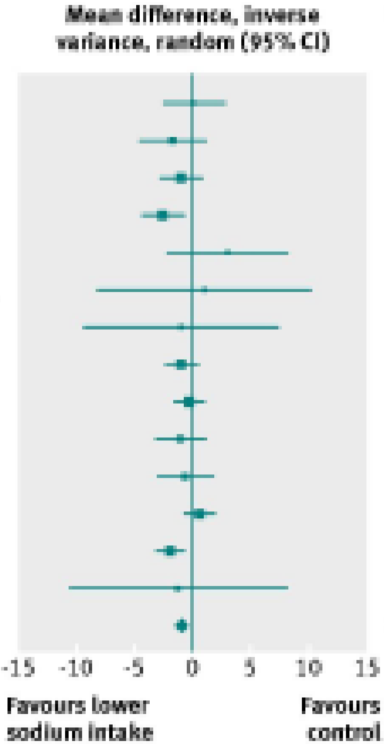
Cappuccio FP & Capewell S. Functional Food Rev 2015; in press

… and children

Study	Mean (SD)/Total No of participants: Lower sodium intake	Mean (SD)/Total No of participants: Control	Weight (%)	Mean difference, inverse variance, random (95% CI)
All				
Calabrese 1985 (males)[119]	-2.4 (6.00)/26	-2.5 (3.90)/52	4.80	0.10 (-2.44 to 2.64)
Calabrese 1985 (females)[119]	-5.3 (6.60)/25	-3.6 (3.90)/50	4.00	-1.73 (-4.53 to 1.07)
Ellison 1989 (males)[114]	0.0 (8.23)/152	0.9 (8.23)/193	8.80	-0.94 (-2.69 to 0.81)
Ellison 1989 (females)[114]	-2.5 (7.74)/157	0.0 (7.74)/148	8.90	-2.54 (-4.28 to -0.80)
Gillum 1981 (both sexes)[120]	1.0 (8.61)/15	-2.0 (8.46)/36	1.30	3.00 (-2.16 to 8.16)
Howe 1985 (males)[115]	-1.0 (9.95)/11	-2.0 (11.96)/11	0.40	1.00 (-8.19 to 10.19)
Howe 1985 (females)[115]	-5.0 (9.49)/10	-4.0 (9.49)/10	0.50	-1.00 (-9.32 to 7.32)
Howe 1991 (both sexes)[115]	-1.0 (4.56)/90	0.0 (4.56)/90	13.00	-0.97 (-2.30 to 0.36)
Miller 1988 (both sexes)[116]	-0.3 (2.81)/44	0.0 (2.81)/44	15.20	-0.30 (-1.47 to 0.87)
Palacios 2004 (black females)[117]	-6.2 (2.80)/19	-5.2 (3.56)/19	6.90	-1.00 (-3.04 to 1.04)
Palacios 2004 (white females)[117]	-9.9 (2.91)/12	-9.3 (2.52)/10	5.80	-0.60 (-2.87 to 1.67)
Sinaiko 1993 (males)[122]	2.2 (2.96)/35	1.6 (2.32)/34	14.00	0.60 (-0.65 to 1.85)
Sinaiko 1993 (females)[122]	-0.5 (2.37)/35	1.4 (2.37)/35	16.20	-1.90 (-3.01 to -0.79)
Trevisan 1981 (both sexes)[118]	-1.3 (12.40)/12	0.0 (9.40)/9	0.40	-1.25 (-10.57 to 8.07)
Subtotal	643	761	100.00	-0.84 (-1.43 to -0.25)

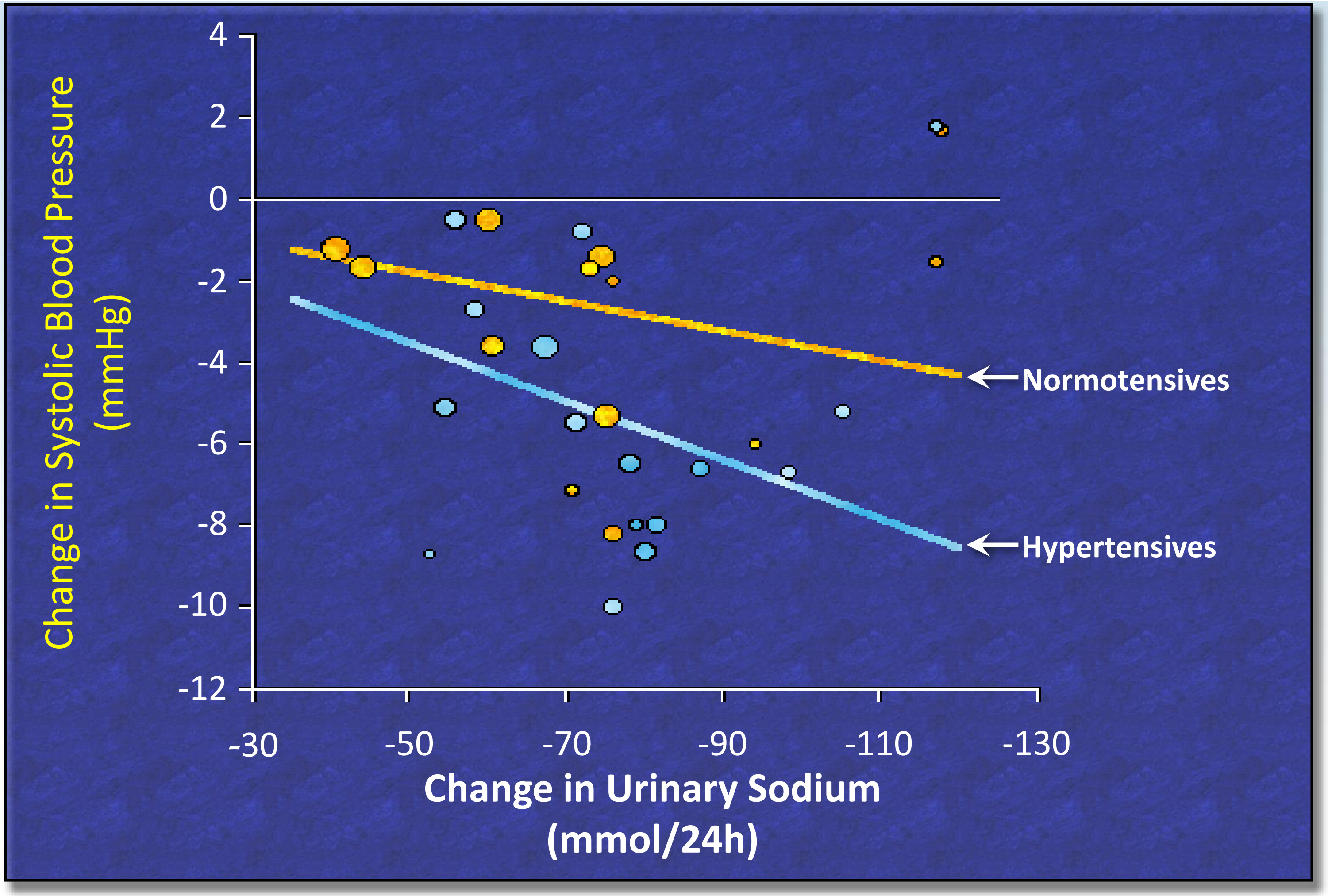
Test for heterogeneity: τ^2=0.24, χ^2=16.38, df=13, P=0.23, I^2=21%

Test for overall effect: z=2.78, P=0.005



Aburto NJ et al. BMJ 2013; 346: f1326

The lower the salt, the lower the blood pressure

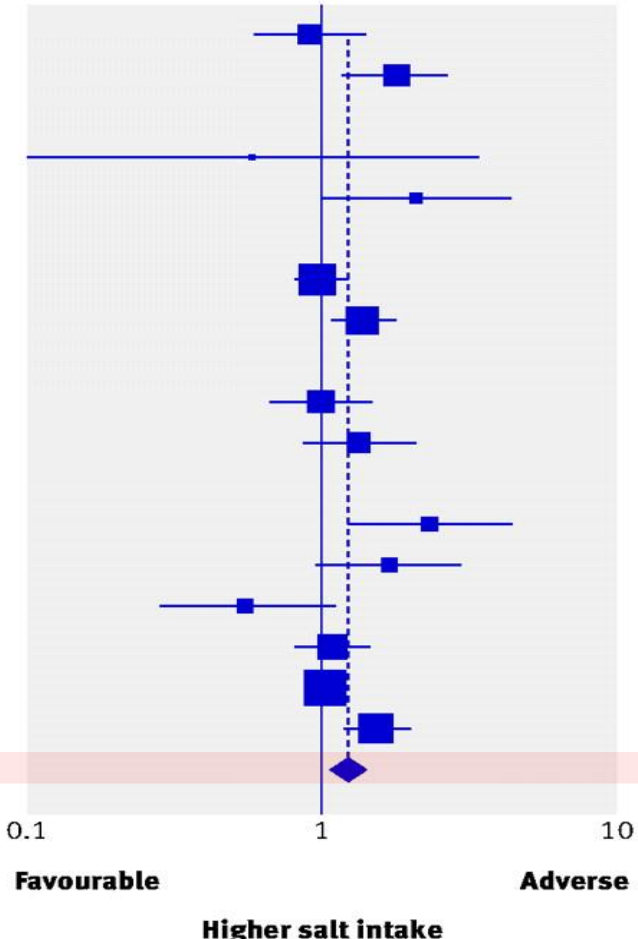


He FJ, MacGregor GA. J Hum Hypertens. 2002;16:761-70

Risk of stroke associated with salt intake in population

Study	Sample size	Events	Follow-up (years)	Relative risk (95% CI)	Sodium difference (mmol/day)	Relative risk (95% CI)
Kagan 1985[10]	7895	238	10		100	0.92 (0.60 to 1.42)
Hu 1992[11]	8562	104	4			1.79 (1.18 to 2.70)
Alderman 1995[6]						
Men	1900	17	3.5		150	0.59 (0.10 to 3.43)
Women	1037	6			120	2.10 (1.01 to 4.33)
He 1999[9]						
Normal weight	6797	430	19		100	0.99 (0.81 to 1.20)
Overweight	2688	250			100	1.39 (1.10 to 1.76)
Tuomilheto 2001[13]						
Men	1173	43	13		100	1.00 (0.68 to 1.48)
Women	1263	41			100	1.34 (0.87 to 2.06)
Nagata 2004[14]						
Men	13 355	137	7		110	2.34 (1.23 to 4.47)
Women	15 724	132			92	1.70 (0.96 to 3.00)
Cohen 2006[15]	7154	79	13.7		92	0.56 (0.28 to 1.11)
Geleijnse 2007[16]	1448	181	5		69	1.08 (0.81 to 1.45)
Larsson 2008[18]	26 556	2702	13.6		84	1.04 (0.93 to 1.17)
Umesawa 2008[19]	58 730	986	12.7		85	1.55 (1.20 to 2.00)
Combined effect: P=0.007	154 282	5346				1.23 (1.06 to 1.43)

Heterogeneity: P=0.04, Egger's test: P=0.26



Strazzullo P et al. BMJ 2009; 339: b4567

Salt reduction lowers cardiovascular risk: meta-analysis of outcome trials

Study*	Reduced-salt		Control		Relative risk (95% CI)
	Events	Total	Events	Total	
TOHP I	17	321	32	311	0·51 (0·29–0·91)
TOHP II	71	938	80	935	0·88 (0·65–1·20)
Morgan	6	34	5	33	1·16 (0·39–3·45)
TONE	36	322	46	331	0·80 (0·53–1·21)
Total	**130**	**1615**	**163**	**1610**	**0·80 (0·64–0·99)**

Relative risk of CVD events (95% CI)

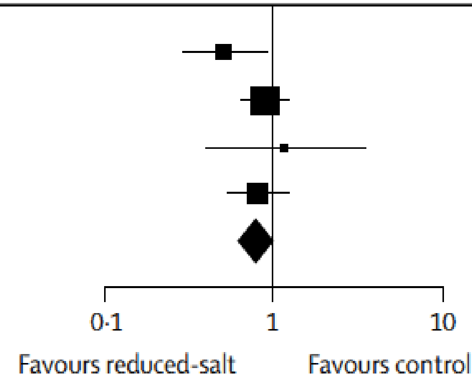


Figure: **Relative risk of cardiovascular disease (CVD) events in our meta-analysis of outcome trials of salt reduction at longest follow-up combining hypertensive and normotensive individuals**

Duration of follow-up ranged from 7 months to 11·5 years. We used fixed effect model with normotensives and hypertensives combined. Heterogeneity χ^2=3·20, df=3 (p=0·36); I^2=6%.Test for overall effect Z=2·02 (p=0·04). TOHP I=Trial of Hypertension Prevention, phase 1. TOHP II=Trial of Hypertension Prevention, phase 2. TONE=Trial of Nonpharmacologic Interventions in Elderly. *Data for individual trials taken from Taylor and colleagues' meta-analysis.[1]

He FJ, MacGregor GA. Lancet 2011:378:380-2

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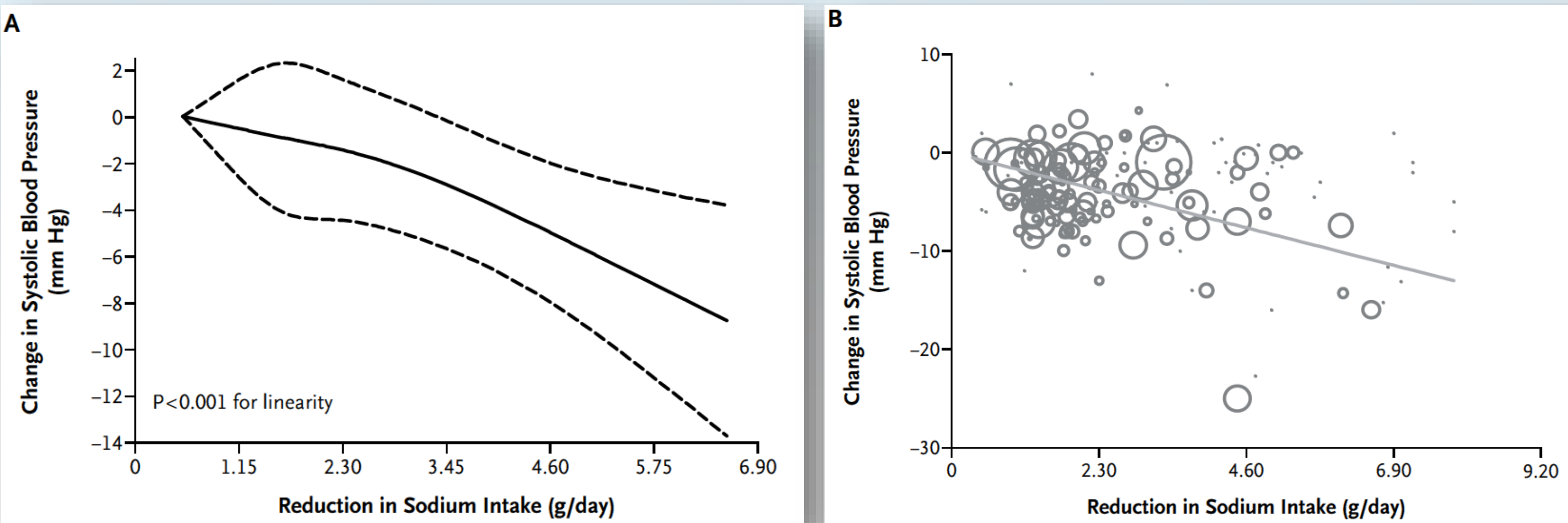
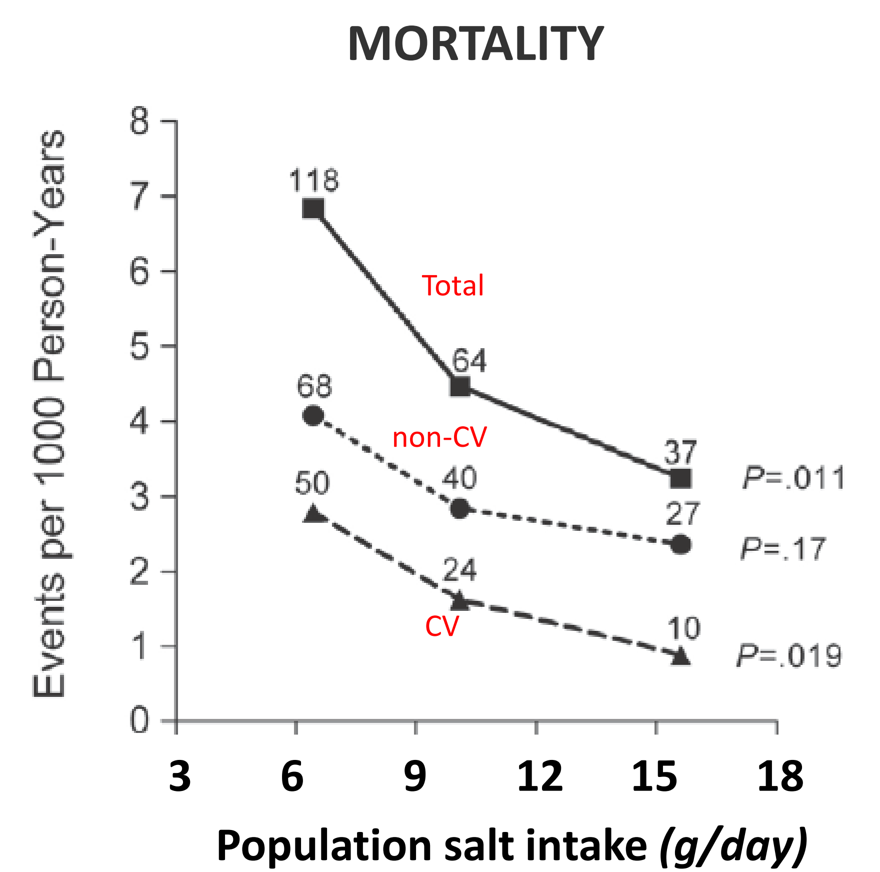
Global Sodium Consumption and Death from Cardiovascular Causes

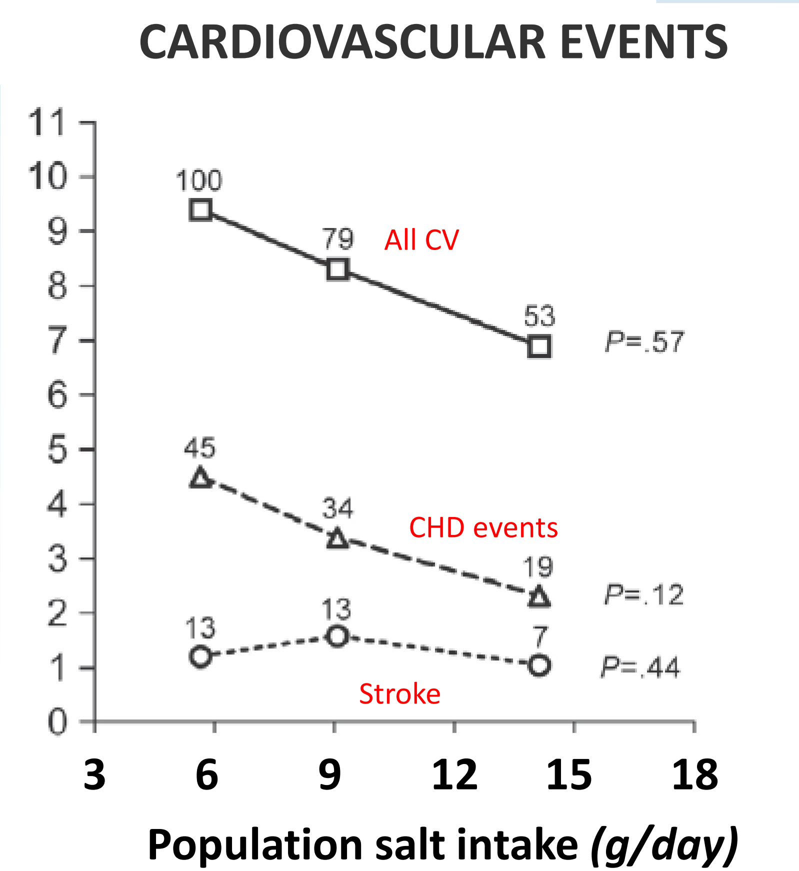
Figure 1. Effects of Reduced Sodium Intake on Systolic Blood Pressure.



Mozaffarian D et al. NEJM 2014:371:624-34

EPOGH Study: mortality rates and CV events by thirds of 24h urinary sodium excretion





Stolarz-Skrzypek et al, JAMA 2011;305:1777–85

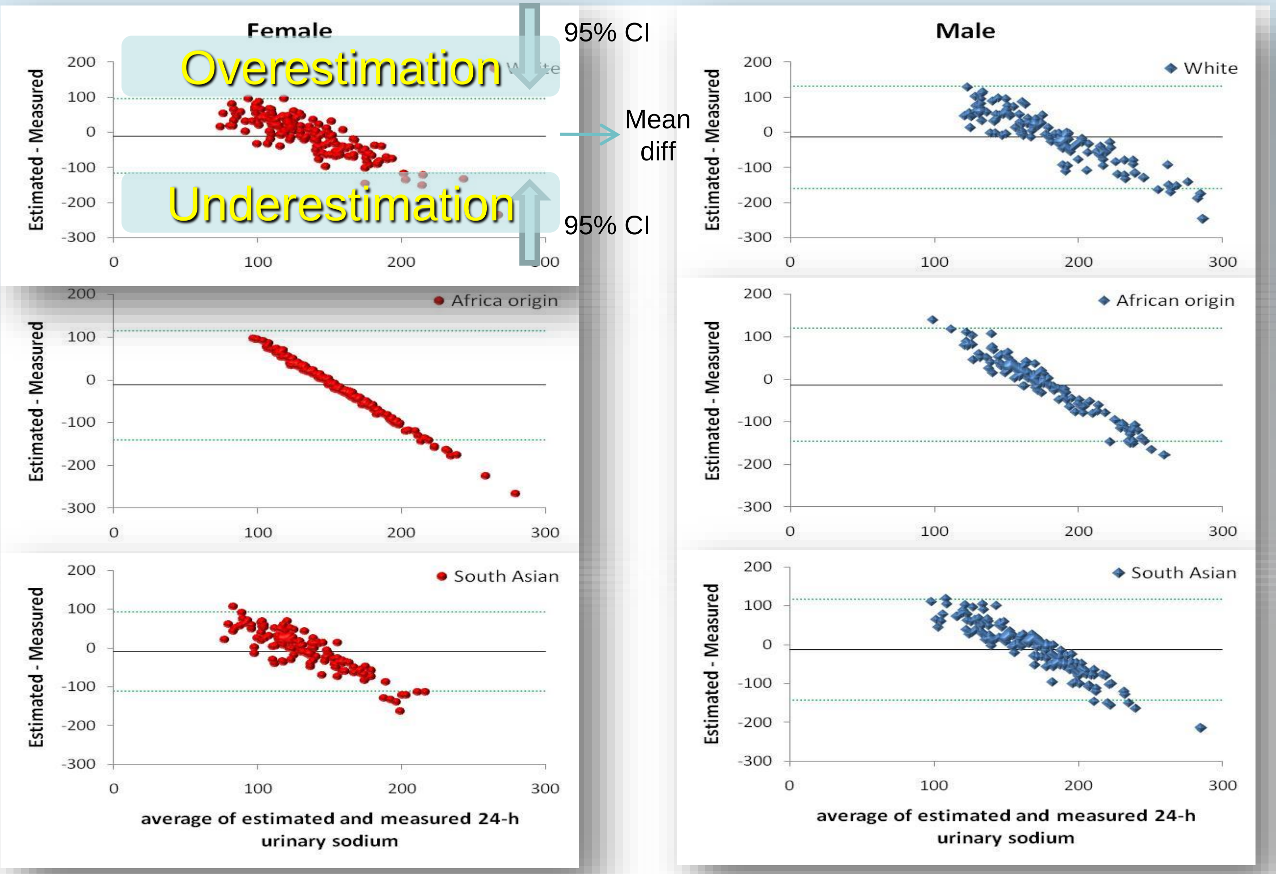
EPOGH Study: characteristics of male participants

Variable	Sodium intake tertile Lowest	Highest	*p*
24h UNa excr. (mmol)	**120**	**290**	**<0.05**
24h urine volume (L)	**1.3**	**1.8**	**<0.05**
24h creat. excr. (mmol)	**12**	**16**	**<0.05**
24h UK excr. (mmol)	**62**	**85**	**<0.05**
≤ Elementary school educ.	**35%**	**20%**	

EXCLUSIONS: only if 24h urine volume < 300 mL

Stolarz-Skrzypek et al, JAMA 2011;305:1777–85
He FJ et al. Kidney Int 2011;80:696-698

Bland-Altman plot comparing estimated 24h UNa by Tanaka's method and actually measured 24h UNa



Ji C et al. Nutr Metab Cardiovasc Dis 2014; 24: 140-7

Association of Urinary Sodium and Potassium Excretion with Blood Pressure

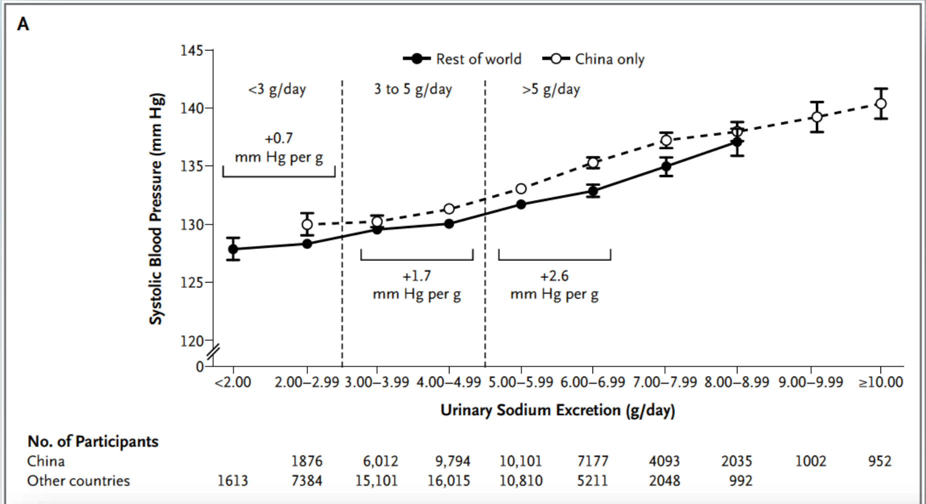


Figure 2. Mean Systolic and Diastolic Blood Pressure According to Sodium Excretion.

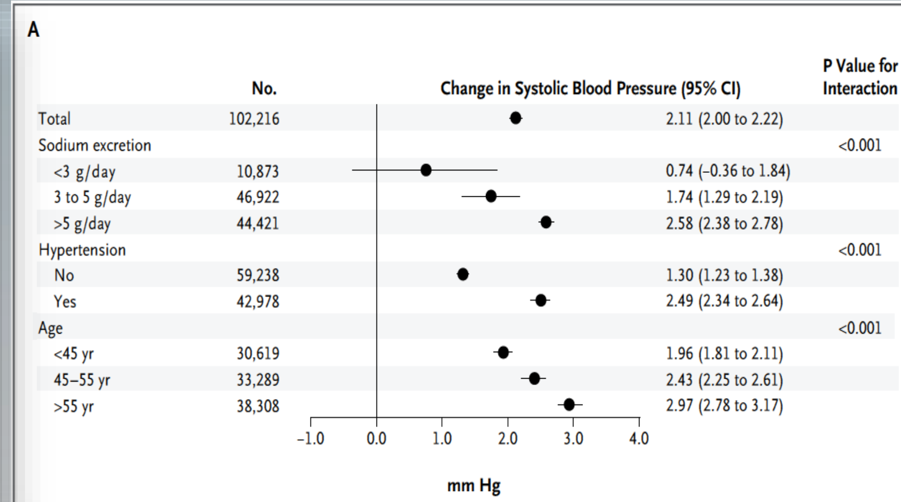


Figure 3. Forest Plots of Changes in Systolic and Diastolic Blood Pressure for Every 1-g Increase in Sodium Excretion.

- Sodium estimated by single fasting morning urine – unreliable and biased
- Sodium Study (n~100K) not comparable to Overall Study (n~160K) – selection bias
  Fewer from India (5 v 18%) and more from China (42% v 30%)
  More participants with ill-health (hypertension, BP medication, CHD, CVD)
- Lower sodium excretion group (*see Table 1, p. 603*):
  <3g per day (<7.5g of salt per day) – unable to discriminate on low sodium intake
  Small sample size - wide confidence intervals

Mente A et al. NEJM 2014:371:601-11

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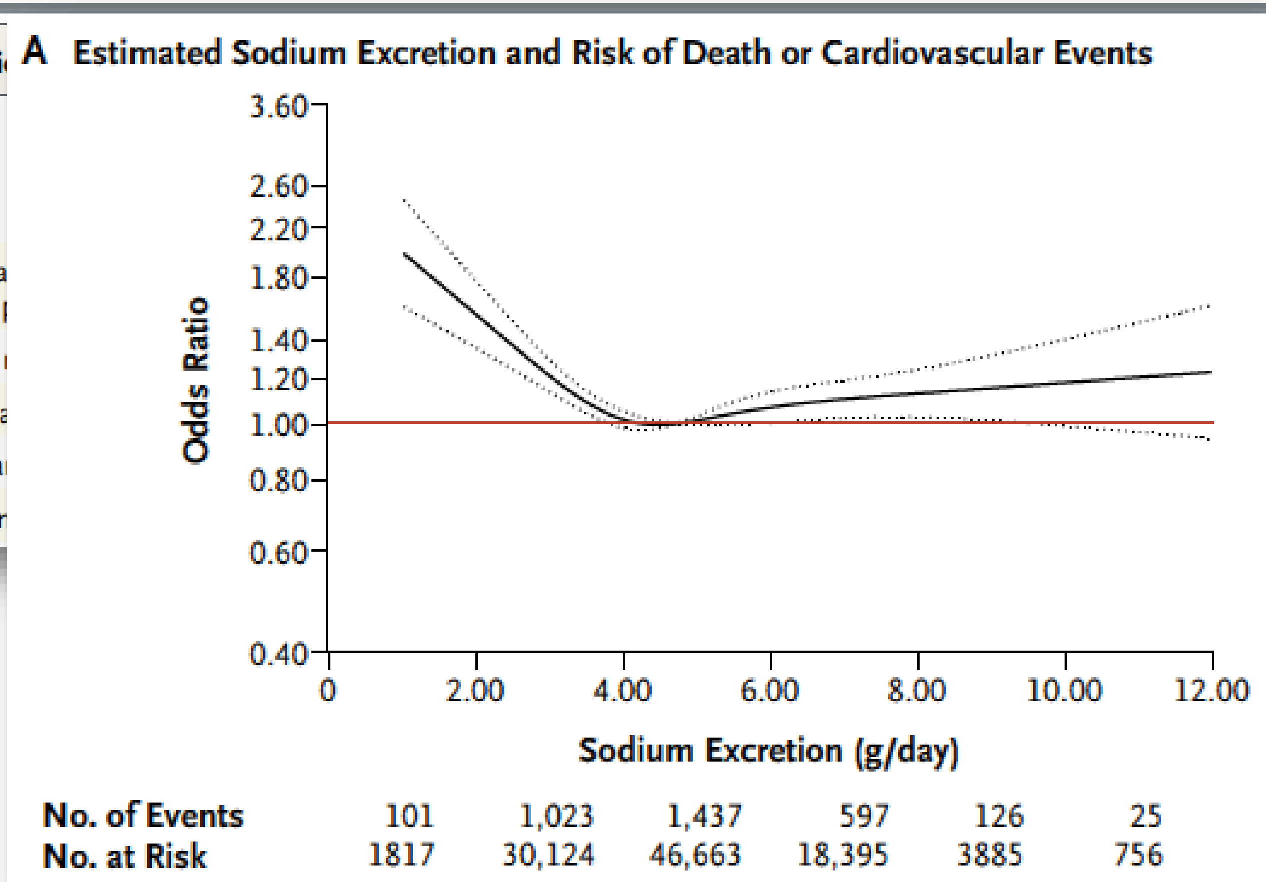
Urinary Sodium and Potassium Excretion, Mortality, and Cardiovascular Events

Table 2. Associati	
Variable	≥7.00 g/day (N=11,017)
Death or cardiova no. of	365 (3.3)
Analysis — odds	
Univariate ana	1.18 (1.05–1.32)
Multivariate a	
Primary ar	1.15 (1.02–1.30)



O'Donnell M et al. et al. NEJM 2014:371:612-23

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Urinary Sodium and Potassium Excretion, Mortality, and Cardiovascular Events

- Sodium estimated by single fasting morning urine – unreliable and biased
- Sodium Study (n~100K) not comparable to Overall Study (n~160K) – selection bias

  Fewer from India (5 v 18%) and more from China (42% v 30%)

  More participants with ill-health (hypertension, BP medication, CHD, CVD)
- Lower sodium excretion group (*see Table 1, p.616*):

  <3g per day (<7.5g of salt per day) – unable to discriminate on low sodium intake

  compared to higher sodium: 3y older; fewer men, Asians, smokers; more Africans and non-Asians, urban; lower blood pressure; higher LDL-cholesterol, history of CVD and diabetes, F&V intake, medication use – biased towards lower sodium excretion due to age and gender, and presence of ill-health (reverse causality)

O'Donnell M et al. et al. NEJM 2014:371:612-23
Cappuccio FP et al. Eur Heart J 2013; May 8: on-line

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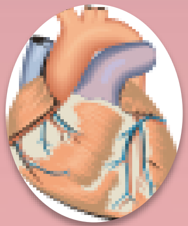
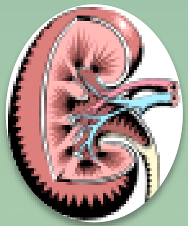
EFFECTS OF A MODERATE REDUCTION IN SALT INTAKE

REDUCES
High BP

PREVENTS
Stroke



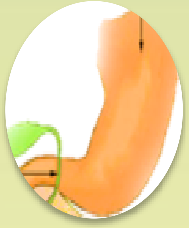
PREVENTS
CHD
LVH



REDUCES
Fluid retention,
High GFR,
albumin,
calcium

PREVENTS
High PTH

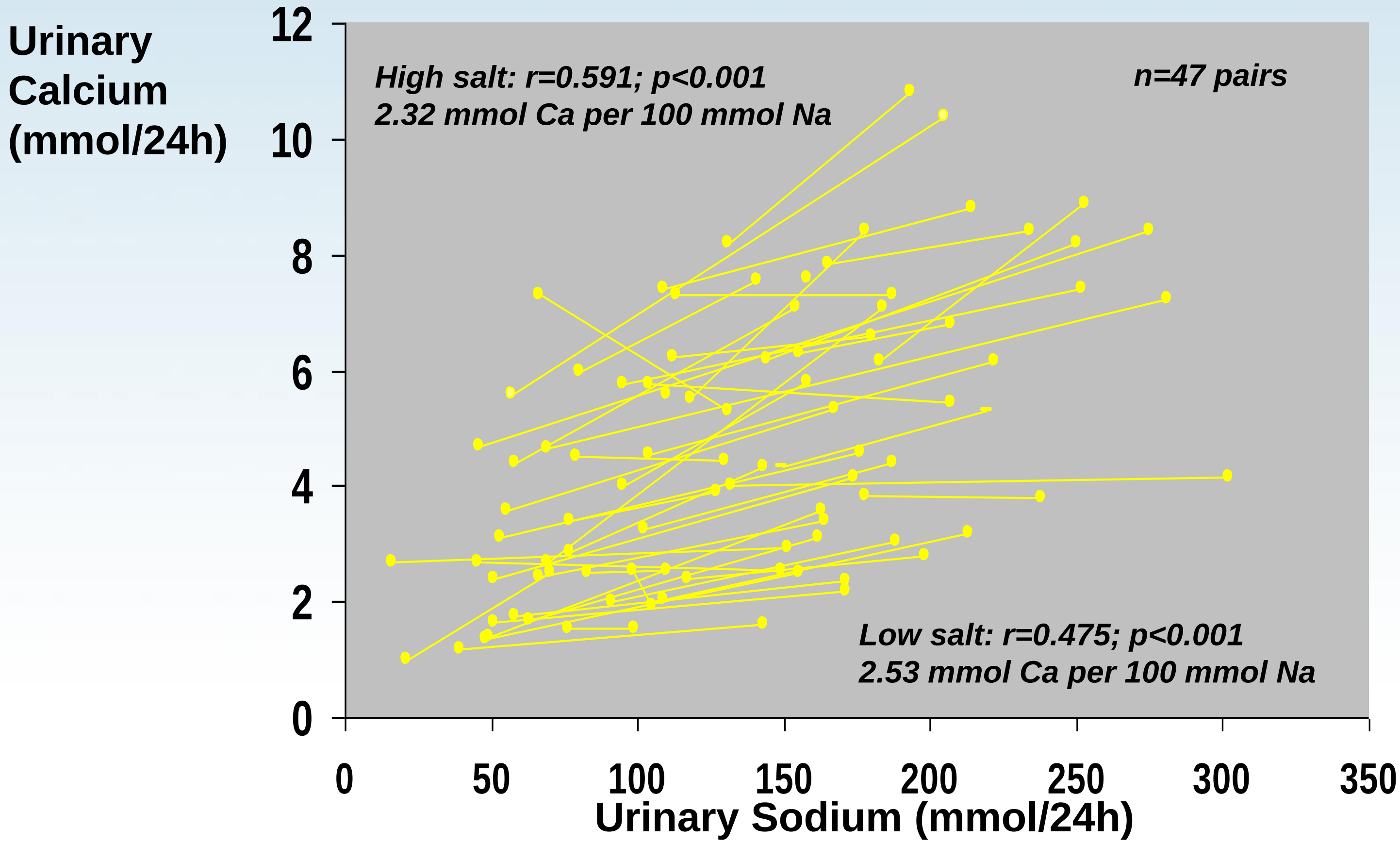
REDUCES
Bone
mineral loss



MAY REDUCE
Stomach cancer

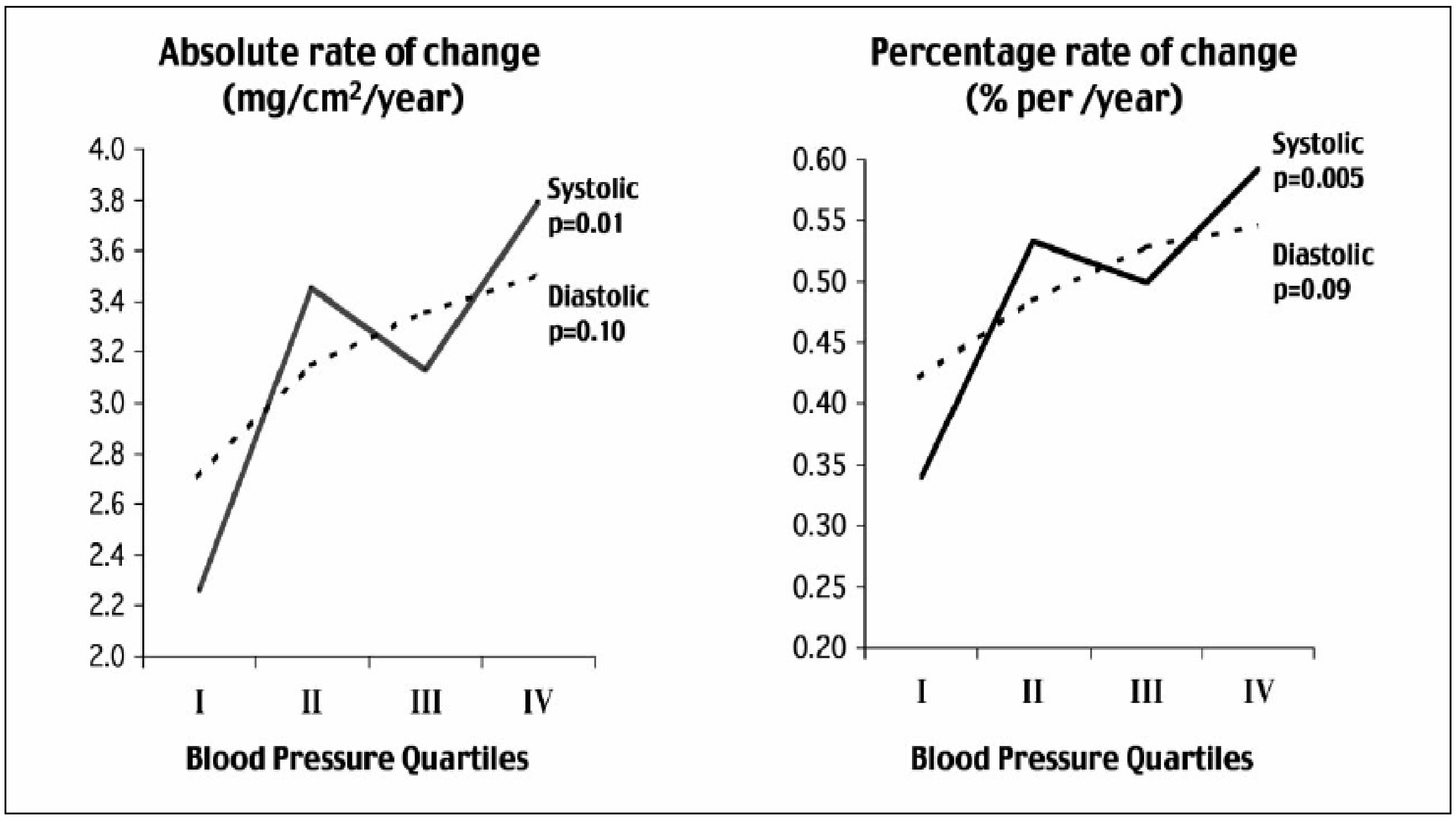
MAY
REDUCE
Cataract

Relationship between sodium and calcium excretion in 47 elderly subjects on a high and a low sodium intake



Cappuccio FP et al. J Nephrol 2000;13:169-77

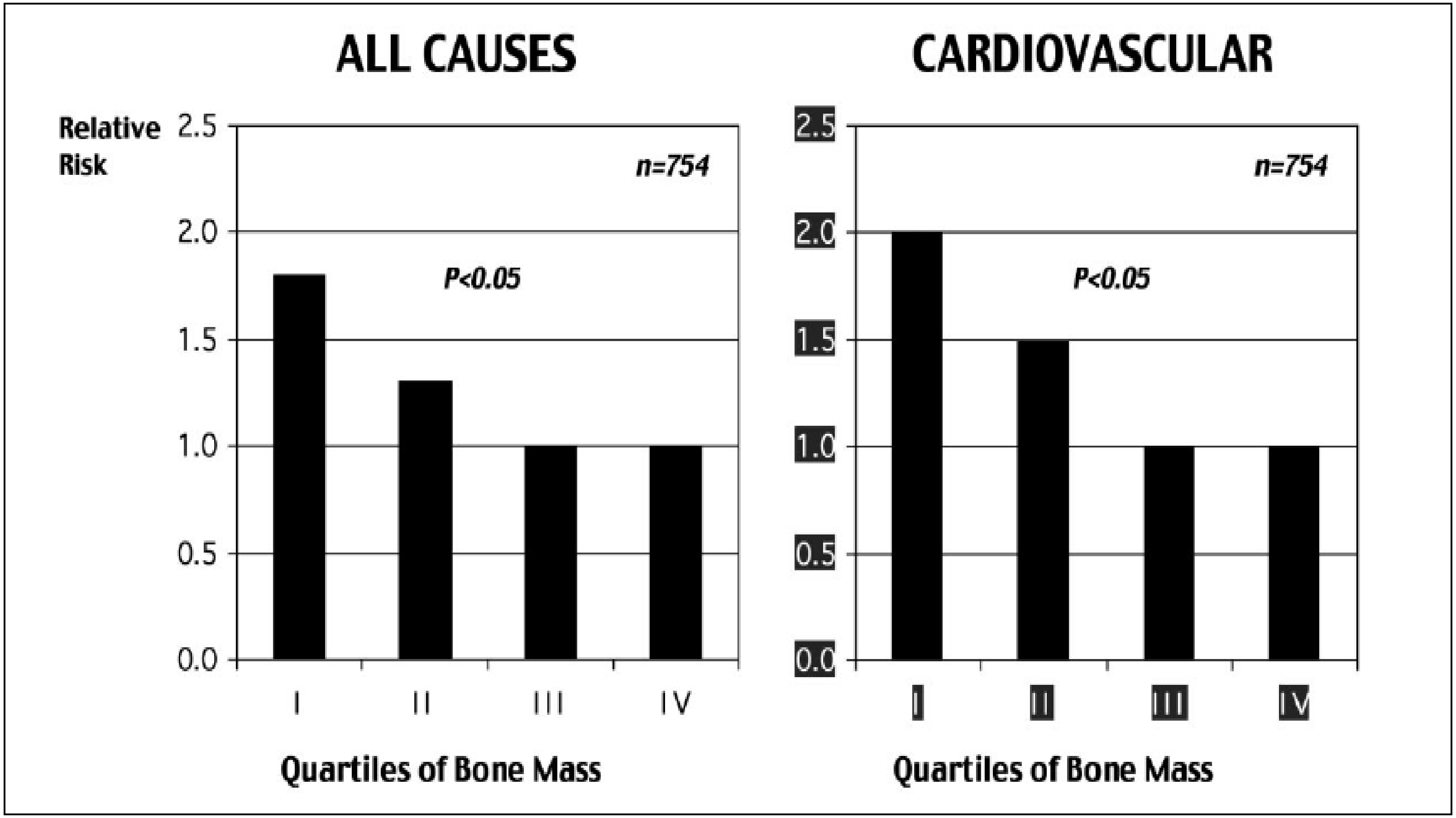
High BP and faster BMD loss over 3.5 years in 3,676 white women (66-91 yrs) not taking thiazide diuretics



Results are adjusted for age, initial bone-mineral density, body weight, weight change, smoking and use of hormone-replacement therapy.

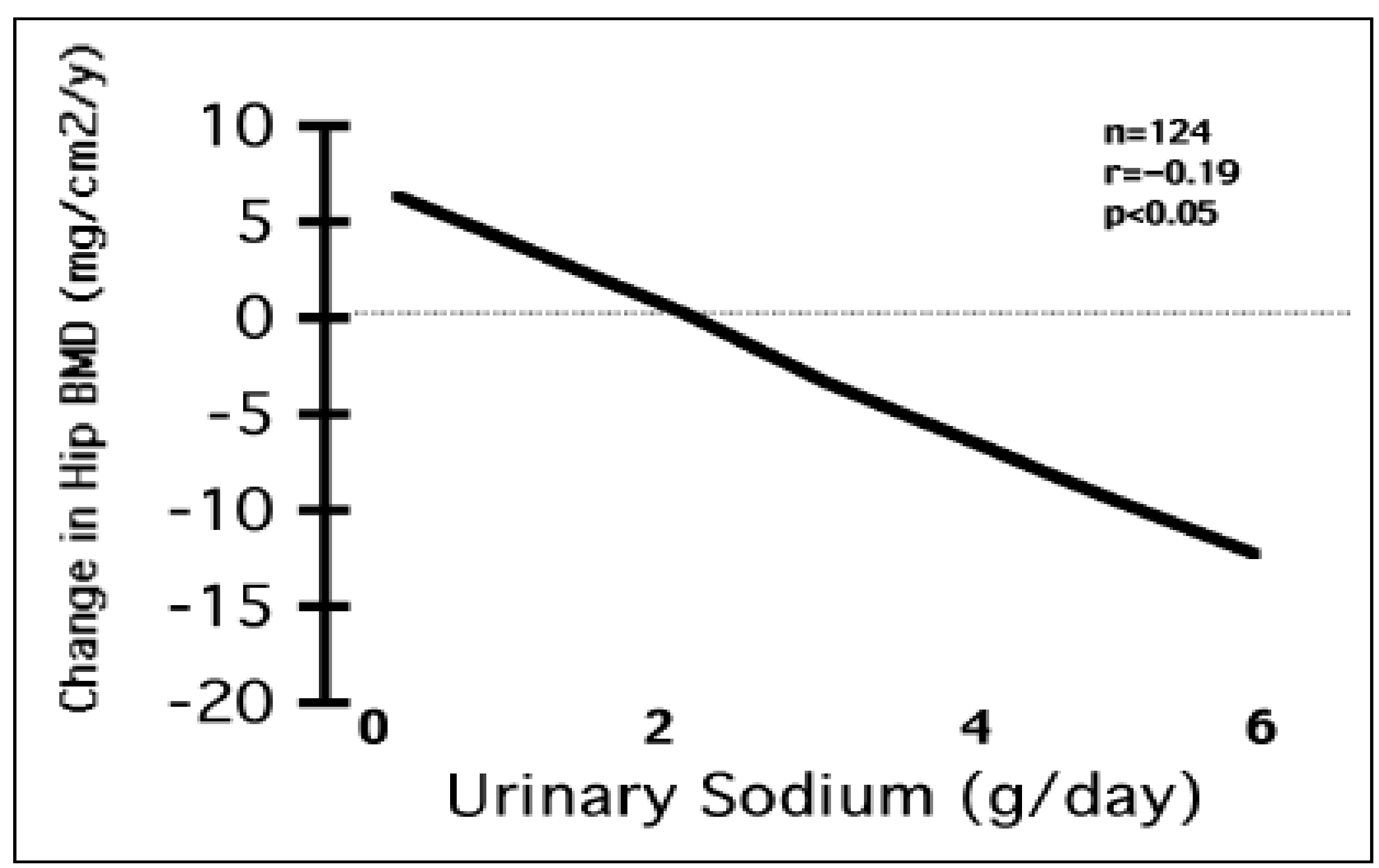
Cappuccio FP et al. Lancet 1999;354:971-5

Low bone mineral content and CVD mortality in postmenopausal women (>60 yrs)



Von der Recke P et al. Am J Med 1999 ;106:273-8

High salt intake and faster BMD loss at the hip in a 2-year follow-up study of postmenopausal women



Devine A et al. Am J Clin Nutr 1995; 62: 740-5

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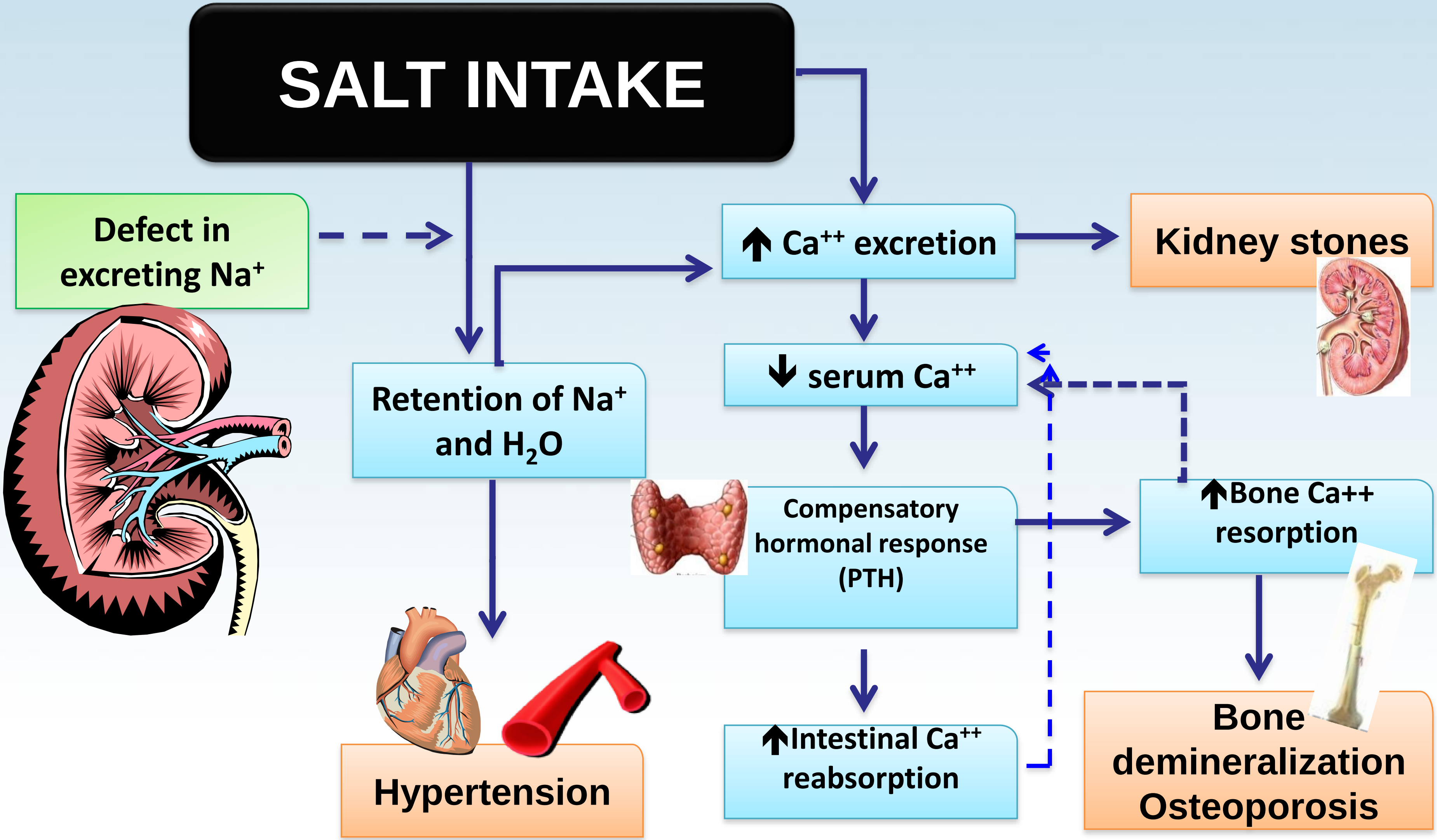
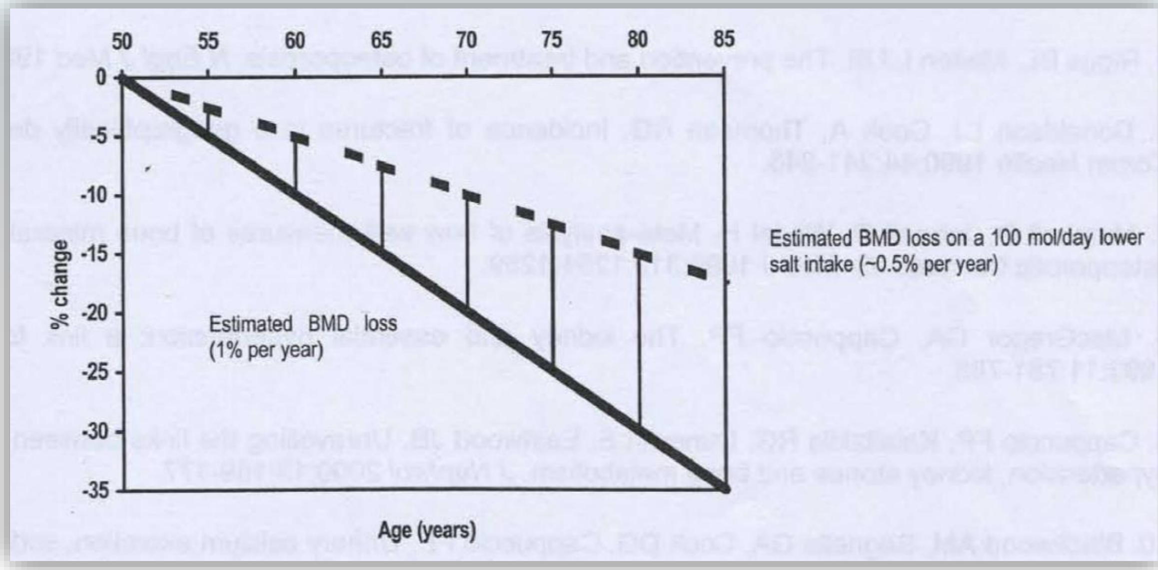


Cappuccio FP et al. Curr Opinion Nephrol Hypert 1997;6:477-82

Implications

- **The estimated effects on calcium excretion are**
  - ***1 mmol calcium per 100 mmol of sodium change***
  - ***0.2 mmol calcium per 10 mmHg mean BP change***

- **These changes, if sustained over decades, may be responsible for the effects on total body calcium balance**



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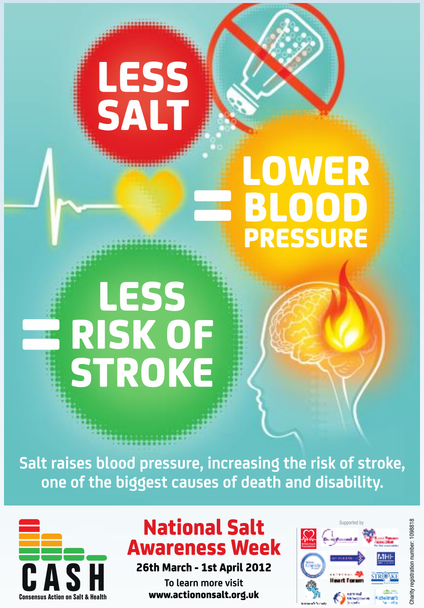
Population approach

- A reduction in salt intake reduces BP
- A reduction of 5g per day may reduce strokes by as much as 23% (i.e. 1.25M deaths worldwide)
- Evidence of benefits as low as 3g salt per day
- Effective in both genders, any age, ethnic group, high, medium and low-income countries
- Population salt reduction programs are both feasible and effective (preventive imperative)
- Salt reduction programs are cost-saving ($6-12 saved for every $ spent)(economic imperative)
- Policies are powerful, rapid, equitable, cost-saving



Components of a strategy to reduce population salt intake

Communication

- **Public Awareness Campaigns**
- Consumers
- Food industry
- Decision makers
- Media
- Health Professionals

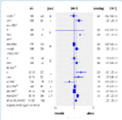
Reformulation

- **Setting Targets**
- Reformulation
- Benchmarking food categories
- Labelling
- **Industry Engagement**
- Motivation
- Costs & Benefits
- Consumer awareness
- Wider support
- Corporate responsibility

- **Voluntary vs Regulatory**

Monitoring

- **Population salt intake**
- Urinary sodium
- Dietary surveys
- **Reformulation progress**
- Salt content of foods (databanks; self-reporting by industry; market surveys)
- **Effectiveness of communication**
- Measuring awareness of campaigns
- Measuring attitudes and behaviour changes

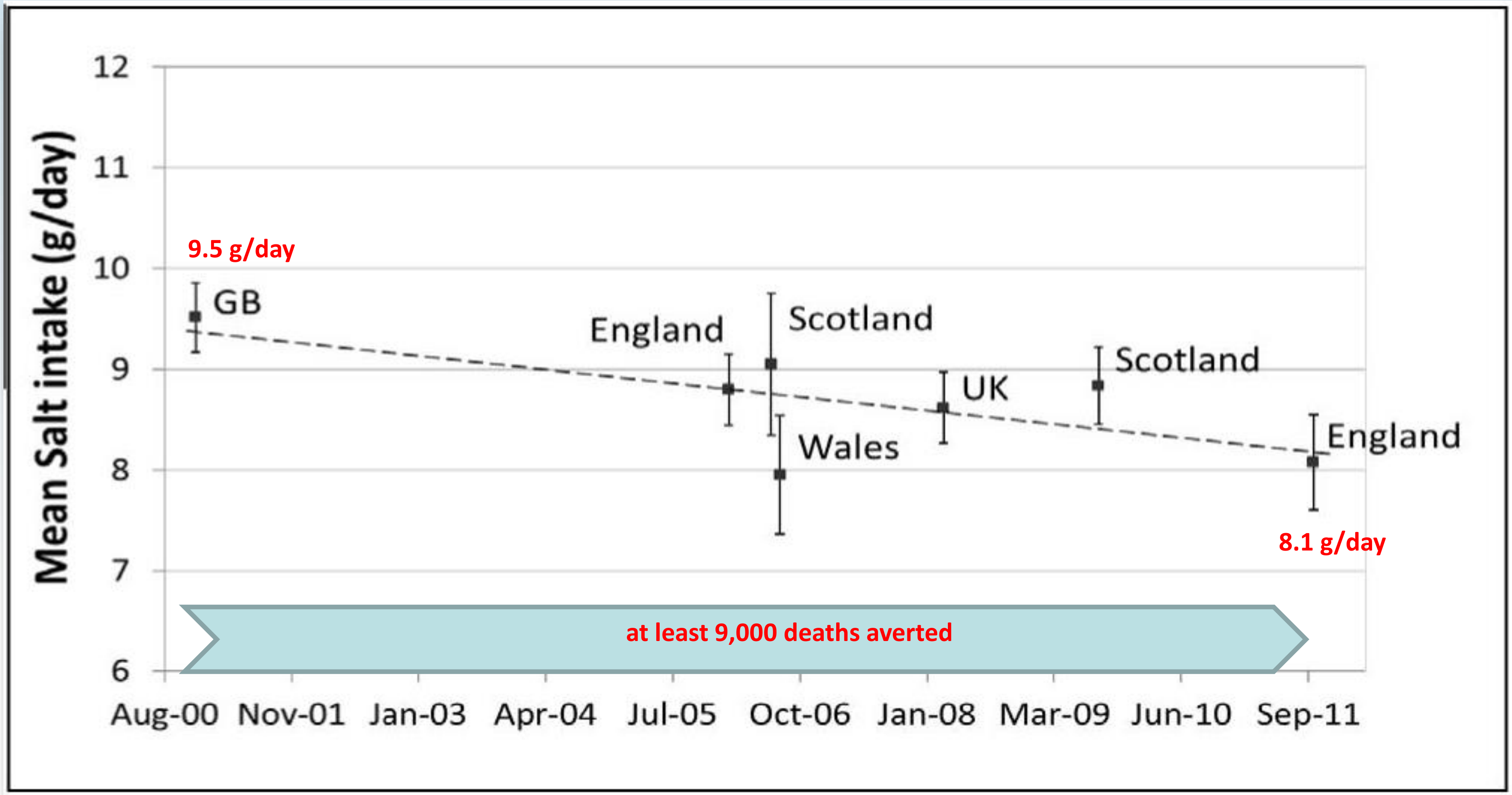


Research

- Epidemiology
- Nutrition
- Public Health
- Food technology
- Behavioural
- Evaluation
- Policy

Cappuccio FP et al. BMJ 2010;343:402-5

Salt intake reduced by 1.4 g/day in the UK between 2000 and 2011



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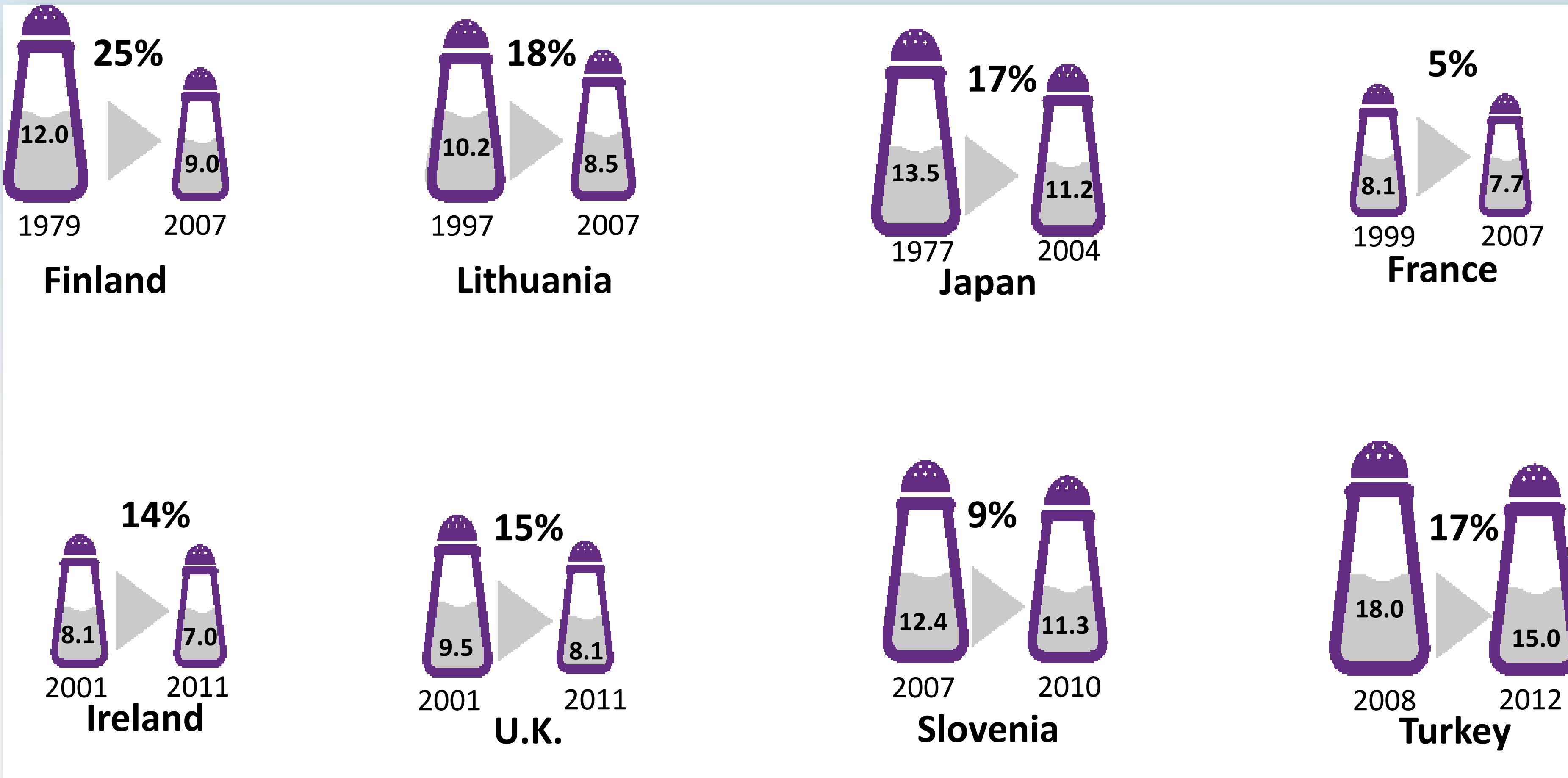
Salt intake reduction (g/day)



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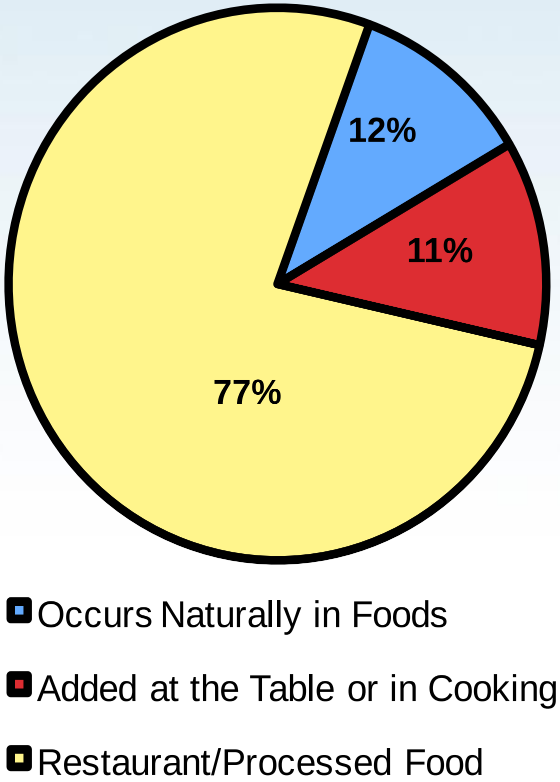
Where in our diet does salt come from?

In regions where most food is processed or eaten in restaurants



- 12% natural content of foods
- "hidden" salt: 77% from processed food – manufactured and restaurants
- "conscious" salt: 11% added at the table (5%) and in cooking (6%)

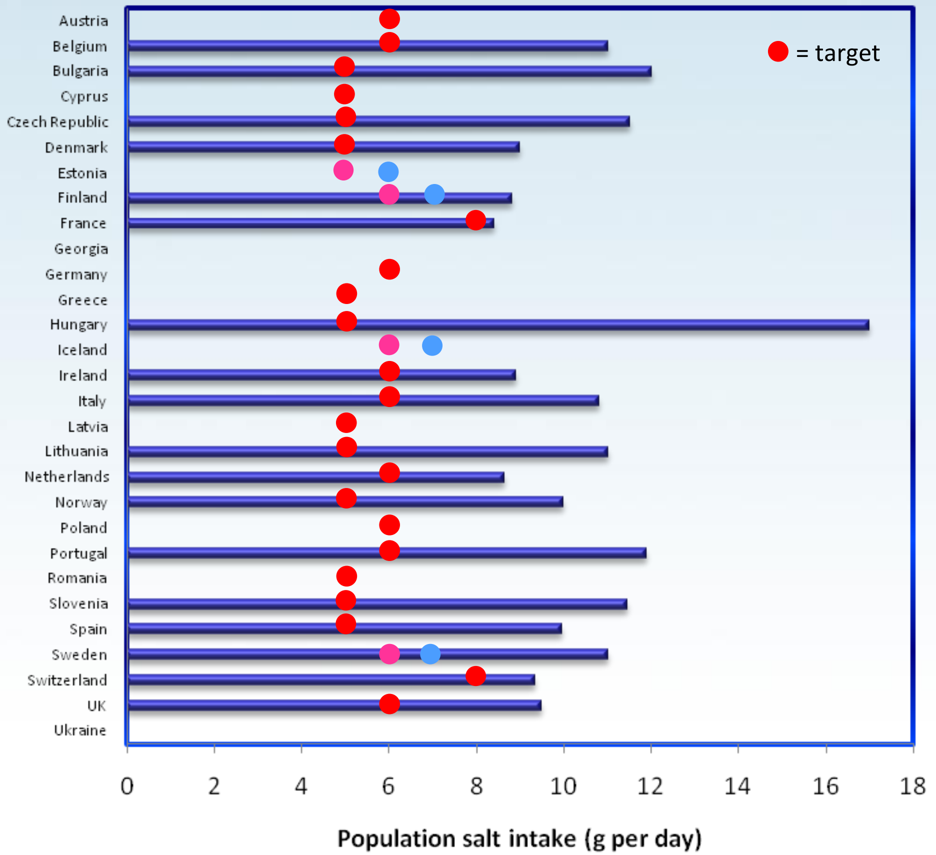
***J Am College of Nutrition.* 1991;10:383-93.**

The food industry and self-regulation

- Benefits of self-regulatory system
  - conserves government resources
  - less adversarial
  - more flexible
  - timelier than government regulation.
- Risk when promises not fulfilled due to weak standards or ineffective enforcement.
- Proposed standards for the Food Industry
  - Transparency
  - Meaningful objectives and benchmarks
  - Accountability and objective evaluation
  - Oversight
- Why does industry engage in self-regulation?
  - Little government involvement, scarce natural resources (e.g. forestry, fisheries)
  - Government perceived as a threat, hence to prevent or forestall, to deflect government regulation (e.g. alcohol, tobacco, food industry?)

Sharma LL et al. Am J Public Health 2010;100:240-6

Salt intake, targets, policies and strategies in Europe



Country	1	2	3	4	5
Austria					
Belgium	✓	✓	✓	✓	✓
Bulgaria	✓		✓	✓	
Cyprus		✓	✓	✓	✓
Czech Rep					
Denmark	✓		✓	✓	✓
Estonia					
Finland	✓		✓	✓	✓
France	✓		✓	✓	✓
Georgia		✓			
Germany					
Greece					
Hungary	✓	✓	✓	✓	✓
Iceland					
Ireland	✓	✓	✓	✓	✓
Italy	✓		✓	✓	✓
Latvia	✓	✓	✓	✓	✓
Lithuania				✓	✓
Netherlands	✓	✓	✓	✓	✓
Norway	✓			✓	✓
Poland				✓	✓
Portugal				✓	✓
Romania					
Slovenia	✓	✓	✓	✓	✓
Spain	✓			✓	✓
Sweden					
Switzerland	✓	✓		✓	✓
UK	✓	✓	✓	✓	✓
Ukraine	✓	✓			

1 = salt in food
2 = consumer behaviours
3 = monitoring
4 = reformulation
5 = education

Cappuccio FP et al. BMJ 2010; 343: 402-5

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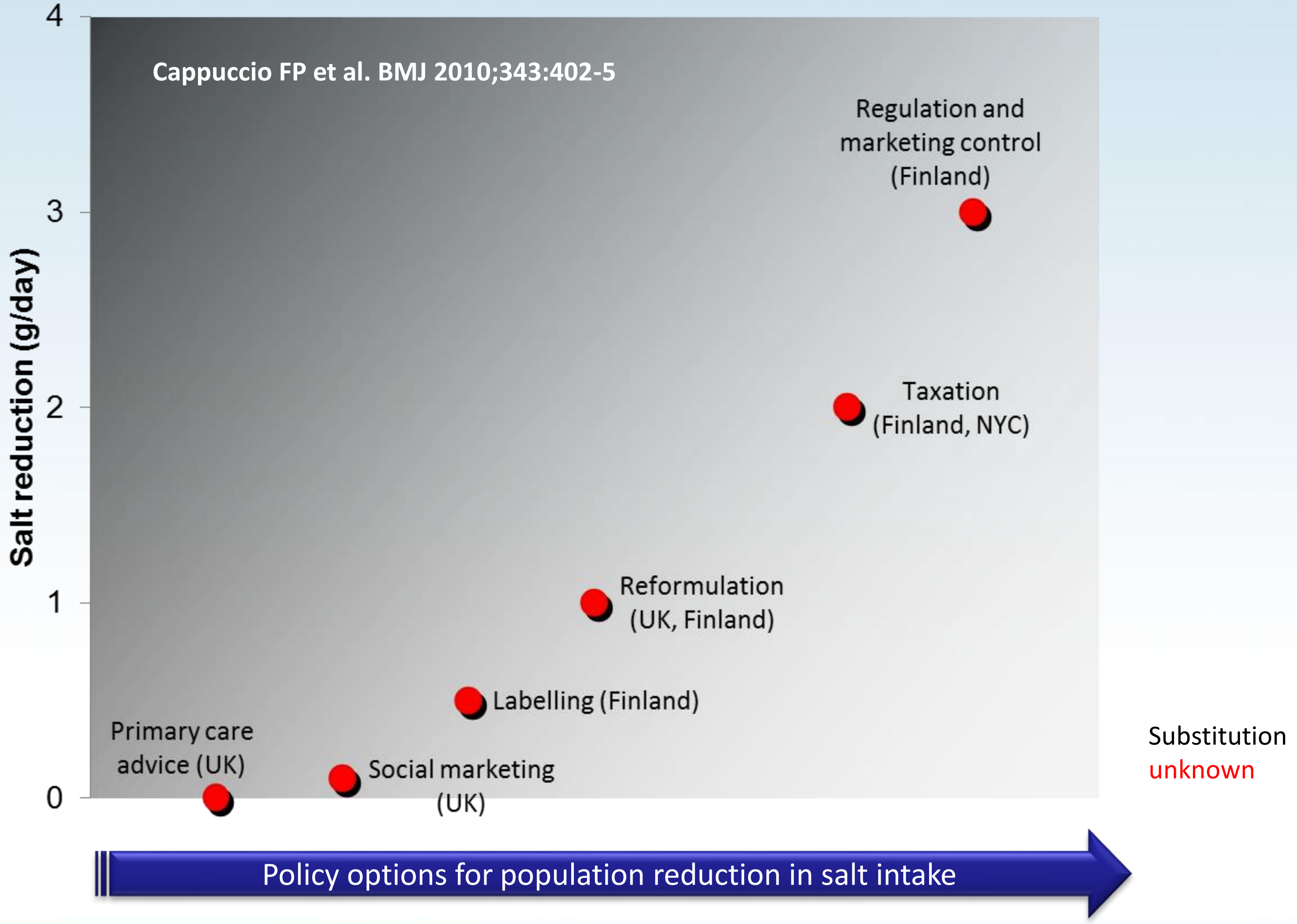
Estimated effects of different policy options



Salt and cardiovascular disease

Legislation to cut levels of salt in processed food is necessary and justified

RESEARCH, p 885

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cvme@warwick.ac.uk

Competing interests: None declared.

Provenance and peer review: Commissioned; not externally peer reviewed.

BMJ 2007;334:859–60
doi:10.1136/bmj.39175.364954.BE

Blood pressure is the most powerful predictor of stroke and other cardiovascular events. The importance of salt (sodium chloride) intake in determining blood pressure and the incidence of hypertension is well established. Furthermore, randomised controlled clinical trials of moderate reductions in salt intake show a dose dependent cause-effect relation and lack of a threshold effect within usual levels of salt intake in populations worldwide.[1] The effect is independent of age, sex, ethnic origin, baseline blood pressure, and body mass.

Prospective studies,[2-5] with one exception,[6] also indicate that higher salt intake predicts the incidence of cardiovascular events. While widespread support exists for reducing salt intake to prevent cardiovascular disease, the lack of large and long randomised trials on the effects of salt reduction on clinical outcomes has encouraged some people to argue against a policy of salt reduction in populations.[6]

In this week's *BMJ*, Cook and colleagues[7] report the long term effects of reduced dietary sodium on cardiovascular disease in people participating in the controlled randomised trials of hypertension prevention follow-up studies (TOHP I and II). More than 3000 participants without hypertension were randomised to a reduced sodium intake for 18 months (TOHP I) or 36-48 months (TOHP II), or to a control arm. The reductions in sodium intake were 44 mmol/day and 33 mmol/day (equivalent to −2.6 g and −2.0 g of salt), respectively. The results show that people originally allocated to either sodium reduction group had a 30% lower incidence of cardiovascular events in the next 10-15 years, irrespective of sex, ethnic origin, age, body mass, and blood pressure. The benefits exceed those estimated by a recent meta-analysis.[8] Cook and colleagues' study is the first to report a beneficial effect of dietary salt reduction on cardiovascular outcomes based on randomised trial data.

The study strengthens the support for dietary recommendations for lower salt intake to prevent cardiovascular disease in the general population. In 1985, the World Health Organization recommended that the average salt intake should be reduced to 5 g per day or less. However, few countries have policies for targeted reduction in salt intake.

Differences exist between developed and developing countries. In Westernised countries, people derive salt mostly from bread and processed food and only a small proportion comes from discretionary use (up to 20%). A

population wide policy
countries can only be in
tion of the food industry
need to sustain a profita
from the food industry

In England and Wale
but levels of salt intake a
recommended 6 g of sa
do nothing, to establish
for a wide range of food
industry has to comply.
years, the first option w
The "voluntary" option
but it is unlikely to ach
position of the industry
proposal for labelling,
would carry a red alert
gap still remaining. The
the food industry to red
food to within set levels.
gests that legislation ha
option and at this stage

Conversely, in many
of sub-Saharan Africa, v
still discretionary, com
cific initiatives can be ef
given the increasing bu
related to hypertension

Without considerably
allowing greater availability of low salt foods, people in developed countries will find it difficult to exercise their "choice" when trying to reduce dietary salt. Doctors and health professionals have long used dietary counselling to deliver non-pharmacological management of hypertension. Advising patients to reduce salt intake with a lifestyle package quickly delivered in a busy primary care setting is ineffective, however.[11] A baseline assessment of salt intake (through a 24 h urinary collection for the measurement of sodium) is not part of the UK's National Service Framework requirements and is not included in the Quality and Outcome Framework. The current system is therefore unlikely to make health professionals and consumers more aware of how much salt people eat or to increase motivation and knowledge on how to reduce it. In a climate of scarce healthcare resources, one of the most cost effective ways to reduce the burden of cardiovascular disease is being overlooked.[13] And yet the evidence gets stronger.

In England and Wales … levels of salt intake are still far from the government's recommended 6 g of salt per day. Future options are to do nothing, to establish voluntary target levels of salt for a wide range of foods, or to legislate so that the food industry has to comply. Given the inertia of the past 20 years, the first option would not contribute to progress. The "voluntary" option would support existing work, but it is unlikely to achieve the set targets. … The "legislation" option would require the food industry to reduce the salt content of processed food to within set levels. The experience in Finland suggests that legislation has added value to the previous option and at this stage is necessary and justified.

e.g. creating incentives rather than disincentives

Cappuccio FP. BMJ 2007;334:859-60

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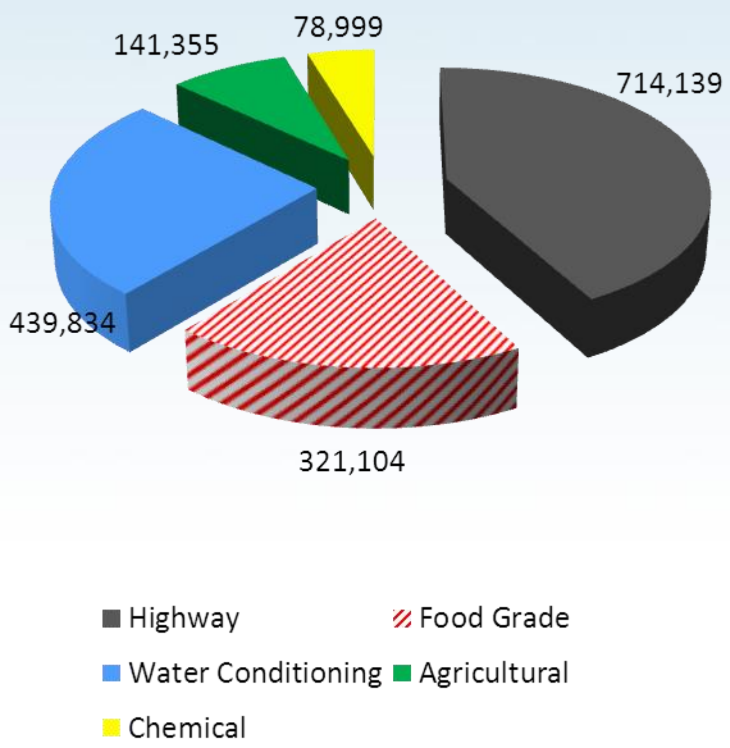
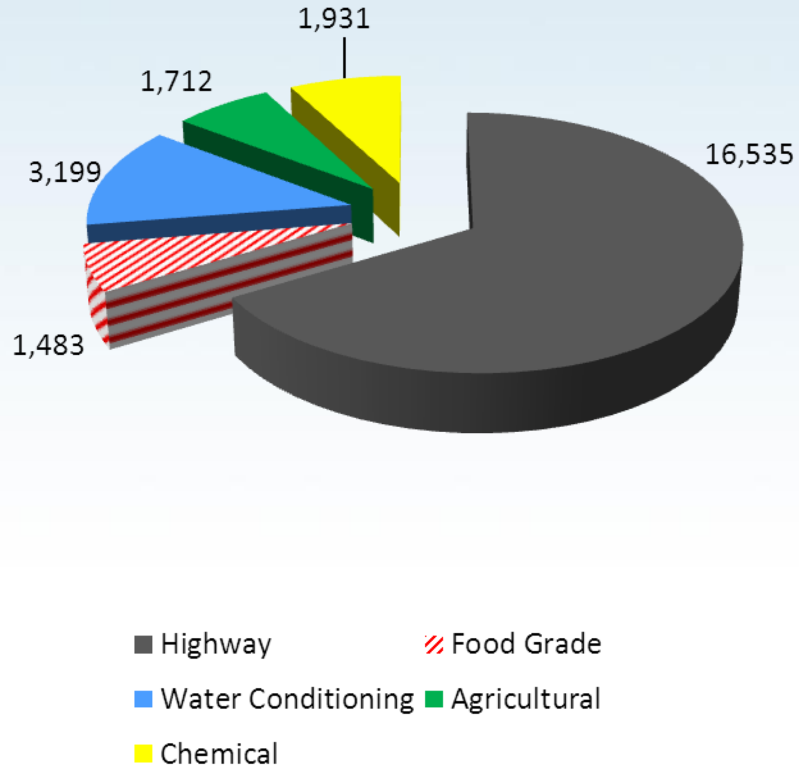
US Salt Sales and Revenues (2009)

Sales Tonns (x1000)



Revenue US $ (x1000)



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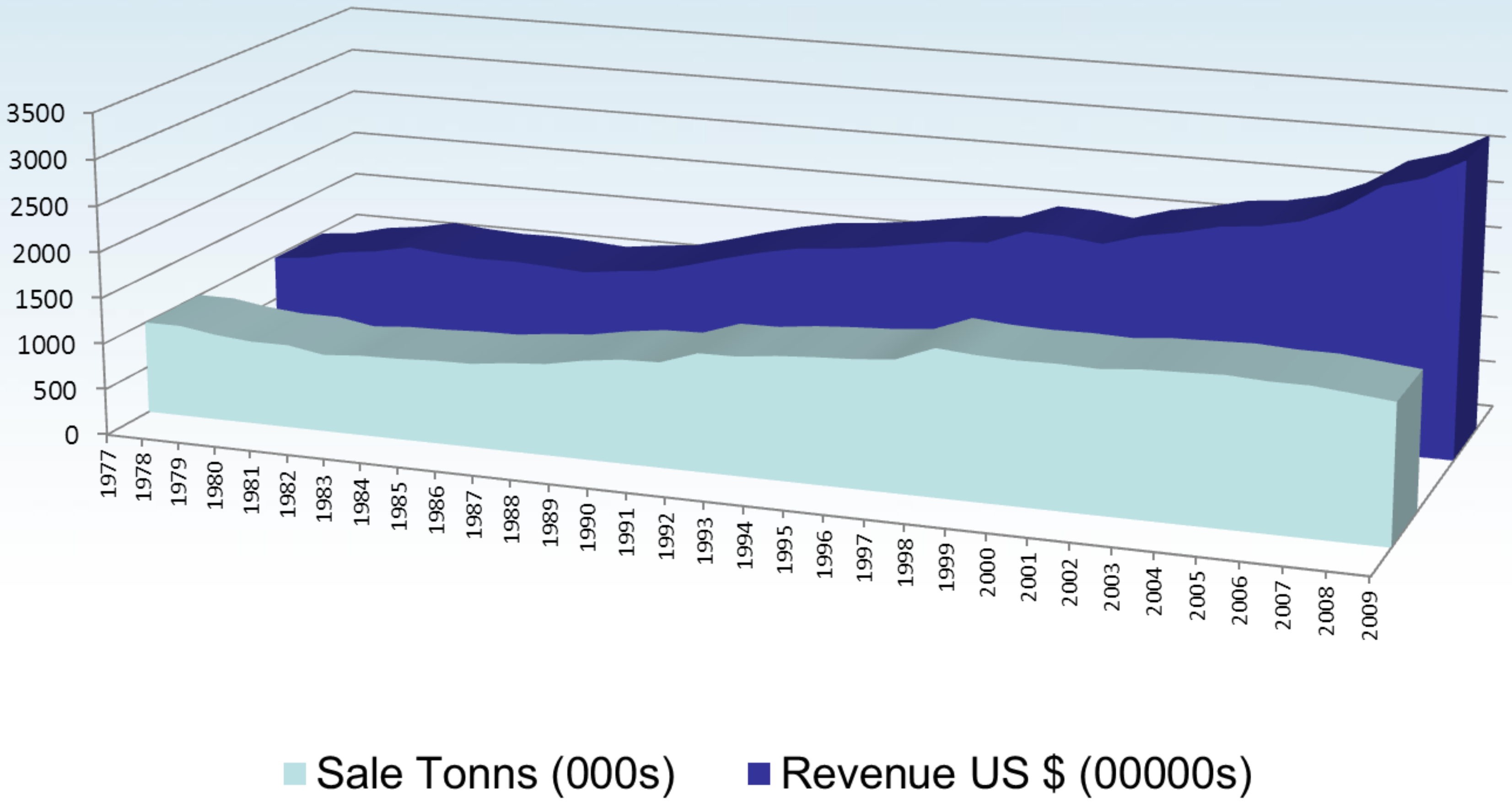
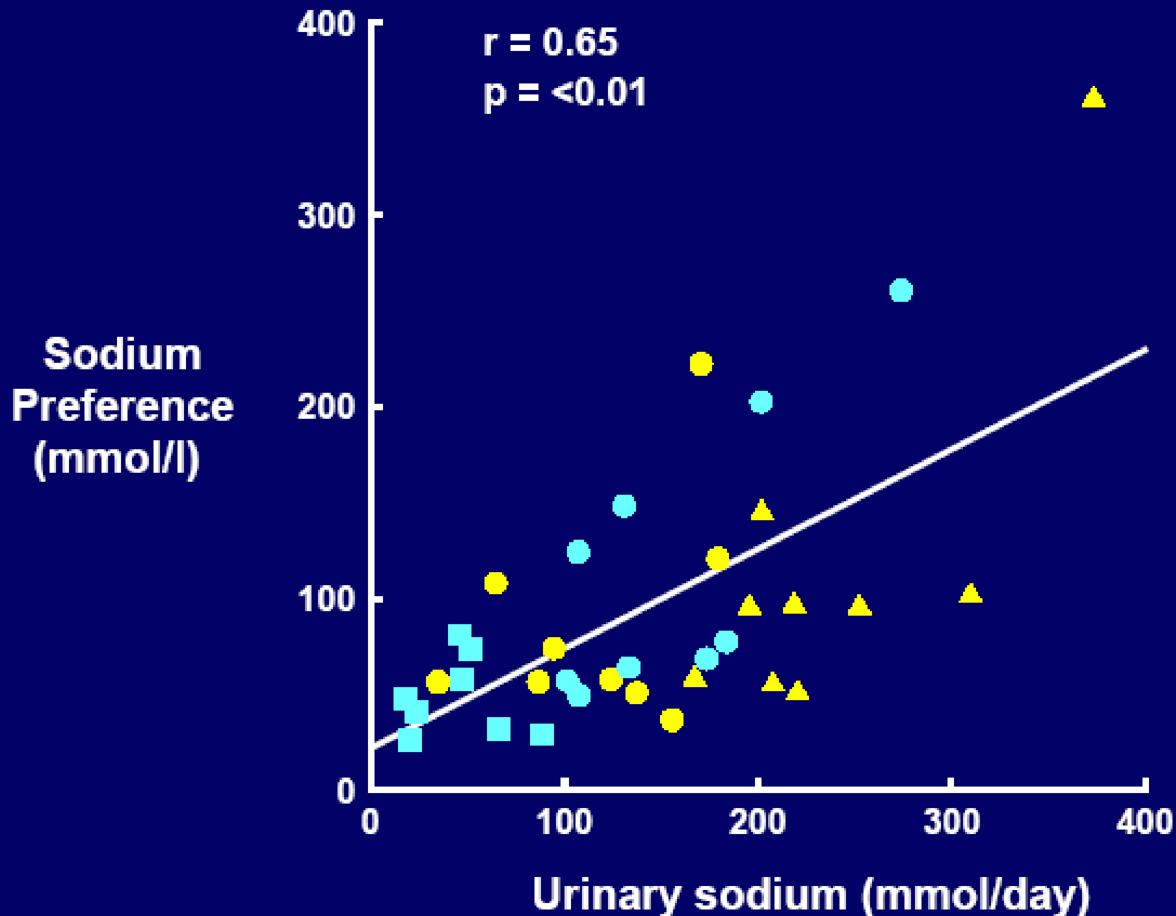
US Food Grade Salt Sales (1977-2009)



The more salt we eat, the more salt we demand!

Teow et al. Clin. Exper. 1986;A7(12):1681-95



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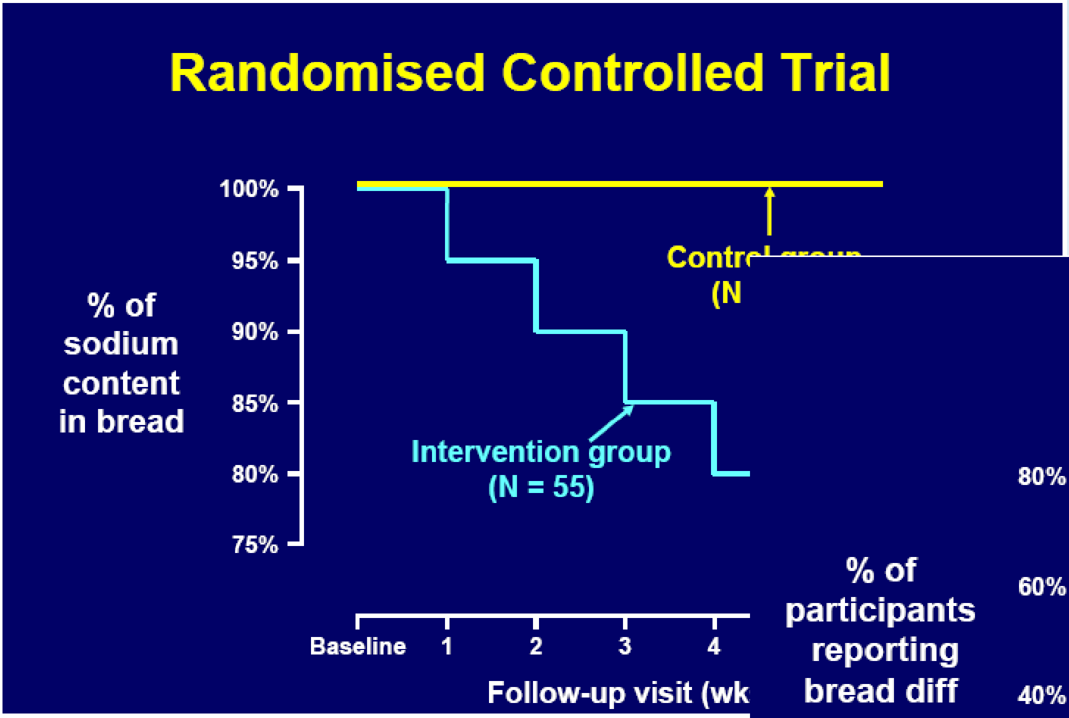
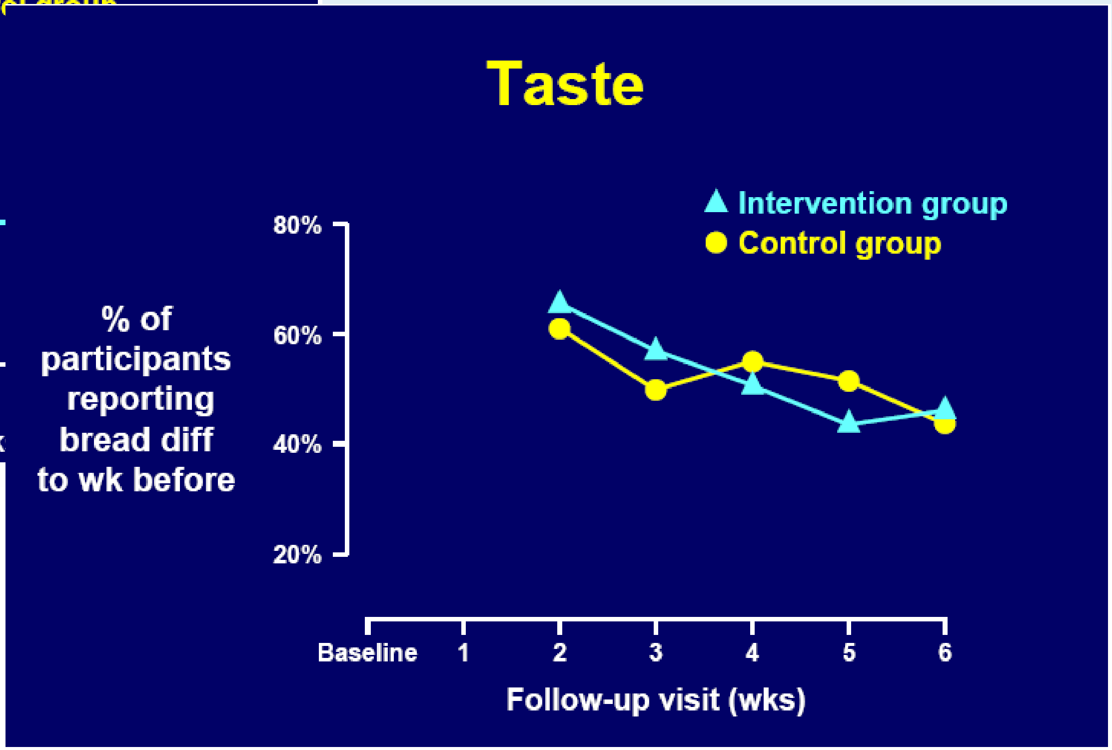
Gradual reduction in salt content is not detected by consumers!





Girgis et al. Eur J Clin Nutr 2003;57:616-620

Cost-effectiveness

- A reduction in salt intake of 3g per day would save 194,000-392,000 QALYs and $10-24b in health care costs annually in the US, i.e. a return of $6-12 for every $ spent[1]
- Even modest reduction of 1g per day would be cost saving and more cost-effective that using medications to lower blood pressure[1]
- Population reductions in salt intake through food reformulation from industry would be cost-saving.
- However, whilst ‘voluntary ‘ action by the food industry is cost-effective, population health benefits could be 20 times greater with Government legislation of moderate salt limits in processed foods[2]

[1]Bibbins-Domingo K et al. NEJM 2010;362:590-9
[2]Cobiac LJ et al. Heart 2010;96:1920-5

Industry vs Public Health Priorities

- Salt contributes to food safety
- Salt increases shelf-life
- Salt makes unpalatable food edible at virtually no cost
- Habituation to high salt foods increases demand – Profit on these foods tends to be greater
- Increasing salt concentration in meat products increases water binding capacity by up to 20%
- Salt intake is the main drive to thirst and thereby increases soft drink, beer and mineral water consumption

- High salt intake increases preventable ill-health (CV and non-CV)
- High salt intake increases the consumption of sugar-containing drinks, alcohol, hence calories.
- High salt intake is economically costly to society (healthcare costs)
- High salt intake creates addiction
- Moderate population reduction in salt intake is feasible, efficacious, cost-effective.

Who owns what in the food industry?

Source: Fritz Kreiss/Occupy Monsanto

"The world's 10 largest food and non-alcoholic beverage companies feed daily an estimated global population of several hundred million in >200 countries, generating a combined annual revenue of >$422b" (Source: IFBA, 2012)

Potassium, Blood pressure and Stroke.

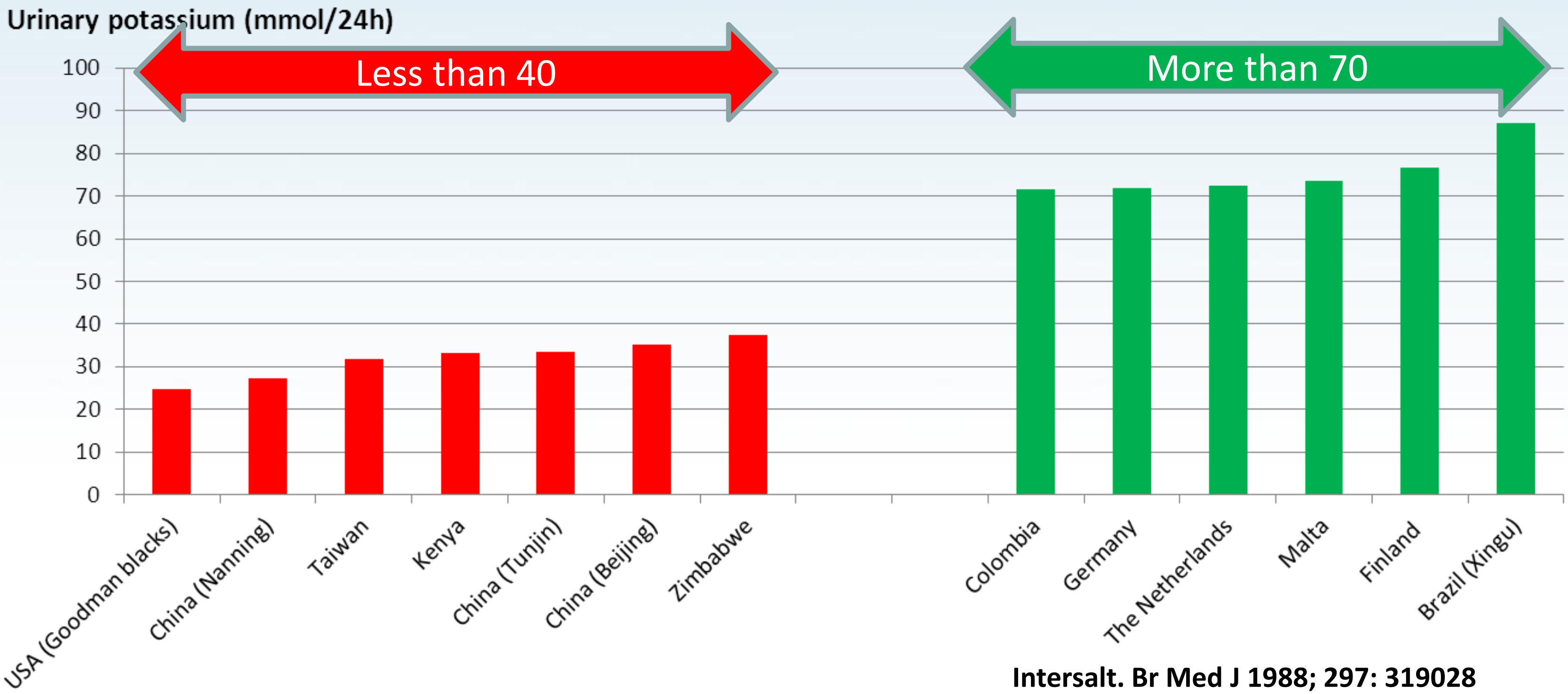
Outline

- Evolutionary diet
- Epidemiology
- Clinical trials
- Animal experiments
- Safety
- Gaps in knowledge (What's next?)

Hunt BD & Cappuccio FP. Stroke 2014; 45: 1519-22

INTERSALT Study

- 10,079 participants aged 20-59 years from 52 centres around the world
- All provide 24h urinary collections for sodium and potassium and had BP taken
- The lower the potassium the higher the blood pressure



Intersalt. Br Med J 1988; 297: 319028

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Clinical trials: K^+ supplements and BP

Author (year)	RCTs	Participants	SBP difference (mmHg)	95% C.I. (mmHg)
Cappuccio et al. (1991)	***19***	***586***	***5.9***	***5.2 - 6.6***
Whelton et al. (1997)	***32***	***2,609***	***3.11***	***1.91 - 4.31***
Geleijnse et al. (2003)	***27***	***-***	***2.42***	***1.08 - 3.75***
Dickinson et al. (2006)	5 4	425	11.2 3.9	-2.5 - 25.2 -0.8 - 8.6
Aburto et al. (2012)	***22***	***1,606***	***3.49***	***1.82 - 5.15***

Effect of increased potassium intake on health: systematic review and meta-analyses

RCTs: K supplementation
1,892 adult participants

SBP diff: -3.49mmHg
95% CI -5.15; -1.82
P < 0.0001

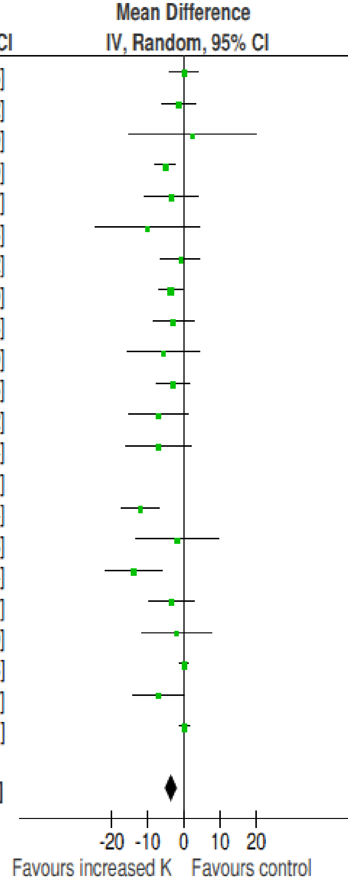
Additional results:
DBP diff: -3.02mmHg
95% CI -4.86; -1.17
P = 0.001
No effect on:
- Lipids
- Catecholamines
- Renal function

- **No dose-response**
- Effect within 4 weeks
- Greater effect the higher the salt intake

Figure 4 - Resting systolic blood pressure - All Adults

Study or Subgroup	Increased potassium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Barden BPARA1986	113.67	8.87	43	113.69	9.44	43	6.9%	-0.02 [-3.89, 3.85]
Berry BPA2010	120.7	9.9	48	122.2	13	48	6.0%	-1.50 [-6.12, 3.12]
Bulpitt BPA1985	-5.2	27.5	19	-7.5	23.9	14	0.8%	2.30 [-15.30, 19.90]
Chalmers BPA1986	-8.9	7	49	-3.8	7.4	52	8.4%	-5.10 [-7.91, -2.29]
Forrester BPA1988	129.8	13.5	23	133.2	12.7	23	3.4%	-3.40 [-10.97, 4.17]
Fotherby BPA1992	176	20	18	186	24	18	1.2%	-10.00 [-24.43, 4.43]
Grobbee BPA1987	135	13.28	40	135.9	11.38	40	5.1%	-0.90 [-6.32, 4.52]
Gu BPA2001	-13.1	10.7	68	-9.4	9	69	7.7%	-3.70 [-7.01, -0.39]
He BPA2010	142	11	42	145	15	42	4.9%	-3.00 [-8.63, 2.63]
Kaplan BPA1985	127.6	11.6	16	133.2	16.8	16	2.2%	-5.60 [-15.60, 4.40]
Kawano BPA1998	147.9	11.7	55	150.8	12.61	55	6.1%	-2.90 [-7.45, 1.65]
MacGregor AEBPA1982	148	13.91	23	155	14.87	23	2.9%	-7.00 [-15.32, 1.32]
Matlou BPA1986	144	18.1	32	151	19.2	32	2.6%	-7.00 [-16.14, 2.14]
Obel BPA1989	133	4	24	172	7	24	0.0%	-39.00 [-42.23, -35.77]
Patki BPARA1990	143.6	10.8	37	155.7	11.4	37	5.5%	-12.10 [-17.16, -7.04]
Richards BPAAEA1984	148	14.2	12	149.9	14.5	12	1.8%	-1.90 [-13.38, 9.58]
Siani BPA1987	131.8	12.7	18	145.8	11.3	19	3.3%	-14.00 [-21.76, -6.24]
Siani BPARA1991	142.1	11.5	21	145.5	9.7	26	4.4%	-3.40 [-9.57, 2.77]
Smith BPARA1985	160	16.1	20	162	15.2	20	2.3%	-2.00 [-11.70, 7.70]
Trial Hyp Prv Col BPA1992	-0.78	5.88	178	-0.84	5.82	175	10.5%	0.06 [-1.16, 1.28]
Valdes BPA1991	138	14.7	24	145	9.8	24	3.7%	-7.00 [-14.07, 0.07]
Whelton BPA1995	-0.87	5.94	161	-1	5.69	157	10.4%	0.13 [-1.15, 1.41]
Total (95% CI)			**947**			**945**	**100.0%**	**-3.49 [-5.15, -1.82]**

Heterogeneity: Tau² = 6.52; Chi² = 56.52, df = 20 (P < 0.0001); I² = 65%
Test for overall effect: Z = 4.10 (P < 0.0001)



Aburto NJ et al. Br Med J 2013; 346: f1378

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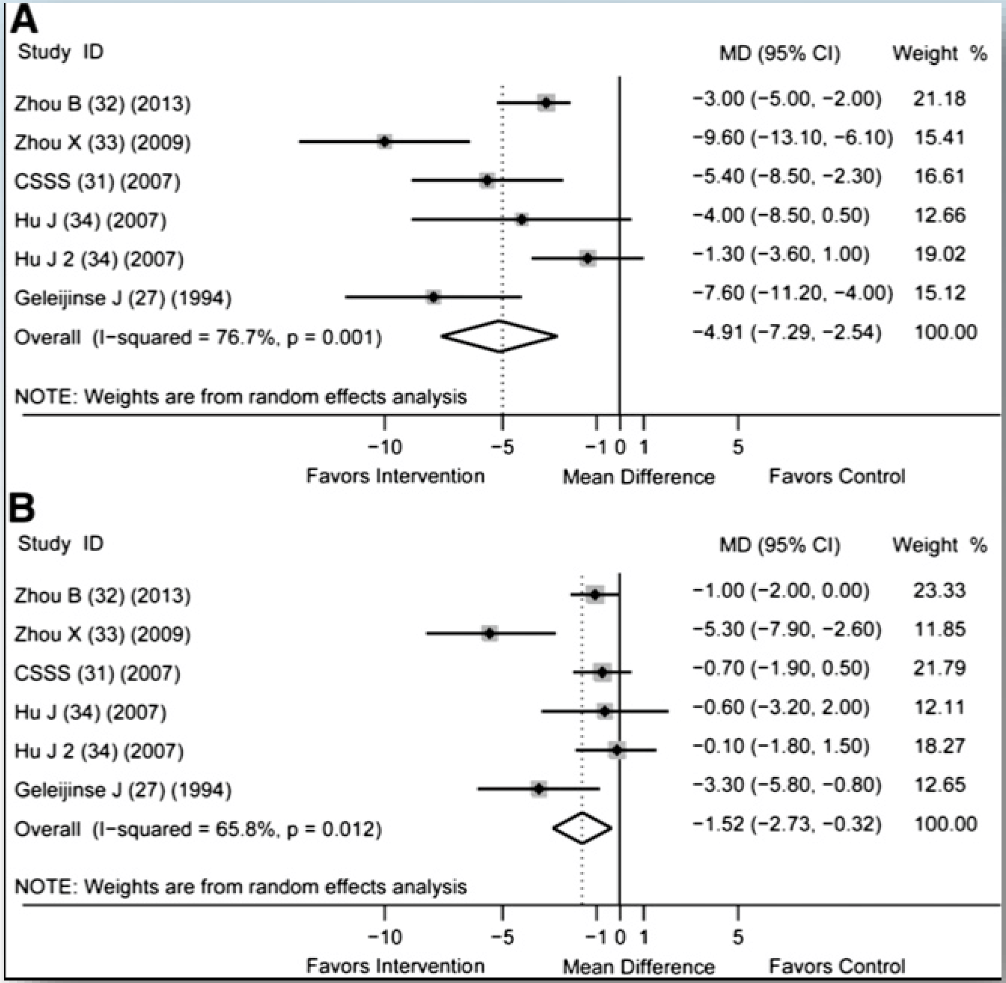
Increasing the dietary potassium intake reduces the need for antihypertensive medication

- RCT; 1-year follow-up.
- 54 patients with well-controlled hypertension, 47 completed follow-up.
- Random allocation to (1): dietary advice aimed at increasing K^+ intake (2) keeping customary diet unchanged.
- Drug therapy titrated in stepwise fashion, provided BP remained on target.
- K^+ intake checked monthly by 3-day food records and 24-h urinary K^+ excretion. K^+ intake increased in group 1 and did not change in group 2 (P<0.001).
- BP could be controlled using less than 50% of the initial therapy in 81% of group 1 (Cl, 66% to 96%) compared with 29% of group 2 (Cl, 10% to 48%) (P = 0.001).
- Increasing the dietary K^+ intake from natural foods is a feasible and effective measure to reduce antihypertensive drug treatment.

Siani A et al. Ann Intern Med 1991;115:753-9

Effects of salt-substitutes on BP



5 RCTs

6 samples

N=1,974

5 China

1 Netherlands

Peng Y-G et al. Am J Clin Nutr 2014;100:1448-54

Potassium Intake, Stroke, and Cardiovascular Disease

A Meta-Analysis of Prospective Studies

Lanfranco D'Elia, MD, PHD,* Gianvincenzo Barba, MD,† Francesco P. Cappuccio, MD,‡
Pasquale Strazzullo, MD*

Naples and Avellino, Italy; and Coventry, United Kingdom

J Am Coll Cardiol 2011;57:1210-9

9 studies, 11 cohorts
Population, prospective
233,606 participants
7,077 strokes

K diff: 42.1mmol (1,640mg)

RR:	0.79
95% CI:	0.68 – 0.90
P =	0.0007

First author	Year	Gender	K intake difference g (mmol) / day	Weight	Relative Risk (95% CI)
Khaw	1987	Men	0.39 (10.0)	6%	0.65 (0.41, 1.00)
Khaw	1987	Women	0.39 (10.0)	8%	0.56 (0.38, 0.82)
Ascherio	1998	Men	1.90 (48.7)	7%	0.69 (0.45, 1.07)
Iso	1999	Women	1.54 (39.4)	12%	0.83 (0.66, 1.04)
Bazzano	2001	Men & Women	2.66 (68.2)	11%	0.76 (0.58, 1.01)
Green (diur)	2002	Men & Women	2.43 (62.3)	6%	1.15 (0.71, 1.85)
Green (not diur)	2002	Men & Women	2.43 (62.3)	8%	0.57 (0.39, 0.83)
Geleijnse	2007	Men & Women	0.86 (22.0)	10%	1.17 (0.86, 1.58)
Weng	2008	Men & Women	1.19 (30.5)	7%	0.59 (0.39, 0.89)
Larsson	2008	Men	1.95 (49.9)	16%	0.92 (0.81, 1.04)
Umesawa	2008	Men & Women	1.29 (33.0)	9%	0.83 (0.60, 1.14)
Combined Effect:	p=0.0007	z=3.38	**1.64 (42.1)**	100%	**0.79 (0.68, 0.90)**
Heterogeneity:	Q=22.0	p=0.01 I^2=55%			
Egger's test:	p=0.11				

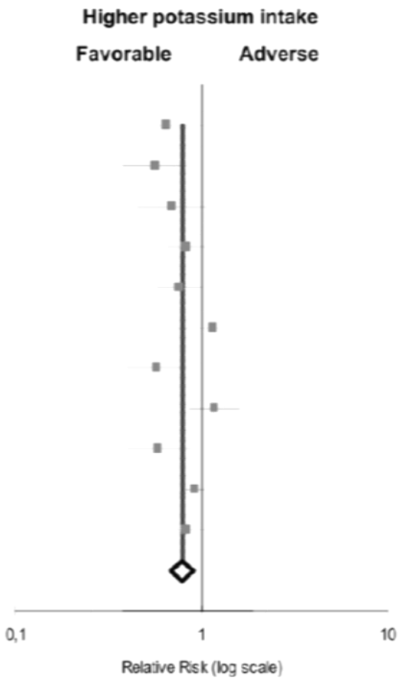


Figure 2 Risk of Stroke

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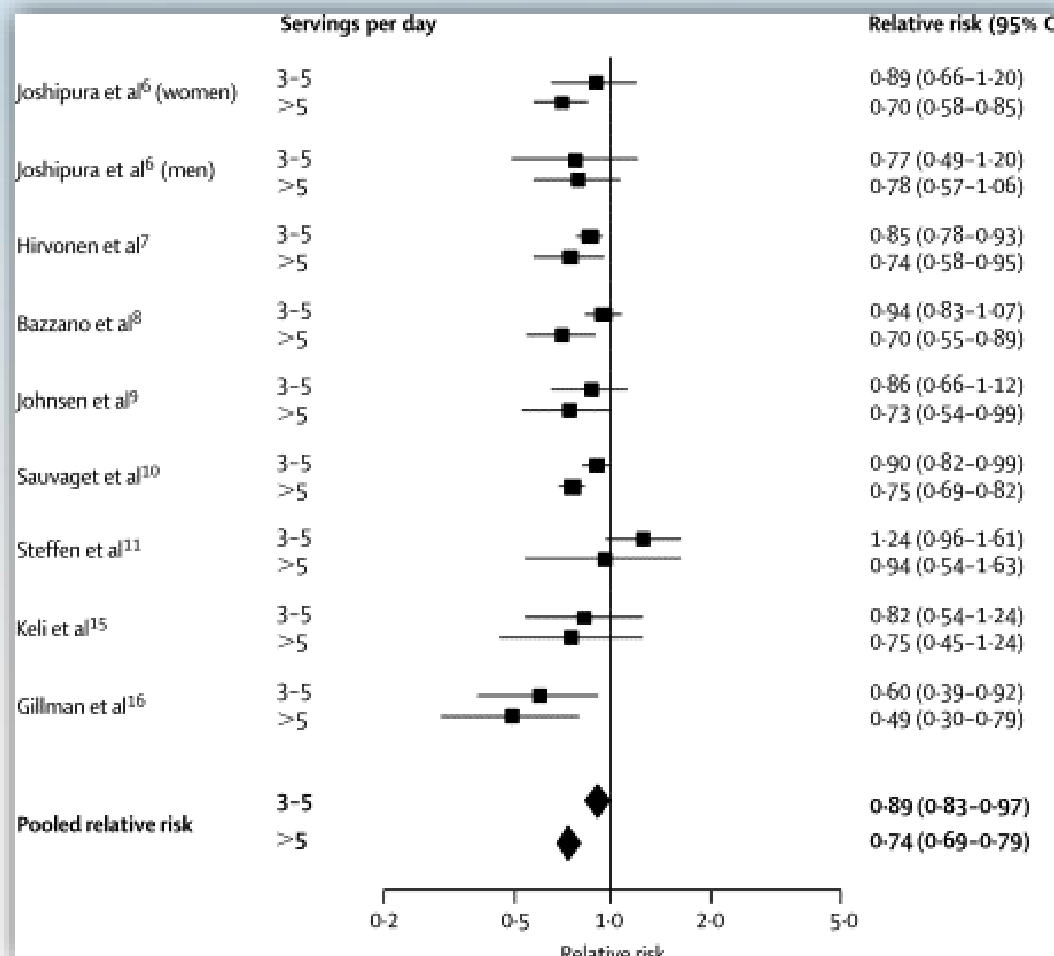
Fruit and vegetable consumption and stroke

Eight studies, 9 cohorts
257,551 participants
4,917 stroke events
Follow up 13 yrs
Comparator <3 a day



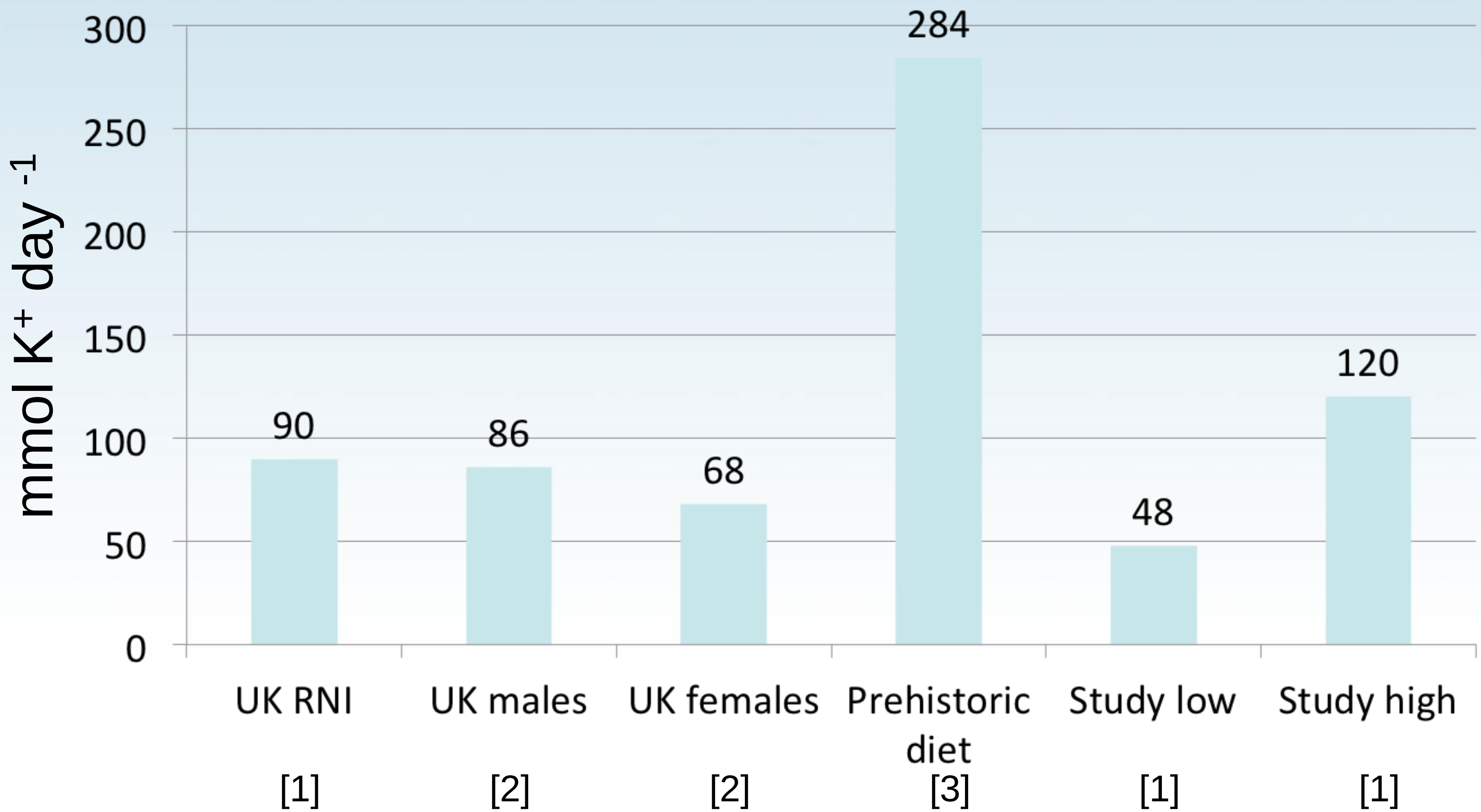
He FJ et al. Lancet 2006;367: 320-6

Safety

- No ill effects reported with the use of high K^+ diets in healthy people
- Major risks of treatment with K^+Cl^- are hyperkalaemia, cardiac arrest, oesophageal and small bowel ulceration.
- K^+ toxicity more likely to result from reduced kidney function than from excess consumption.
- Supplementation trials found no adverse effects of K^+Cl^- at doses between 25-104 mmol/d.

Saggar-Malik A & Cappuccio FP. Drugs 1993; 46: 986-1008
Hathcock JN. Vitamin & mineral safety, 2004

How Much Potassium?



[1] Vitamin and mineral safety, 2nd ed. J.N.Hathcock, (2004); [2] The National Diet and Nutrition Survey, DoH (2003); [3] Tobian, L. Jeremiah Metzger Lecture (1986) TACCA (97) p123-40

Conclusions

- Average salt intake around the world is too high.
- It is responsible for avoidable ill-health with associated healthcare and social costs
- A moderate reduction in salt intake is feasible, achievable and cost-effective for society.
- Different economies around the world have different sources of dietary salt (from processed food and industrial food production to social and cultural behaviour in salt use).
- Strategies to reduce population salt intake include public awareness campaigns, comprehensive reformulation programmes and surveillance of salt intake and food salt content.
- The food manufacturing and retail industries have the capability and the responsibility to contribute substantially to these aims given their outreach.
- Voluntary and effective food reformulation is the preferred choice.
- Where ineffective, mandatory actions and state-led market interventions are available.
- Further research in the feasibility of substitution with potassium chloride in food manufacturing.