Salt Intake and Cardiovascular Risk

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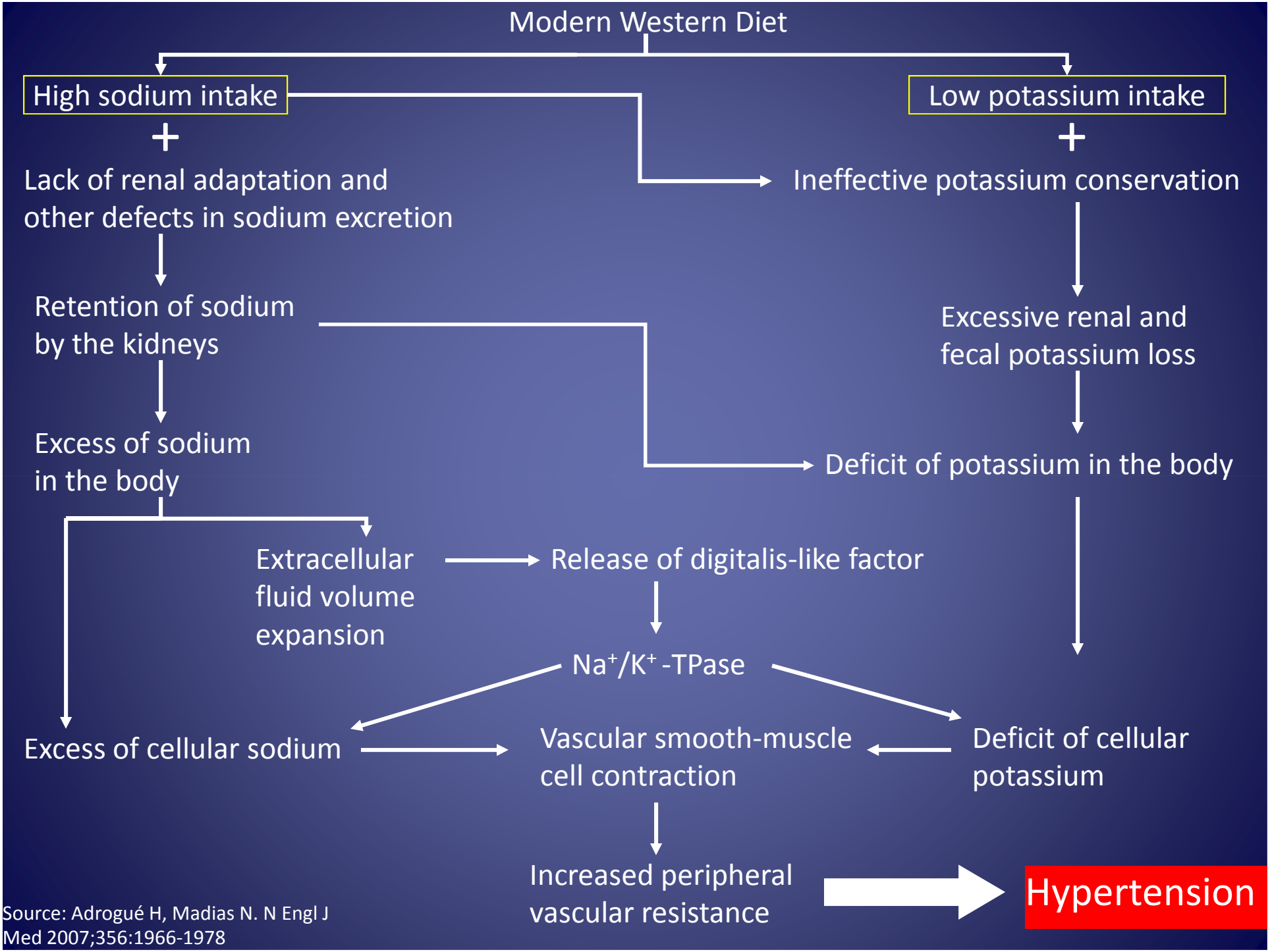
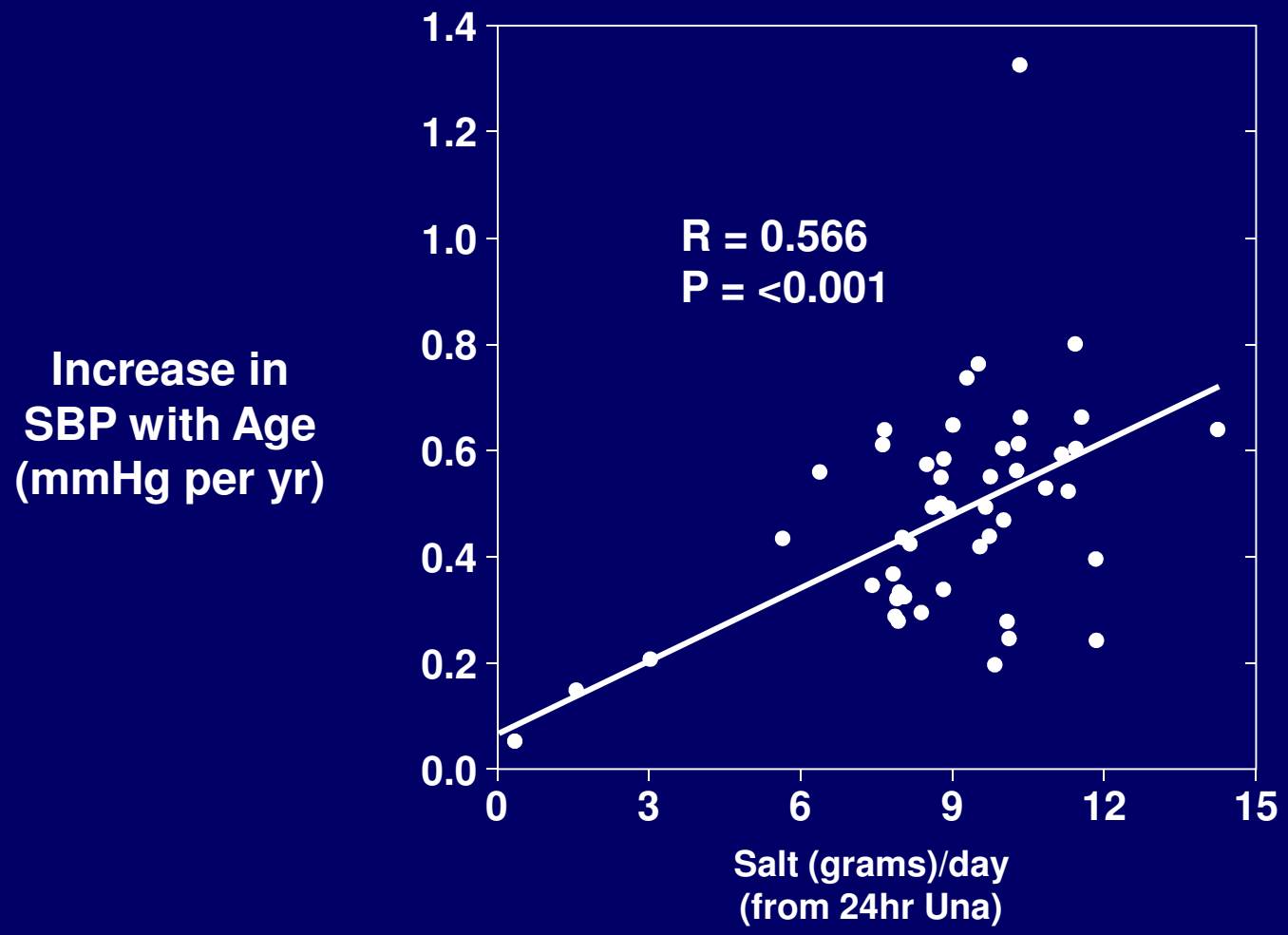
Outline

- Evidence linking salt and blood pressure
- Evidence linking salt and cardiovascular disease
- Challenges studying salt and cardiovascular disease
- Salt, CKD, and cardiovascular disease



Source: Adrogué H, Madias N. N Engl J Med 2007;356:1966-1978

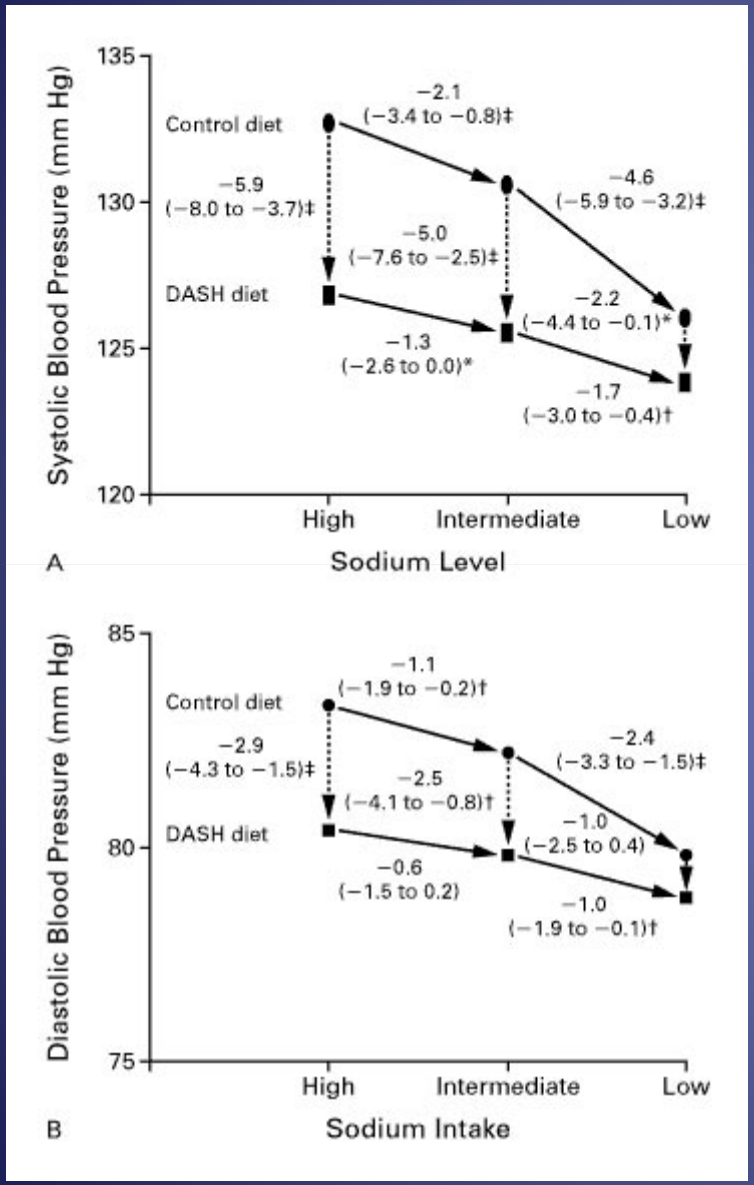
↑ BP with age associated with higher salt intake (INTERSALT) – 52 communities worldwide, n=10,079



↑ 6 gm/day (100 mmol sodium) over 30 years → ↑ SBP 9mmHg

Adapted Intersalt, BMJ 1988;297:319-32

The Effect on Systolic and Diastolic Blood Pressure of Reduced Sodium Intake and the DASH Diet



- 412 participants with prehypertension or Stage 1 hypertension
- High Sodium 140-150 mmol
- Intermediate 100-110 mmol
- Low Sodium 60-70 mmol

Sacks F et al. N Engl J Med 2001;344:3-10

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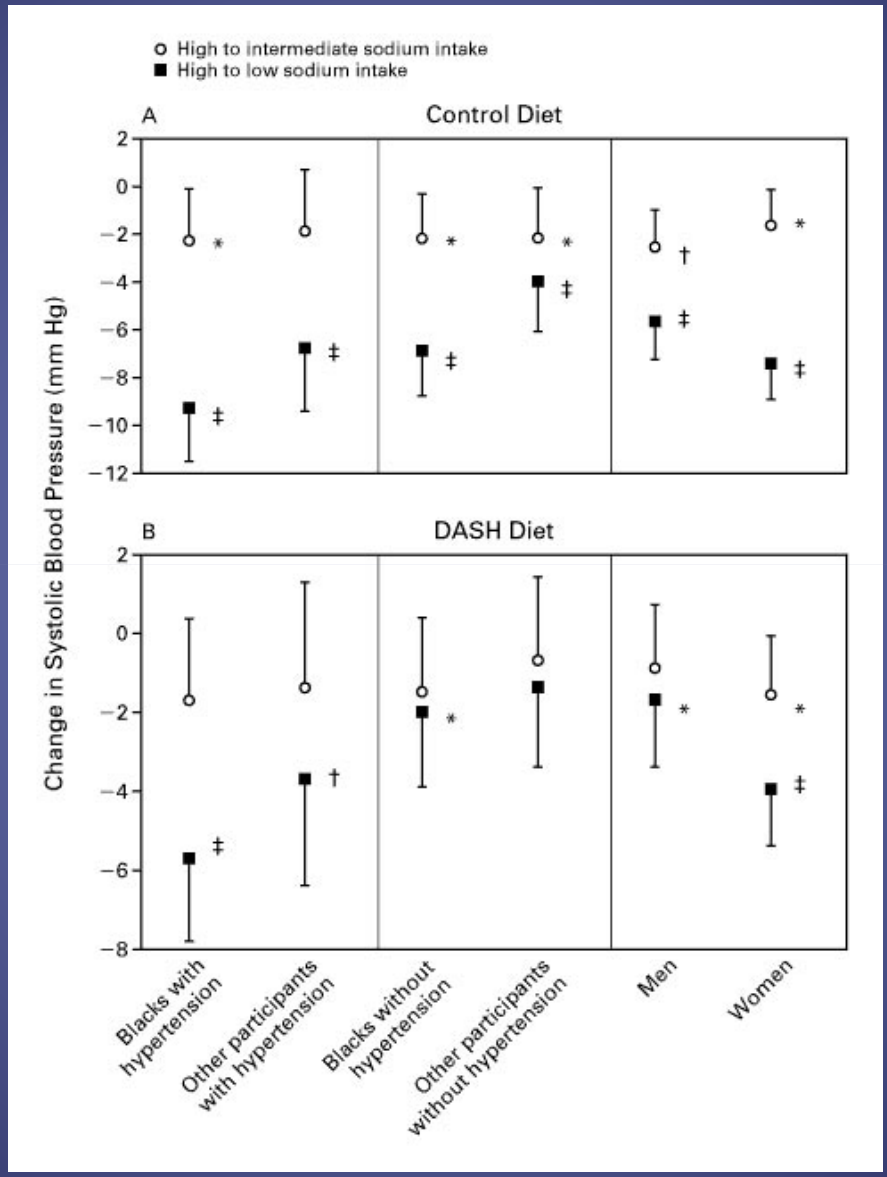
The Effect on Systolic Blood Pressure of Dietary Sodium Intake, According to Subgroup



Sacks F et al. N Engl J Med 2001;344:3-10

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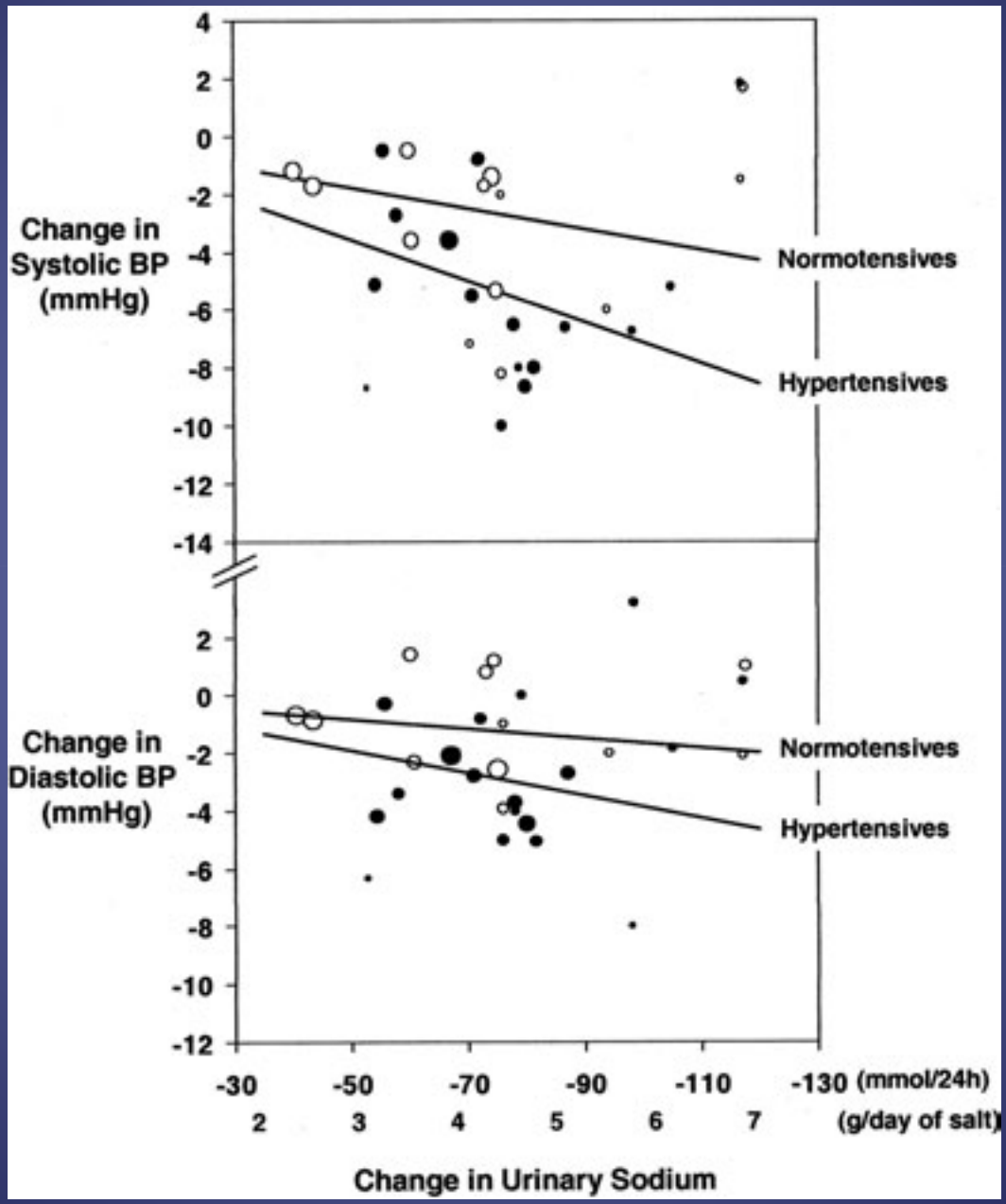
Relation between the net change in 24-hour urinary sodium excretion and blood pressure in the meta-analysis



Hypertension

He, F. J. et al. Hypertension 2003;42:1093-1099

Outline

- Evidence linking salt and blood pressure
- Evidence linking salt and cardiovascular disease

Direct evidence for salt and CVD

Possibly independent of blood pressure

- Endothelial damage, direct effect on LVH, vascular reactivity
- Adverse effects of sympathetic, RAAS activation

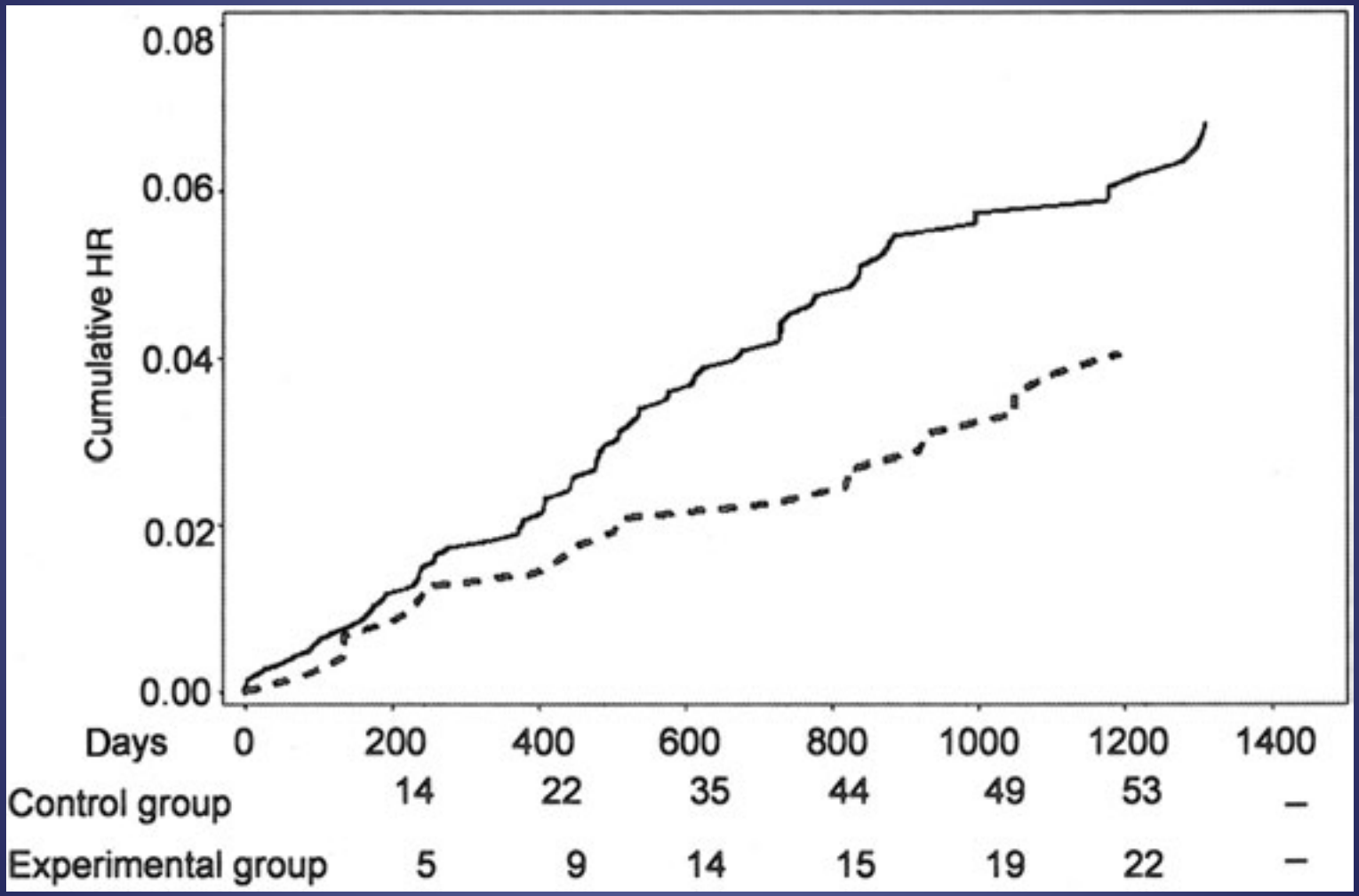
Observational studies of CVD:

- Meta-analysis (Strazullo, BMJ 2009) per 6 gm salt
- Stroke: RR=1.23 (95% CI=1.06-1.43), p=0.007
- CVD: RR=1.14 (95% CI=0.99-1.32), p=0.07

Chang (AJCN 2006)

- Five kitchens of veterans' home in Taiwan
  - 1981 veterans
  - 40% were hypertensive
- Kitchens cluster-randomized to potassium-enriched (lower Na) or regular salt ('95-'99)
- Significant reduction in CVD mortality
  - RR = 0.59 (95% CI = 0.37-0.95)
- Experimental group lived longer (0.3-0.9 yrs)
  - Spent less ($426/yr) on inpatient care for CVD

Cumulative hazard ratios (HRs) of cardiovascular disease-related deaths for the treatment and control groups



Chang, H.-Y. et al. Am J Clin Nutr 2006;83:1289-1296

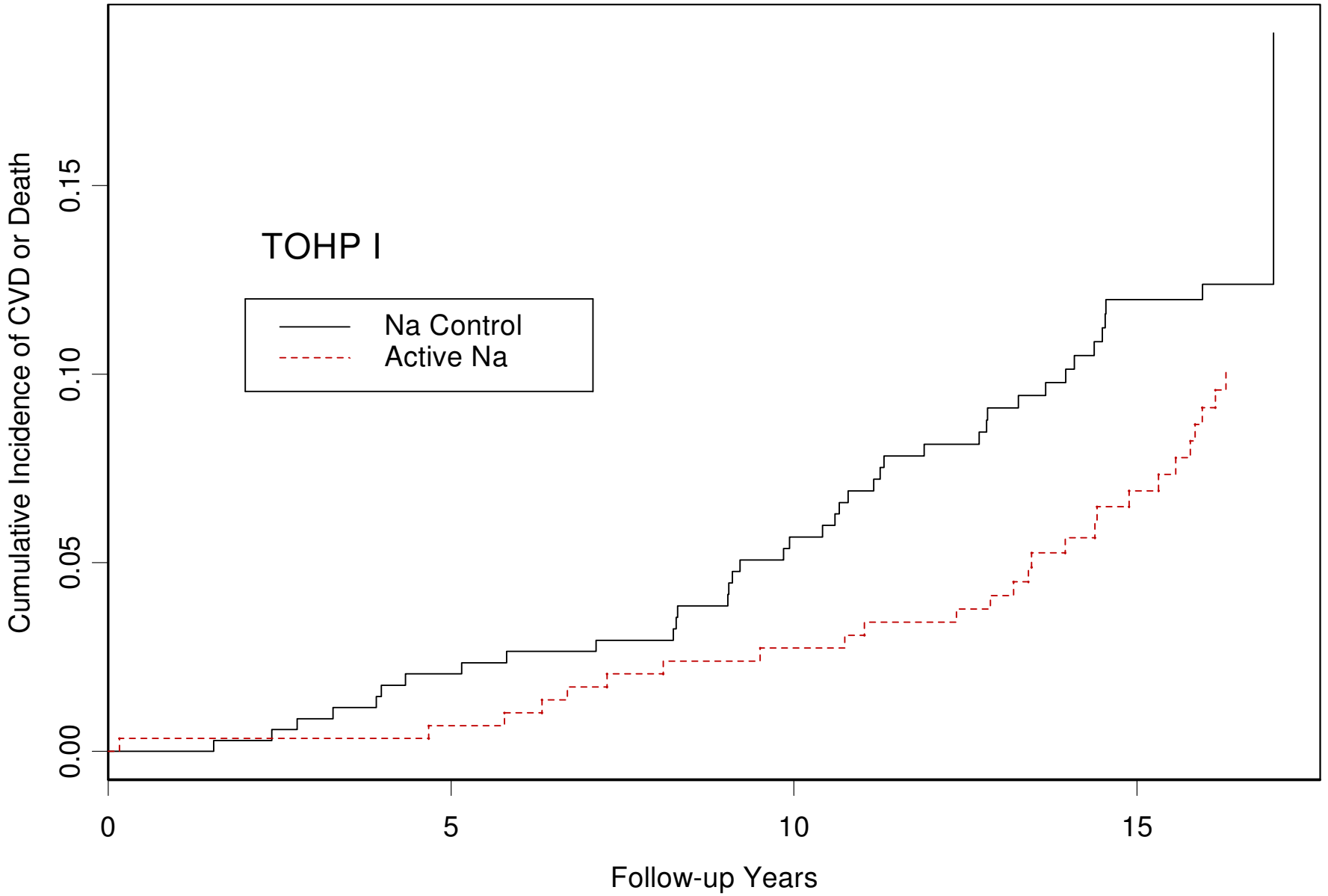
TOHP I and II Trials of Blood Pressure

- TOHP I (1987-1990)
  - DBP 80-89, aged 30-54 years, **18-month** fu, 10 sites
  - 2,182 randomized participants, 744 in sodium arm
- TOHP II (1990-1995)
  - DBP 83-89, aged 30-54 years, overweight, **3-4 year** fu
  - 2,382 randomized participants
- TOHP Follow-up
  - Observational follow-up 10-15 and 5-10 yrs after I and II
  - 4,526 participants
  - Medical records/death linkage
  - Intent to treat

TOTAL CVD by Randomized Sodium Intervention in TOHP Follow-up Study

	RR	95% CI	p
Adjusted for Demographics			
Overall	**0.75**	**0.57-0.99**	**0.044**
Adjusted for Demographics, BS Wt and Na			
Overall	**0.70**	**0.53-0.94**	**0.018**
Phase I	0.48	0.25-0.92	0.027
Phase II	0.79	0.57-1.09	0.16

Cumulative Incidence of CVD Adjusted for Clinic, Age and Sex



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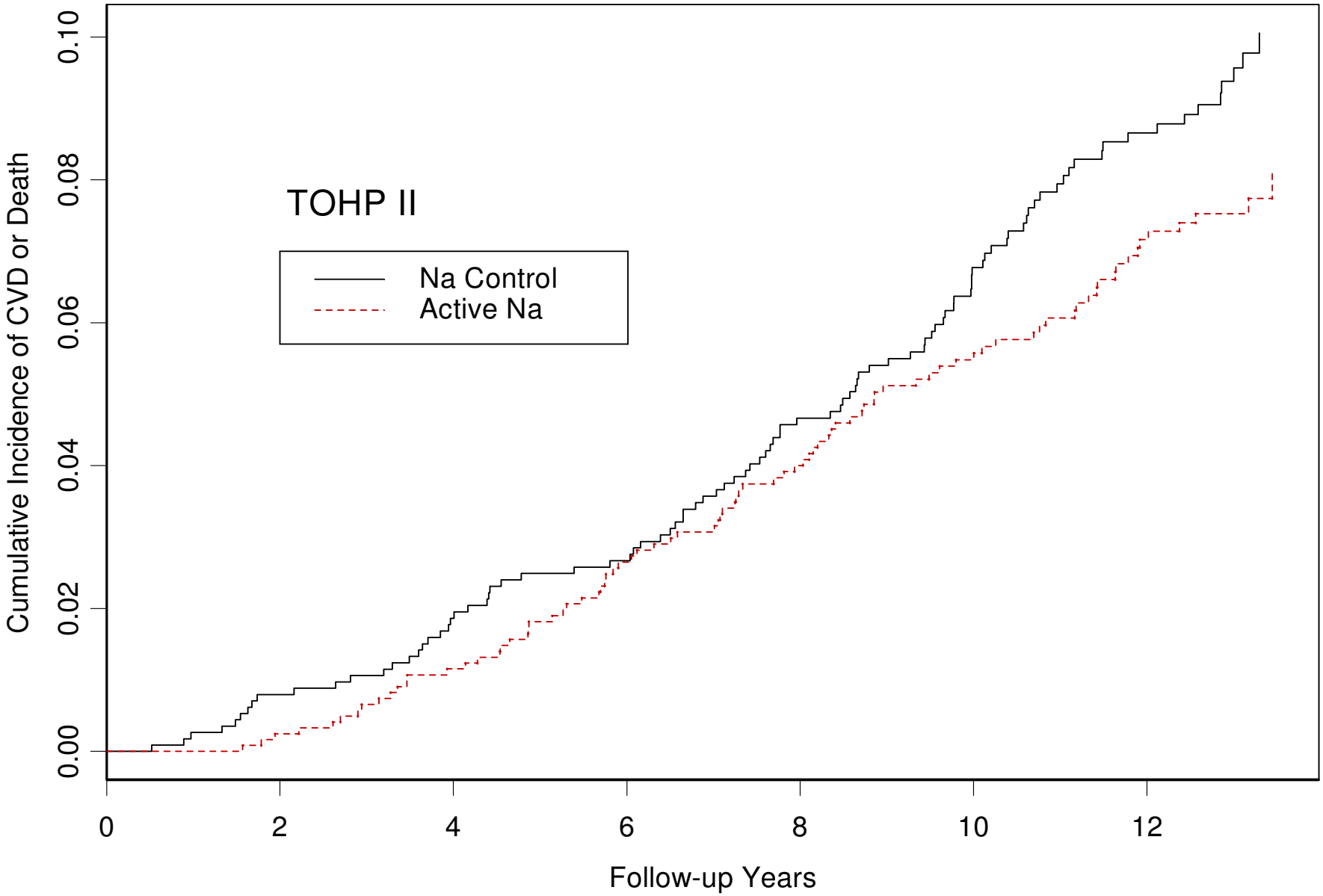

Outline

- Evidence linking salt and blood pressure
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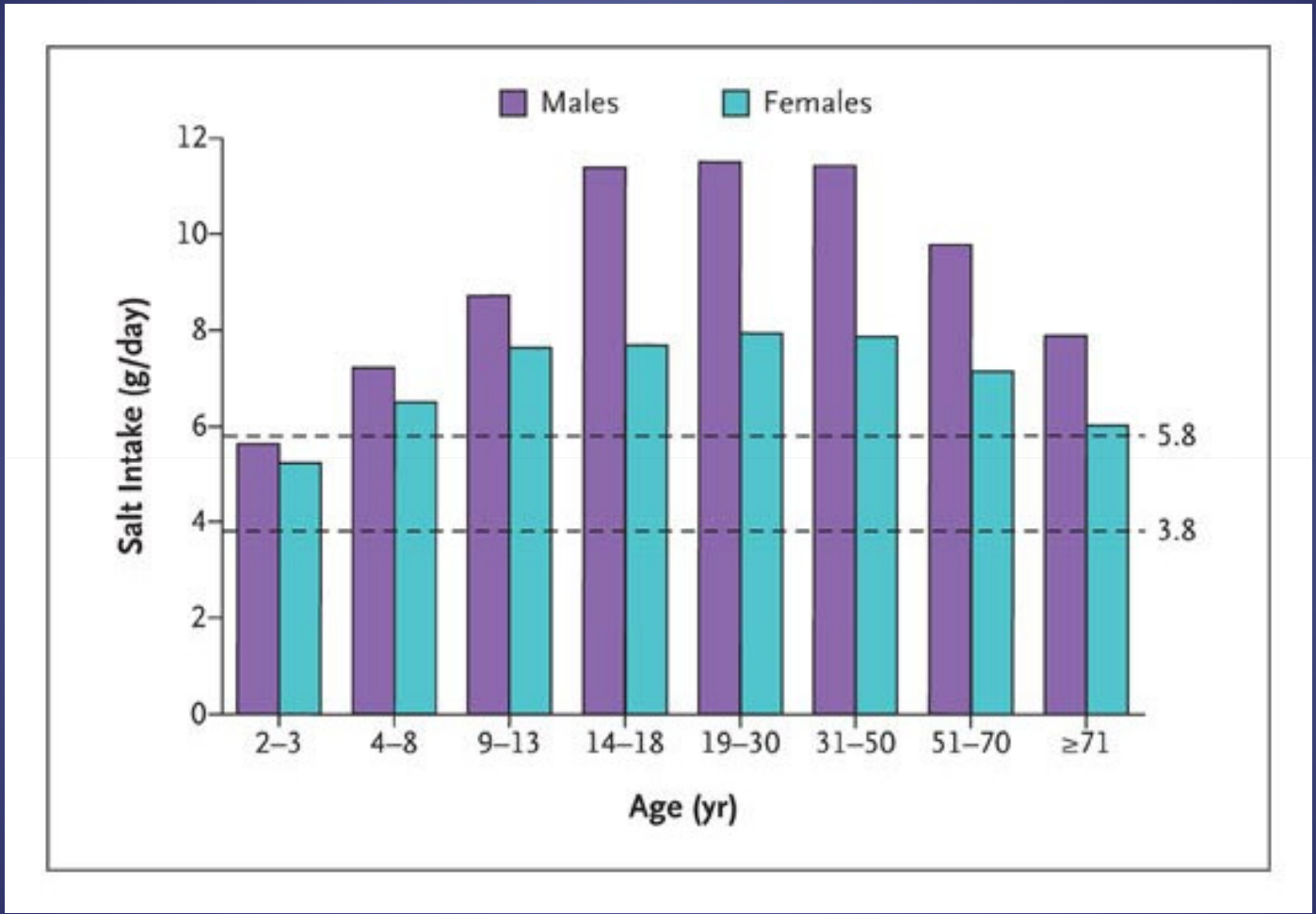
- Challenges studying salt and cardiovascular disease

Salt intake in the United States

- Recommended daily salt intake:
  - **< 5.8gm/day** (<100 mmol sodium or **2300 mg**)
    - 1 gm salt = approx 17 mmol or 400 mg sodium
- WHO recommendations
  - <5 gm/day (<85 mmol sodium or 2000 mg)
- Current daily intake in US:
  - 9.4 gm/day (3700 mg sodium)

Average daily salt intake in male and female Americans, as ascertained from 24-hour dietary recall, 2005-2006



Source: Appel L and Anderson C. N Engl J Med 2010;362:650-652

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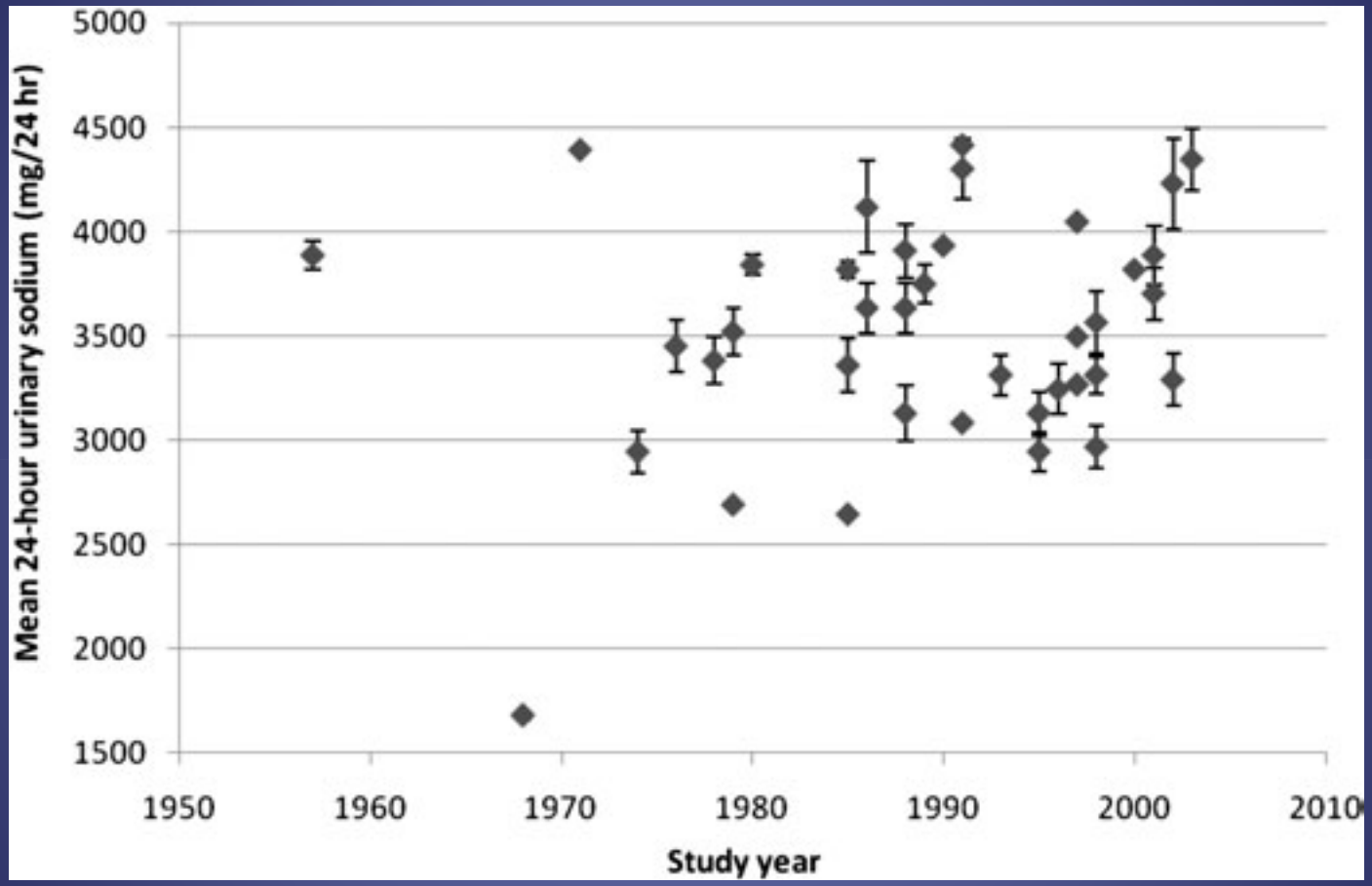
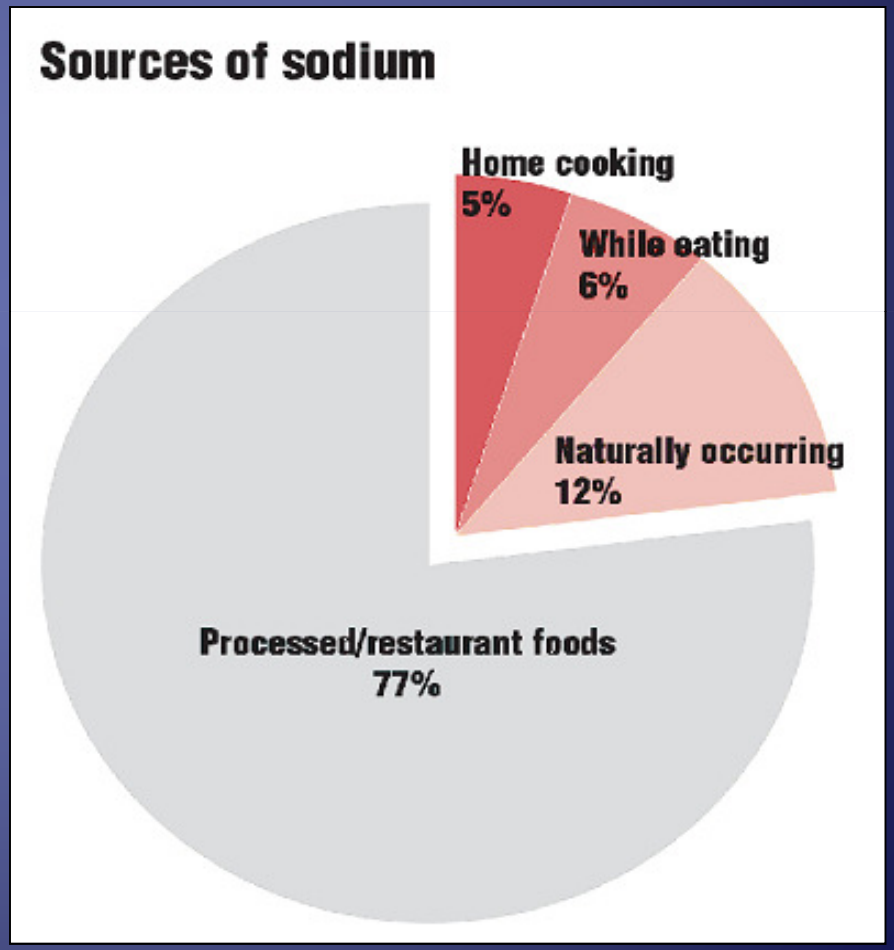
Mean (95% CI) 24-h urinary sodium excretion (mg/24 h) by study year (US studies)



Bernstein, A. M. et al. Am J Clin Nutr 2010;92:1172-1180

Where is the salt?

80% in processed or pre-prepared foods



Sources: Mattes et al.

Cancer Control and Population Sciences Home
Applied Research Home
Risk Factor Monitoring and Methods Home
Diet

Sources of Sodium among the US Population, 2005–06:

Introduction
List of specific foods

Mean Intakes & Percentage Contribution of Foods:

Among US Population, by Age

Among US Males, by Age
Among US Females, by Age
Among US Population, by Race/Ethnicity & Family Income

Mean Intakes & Mean Contribution of Foods:

Among US Population, by Age
Among US Males, by Age
Among US Females, by Age
Among US Population, by Race/Ethnicity & Family Income

Table 1a. Mean Intake of Sodium, Mean Intake of Energy, and Percentage Sodium Contribution of Various Foods Among US Population, by Age, NHANES 2005–06

		All Persons	Age Group (years)									
			2-18	2-3	4-8	9-13	14-18	19+	19-30	31-50	51-70	71+
Sample Size		8549	3778	497	899	1047	1335	4771	1310	1537	1224	700
Mean Intake of Sodium (mg)		3436	3129	2144	2694	3227	3793	3535	3814	3781	3306	2686
Mean Intake of Energy (kcal)		2157	2027	1471	1802	2035	2427	2199	2407	2354	2020	1691
Rank[1]	Food Group[2,3]											
1	Yeast breads	7.3	7.2	6.1	7.4	6.8	7.6	7.3	5.9	6.5	8.8	10.6
2	Chicken and chicken mixed dishes	6.8	7.4	5.1	6.8	7.3	8.3	6.6	7.6	7.1	5.5	4.6
3	Pizza	6.3	9.4	4.7	7.6	8.7	12.1	5.4	7.5	6.4	3.3	1.9
4	Pasta and pasta dishes	5.1	6.7	9.8	8.3	7.0	4.8	4.6	5.3	4.3	4.7	3.9
5	Cold cuts	4.5	4.3	3.9	3.8	4.4	4.6	4.6	3.9	5.3	4.0	4.8
6	Condiments	4.4	4.1	3.4	3.4	4.4	4.5	4.4	4.4	4.9	4.1	3.0
7	Mexican mixed dishes	4.1	3.9	2.1	2.7	4.5	4.2	4.2	6.0	4.7	2.4	0.5
8	Sausage, franks, bacon, and ribs	4.1	4.6	6.2	4.9	5.1	3.6	4.0	3.4	3.8	4.6	4.5
9	Regular cheese	3.5	3.5	4.1	3.2	3.1	3.9	3.5	3.9	3.5	3.5	3.1
10	Grain-based desserts	3.4	3.7	2.5	4.2	3.9	3.5	3.4	2.8	3.3	3.5	4.6
11	Soups	3.3	2.4	3.2	3.0	2.4	1.9	3.6	3.1	2.7	5.1	5.1
12	Beef and beef mixed dishes	3.3	2.5	1.9	1.6	2.8	2.9	3.5	3.9	3.5	3.0	3.6
13	Rice and rice mixed dishes	2.6	1.9	2.1	1.9	2.2	1.6	2.9	3.3	3.1	2.2	1.9
14	Eggs and egg mixed dishes	2.6	2.0	1.9	1.8	1.9	2.4	2.7	2.4	2.7	3.0	2.9

Sources of salt in our grocery bags

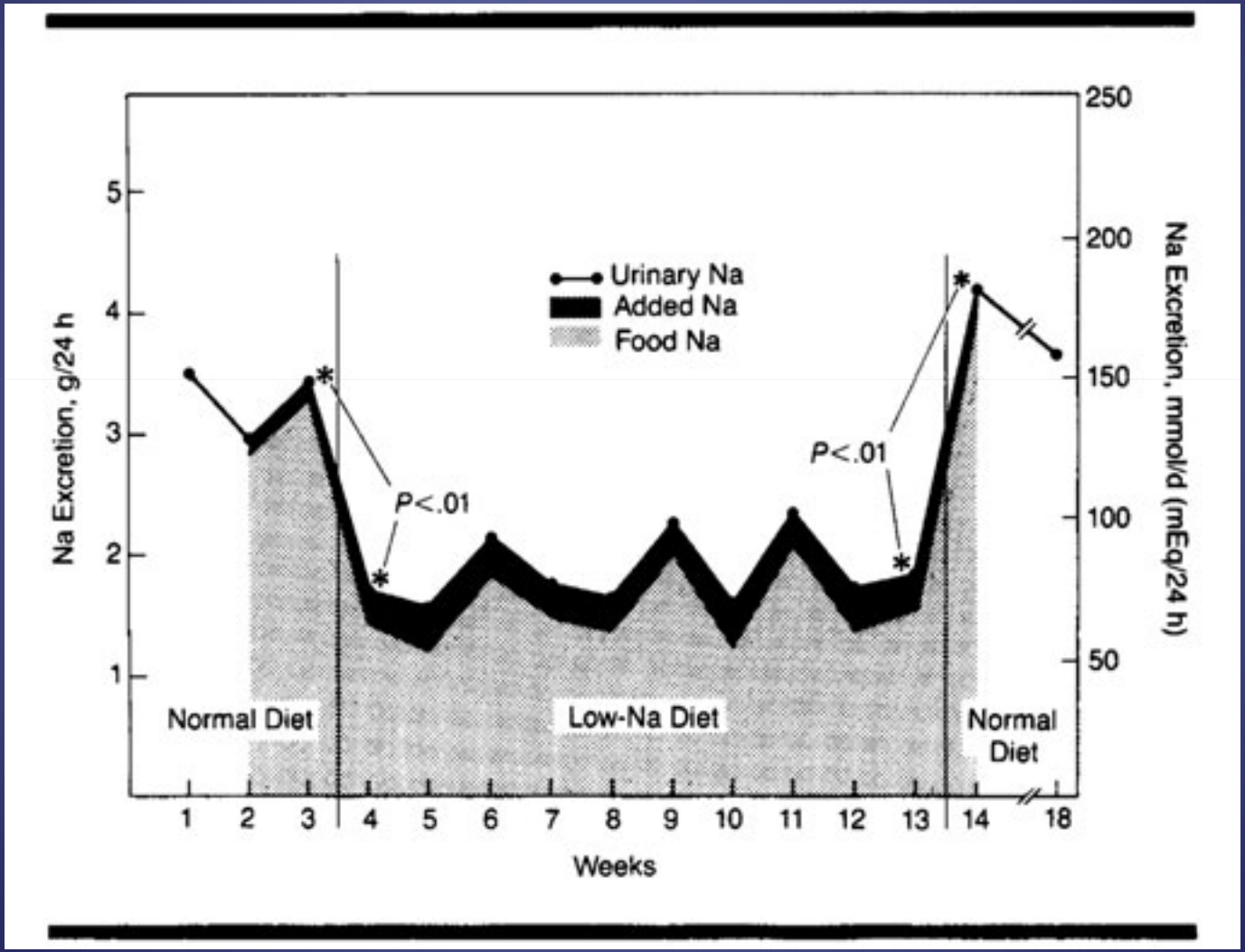
- 35% from cereal & cereal products
  - breads, cereals, pastries
- 26% from meat & meat products
- 8% from milk & milk products
  - milk, cheese

Source: http://www.actiononsalt.org.uk

Why do food manufacturers use so much salt?

- Preservative
- Weight of food
- Taste
  - Inexpensive way to add flavor
  - Habituated to very salty food
  - Can be unlearned
    - (6 wk down regulation of salt taste receptors)

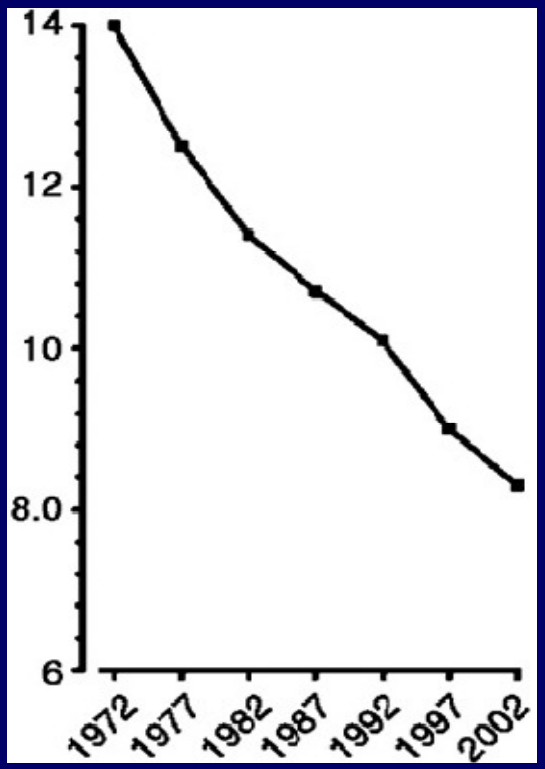
Less sodium intake when adding salt at the table



Beauchamp et al. JAMA 1987

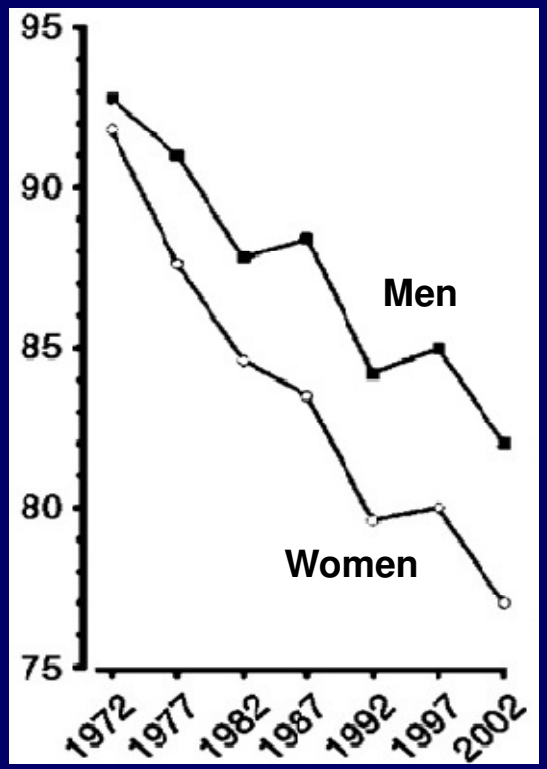
Finland

Salt intake (g/day by 24 hr urine)



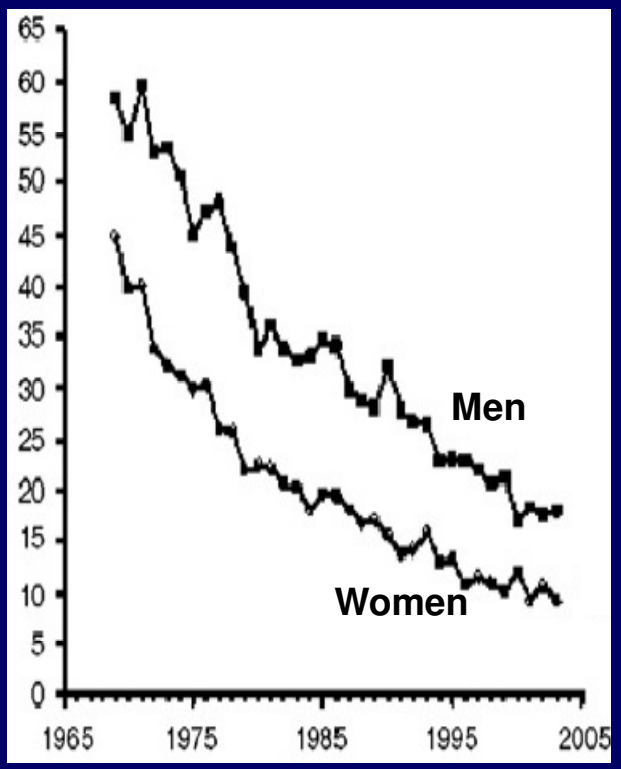
Year

Diastolic BP (mmHg)



Year

Stroke mortality (1/100000)



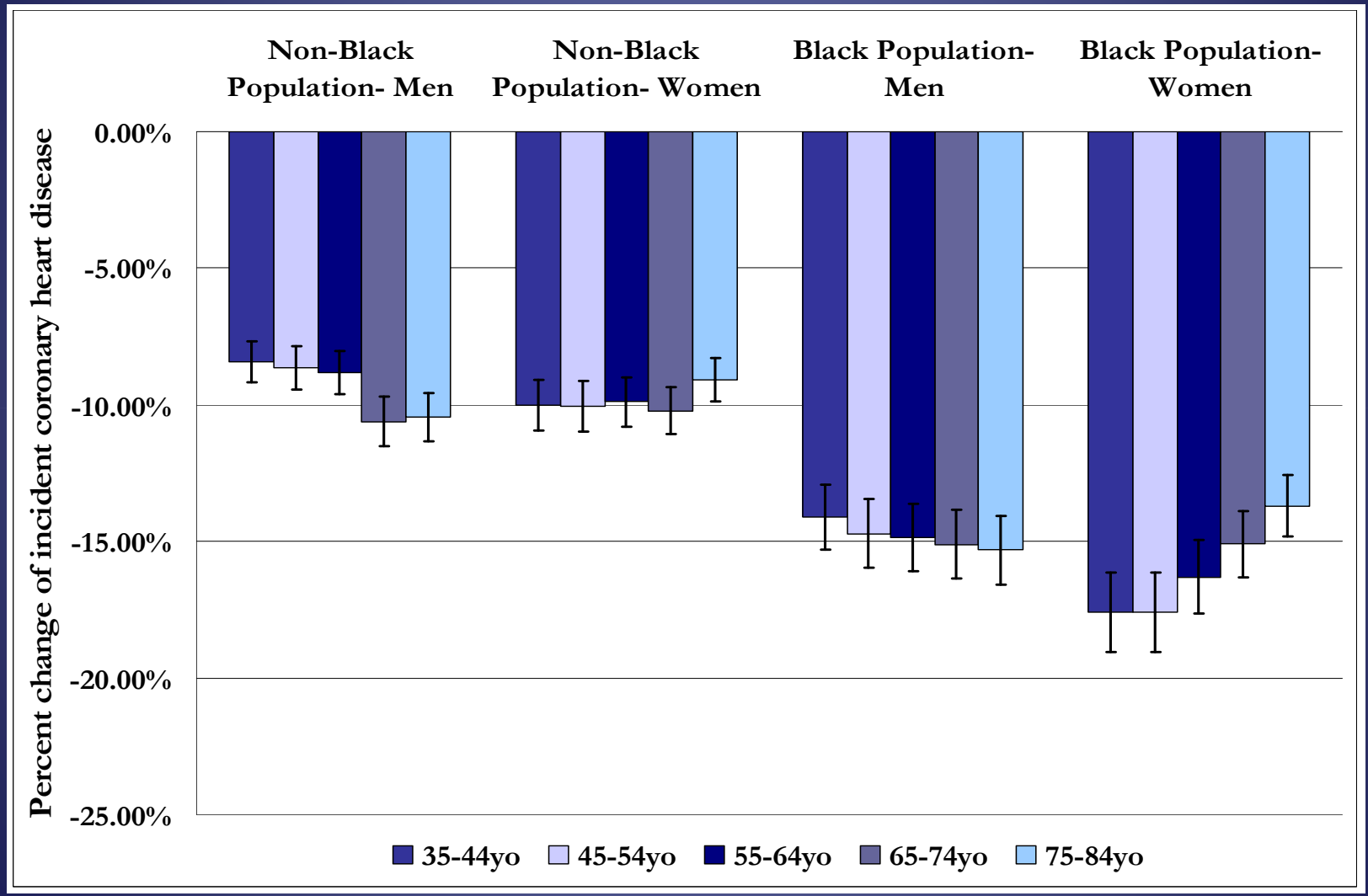
Year

Karppanen & Mervaala. Prog Cardiovasc Dis 2006;49:59-75.

Experience around the world

- Japan
  - Educational efforts in the 60's resulted in measurable decreases in salt intake, blood pressure, and stroke
  - Targeted individual education because most intake from salt added during cooking and on table.
- UK
  - Mostly salt from processed/prepared foods. Set standards, efforts directly with food manufacturers, 10% over the first 3 years
- Other countries with sodium reduction efforts

Percent change in incident CHD with 3 gm/day reduction in dietary salt



Bibbins-Domingo, K. et. al. NEJM, 2010, 362 (7):590-99.

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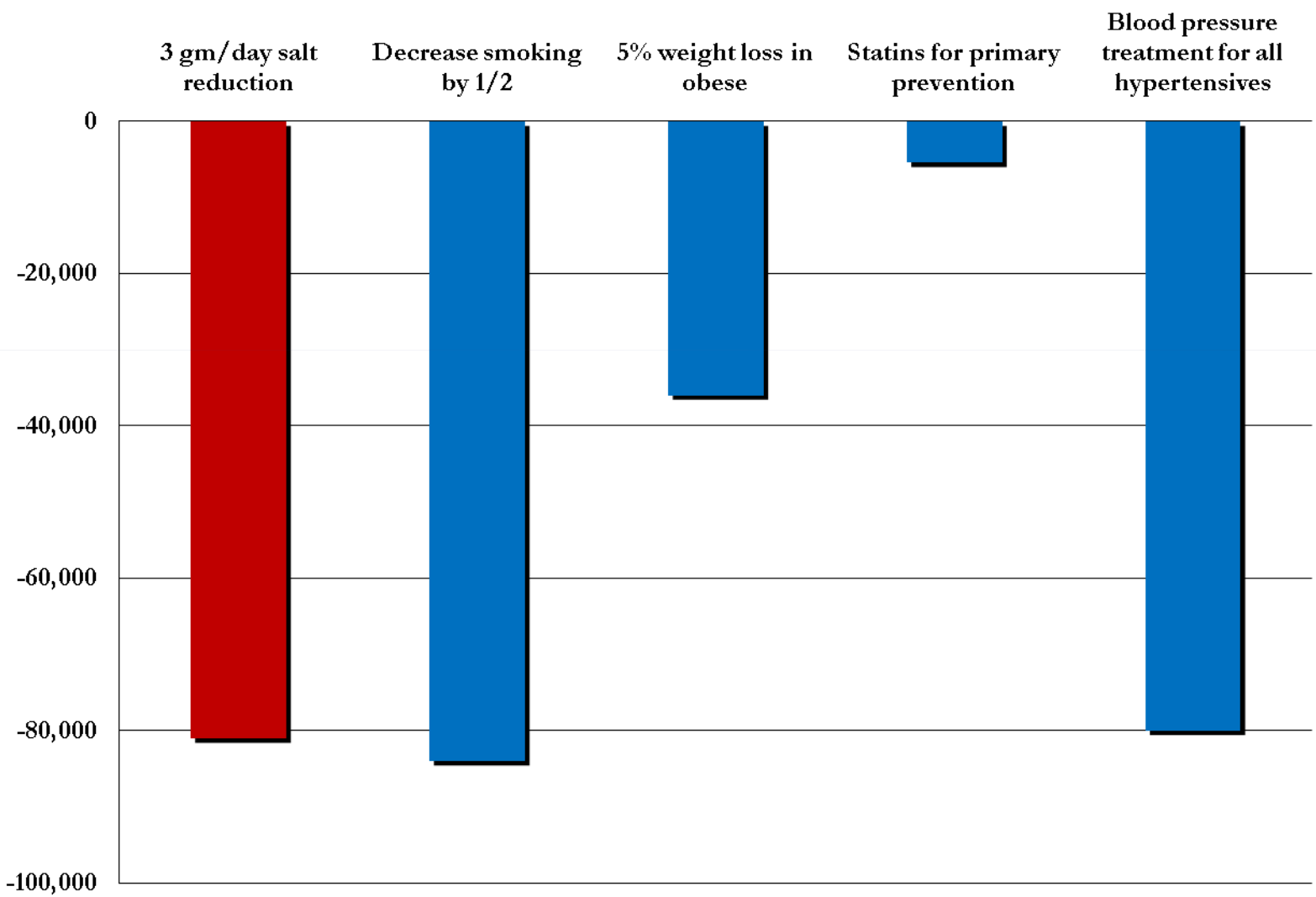
Comparing salt reduction to other preventive measures (deaths 2010-2019)



Reducing salt → reducing costs

- WHO estimates $1 per person to reduce salt through regulatory means, public campaigns, monitoring.
  - More cost effective than treating all hypertensives
  - Actually cost savings even if only modest reductions in salt achieved.
    - Gradual reduction over the decade to 1 gm/day reduction -> 7 dollars saved in healthcare for 1 dollar spent.

Outline

- Evidence linking salt and blood pressure
- Evidence linking salt and cardiovascular disease
- Challenges studying salt and cardiovascular disease
- Salt, CKD, and cardiovascular disease

Salt, CKD, and cardiovascular disease

- CKD is a salt-sensitive state (Koomans HA, Roos JC, Boer P, et al. Miner Electrolyte Metab 1982; 7:134–145; Weir MR, Dengel DR, Behrens MT, Goldberg AP. Hypertension 1995; 25:1339–44)
- Night-time "non-dipping" in CKD may contribute to CVD risk
  - Nocturnal hypertension compensates for diminished daytime natriuresis - enhances pressure natriuresis at night. Kimura, Dohi, Fukuda, Hypertension Research **33**, 515-520 (June 2010)
- Low sodium enhances antihypertensive and antiproteinuric properties of ACE inhibition (Navis G, et al. Kidney Int .31:815-819, 1985)

Sodium restriction in ESRD

2 site dialysis unit comparison (Kayikcioglu…Ok, *Nephrol. Dial. Transplant. (2009) 24 (3): 956-962)*

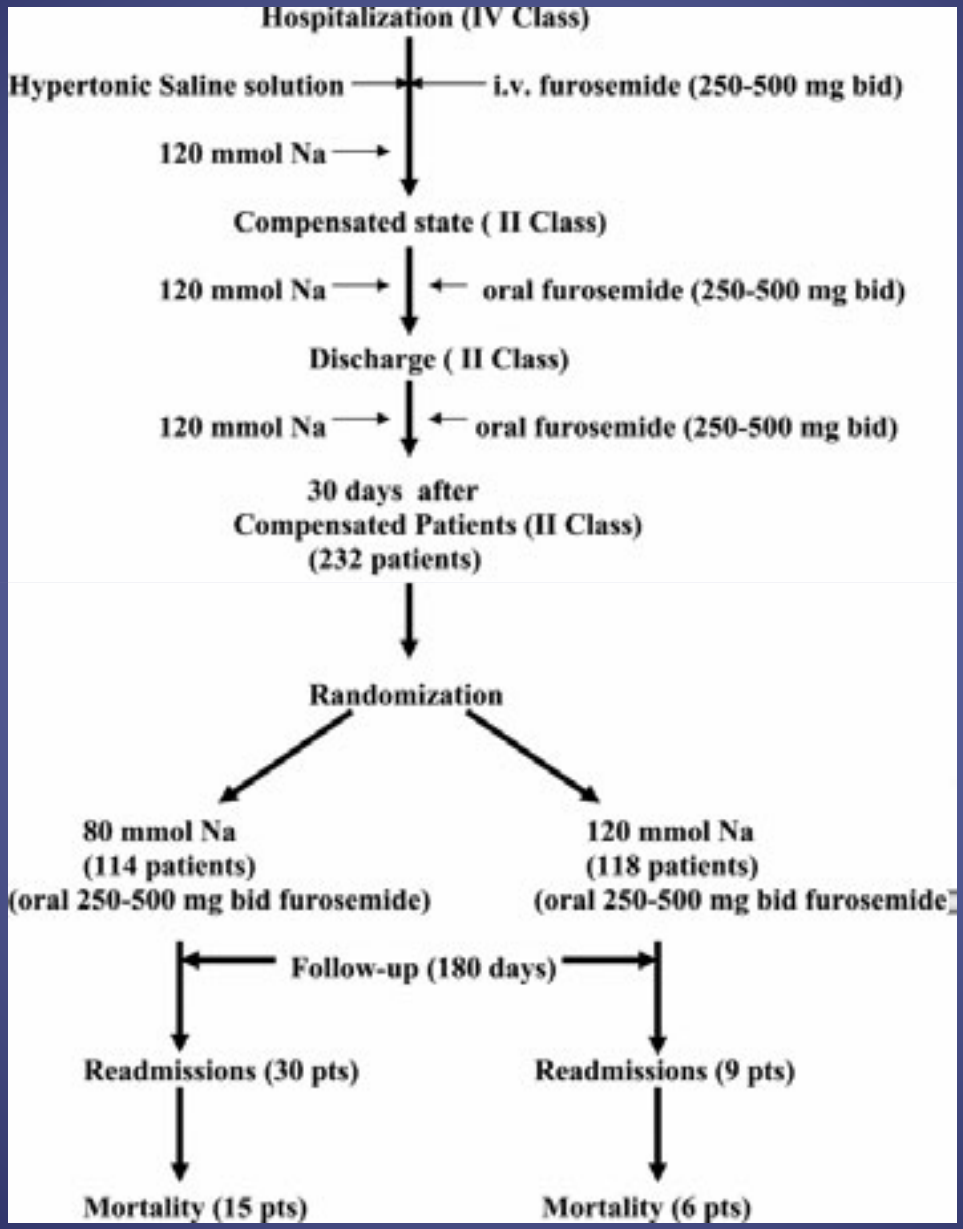
- Site A - Salt <5 gm, intensive ultrafiltration to maintain pre-dialysis BP <140/90 without meds
- Site B – Medications to control blood pressure

- Comparison of patients at each center at least one year.
- Age and dialysis duration distribution similar between centers.

	Centre A (n = 190)	Centre B (n = 204)	P-value
Use of antihypertensive medication (n = %)	13 (7%)	86 (42%)	0.001
ACE-/I or ARB	8	27	
Calcium channel blocker	1	43	
Beta blocker	2	3	
Furosemide	1	1	
Combination of two medications	1	12	
Interdialytic weight gain (kg)	2.29 ± 0.83	3.31 ± 1.12	0.0001
Interdialytic weight gain (kg for 70 kg man)	2.61 ± 0.98	4.05 ± 1.52	0.0001
Systolic BP (mmHg)	126 ± 15	126 ± 21	ns
Diastolic BP (mmHg)	75 ± 12	76 ± 11	ns
Pulse pressure (mmHg)	51 ± 9	50 ± 12	ns
Systolic BP ≥140 (%)	18	37	0.001
Diastolic BP ≥90 (%)	12	8	ns
Patients with systolic BP ≥140 and/or diastolic BP ≥90			
At the time of starting the HD programme	78	83	ns
Current situation	19	37	0.001
Intradialytic hypotension (number of episode per 100 HD sessions)	11	27	0.009

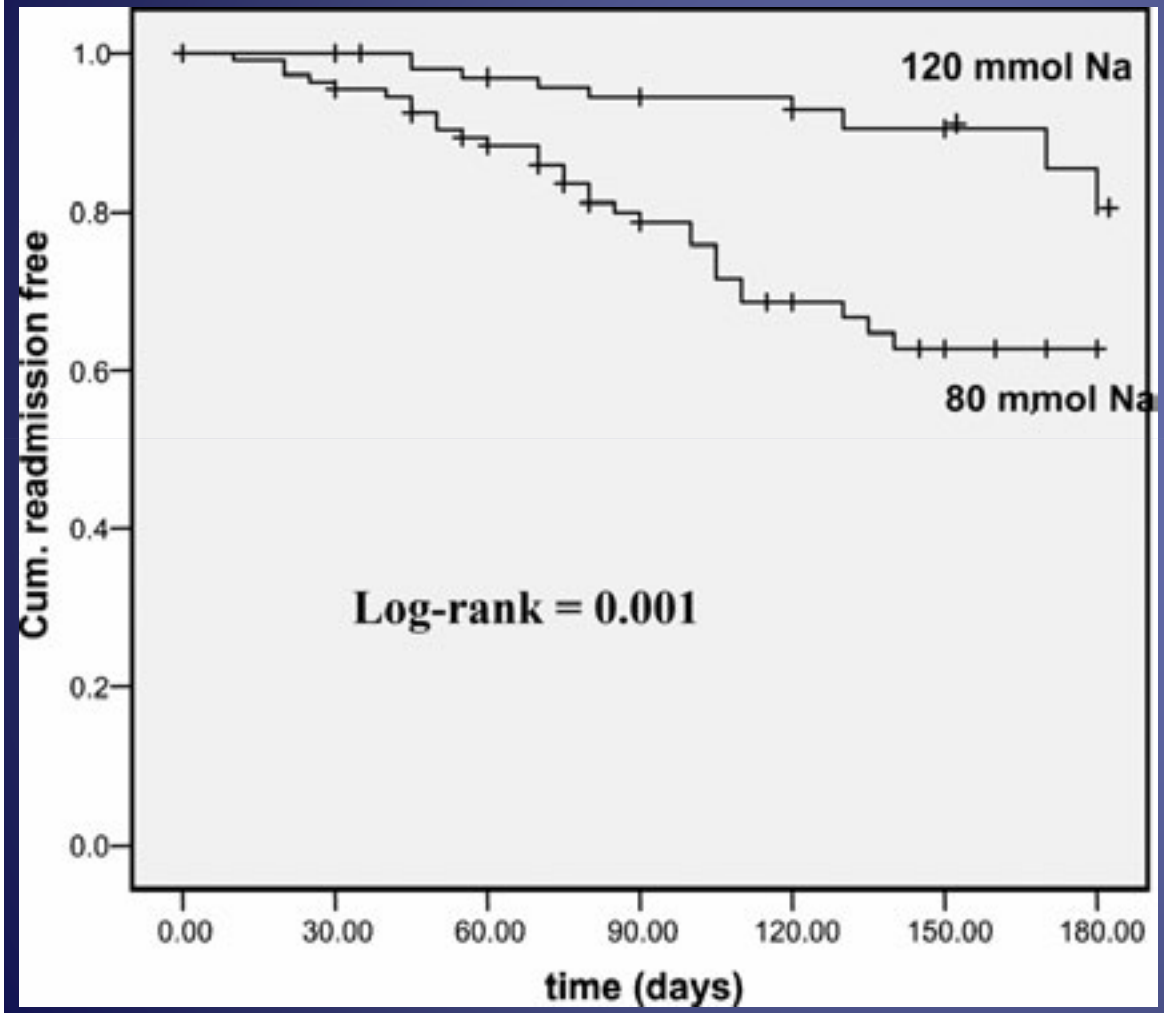
	Centre-A (n = 190)	Centre-B (n = 204)	P-value
LA indices			
LA index (cm/m^2)	2.40 ± 0.34	2.74 ± 0.53	0.0001
LA volume index (mL/m^2)	29.5 ± 10.0	36.7 ± 21.7	0.0001
LV measurements and indices			
LV diastolic index (cm/m^2)	2.61 ± 0.33	2.97 ± 0.64	0.0001
LV end-systolic index (cm/m^2)	1.60 ± 0.29	1.96 ± 0.47	0.0001
Interventricular septalindex (cm/m^2)	0.79 ± 0.13	0.83 ± 0.14	0.018
Posterior wall index (cm/m^2)	0.76 ± 0.11	0.83 ± 0.11	0.0001
LV ejection fraction (%)	68 ± 10	63 ± 09	0.0001
LV fractional shortening (%)	39 ± 8	35 ± 6	0.0001
LV mass indexed to height$^{2.7}$ ($g/m^{2.7}$)	59 ± 16	74 ± 27	0.0001
LV hypertrophy (%)[a]	124 (74%)	171 (88%)	0.001
Pulsed Doppler parameters			
Mitral-inflow E (cm/s)	73 ± 22	76 ± 27	ns
Mitral-inflow A (cm/s)	83 ± 18	82 ± 25	ns
Deceleration time (min/s)	0.23 ± 0.06	0.28 ± 0.07	0.0001
Isovolumic relaxation time (min/s)	0.08 ± 0.01	0.12 ± 0.02	0.0001
Mitral-inflow A-wave duration (min/s)	0.14 ± 0.02	0.16 ± 0.03	0.0001
E/A ratio	0.90 ± 0.31	0.96 ± 0.33	0.076
Mitral valve lateral annulus Ee/Ae (min/s)	0.99 ± 0.43	0.89 ± 0.41	0.034

Sodium restriction in heart failure



Clinical Science www.clinsci.org Clin. Sci. (2008) 114, 221-230

Outcomes at 180 days



In normal sodium arm vs. low at 180 days:

- Greater diuresis
- Lower body weight
- Lower creatinine
  - (2.1 vs. 1.4 mg/ml)
- Lower BUN
- Lower BNP

<u>In low sodium arm</u>

- Increased aldosterone
- Increased PRA

Conclusions

- Lower dietary salt lowers blood pressure
  - May be particularly beneficial in CKD as a salt-sensitive state
- Lower dietary salt lowers CVD risk.
  - Via blood pressure lowering, possibly other direct mechanisms

Conclusions

- Both clinical management and research are complicated by high salt food environment.
  - Most of our patients are consuming well above guideline targets, cannot comply with recommendations without substantial personal or environment changes.
- Only few studies examining salt reduction in CKD or ESRD and CVD outcomes
  - Have the potential for high yield results