

# Plan of Research on Sodium Intake in Diabetic Patients in Korea

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# Contents

- Significance of Research on Sodium Intake
- Study Design and Potential Research Design
- Issues to Consider
- Future Direction

나트륨 섭취량 세계 최고수준... WHO 권장량의 3배

# 외식 잦은 30~40대 직장인들 '나트륨 비상'

가장 큰 이유는? 직장인들 두끼 이상 외식 식당은 맛 살리려 소금 과용

과다 섭취 왜 나쁜가? 고혈압·심장병 유발하고 뇌졸중·위암 위험 요인도

**과다한 소금 섭취가 초래하는 질병**

- ◆ 나트륨**
- ◆ 한국 직장인 남성 '나트륨 비상'**
- ◆ 나트륨의 사회학**
- ◆ 나트륨 과잉섭취는 심장병 요인**

**체내 나트륨 농도가 높아지면**

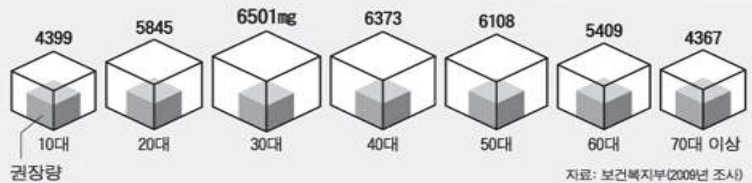
- ◆ 골다공증**  
체내에서 나트륨이 빠져나갈 때 칼슘이 함께 빠져나가기도 함
- ◆ 고혈압**  
혈중 나트륨 농도가 높으면 삼투압 현상에 의해 세포에서 수분이 혈관으로 빠져나옴 → 혈류량 증가 → 혈압 상승
- ◆ 심장병·뇌졸중**  
고혈압이 혈관에 손상이 생기면서 심장·뇌의 혈관이 막히거나 터짐
- ◆ 위암**  
염분이 위 점막을 자극해 위염을 일으키고 만성적 위염이 위암으로 발전
- ◆ 만성신부전**  
고혈압으로 신장의 모세혈관이 망가지면서 신장 기능 쇠퇴

외국에선...

핀란드,  
나트륨 줄인 '팬솔트'로  
평균 수명 5년 늘어

美, 전국민  
소금줄이기 운동

한국 남성의 연령별 하루 나트륨 섭취량  
단위: mg

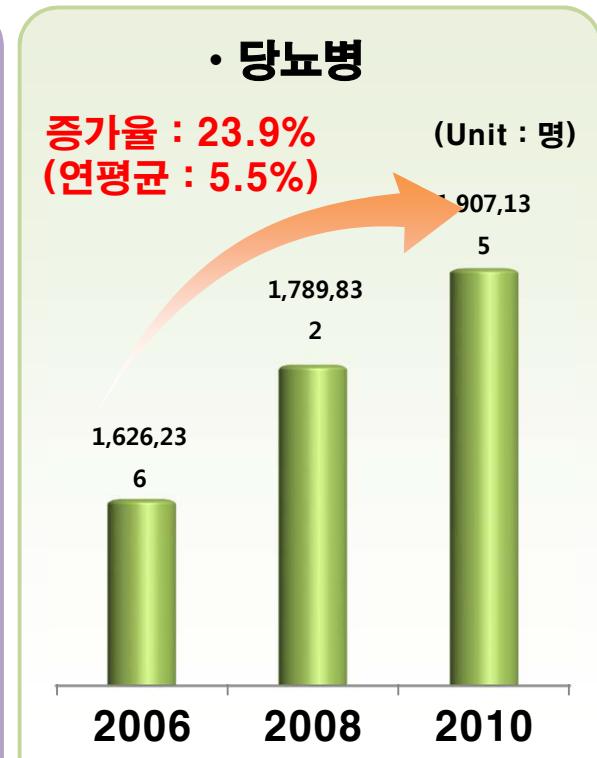
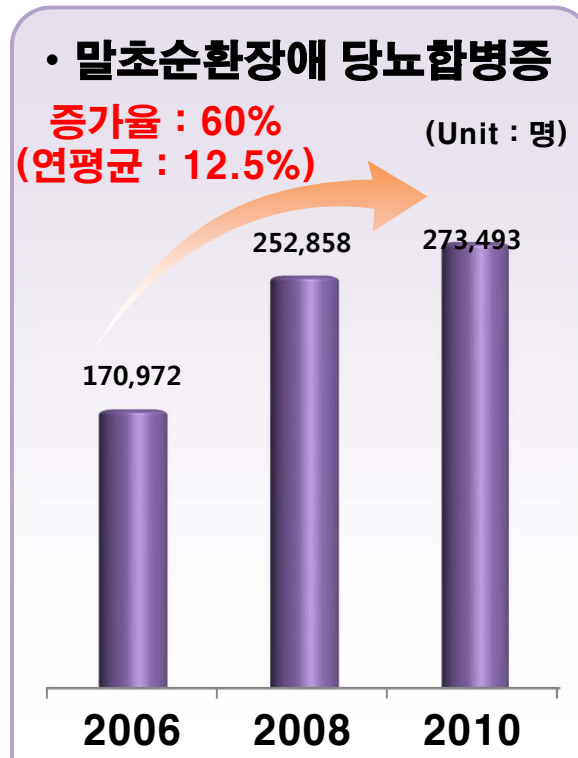
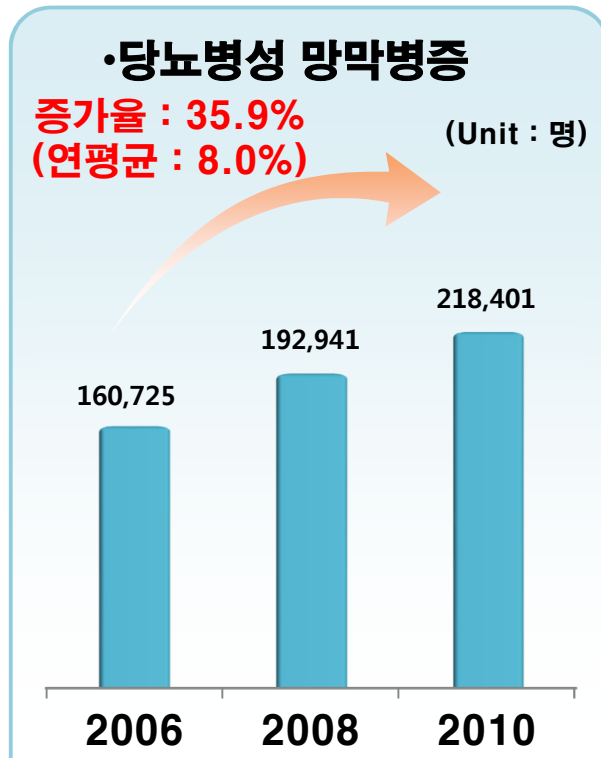


하루 평균 나트륨 섭취량  
단위: mg



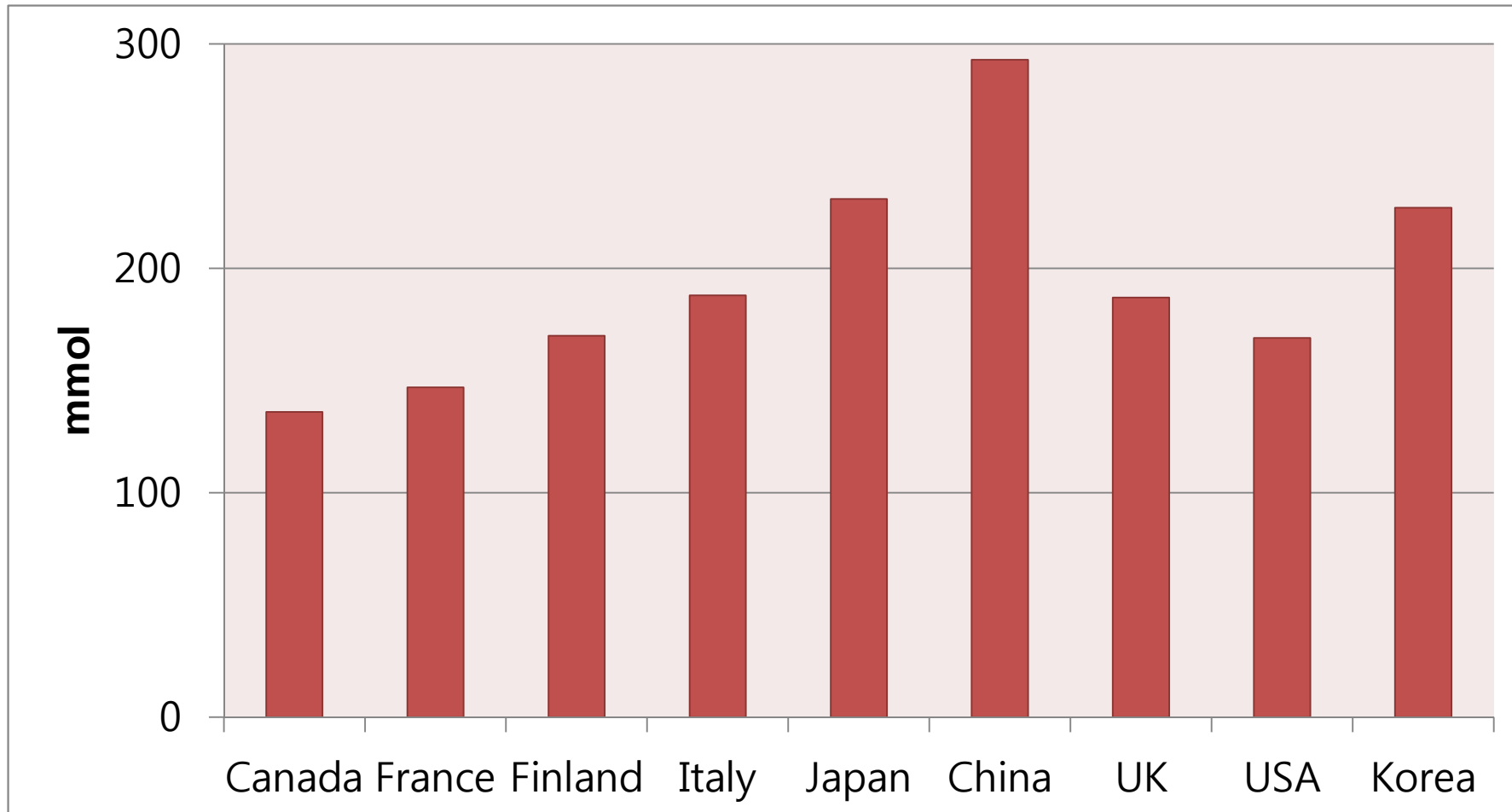
**→ 나트륨(Na)**  
짠맛을 내는 소금의 주성분으로 인체 필수 원소이지만, 과잉 섭취할 경우 고혈압·심장병·뇌졸중·만성신부전 등을 일으키고 골다공증의 위험이 높아진다고 의학계는 경고한다. 우리나라 사람들은 면류(23%), 김치(15%), 국·탕·찌개(11%)를 통한 나트륨 섭취가 많은 편이다.

# 당뇨병과 당뇨합병증 환자 증가 추이



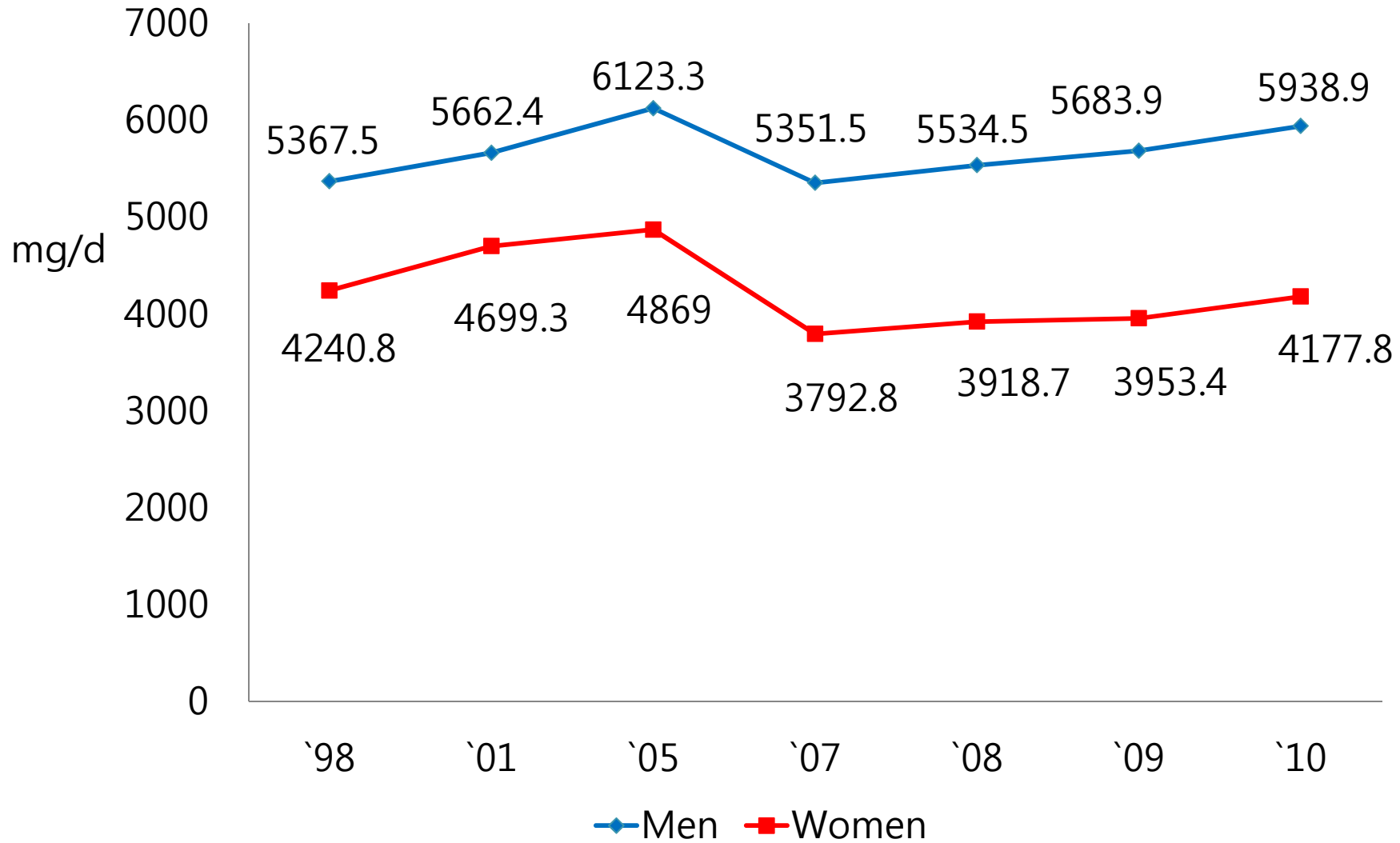
출처 : 국민건강보험공단

# Sodium Excretion from 24-hour urine



Brown IJ 2009; Son SM 2007

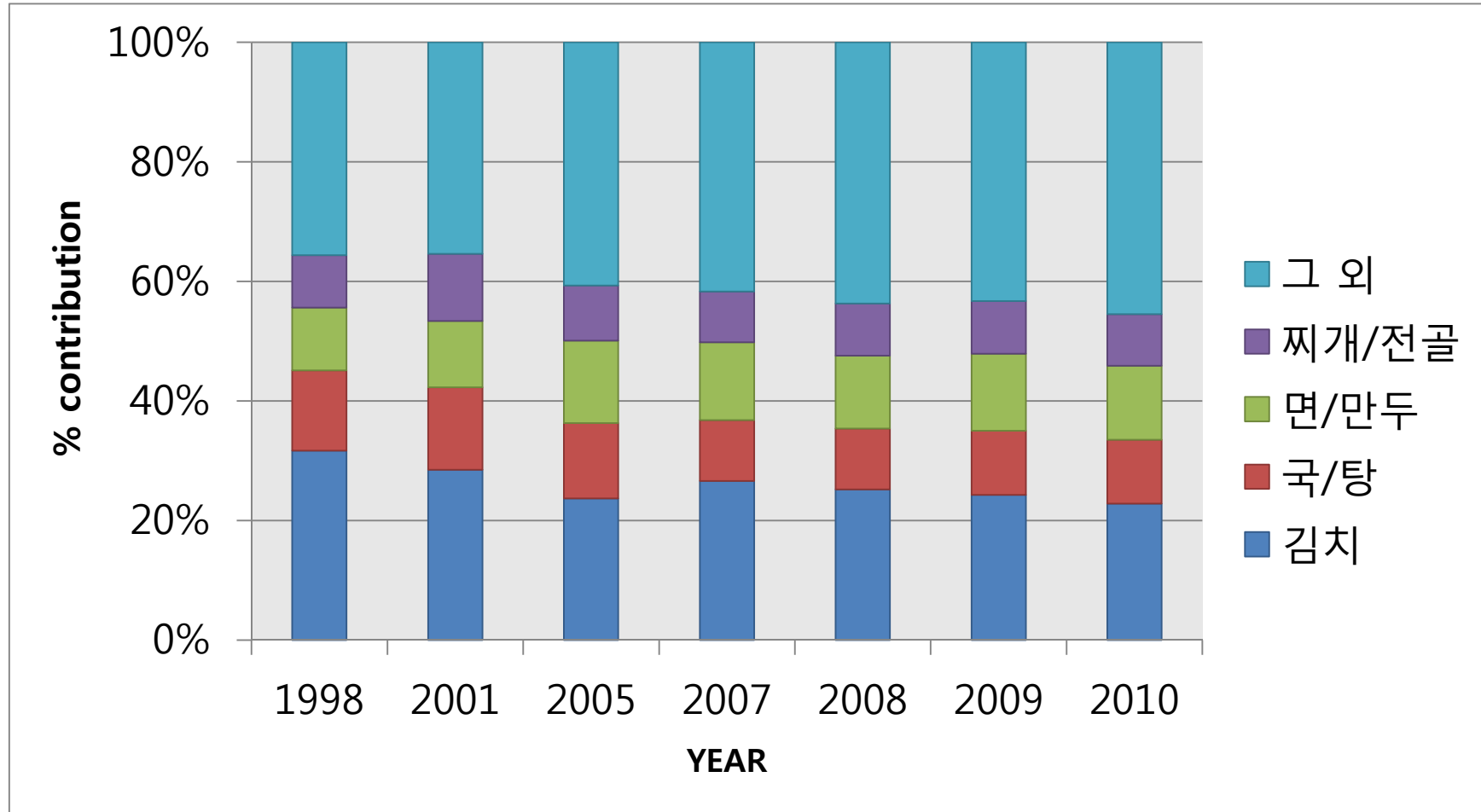
# Trends in Sodium Intake among Koreans 1998-2010 NHANES



# Food Sources Contributing to Na Intake

순위	1998		2001		2005		2007		2008		2009		2010	
	음식군	%	음식군	%	음식군	%	음식군	%	음식군	%	음식군	%	음식군	%
1	김치	31.7	김치	28.3	김치	23.7	김치	26.6	김치	25.2	김치	24.3	김치	22.8
2	국/탕	13.4	국/탕	13.8	면/만두	13.8	면/만두	13.0	면/만두	12.2	면/만두	12.9	면/만두	12.4
3	면/만두	10.5	찌개/전골	11.2	국/탕	12.6	국/탕	10.2	국/탕	10.2	국/탕	10.7	국/탕	10.7
4	찌개/전골	8.8	면/만두	11.1	찌개/전골	9.2	찌개/전골	8.5	찌개/전골	8.7	찌개/전골	8.8	찌개/전골	8.6
5	볶음	4.9	밥	5.3	밥	6.4	밥	5.5	밥	6.4	밥	5.8	밥	5.5
6	구이	3.7	볶음	4.5	볶음	4.8	구이	5.0	구이	5.1	장/양념	5.3	구이	5.4
7	장/양념	3.4	구이	3.3	구이	4.7	장/양념	4.9	장/양념	4.9	구이	5.2	장/양념	5.3
8	생채/무침	2.7	생채/무침	2.5	생채/무침	3.6	볶음	4.6	볶음	4.7	볶음	4.8	볶음	4.8
9	밥	2.5	장/양념	2.5	장/양념	3.5	생채/무침	2.9	생채/무침	3.0	장아찌/절임	3.8	장아찌/절임	4.0
10	빵/과자	2.4	나물/숙채	2.2	나물/숙채	2.6	장아찌/절임	2.4	장아찌/절임	2.8	생채/무침	3.2	생채/무침	3.6

# Food Sources of Na Intake KNHANES

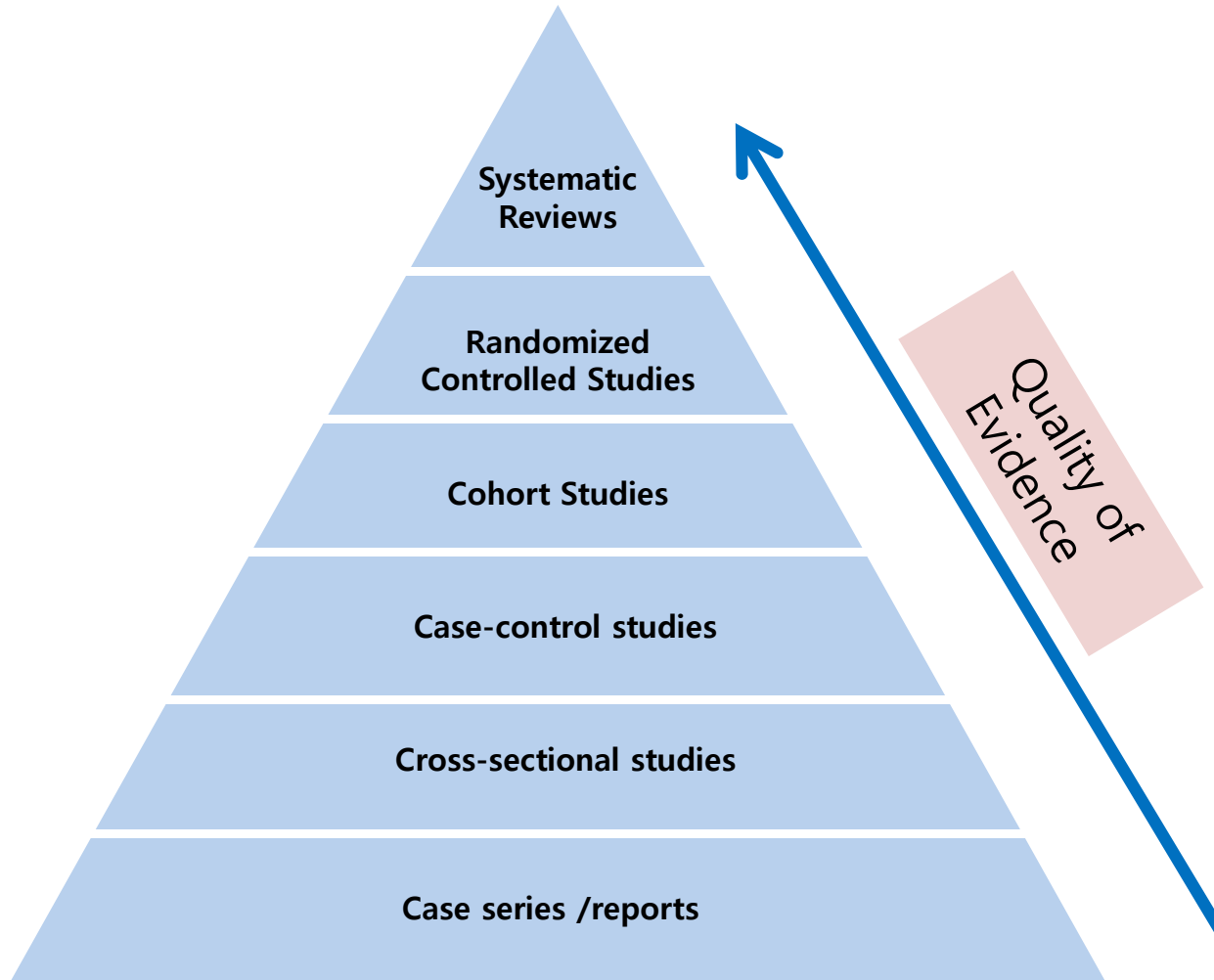




# Top Food Sources of Sodium in Other Countries

- UK
  - Cereal products (bread, other baked goods and breakfast cereals) ~ 38%.
  - Meat products (incl. processed meats) ~ 21%
- USA
  - Cereals and baked goods > 16%
  - Meat products incl. hot dogs and bacon >13%
- Japan
  - Soy sauce, salted vegetables and fruits, miso soup, fresh and salted fish and salt added
- China
  - Salt added and soy sauce

# Study Design



# Epidemiologic Studies

## **DISTRIBUTION: DESCRIPTIVE STUDIES**

- Correlational or ecologic study
- Cross-sectional study

## **DETERMINANTS: ANALYTIC STUDIES**

Search for factors associated with or predictive of outcome

- Observational study
  - case-control
  - cohort
- Intervention study  
e.g. randomized clinical trial

# Cross-sectional study

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## Sodium Intake Among People with Normal and High Blood Pressure

Umed A. Ajani, MBBS, MPH, Sandra B. Dunbar, RN, DSN, Earl S. Ford, MD, MPH, Ali H. Mokdad, PhD, George A. Mensah, MD

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**Table 2.** Sodium intake (mg) among participants with normal and high blood pressure, NHANES 1999–2000

	High blood pressure	No high blood pressure	<i>p</i> value*
Sample size	1673	2338	
Weighted sample	58 723 759	118 441 907	
Mean	3330	3600	
Median	2987	3243	
Geometric mean	2885	3146	<0.001
Adjusted geometric mean	2992	3089	0.032

NHANES, National Health and Nutrition Examination Survey.

\*Determined from log-transformed sodium intake.

Ajani UA Am J Prev Med 2005

# Cross-sectional study

- **Snapshot in time: information on exposure and outcome of individuals assessed simultaneously**
- **Time saving, data often available and regularly updated**
- **Limitations:**

**No temporal sequence, so ability to test hypothesis will depend on the exposure. If exposure cannot or unlikely to change as a result of the disease, could be hypothesis testing.**

# Analytic Study

1. Among individuals, with appropriate comparison group, with appropriate time sequence, and with adequate control of confounding.
2. Observational studies (exposures are self-selected)
  - Case-control
  - Cohort
3. Intervention studies (exposures are allocated by investigators)  
e.g. randomized clinical trial

Case-Control Study:  
status

Selection into study on basis of disease

EXPOSURE

DISEASE

?



?



PRESENT



ABSENT



Basis on which groups are selected at  
beginning of study



INVESTIGATOR

## **Case-control design:**

### **STRENGTHS:**

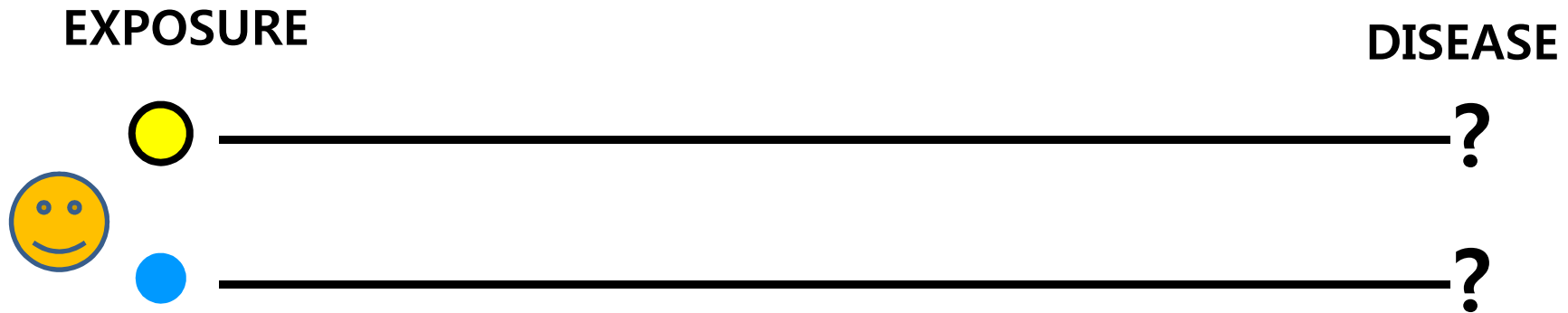
- **Efficient in terms of time and money, since disease already occurred**
- **Efficient way to deal with long latent period**
- **Can examine effects of other risk factors**

### **LIMITATIONS:**

- **Worried about ability to get accurate exposure information for right time period  
(1 year? 5 years? 10 years?)**



# Cohort Study: Selection into study on basis of exposure status



PRESENT



ABSENT



Basis on which groups are selected at beginning of study



INVESTIGATOR

## **Cohort design:**

### **STRENGTHS:**

- **More accurate exposure information.**
- **Can elucidate temporal relationship (analysis by time).**
- **Can look at multiple outcomes**

### **LIMITATIONS:**

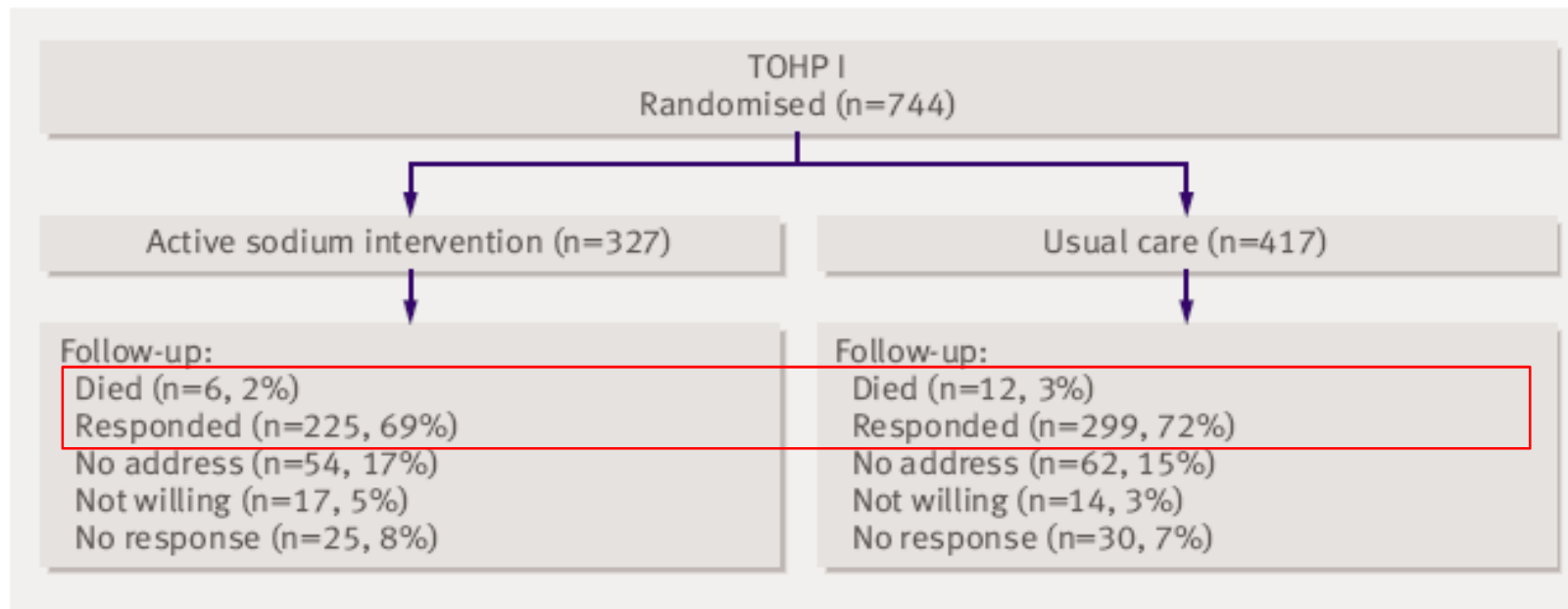
- **Will take longer in time (latent period), and be more expensive.**
- **Need relevant data to be available**
- **Need to follow-up participants for long periods of time.**

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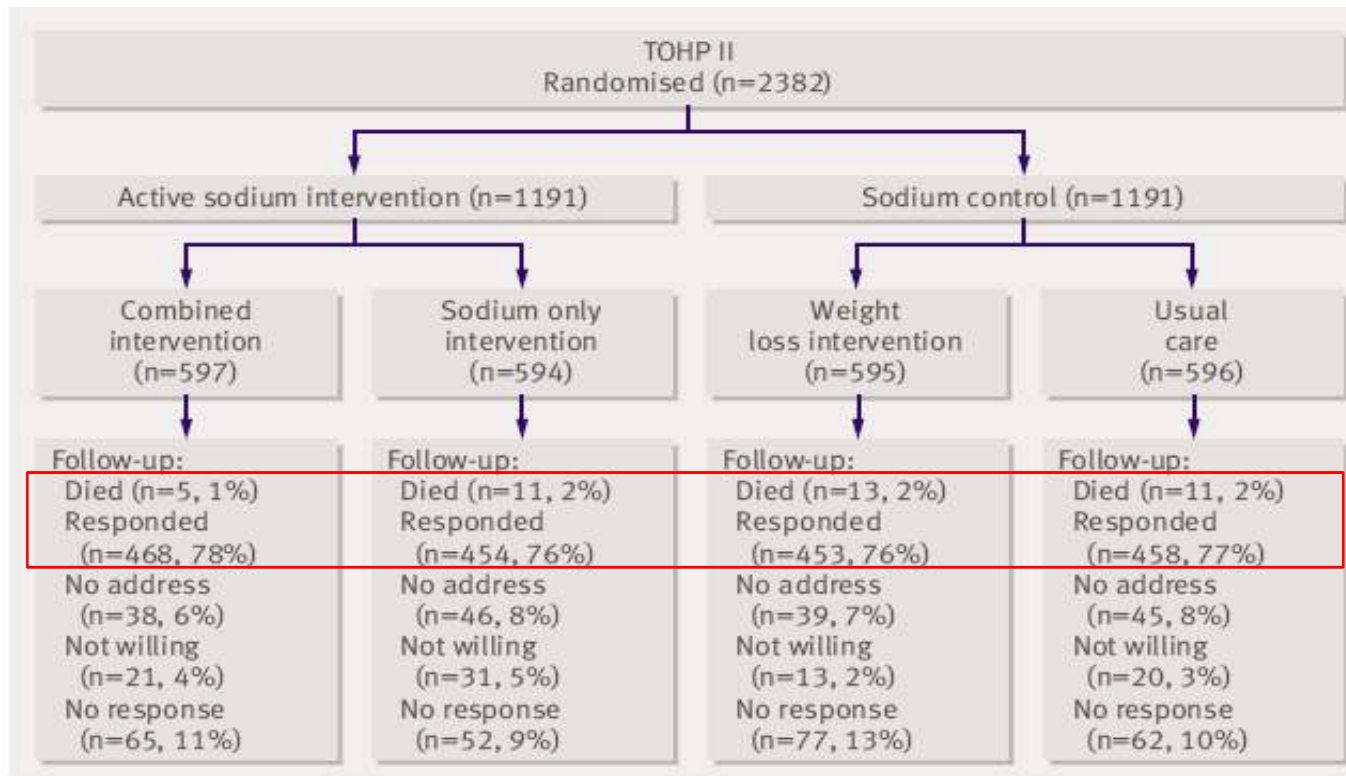
### Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP)

Nancy R Cook, associate professor,<sup>1</sup> Jeffrey A Cutler, former senior scientific adviser,<sup>2</sup> Eva Obarzanek, research nutritionist,<sup>2</sup> Julie E Buring, professor,<sup>1</sup> Kathryn M Rexrode, assistant professor of medicine,<sup>1</sup> Shiriki K Kumanyika, professor of epidemiology,<sup>3</sup> Lawrence J Appel, professor of medicine,<sup>4</sup> Paul K Whelton, president and chief executive officer,<sup>5</sup> for the Trials of Hypertension Prevention Collaborative Research Group

# TOHP study



- The first TOHP trial tested the feasibility and efficacy of seven non-pharmacological interventions in reducing blood pressure in people with high normal blood pressure.
- Interventions : weight loss, sodium reduction, stress management, and nutritional supplements (calcium, magnesium, potassium, and fish oil).



- The second TOHP trial tested the effects of weight loss and sodium reduction on incident hypertension and blood pressure.
- 2×2 factorial design → effects of the sodium reduction intervention were analysed by grouping data for the 2 sodium reduction interventions (alone or with weight loss) and for the 2 non-sodium reduction groups (usual care or weight loss alone).

# Follow up study

- The observational follow-up for cardiovascular disease began in 2000, and ended in 2004-5.
- Data on all events occurring since the end of the trials was collected by mail and phone.
- Information on self reported sodium intake was collected on the final follow-up questionnaire sent in 2004-5.

**Table 1 | Characteristics of participants in TOHP I and II according to allocation to sodium reduction intervention or control group. Numbers are means (SDs) unless stated otherwise**

	TOHP I			TOHP II*		
	Intervention (n=327)	Control (n=417)	P value	Intervention (n=1191)	Control(n=1191)	P value
<b>Baseline</b>						
No (%) of men	232 (71.0)	299 (71.7)	0.82	784 (65.8)	782 (65.7)	0.93
<b>No (%) according to race:</b>						
White	255 (78.0)	319 (76.5)	0.89	950 (79.8)	938 (78.8)	0.20
Black	64 (19.6)	87 (20.9)		212 (17.8)	209 (17.6)	
Other	8 (2.4)	11 (2.6)		29 (2.4)	44 (3.7)	
Age (year)	43.4 (6.6)	42.6 (6.5)	0.074	43.9 (6.2)	43.3 (6.1)	0.015
Weight (kg)	82.7 (14.3)	82.8 (13.9)	0.90	93.8 (14.3)	93.5 (13.8)	0.66
BMI (kg/m <sup>2</sup> )	27.1 (3.8)	27.1 (3.6)	0.88	30.9 (3.1)	30.9 (3.1)	0.87
SBP (mm Hg)	124.8 (8.5)	125.1 (8.1)	0.57	127.5 (6.6)	127.4 (6.2)	0.70
DBP (mm Hg)	83.7 (2.7)	83.9 (2.8)	0.43	86.0 (1.9)	85.9 (1.9)	0.11
Sodium excretion (mmol/24 h)	154.6 (59.9)	156.4 (60.5)	0.70	182.9 (78.4)	184.5 (76.8)	0.62
<b>Change to end of trial</b>						
Change in weight (kg)	-0.2 (3.8)	0.2 (3.9)	0.19	0.7 (5.5)	0.8 (5.7)	0.67
<b>Change in sodium excretion (mmol/24 h)</b>	<b>-55.2 (76.9)</b>	<b>-11.3 (77.7)</b>	<b>&lt;0.0001</b>	<b>-42.5 (89.0)</b>	<b>-9.8 (87.7)</b>	<b>&lt;0.0001</b>

BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure.

\*In TOHP II (a 2x2 factorial trial), participants were grouped according to whether they did or did not receive reduced sodium intervention. Hence, active sodium reduction group includes those assigned to sodium reduction alone and to sodium reduction plus weight loss, while control group includes those assigned to weight loss alone and to usual care.

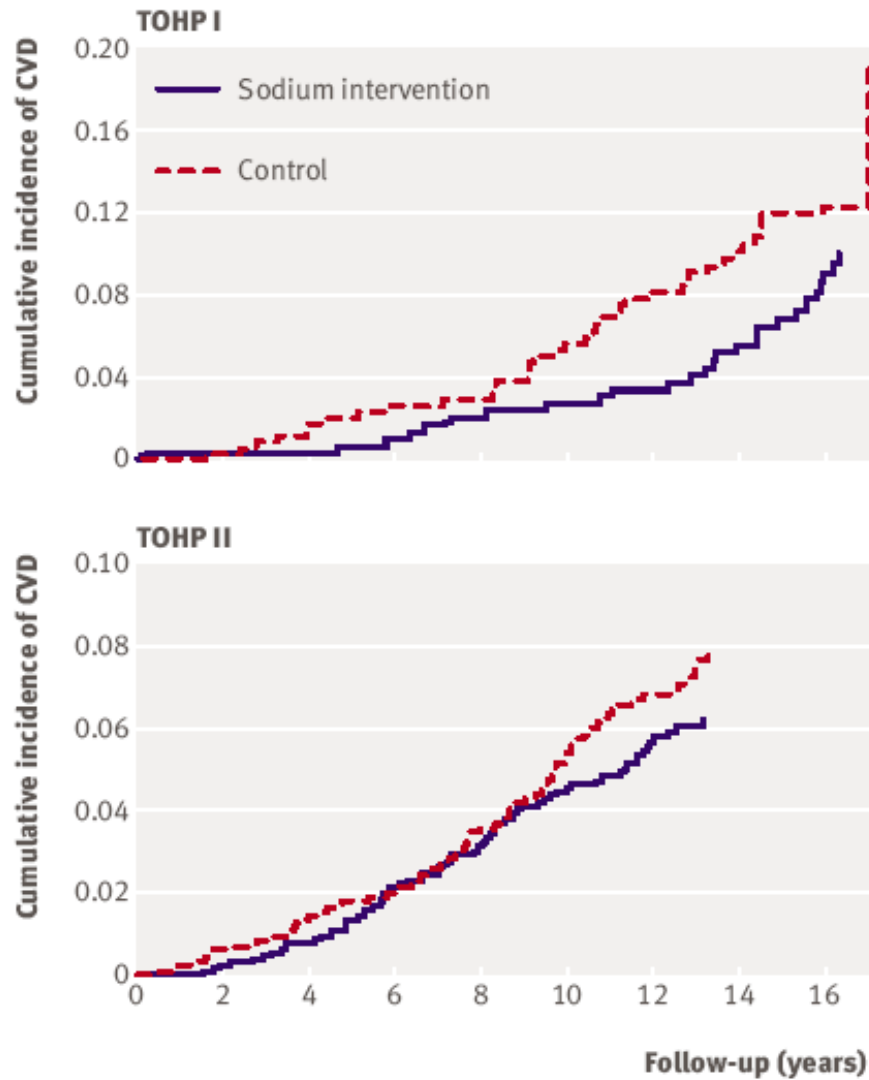


Fig 2 | Cumulative incidence of cardiovascular disease (CVD) by sodium intervention group in TOHP I and II, adjusted for age, sex, and clinic

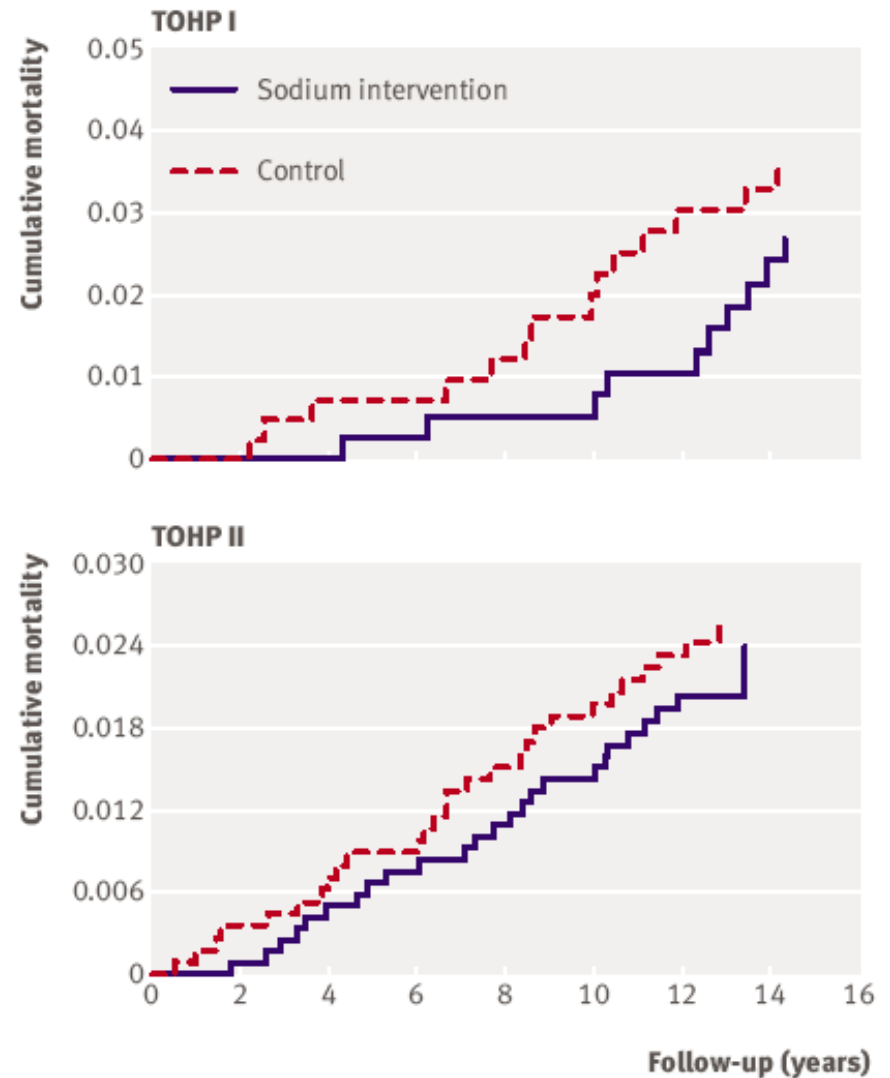


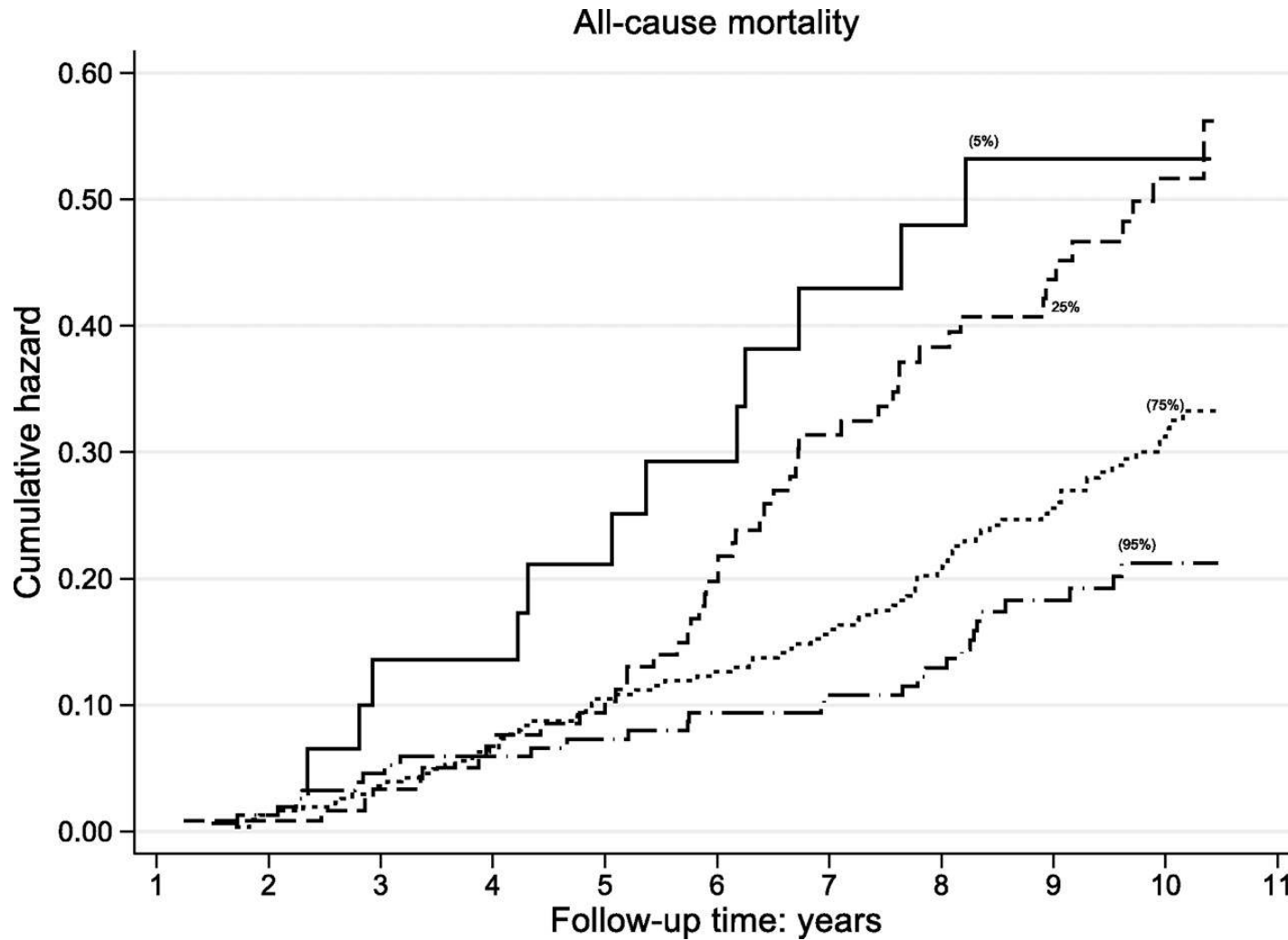
Fig 3 | Total mortality by sodium intervention group in TOHP I and II, adjusted for age, sex, and clinic



# Dietary Salt Intake and Mortality in Patients With Type 2 Diabetes

- 638 patients attending a single diabetes clinic in Melbourne, Australia were followed in a prospective cohort study for a median of 9.9 years.
- Baseline sodium excretion was estimated from 24-h urinary collections.
- 175 deaths, 75 (43%) of which were secondary to cardiovascular events.

**Cumulative hazard (Nelson-Aalen) of all-cause mortality, stratified by percentiles (5th, 25th, 75th, and 95th) of 24-h urinary sodium excretion.**



Ekinci E I et al. Diabetes Care 2011

All-cause mortality was inversely associated with 24-h urinary sodium excretion.

**Intervention Study: Type of prospective cohort study in which exposure is allocated by investigator**

**EXPOSURE**

**DISEASE**



 **PRESENT**

 **ABSENT**

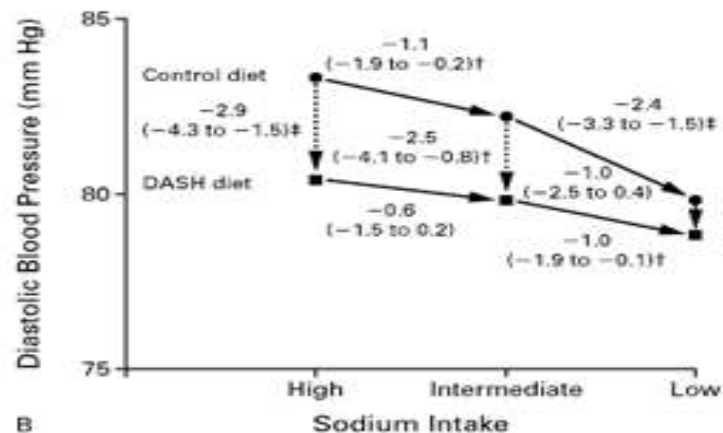
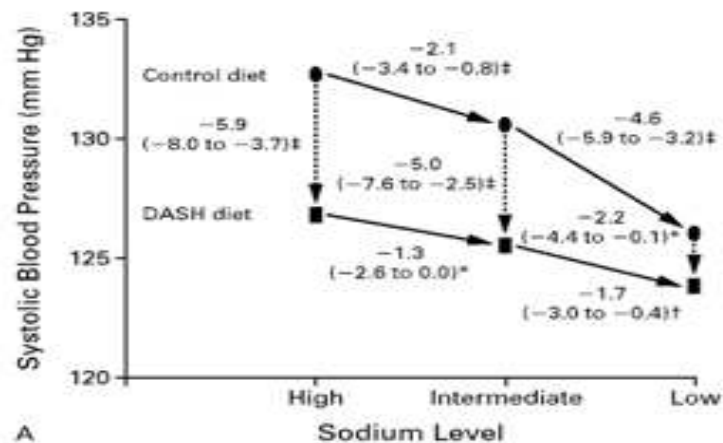
} Exposure is allocated to participants at beginning of study



**INVESTIGATOR at beginning of study**

# DASH-sodium

## Reduced Sodium Intake and Hypertension



The Effect on Systolic Blood Pressure (Panel A) and Diastolic Blood Pressure (Panel B) of Reduced Sodium Intake and the DASH Diet

The reduction of sodium intake to levels below the current recommendation and the DASH diet both lower blood pressure substantially, with greater effects in combination than singly. Long-term health benefits will depend on the ability of people to make long-lasting dietary changes and the increased availability of lower-sodium foods.

## **Intervention study:**

### **STRENGTHS:**

- **True control of exposure (exercise pattern)**
- **Ability to control confounding**

### **LIMITATIONS:**

- **Most expensive design, needs most resources**
- **Issues of compliance with regimen**

# Meta-analysis

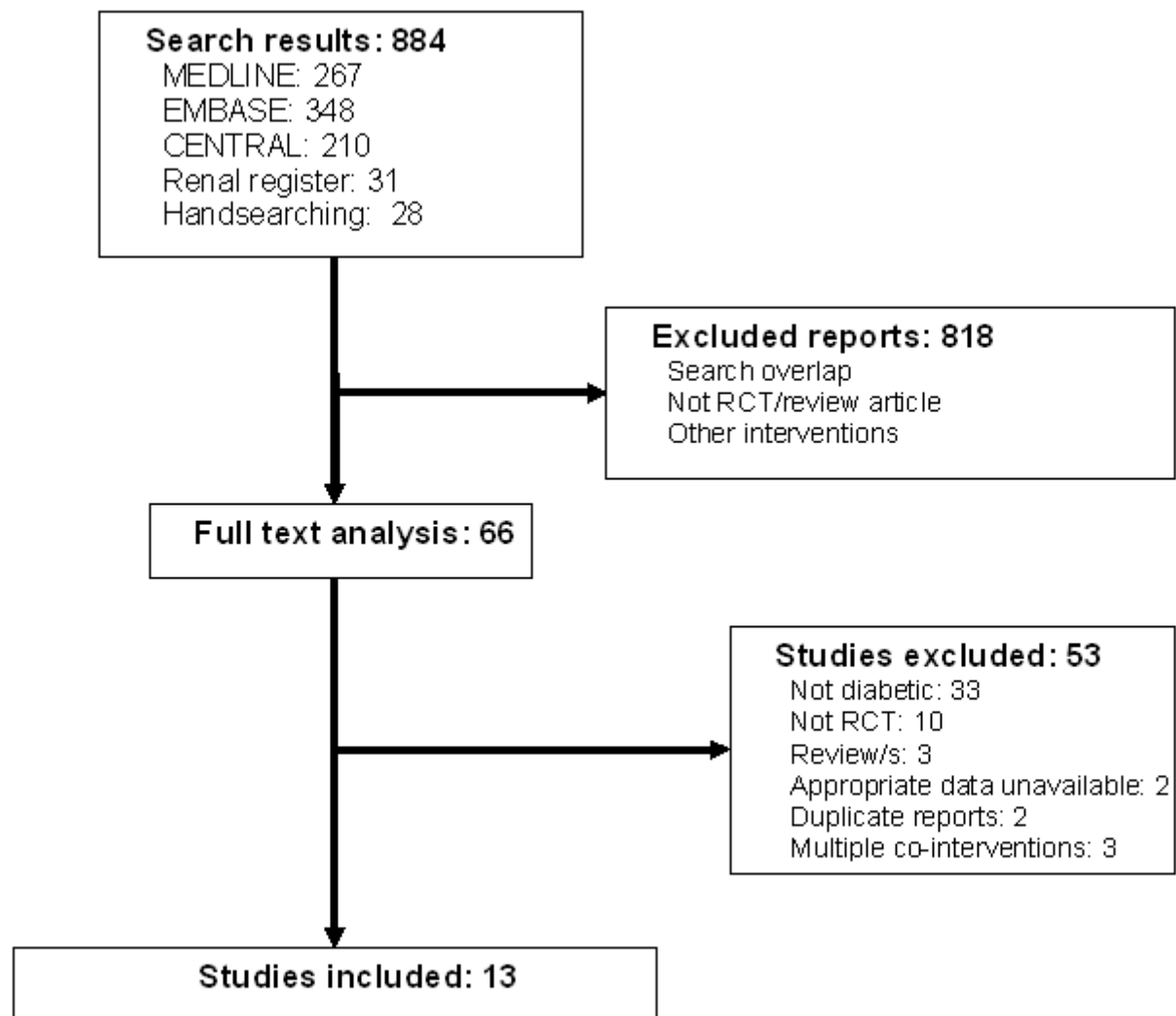
- Quantitative review and synthesis of similar but independent studies
- Combine information over several studies to increase power and generalizeability
- Estimate an average or pooled effect over studies
- Examine differences across studies to determine modification of treatment effect

# Altered dietary salt intake for preventing and treating diabetic kidney disease (Review)

Suckling RJ, He FJ, MacGregor GA



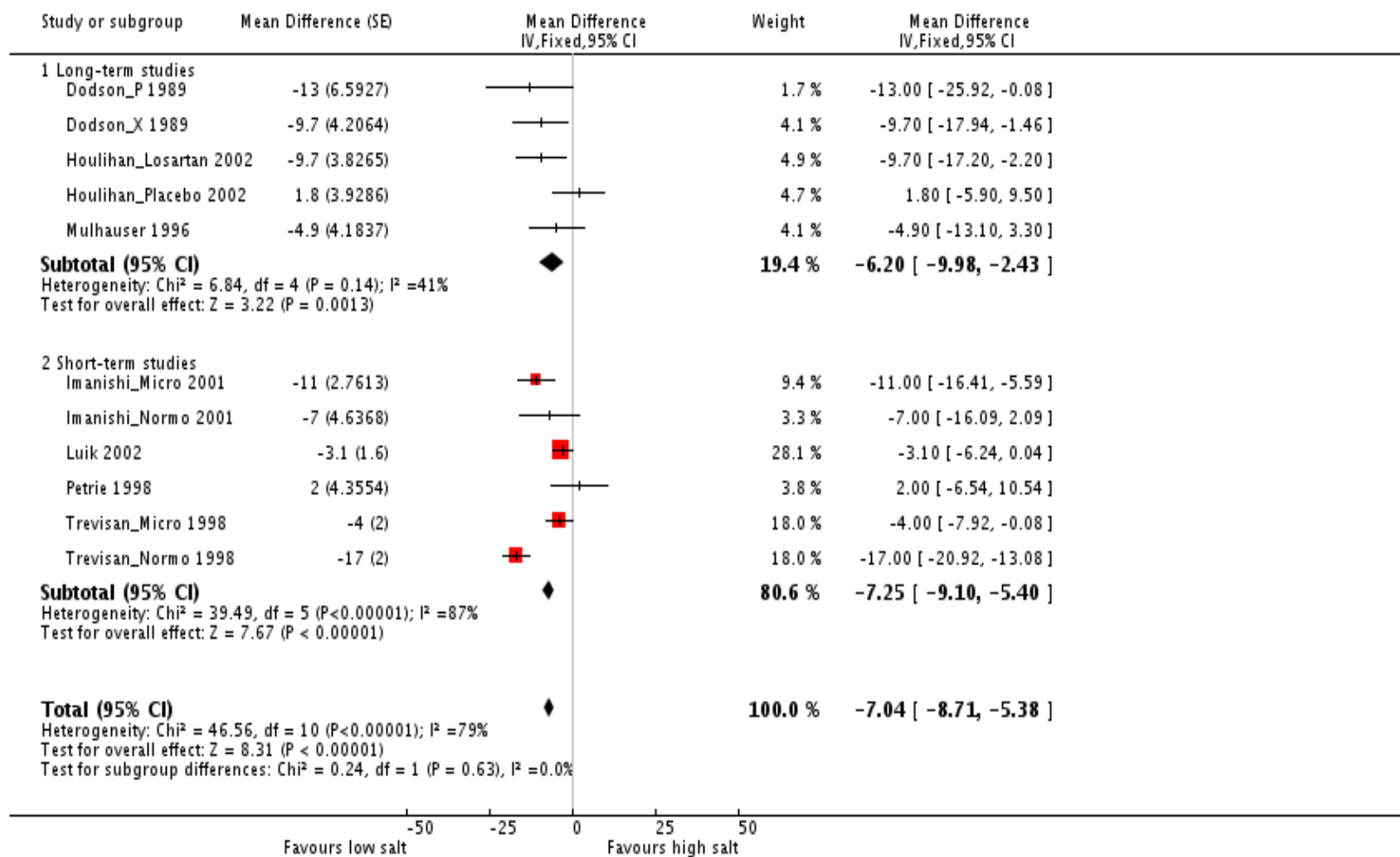
**THE COCHRANE  
COLLABORATION®**





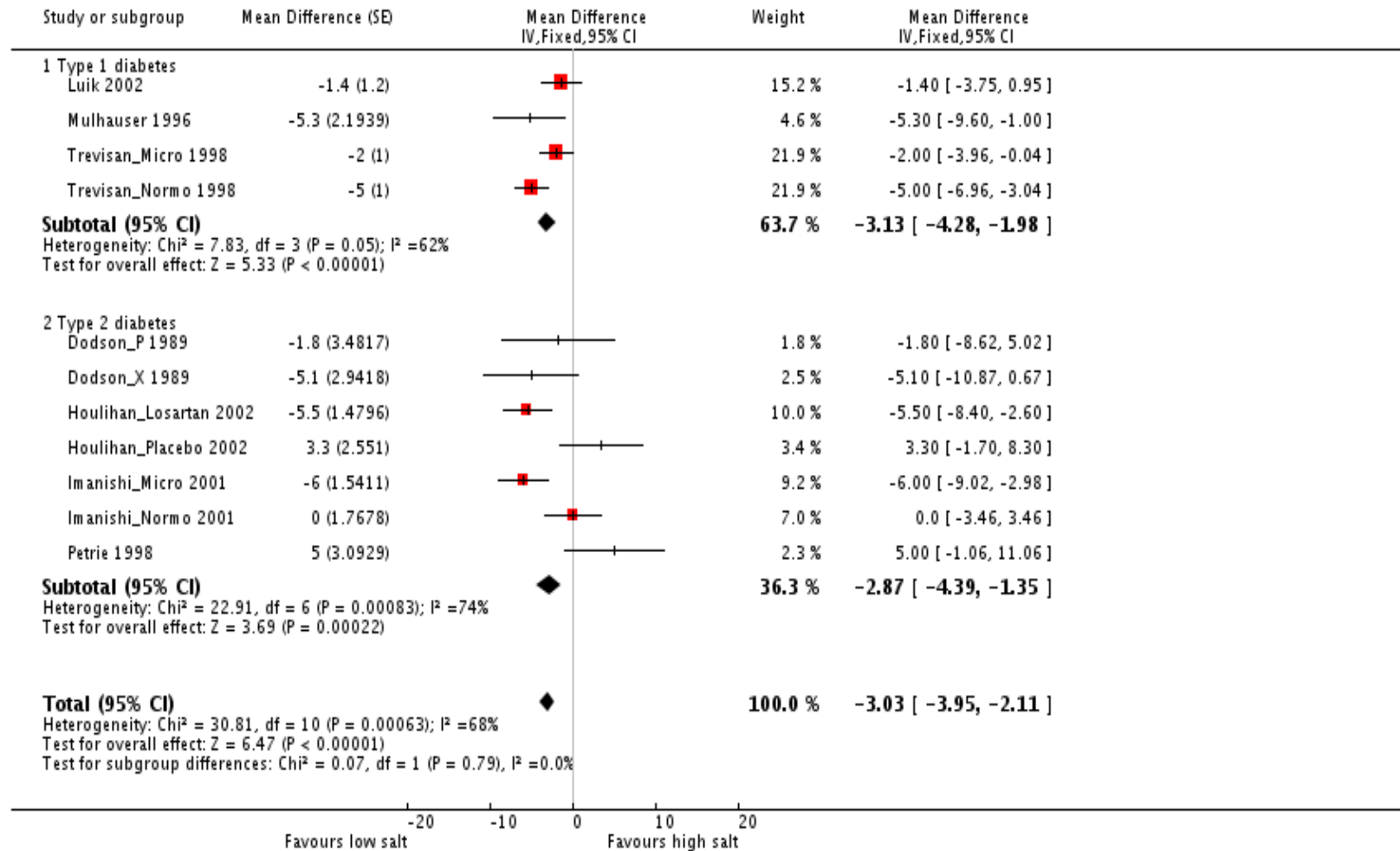
# SBP among Adults with Type 1 or 2 DM

Review: Altered dietary salt intake for preventing and treating diabetic kidney disease  
 Comparison: 1 Net change with altering salt diet  
 Outcome: 1 Systolic BP



# DBP among Adults with Type 1 or 2 DM

Review: Altered dietary salt intake for preventing and treating diabetic kidney disease  
 Comparison: 2 Net change in BP in type 1 and type 2 diabetes  
 Outcome: 2 Diastolic BP



# Issues

- Complexity of diet

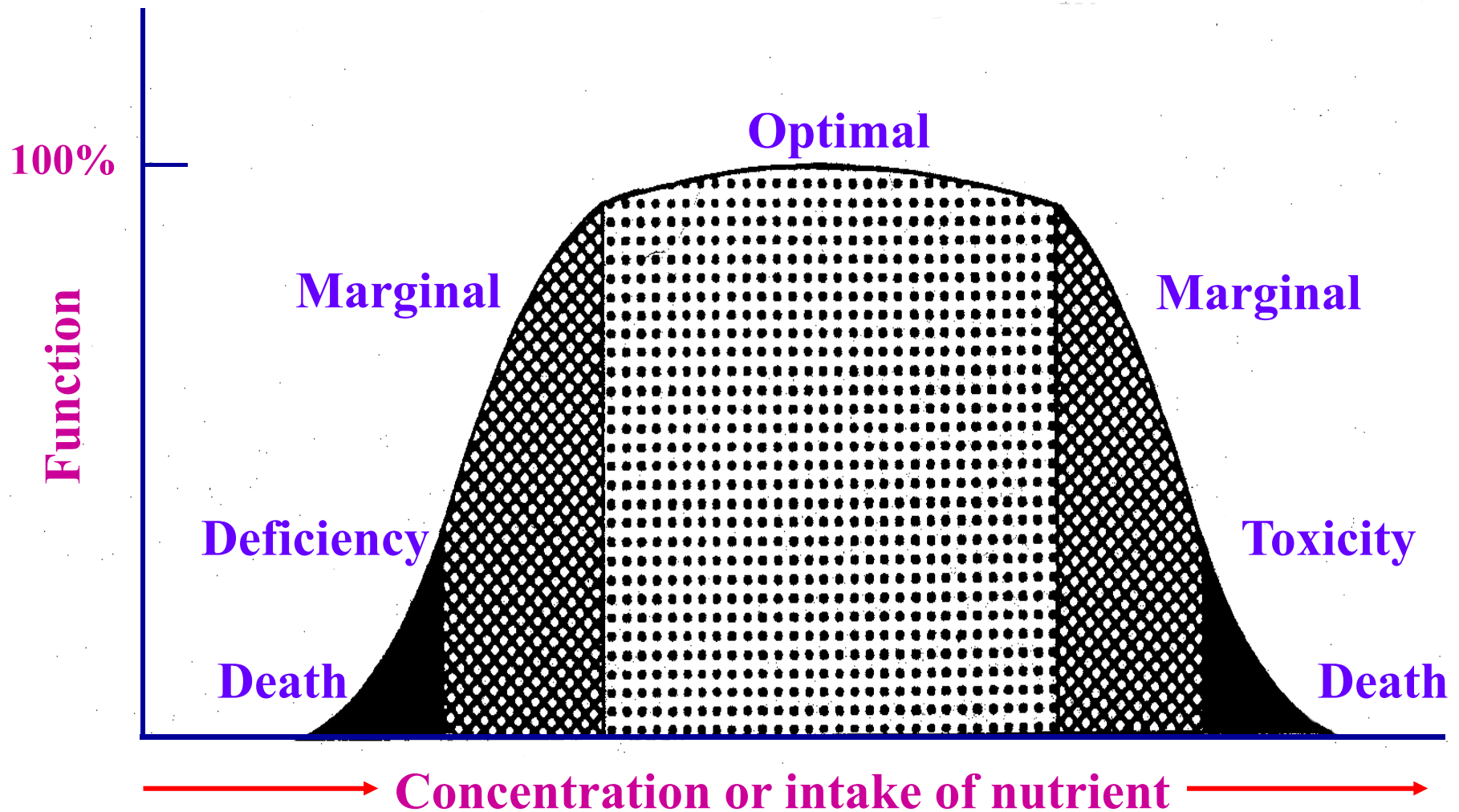
- Components are inter-correlated
- Exposure cannot be characterized as present or absent
- Within-person variation
- Measurement error

- Bias

- Confounding factor
- Treatment difference
- Compliance

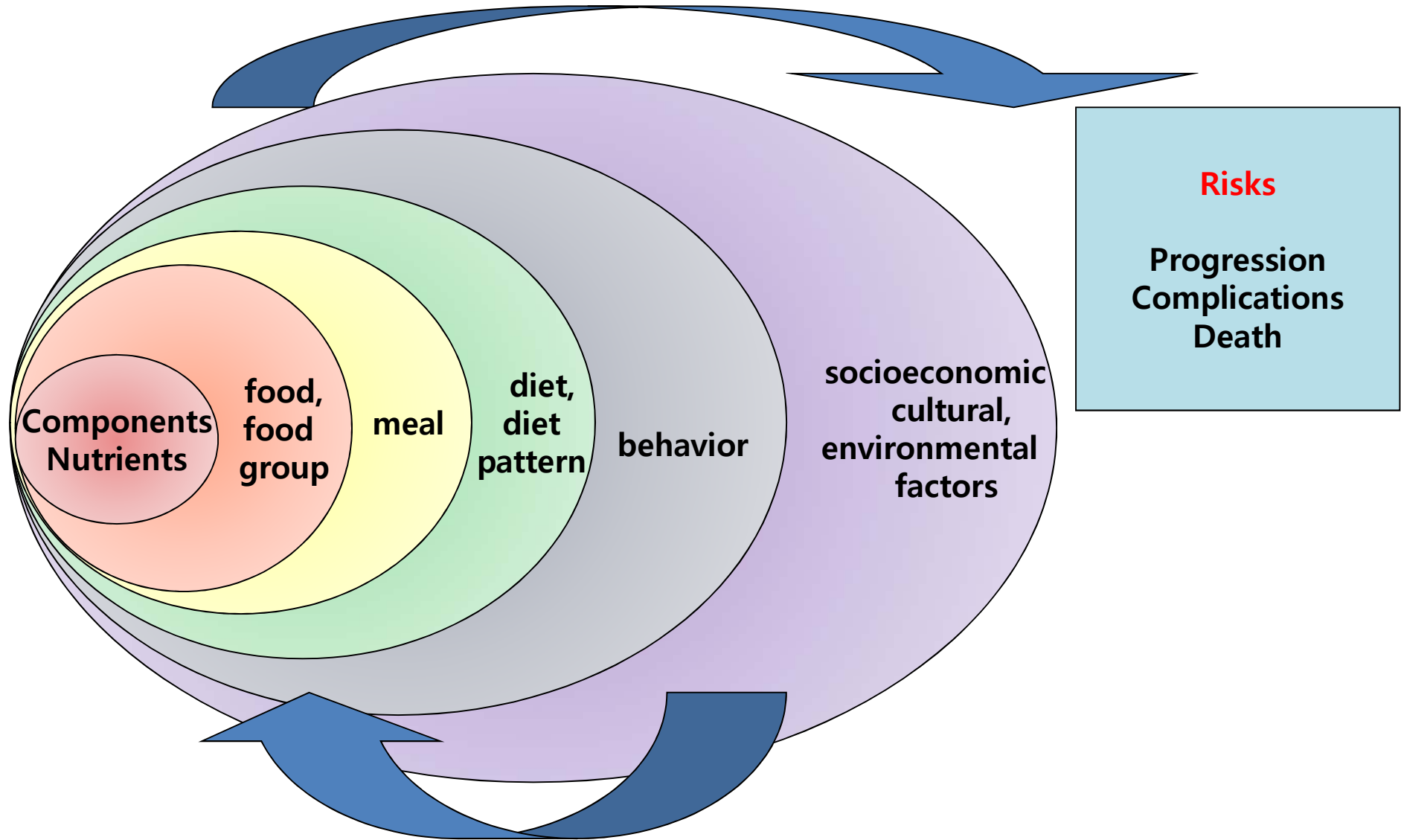
- Interaction

- Treatment
- Genetic factors (incl. sodium sensitivity)



**Hypothetical relationship between intake of an essential dietary factor and health.**

# Multiple Factors



# Issues in Intervention Study

- Study design
  - Cross-over or Parallel design
  - Randomization vs. Non-randomization
  - Blind
- Participants
  - Illness
  - Age, gender, and other factors
- Level of sodium restriction
  - Compliance
  - Effect
  - Application
- Outcome
- Interaction
- Duration of study

# Standards of Medical Care in Diabetes - 2012

- Lifestyle therapy for hypertension consists of weight loss, if overweight; Dietary Approaches to Stop Hypertension (DASH)-style dietary pattern, including reducing sodium and increasing potassium intake; moderation of alcohol intake; and increased physical activity.  
(B)

Although there are no well-controlled studies of diet and exercise in the treatment of hypertension in individuals with diabetes, the Dietary Approaches to Stop Hypertension (DASH) study in nondiabetic individuals has shown antihypertensive effects similar to pharmacologic monotherapy. Lifestyle therapy consists of reducing sodium intake (to <1,500 mg per day) and excess body weight; increasing consumption of fruits, vegetables (8–10 servings per day), and low-fat dairy products (2–3 servings per day); avoiding excessive alcohol consumption (no more than two servings per day in men and no more than one serving per day in women)

Sacks FM et al. NEJM 2001

# 대한당뇨병학회 진료지침 2011

- 당뇨병성 합병증의 발생이나 진행의 지연을 위해서는 혈당뿐만 아니라 혈압의 조절도 중요하므로 나트륨은 4000 mg 이내로 하며 고혈압이나 신장 합병증, 심혈관계 질환을 동반한 경우에는 2000-3000 mg (소금 5-7.5 g) 이내로 제한하는 것이 중요하다.



# Future Direction

Cross-Sectional Study

- **Sodium intake status and morbidity among diabetic patients**

Prospective Study

- **Prospective study of sodium intake or sodium excretion and mortality and morbidity among diabetic patients**

Intervention Study

- **Effect of dietary modification and nutrition education on sodium reduction**
- **Effect of sodium reduction on mortality and morbidity of diabetic patients**

Clinical Implication

- **Sodium reduction strategy**
- **Korean-specific guidelines**

# Summary

- Research on dietary sodium intake and mortality and morbidity among patients with diabetes is sparse.
- Intervention studies in a clinical setting and further prospective studies of diabetic patients are warranted.

# Acknowledgements

- 송다영
- 박종은
- 김영하