Canadian VIGOUR Centre
Bridging Hearts and Minds

Dietary trials in Heart Failure: SODIUM-HF

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Disclosures / COI / RWI / RWA

- Available online: thecvc.ca
- PI of SODIUM-HF trial
- Not a dietician

Salt’n’Pepa

*There are no RCT involving pepper or Salt’n’Pepa for patients with HF

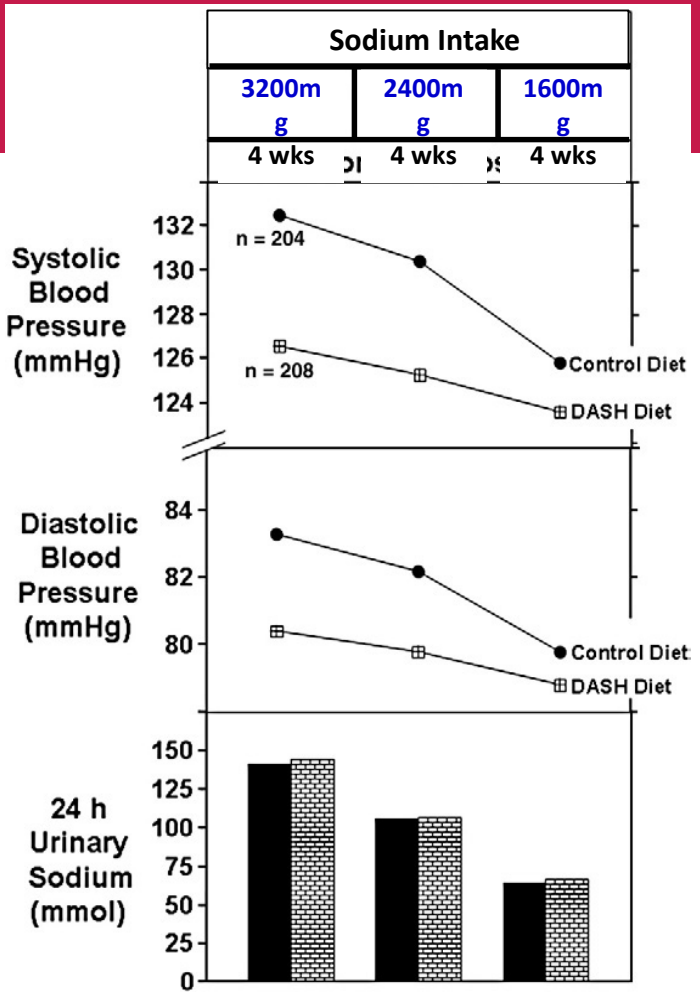
What's the real issue with salt?

- Which population?
  - HTN, CAD, prevention, elderly, kids…..
  - PURE etc is all non-HF
- What dietary context?
  - Eating what, when, with whom, and how?
- Sodium measurement issues?
  - Spot urinary sodium vs diet intake
- What outcome?
  - BP vs. mortality

But where did this salt business all start?

Skipping 1800s till 1970s

DASH Trial

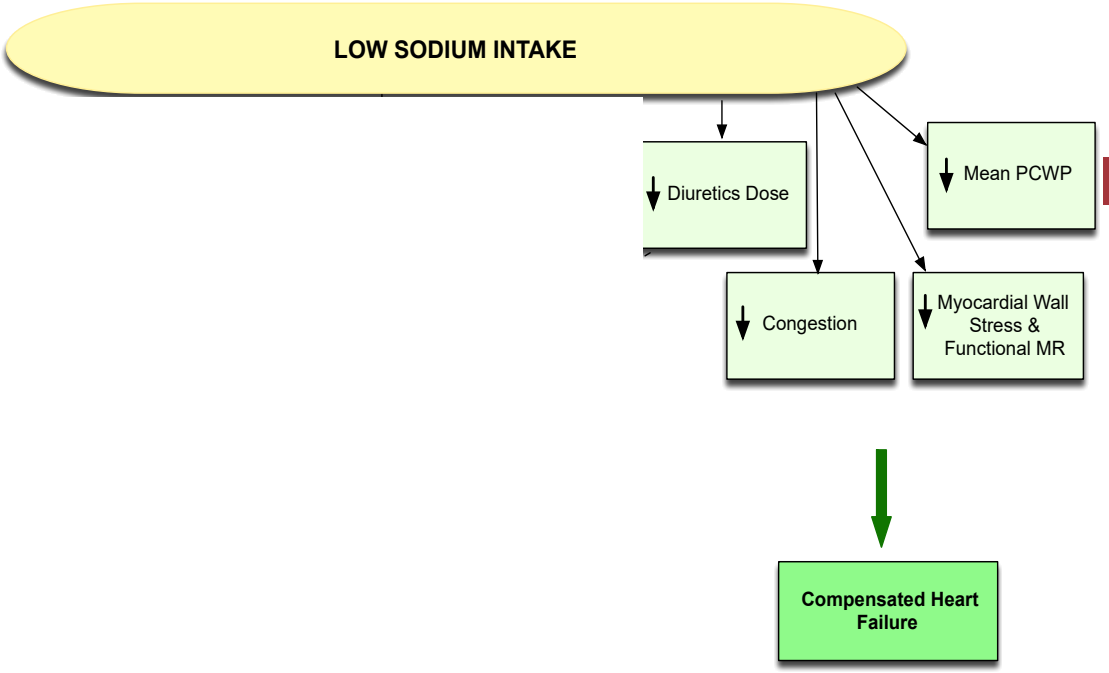


~400 patients w/HTN
Metabolic kitchen making all meals
12 weeks total
Surrogate outcomes

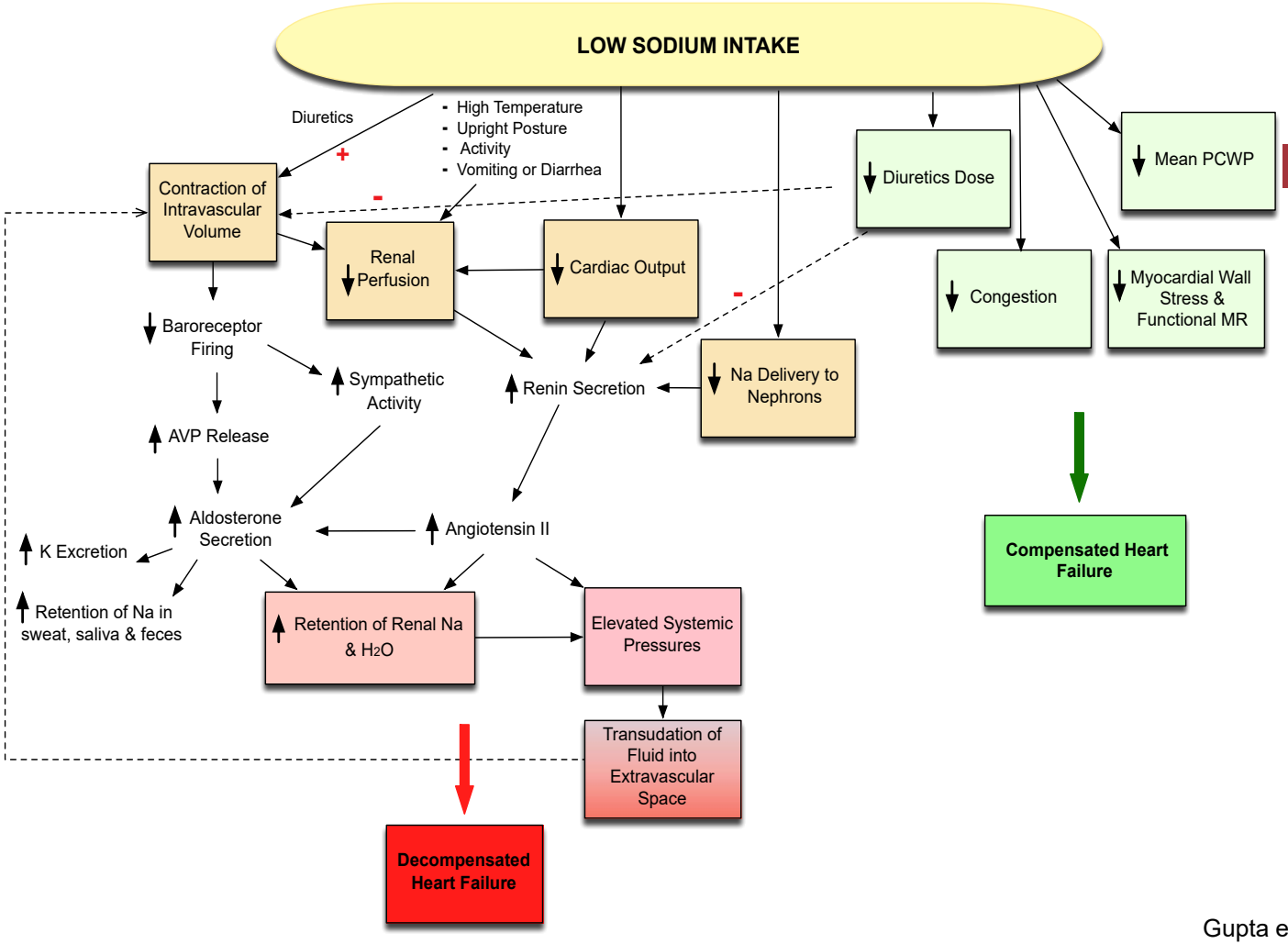
Sacks F et al. N Engl J Med. 2001; 334: 3-10
Figure adapted from: He J and MacGregor GA. Prog in Cardiovasc Dis. 2010; 52:363-82

Heart Failure and Sodium

- Heart failure (HF) is associated with neurohormonal activation and abnormalities in autonomic control that lead to sodium and water retention
- Clinicians have focused on dietary sodium and water restriction to minimize the risk of volume overload
- Little evidence supports this practice
- We spend +++time ($) doing this – **VALUE**?



Gupta et al. Circulation 2012



Gupta et al. Circulation 2012


Observational data

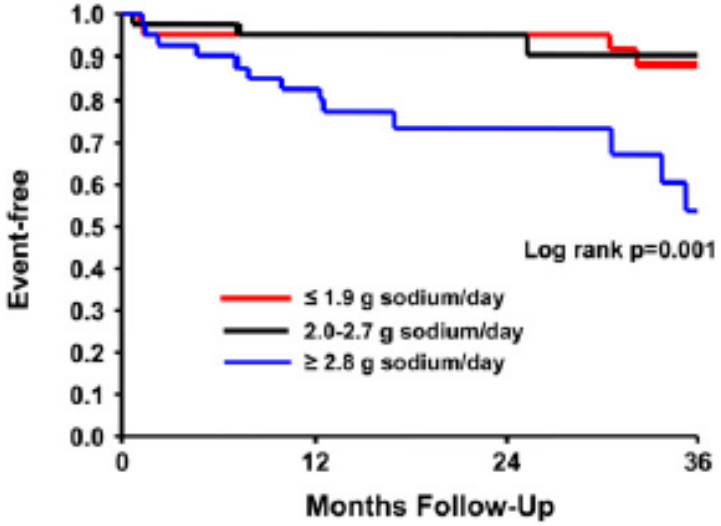
Clinical question

Does advising a patient to lower the amount of sodium in their diet change the clinical outcome?

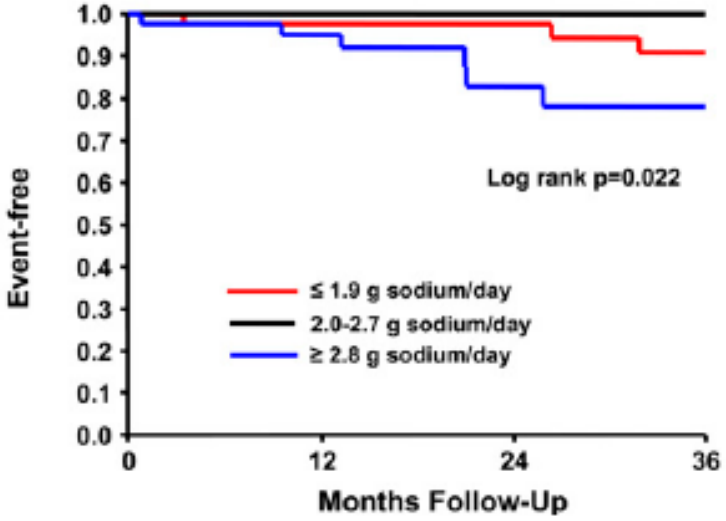
Observational studies: HF

n= 123 patients with HF

HF Hospitalization



Mortality



Arcand et al. Am J Clin Nutr. 2011.
Colin et al. Rev Chil Nutr, 2010.

RCTs

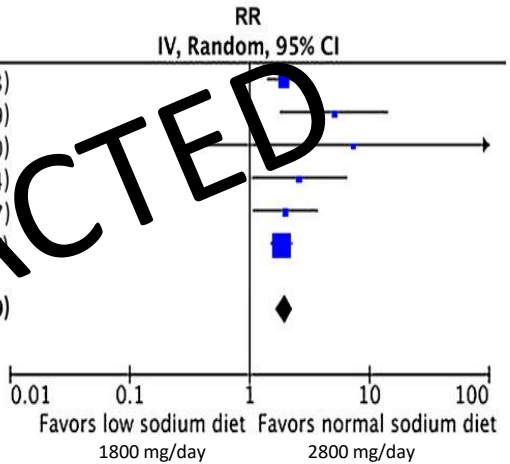
Some other RCTs…..

Forest plot of relative risks for <u>mortality</u>

Study or subgroup	Low sodium Events	Total	Normal sodium Events	Total	Weight	RR IV, Random, 95% CI
Licata *et al*, 2003[9]	47	54	24	53	26.6%	1.92 (1.41 to 2.63)
Parrinello *et al*, 2009[7]	20	86	4	87	2.5%	5.06 (1.80 to 14.19)
Paterna *et al*, 2005[10]	3	46	0	48	0.3%	7.30 (0.39 to 137.50)
Paterna *et al*, 2008[13]	15	114	6	118	3.1%	2.59 (1.04 to 6.44)
Paterna *et al*, 2009[11]	26	179	14	191	6.9%	1.98 (1.07 to 3.67)
Paterna *et al*, 2011[12]	212	890	114	881	60.6%	1.64 (1.30 to 2.2[illegible])
Total (95% CI)		**1369**		137[illegible]	100.0%	1.9[illegible] (1.6[illegible] to 2.29)
Total events	323		162			

Heterogeneity: $\tau^2=0.00$; $\chi^2=4.73$, df=5 (p=0.45); I²=[illegible]%

Test for overall effect: Z=8.08 (p<0.00001)



RETRACTED

Parenterally administered saline solutions
250–1000 mg of furosemide daily
Fluid restriction 1 litre/day

DiNicolantonio JJ et al. Heart 2012. doi:10.1136/heartjnl-2012-302337
<u>Retraction</u> notice. Heart 2013;99:820

Low quality RCTs: helpful?

- Small RCT in AHF w/HFpEF
- N=53 patients, 2 groups, 7 days
- 0.8 g / sodium + 800 mls fluid vs usual care (~4g sodium, unlimited fluid)
- No change in BNP, weight, congestion etc
- Increase in thirst in restricted group

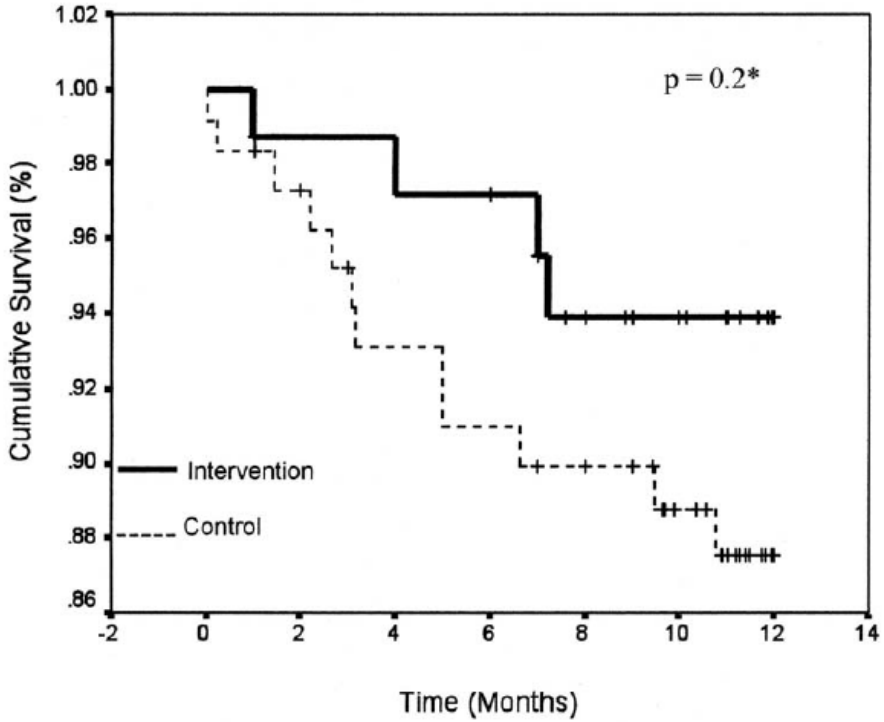
Dalmedia, nutrition 2018

Small RCT

Colin et al. Rev Chil Nutr, 2010.

Small RCT

n= 195 patients with HF, Outpatient, Mexico city



Intervention group: Dietary recommendations for sodium restriction to <2400 mg/day provided by a dietitian.

Control Group: Usual dietary recommendations for dietary sodium reduction.

Colin et al. Rev Chil Nutr, 2010.

Dietary sodium recs in HF

Guideline and year	Sodium restriction recommendation / day
Canadian Cardiovascular Society 2017	<2300 mg
AHA/ ACC/ HFSA 2017	None
European Society of Cardiology 2016	None

IOM = <1500 mg/day for all people

HFC Dietician waiting to pounce….

Measurement

Measuring Sodium/Adherence?

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Plasma
Easy

Tightly regulated, physiologically

Well-validated lab technique

Reflects acute change

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Urine
Easy (spot), hard (24H)

Variability/debate on methods

Depends on excretion /reabsorption

90-95% ingested is excreted (assumed)

Well-validated lab technique

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Easy

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Urine
Easy (spot), hard (24H)

Variability/debate on methods

Depends on excretion /reabsorption

90-95% ingested is excreted (assumed)

Well-validated lab technique

Diet
Easy-Hard

Variability in reporting

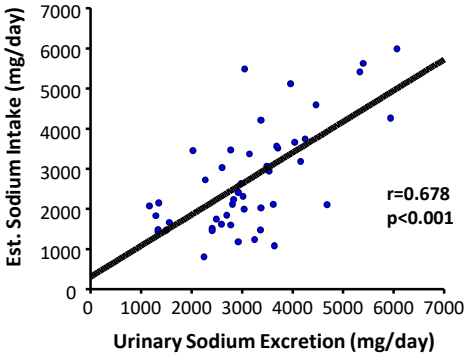
Need to know food (exact)

Well-validated technique

Reflects consumption

Food vs. Urine: Diuretics

Patients with HF not on loop diuretics (n=47)



Arcand, *AJCN* 2011

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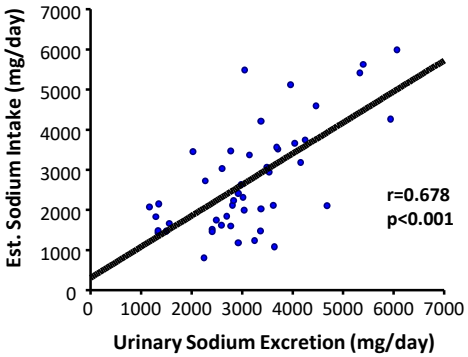
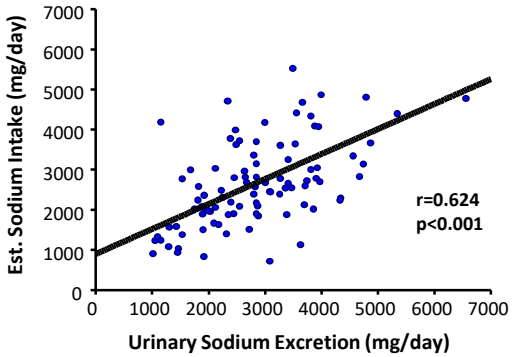


Non-HF cardiac patients (n=96)



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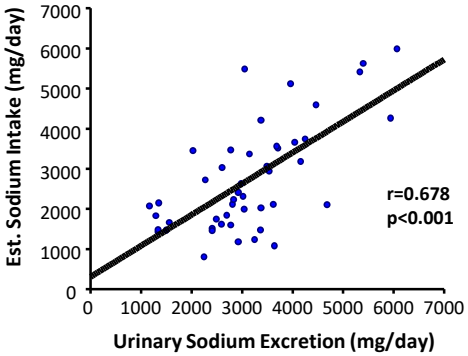

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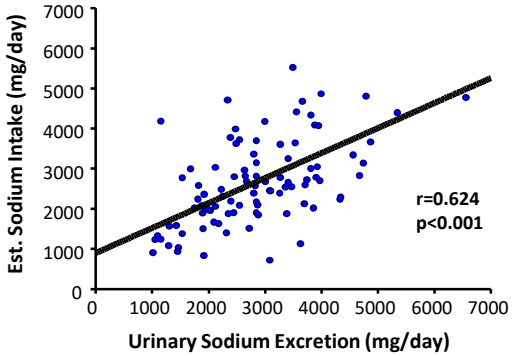
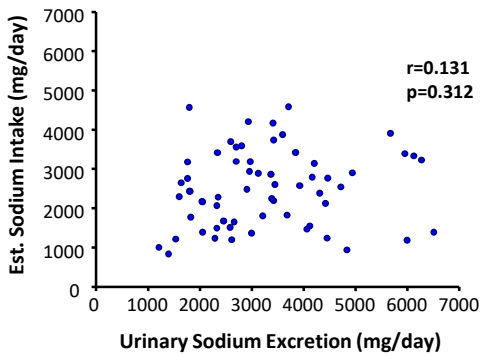


Patients with HF on loop diuretics (n=62)



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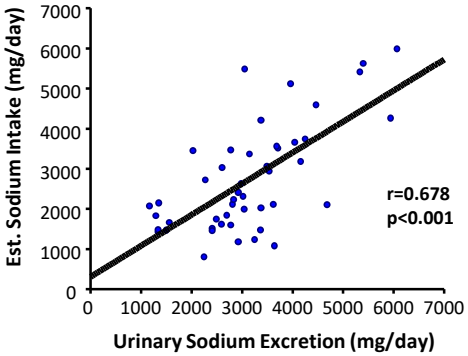

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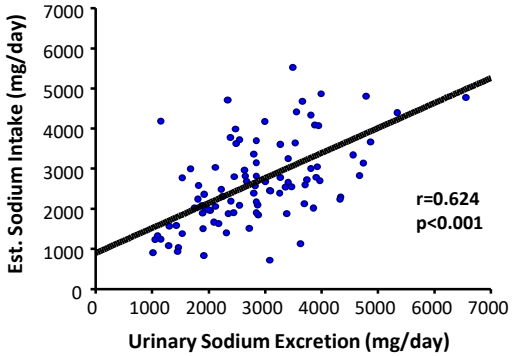

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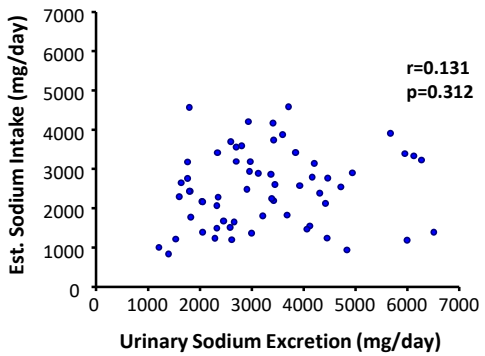

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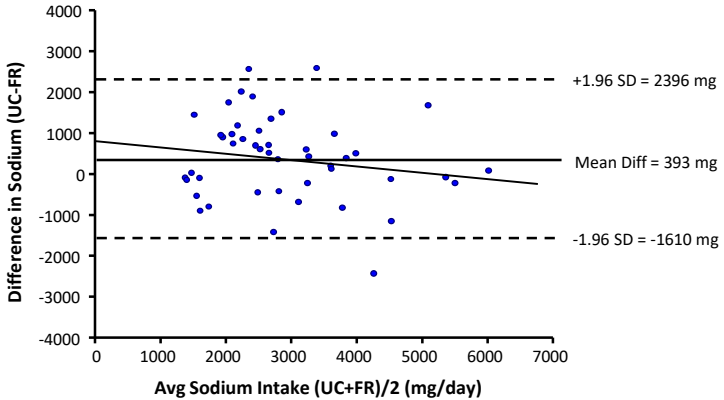

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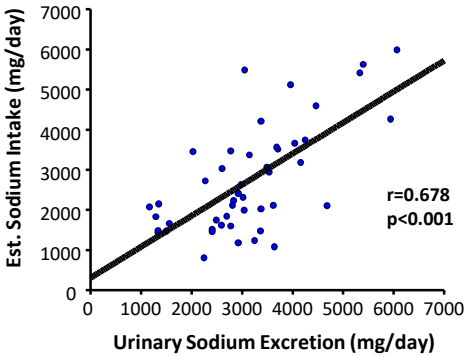

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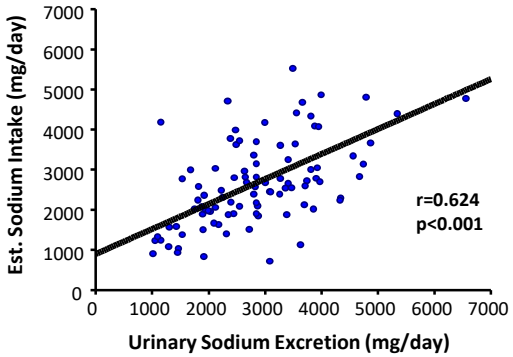

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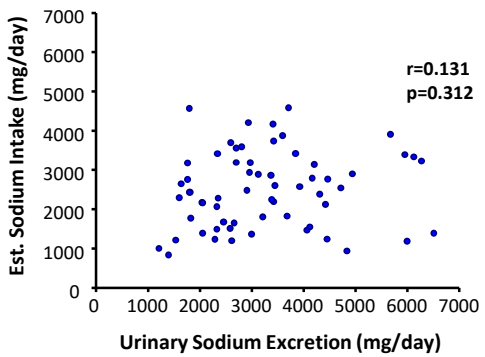

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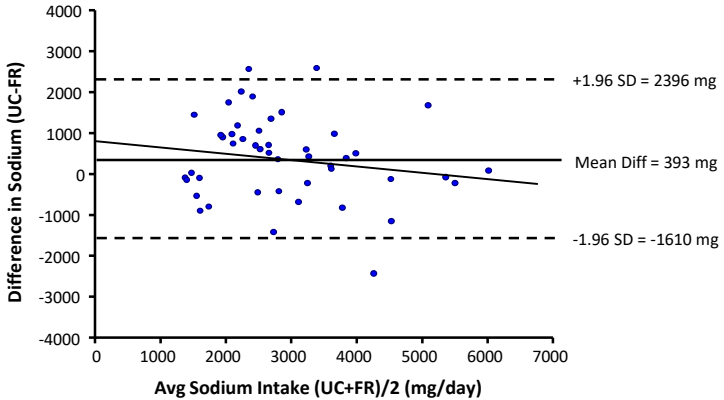

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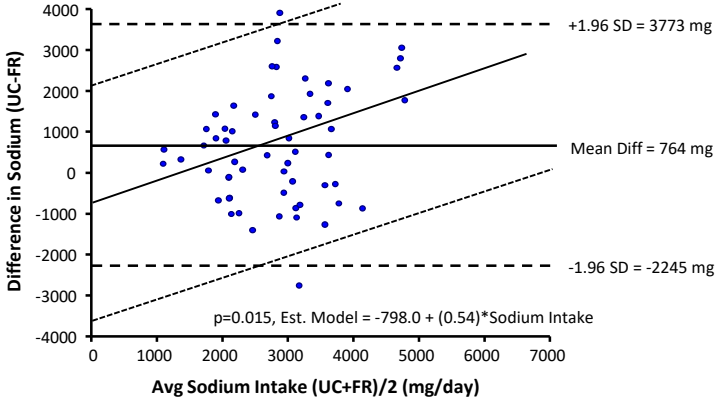


Arcand, *AJCN* 2011

Measurement: Food records

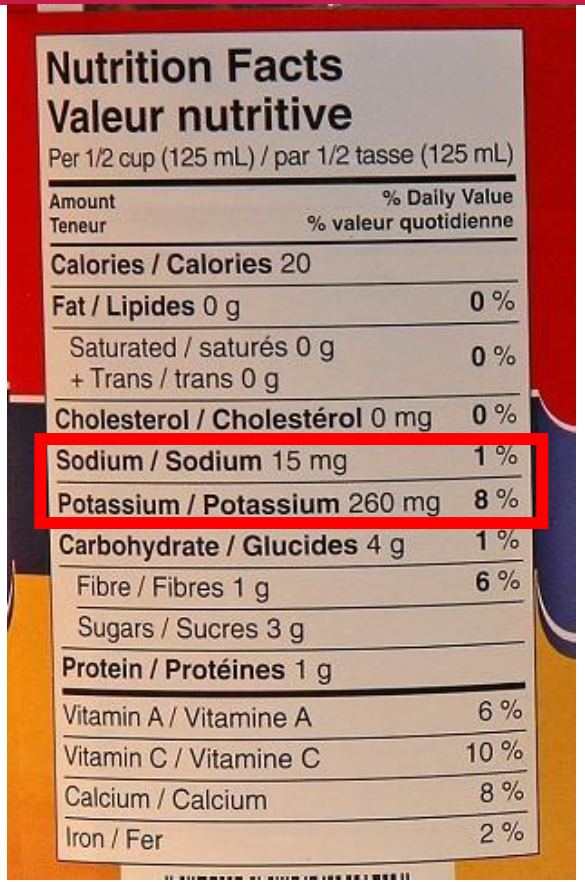
- Food recall: underestimates total c/w 24UNA
  - 15-25% **under**estimate
- Food records:
  - 1-14 days
  - Not much more info after 3-5 days
  - Actual record, not a recall
- Input into program (e.g. Food Processor, ESHA) which spits out every detail

Caggiula AJCN 1985
Espeland AJE 2001
Khaw AJCN 2004

Low Sodium vs Regular

Nutrition Facts
Valeur nutritive
Per 1/2 cup (125 mL) / par 1/2 tasse (125 mL)

Amount / Teneur	% Daily Value / % valeur quotidienne
Calories / Calories 20	
Fat / Lipides 0 g	**0** %
Saturated / saturés 0 g + Trans / trans 0 g	**0** %
Cholesterol / Cholestérol 0 mg	**0** %
Sodium / Sodium 400 mg	**17** %
Carbohydrate / Glucides 4 g	**1** %
Fibre / Fibres 1 g	**4** %
Sugars / Sucres 3 g	
Protein / Protéines 1 g	
Vitamin A / Vitamine A	6 %
Vitamin C / Vitamine C	10 %
Calcium / Calcium	8 %
Iron / Fer	2 %



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Fat / Lipides 0 g	**0** %
Saturated / saturés 0 g + Trans / trans 0 g	**0** %
Cholesterol / Cholestérol 0 mg	**0** %
Sodium / Sodium 15 mg	**1** %
Potassium / Potassium 260 mg	**8** %
Carbohydrate / Glucides 4 g	**1** %
Fibre / Fibres 1 g	**6** %
Sugars / Sucres 3 g	
Protein / Protéines 1 g	
Vitamin A / Vitamine A	6 %
Vitamin C / Vitamine C	10 %
Calcium / Calcium	8 %
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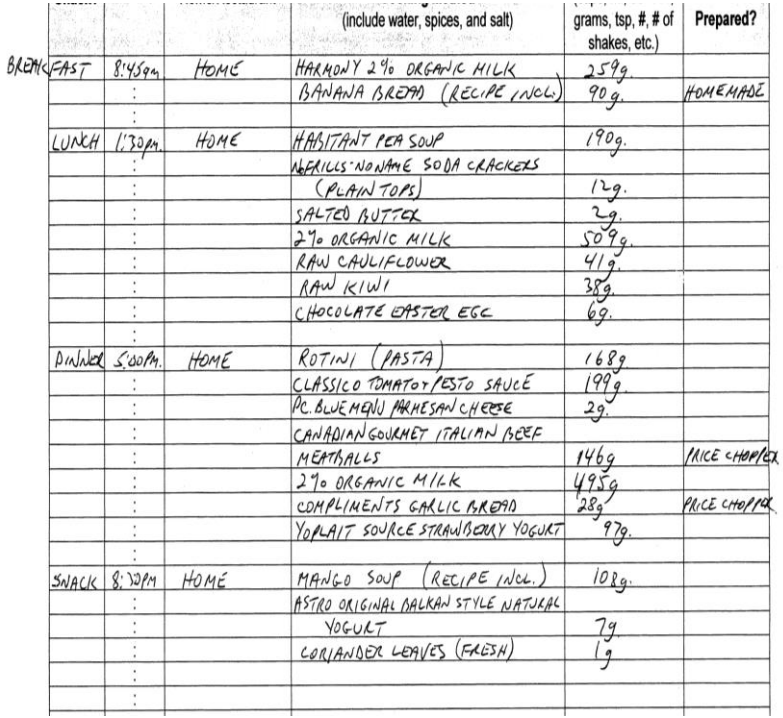
Food Records

- Prospective
- Recording and measurement of all food and beverages each day, for any # of days
- Weighted or volume measurements
- Not dependant on memory



			(include water, spices, and salt)	grams, tsp, #, # of shakes, etc.)	Prepared?
BREAKFAST	8:45am	HOME	HARMONY 2% ORGANIC MILK	259g.	
			BANANA BREAD (RECIPE INCL.)	90g.	HOMEMADE
LUNCH	1:30pm.	HOME	HABITANT PEA SOUP	190g.	
			NATRULS-NO NAME SODA CRACKERS (PLAIN TOPS)	12g.	
			SALTED BUTTER	2g.	
			2% ORGANIC MILK	509g.	
			RAW CAULIFLOWER	41g.	
			RAW KIWI	38g.	
			CHOCOLATE EASTER EGG	6g.	
DINNER	5:00pm.	HOME	ROTINI (PASTA)	168g	
			CLASSICO TOMATO/PESTO SAUCE	199g	
			PC. BLUE MENU PARMESAN CHEESE	2g.	
			CANADIAN GOURMET ITALIAN BEEF MEATBALLS	146g	PRICE CHOPPER
			2% ORGANIC MILK	495g	
			COMPLIMENTS GARLIC BREAD	28g	PRICE CHOPPER
			YOPLAIT SOURCE STRAWBERRY YOGURT	97g.	
SNACK	8:30PM	HOME	MANGO SOUP (RECIPE INCL.)	108g.	
			ASTRO ORIGINAL BALKAN STYLE NATURAL YOGURT	7g.	
			CORIANDER LEAVES (FRESH)	1g	

Corelab approach

Clinical/Research question

Does advising a patient to lower the amount of sodium in their diet change the clinical outcome?

PILOT: Am Heart J. 2015 doi: 10.1016/j.ahj.2014.11.013. **The long-term effects of dietary sodium restriction on clinical outcomes in patients with heart failure. The SODIUM-HF (Study of Dietary Intervention Under 100 mmol in Heart Failure): a pilot study.**

Design paper: Am Heart J. 2018 Nov;205:87-96. doi: 10.1016/j.ahj.2018.08.005. **Rationale and design of the Study of Dietary Intervention Under 100 MMOL in Heart Failure (SODIUM-HF).**

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SODIUM-HF

Study of Dietary Intervention Under 100 MMOL in Heart Failure

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@sodiumhf

https://www.sodiumhftrial.com/

What are the main trial objectives?

- Evaluate the long-term effects of a low-sodium containing diet in patients with HF on a composite clinical outcome of:
  - All-cause mortality
  - CV hospitalizations
  - CV ED visits

- Secondary objectives include the evaluation of a low-sodium containing diet on:
  - Quality of life
  - Exercise capacity
  - NYHA class
  - Clinical outcomes (CV events + mortality) to 24 months

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SODIUM-HF: Trial Design

- Multicentre, multinational
  - 25 sites
  - Canada, Mexico, Chile, Colombia, Australia, New Zealand
  - N=1000 subjects (n=650 enrolled)
  - Randomized, Open-label
  - Blinded adjudicated endpoint

- **Study Population**: patients with chronic HF (REF, PEF are eligible), NYHA 2-3, >1500 mg dietary Na

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SODIUM-HF: Intervention

Patients randomized to one of two study arms:

1. Low-sodium containing diet (65 mmol or 1500 mg daily)

2. Usual care (general advice to limit dietary sodium as provided in routine clinical practice)

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Intervention: Sample menus

Samples of menus at different levels of energy requirement (1400-2200 kcal) are available:

- In accordance with information provided in the meal plan and are intended to guide the patients in following their meal plan.
- Patient might **interchange** any of the **food items** included in the menus by another one included in the **recommended foods lists** of the **same food group** that the original one included in the menu.
- If energy requirements are **adjusted** during a follow-up visit, sample menus should be provided accordingly.

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SODIUM-HF: Challenges

- Enrolment
- New strategies to continually engage site personnel doing the recruiting +RDs
- Lower site budget as a barrier to site participation
- Local logistics unique to each site when implementing dietary intervention
- Changing context of clinical trials research – e.g., online consent, e-signatures for patients, secular trends in volunteerism

SODIUM-HF: Successes

- Intriguing research question for MDs, RNs, NPs, RDs
- Simple, straightforward eCRF
- Top enrolling sites have a 1 FTE coordinator, available dietitian(s) and engaged PI
- Minimal source collected for adjudication of events
- Sites sought independent funding for sub-grants
- 100% remote monitoring
- Low administrative burden for sites
- Every site dietician on a Dietician Working Group
- Steering Committee: includes every site PI

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BRAZIL
AUSTRALIA
INDONESIA
MONGOLIA
NORTH ATLANTIC OCEAN
PACIFIC OCEAN
SOUTH ATLANTIC OCEAN
INDIAN OCEAN
ANTARCTICA

Summary / conclusions

Test unproven dogma
Think about the patient, intervention, control
Time for observation fini; interv'n is needed
SODIUM-HF and other RCT ongoing