Canadian **VIGOUR** Centre
Bridging Hearts and Minds

Diet and Heart Failure: Should we Challenge Current Practice?

Justin A. Ezekowitz, MBBCh MSc
Professor, University of Alberta
Co-Director, Canadian VIGOUR Centre
Cardiologist, Mazankowski Alberta Heart Institute
Montreal Bagel 2022

@sodiumhf

yes

Disclosures / COI / RWI / RWA

- Available online: thecvc.ca
- Funding from:

University Hospital Foundation

@sodiumhf

Diet and HF

1. Food is medicine
2. Food doesn’t matter
3. Food matters but only so much

Clinical question

Does advising a patient to change the amount of

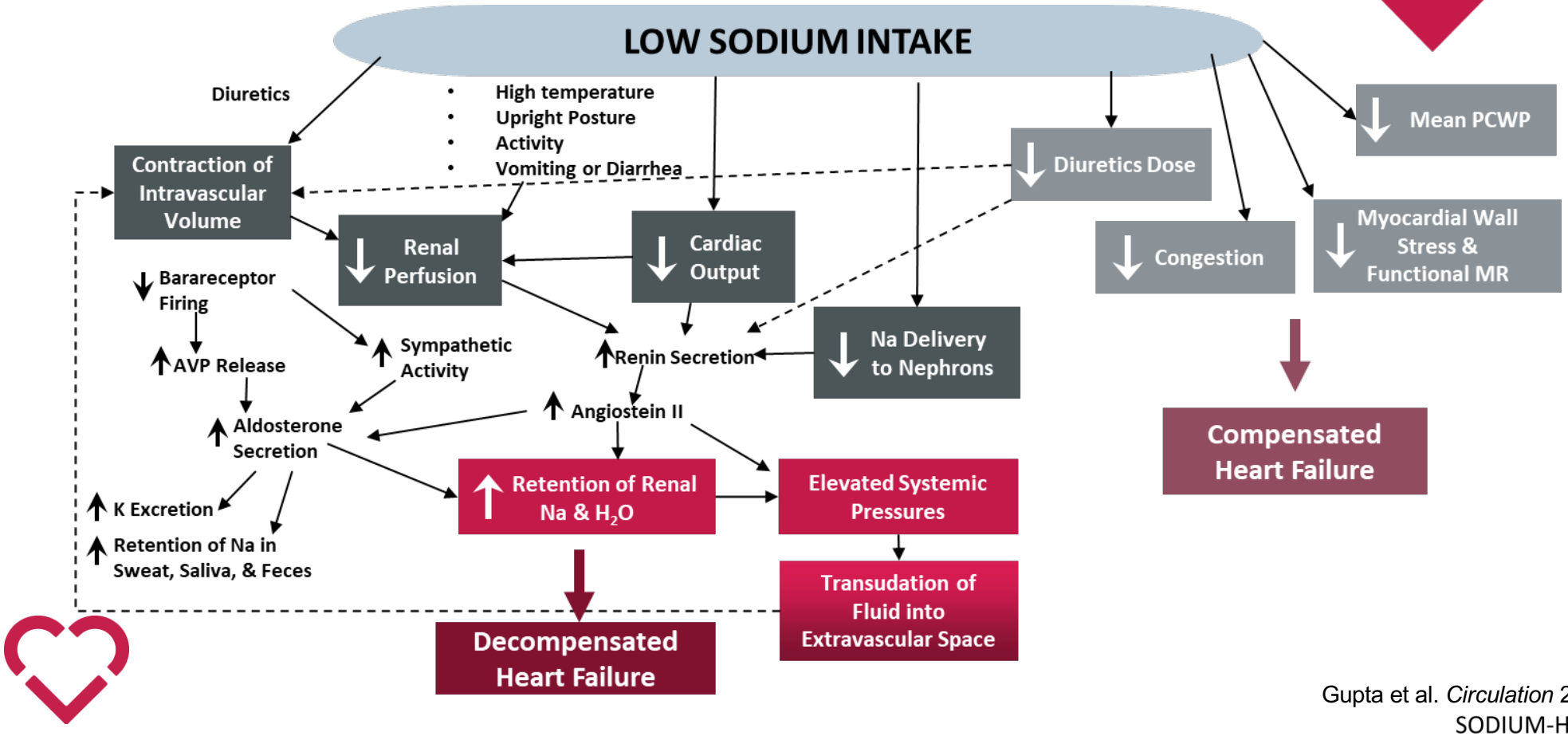
1. **sodium**
2. **potassium**
3. **magnesium**
4. **fluid**
5. **….**

in their diet change the clinical outcome?

Heart Failure and Dietary Sodium

- HF is associated with:
  - neurohormonal activation
  - abnormalities in autonomic control
  - sodium and water retention
- Clinicians have focused on dietary sodium and water restriction to minimize the risk of volume overload for > 100 years
- Little evidence supports this practice

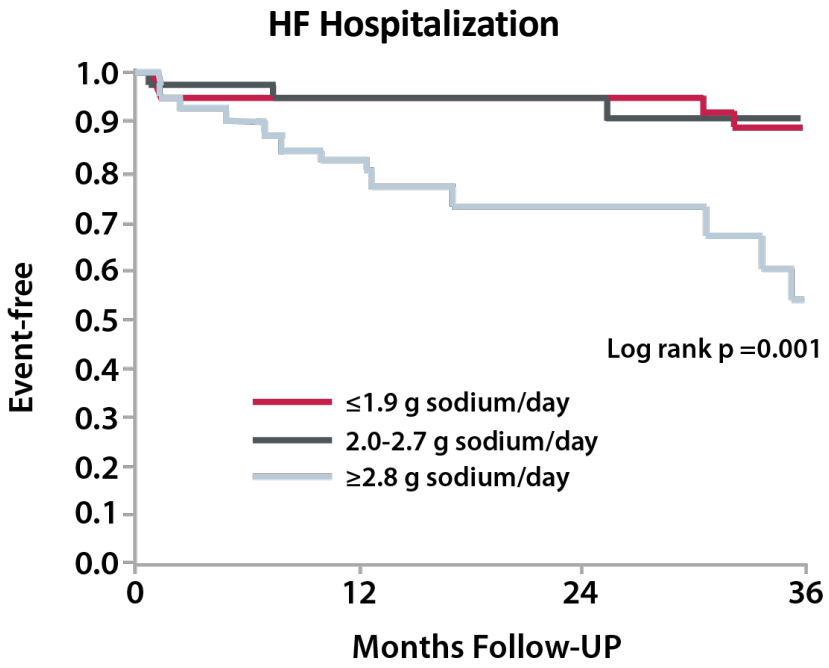
Dietary Sodium Intake

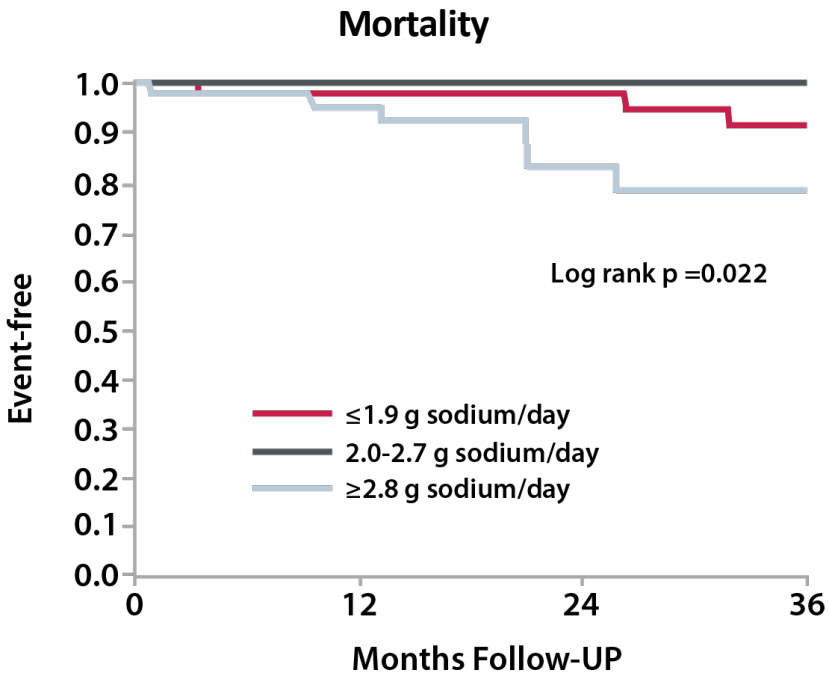


Gupta et al. *Circulation* 2012

SODIUM-HF

Dietary sodium: Observational studies





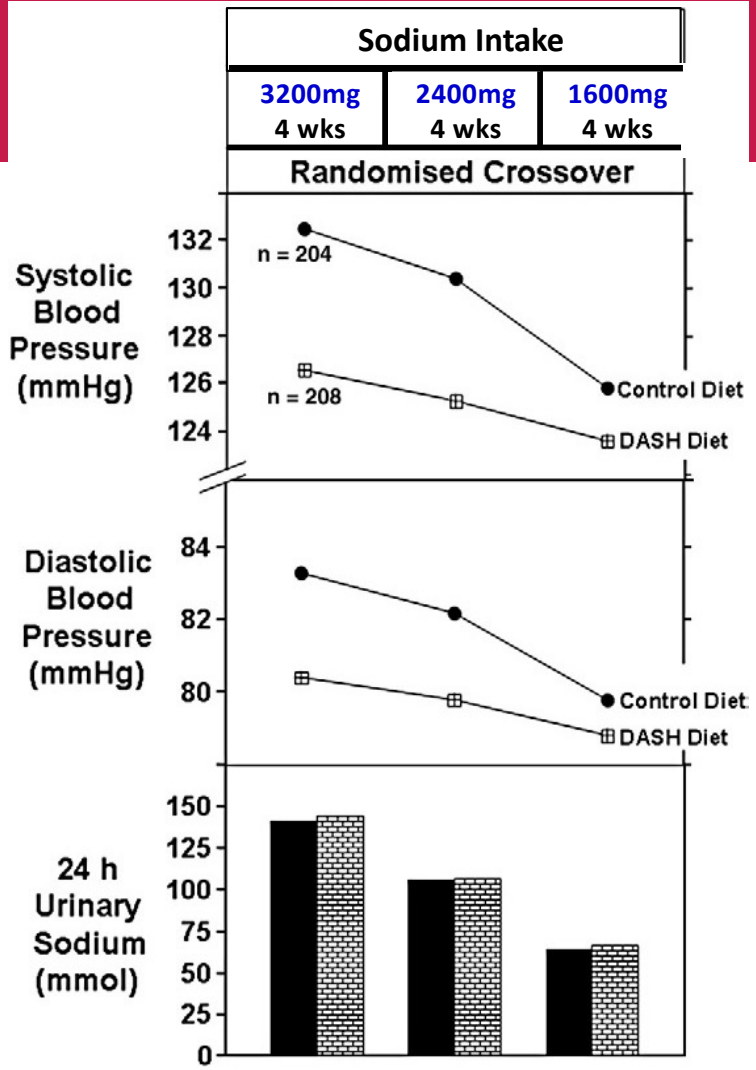
n= 123 patients with HF

Arcand et al. *Am J Clin Nutr*. 2011.

SODIUM-HF

How do we do the trials?

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

RESEARCH SUMMARY

Effect of Salt Substitution on Cardiovascular Events and Death

Neal B et al. DOI: 10.1056/NEJMoa2105675

CLINICAL PROBLEM

Salt substitutes that replace part of the sodium in regular salt with potassium chloride have been shown to decrease blood pressure, but their effects on cardiovascular and safety outcomes are unclear.

CLINICAL TRIAL

Design: An unblinded, cluster-randomized trial examined cardiovascular and safety outcomes with a salt substitute as compared with regular salt in high-risk adults.

Intervention: 600 villages in rural China were assigned to use a salt substitute (75% sodium chloride, 25% potassium chloride) for all household cooking and food preservation or to continue using regular salt (100% sodium chloride). A total of 20,995 adults with a history of stroke or age ≥60 years with poorly controlled blood pressure were included. The primary outcome was stroke.

RESULTS

Efficacy: During a mean follow-up of 4.74 years, the incidence of stroke was significantly lower in the salt-substitute group than in the regular salt group. Secondary outcomes, including major cardiovascular events and death from any cause, also favored the salt substitute.

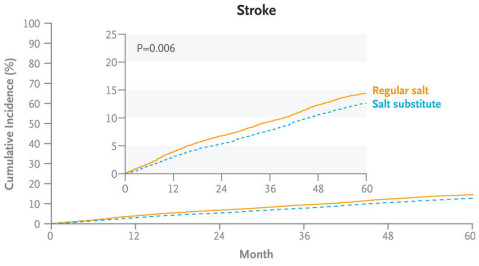
Safety: The incidence of clinical hyperkalemia did not differ between the groups.

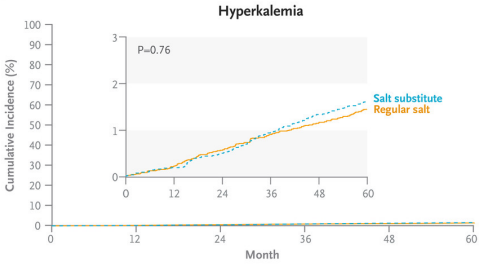
LIMITATIONS AND REMAINING QUESTIONS

- Participants were aware of the trial-group assignments.
- Whether the findings can be generalized to other settings or populations is unknown.
- Serum electrolytes were not measured serially, so some instances of hyperkalemia were likely to have been missed.

Links: Full Article | NEJM Quick Take | Editorial

Outcomes	Salt Substitute	Regular Salt	Rate Ratio (95% CI)	P Value
	no. of events per 1000 person-yr			
Stroke	29.14	33.65	0.86 (0.77–0.96)	P=0.006
Major Adverse CV Events	49.09	56.29	0.87 (0.80–0.94)	P<0.001
Death from Any Cause	39.28	44.61	0.88 (0.82–0.95)	P<0.001
Hyperkalemia	3.35	3.30	1.04 (0.80–1.37)	P=0.76





CONCLUSIONS

In this study among patients with a mean age of 65.4 years and a history of stroke or high blood pressure, use of a salt substitute lowered the risks for stroke, major cardiovascular events, and death from any cause.

SSaSS Trial

~600 villages (21000 people) w/risk
Salt substitute
4.7 years
Clinical outcomes (stroke)

Neal, *NEJM* 2021

SODIUM-HF Objectives

Evaluate the effects of a low-sodium diet, compared to usual care, in patients with HF, on a 12 month outcome of:

- **Primary Endpoint:** Composite clinical outcome of All-cause mortality, CV hospitalizations, CV ED visits

- **Secondary Endpoints:**
  - Quality of life (by KCCQ)
  - Exercise capacity (by 6MWT)
  - NYHA class

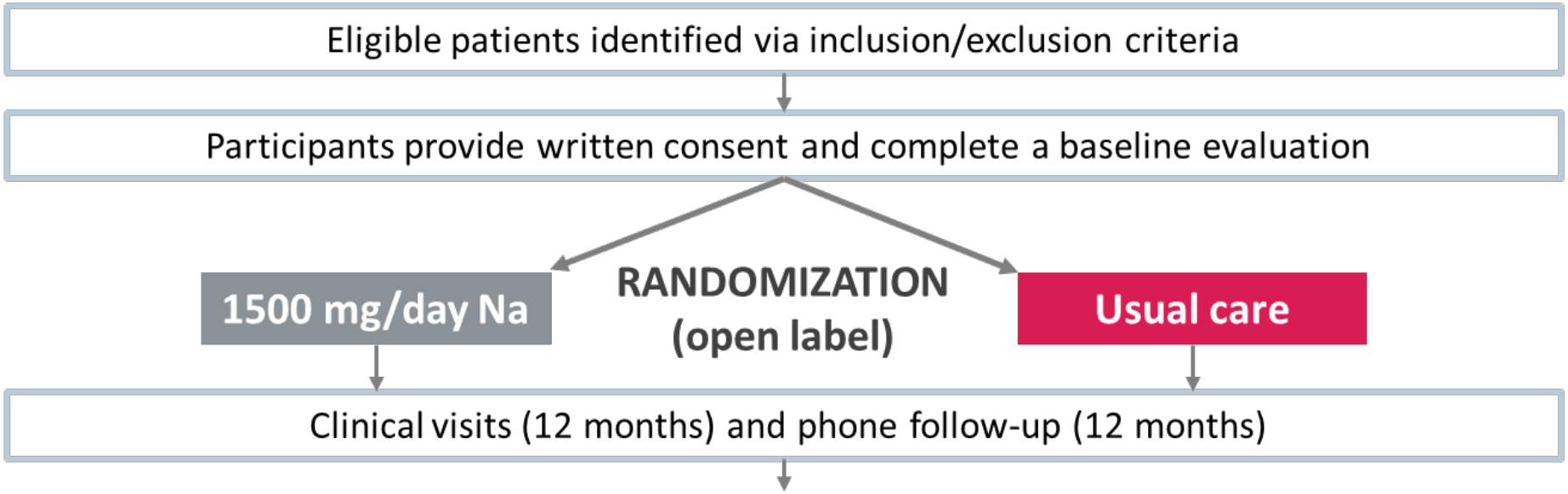
CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

University Hospital Foundation

Colin-Ramirez, *AHJ*, 2018 SODIUM-HF

SODIUM-HF: Trial Design

841 patients with heart failure (NYHA II-III) on optimally tolerated medical therapy



Primary Endpoint:

Composite outcome of all-cause mortality, CV hospitalizations, or CV ED visits

Secondary Endpoints:

Change in KCCQ, 6-minute walk test, and NYHA class

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

University Hospital Foundation

Colin-Ramirez, *AHJ*, 2018

SODIUM-HF

Was it the right population?

- Outpatient vs inpatient
- Relative vs absolute changes or targets
- Sodium intake:
  - Lower than average pt with CVD
  - Large HQ surveys lacking
    - UofT ~2400 mg/d
    - GOURMET-HF ~2900 mg/d

Hummel, Circ-HF 2018; Arcand

SODIUM-HF: Sites

SODIUM-HF

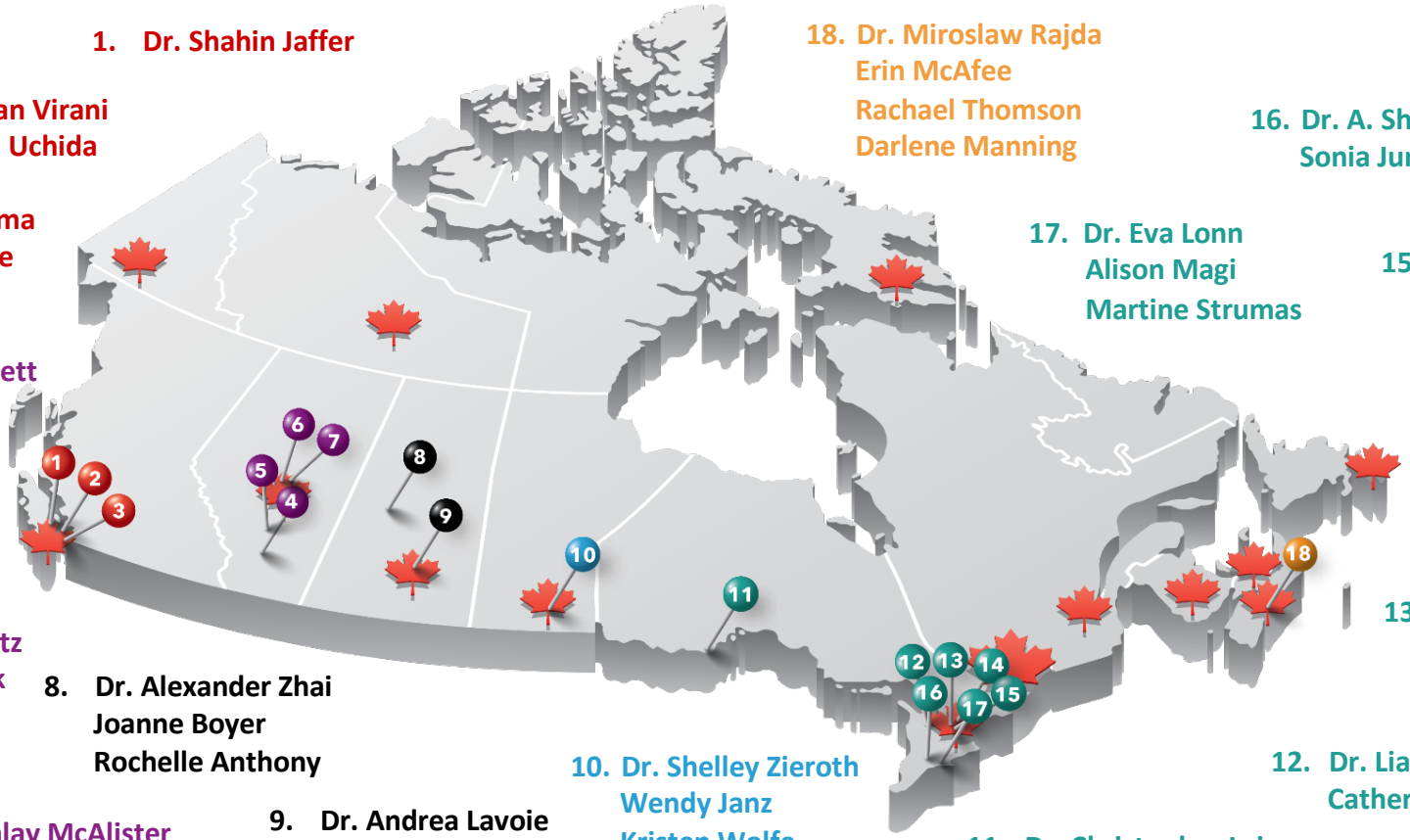
26 sites

Canada, Mexico, Chile, Colombia, Australia, New Zealand

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

University Hospital Foundation

Canadian SODIUM Sites



1. Dr. Shahin Jaffer

2. Dr. Sean Virani
   Naomi Uchida

3. Dr. Mustafa Toma
   Elizabeth Grieve
   Sinead Feeney

4. Dr. Jonathan Howlett
   Sneha Patel

5. Dr. Jitendra Singh
   Kelly Lehmann
   Lauren Padilla

5. Dr. Justin Ezekowitz
   Quentin Kushnerik
   Anita Naicker
   Elizabeth Woo

7. Dr. Finlay McAlister

8. Dr. Alexander Zhai
   Joanne Boyer
   Rochelle Anthony

9. Dr. Andrea Lavoie
   Jo-Anne Kurenoff

10. Dr. Shelley Zieroth
    Wendy Janz
    Kristen Wolfe

11. Dr. Christopher Lai
    Lisa Stein

12. Dr. Liane Porepa
    Catherine McPherson

13. Dr. Gordon Moe
    Carlos Fernando
    Eva Jasielski

14. Dr. Heather Ross
    Enza De Luca
    Margaret Brum

15. Dr. Milan Gupta
    Disha Shasti
    Winnie Christopher

16. Dr. A. Shekhar Pandey
    Sonia Juranics

17. Dr. Eva Lonn
    Alison Magi
    Martine Strumas

18. Dr. Miroslaw Rajda
    Erin McAfee
    Rachael Thomson
    Darlene Manning

SODIUM-HF: Intervention

- Samples of **menus** at different levels of energy requirement (1400-2200 kcal)
- 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.
- Food **individualized** to local region/country
- If energy requirements were adjusted during a follow-up visit, new sample menus were provided.
- **3 day food records** for each visit

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

University Hospital Foundation

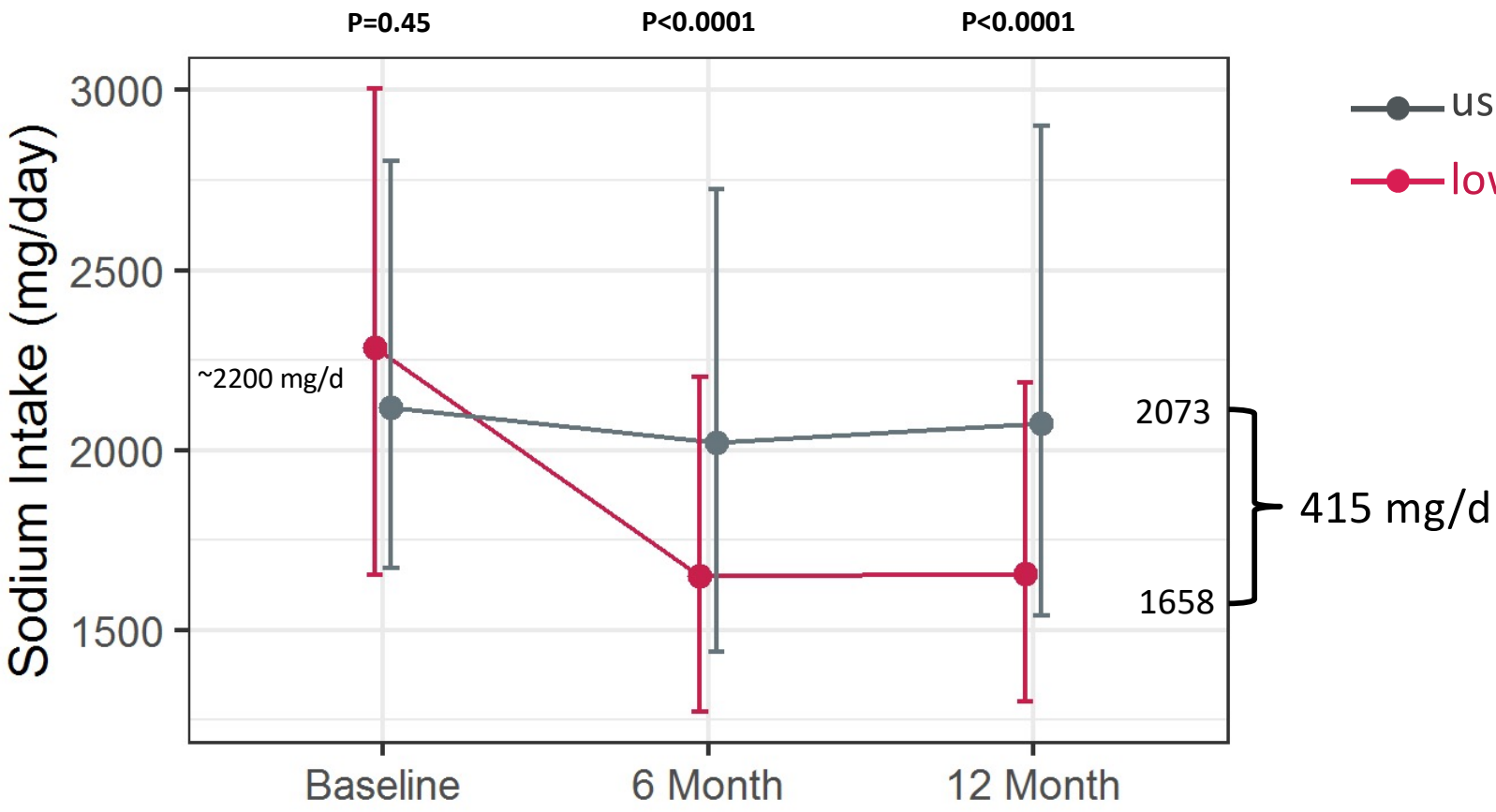
Colin-Ramirez, *AHJ*, 2018
Colin-Ramirez, *CJC Open*, 2019

SODIUM-HF

Did we get the intervention right?

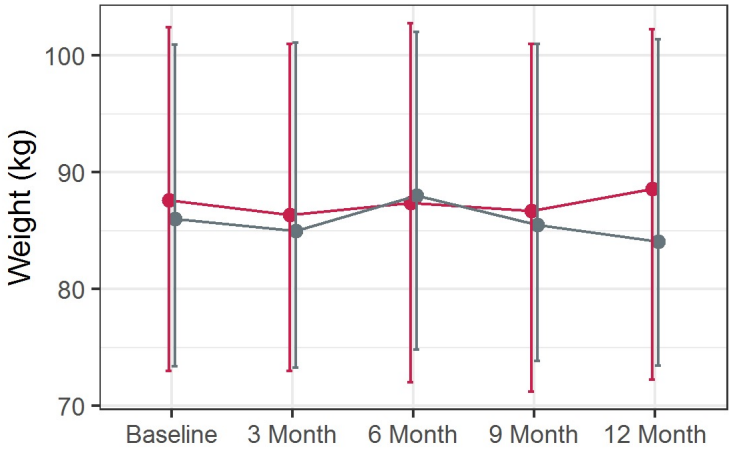
- Feeding trials (DASH)
  - Small, resource intensive, explanatory
  - Non-scalable
- Menu based
  - Low-tech, bespoke, pragmatic
  - Food variability, hard to isolate a nutrient
- Dietician involvement
  - Human effect, clinician time
  - Imbalance across arms

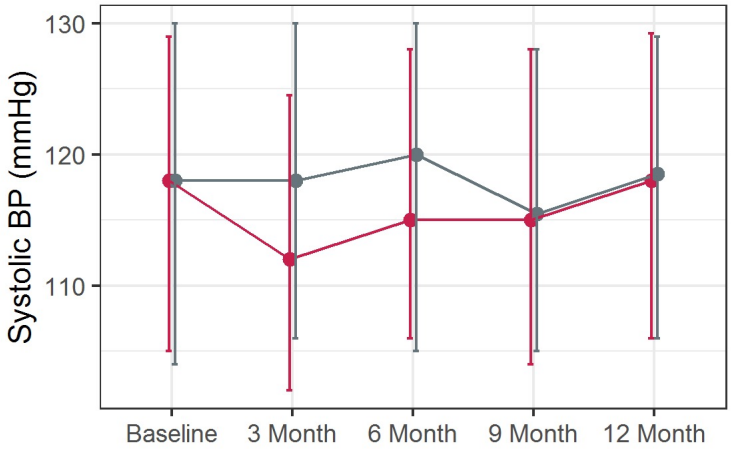
Dietary sodium intake

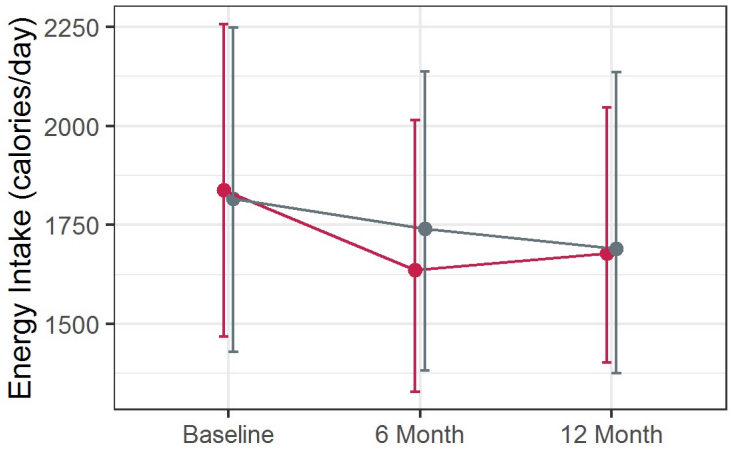


SODIUM-HF

Blood pressure, weight and energy intake







low sodium

usual care

All comparisons p=NS

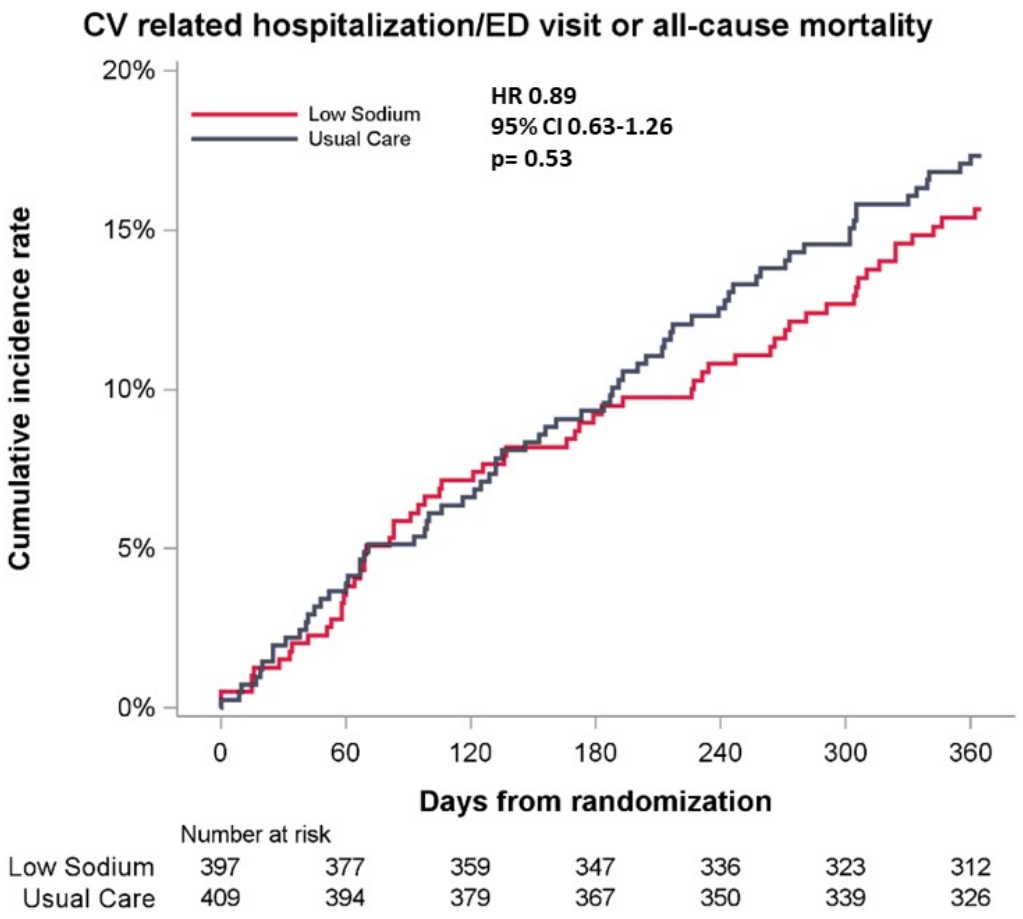
SODIUM-HF

Outcomes

Was this the right outcome?

- CVD/HFH = current standard
- All-cause mortality = totality of badness
- CV hospitalization = HFH + afib + ACS + …
- CV ED = treat/street
- 1 vs 2 vs 5 years…..

Primary Outcome

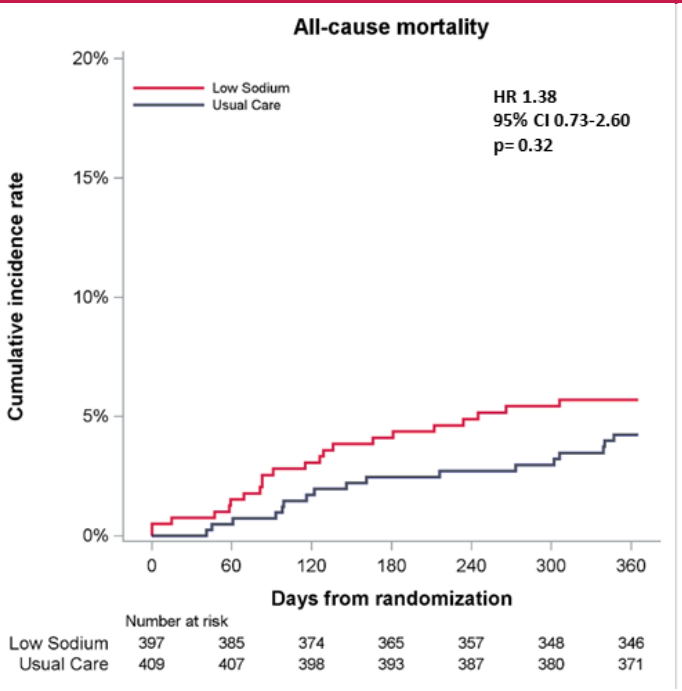


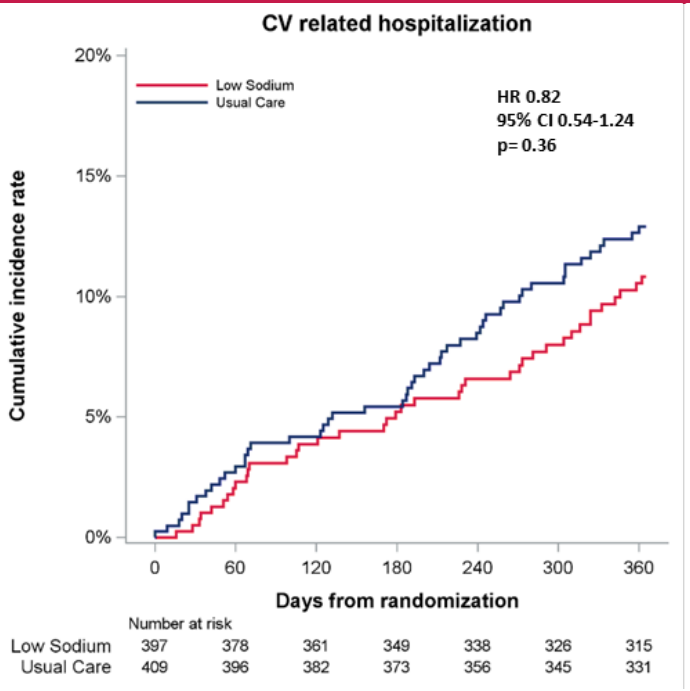
CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

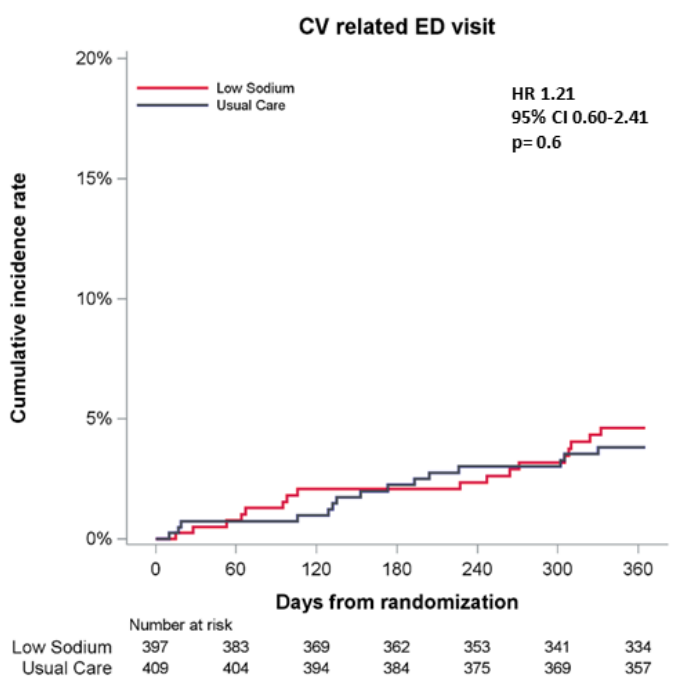
University Hospital Foundation

SODIUM-HF

Secondary Outcomes





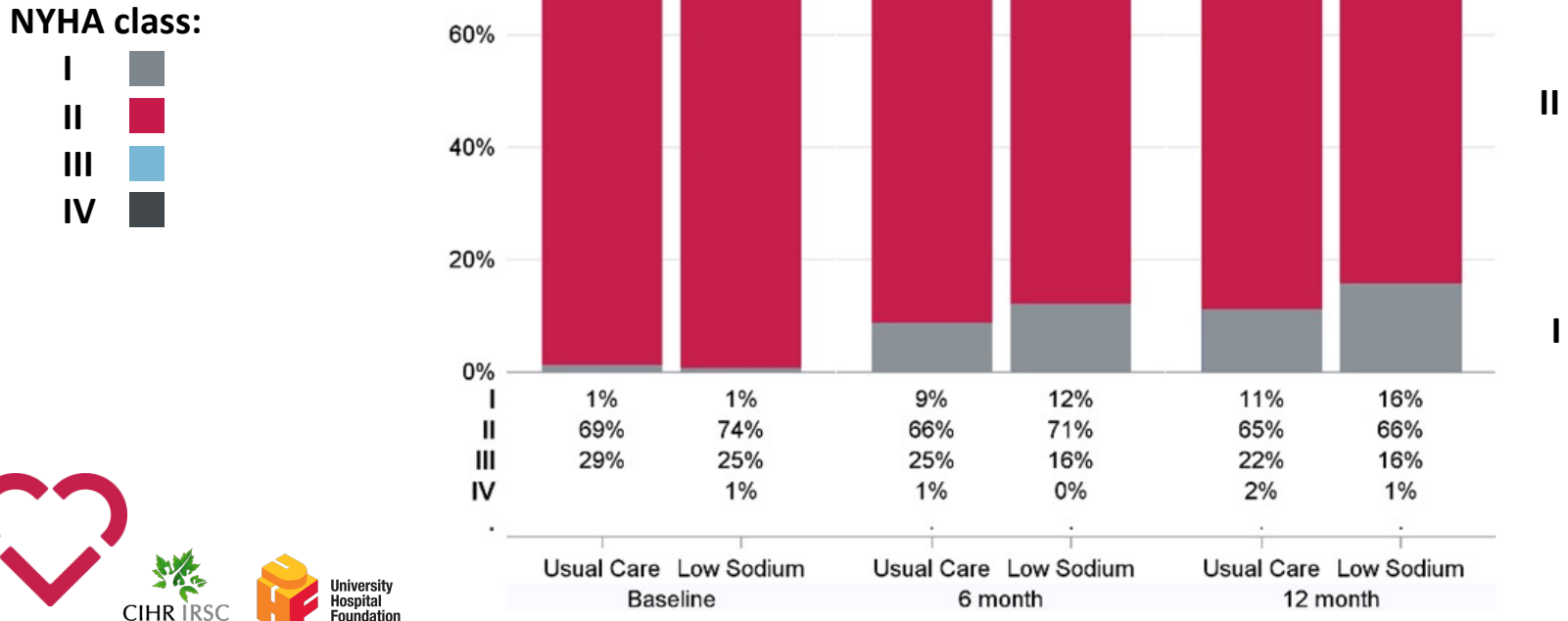


CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

University Hospital Foundation

SODIUM-HF

Change in NYHA class



CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

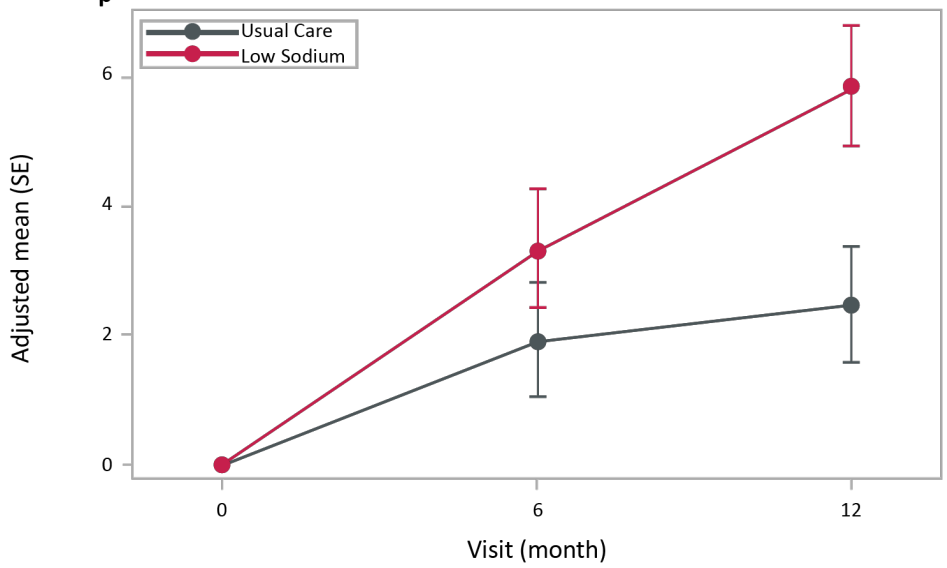
University Hospital Foundation

SODIUM-HF

Change in KCCQ score

KCCQ OSS

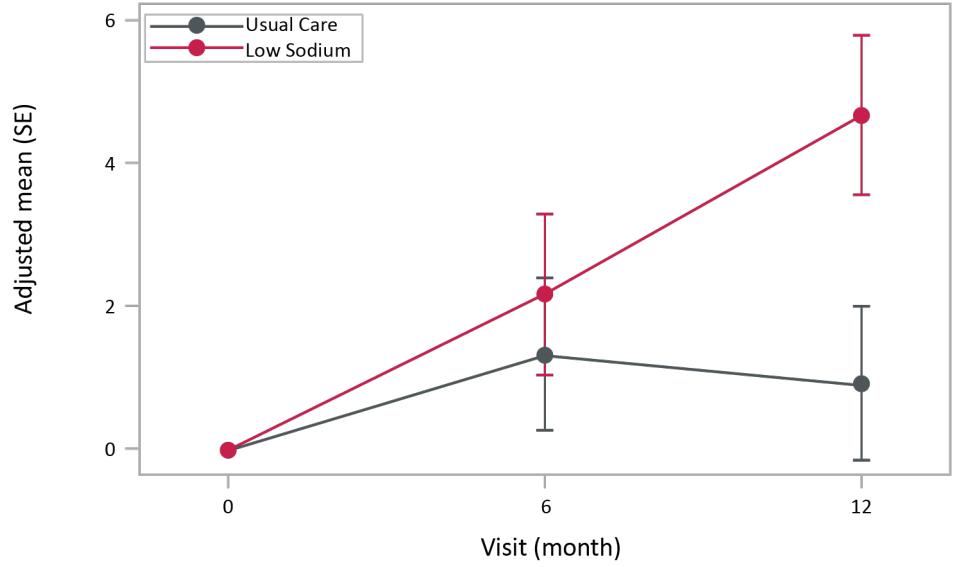
Difference (CI)		1.42 (-1.1, 3.97)	3.38 (0.79, 5.96)
p		0.277	0.011



Usual Care	407	330	316
Low Sodium	393	309	302

KCCQ PLS

Difference (CI)		0.86 (-2.2, 3.93)	3.77 (0.67, 6.87)
p		0.585	0.017



Usual Care	402	320	308
Low Sodium	383	296	295

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

University Hospital Foundation

SODIUM-HF

Limitations

- There was a sodium reduction of 415 mg / day by 12 months, and greater reductions in daily sodium or alternatively, enrolling patients with markedly higher dietary sodium may or may not produce different results.
- The trial was stopped early
- Lower than anticipated event rate
- Inclusion criteria were pragmatic and no NT-proBNP required

Patient comments on Twitter

No real differences. 🤔 Honestly, my first take? This will come as a welcome relief to those patience who, quite honestly, overadhere to the >1200 mg sodium restriction to their detriment (insert ppl like me). Also, reduce the shame in thinking 'I am not doing enough'

Re-emphasis on a balanced diet with moderate activity (as manageable) is much more realistic -

It's massive. The guilt. Your heart is 'failing' you and now you are failing even more because of 'too much sodium' which is in everything?

I think the take home message here is the OCD on extra low sodium which involves a complete overhaul of everyone's diet and lifestyle has far worse and potentially deleterious effects on mental health -

Implications

A low-sodium diet as done in SODIUM-HF:

- Clinicians: as a therapy to improve QOL
- Patients: as part of an overall health strategy
- Guidelines: informs with best evidence

Test unproven dogma

Think about the patient, intervention, control

Time for pragmatic RCTs

SODIUM-HF done; others need to be done