Canadian **VIGOUR** Centre
Bridging Hearts and Minds

# Study of Dietary Intervention Under 100 MMOL in Heart Failure

# SODIUM-HF

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ACC 2022

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- Funding from:


University Hospital Foundation


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# SODIUM-HF team

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# 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

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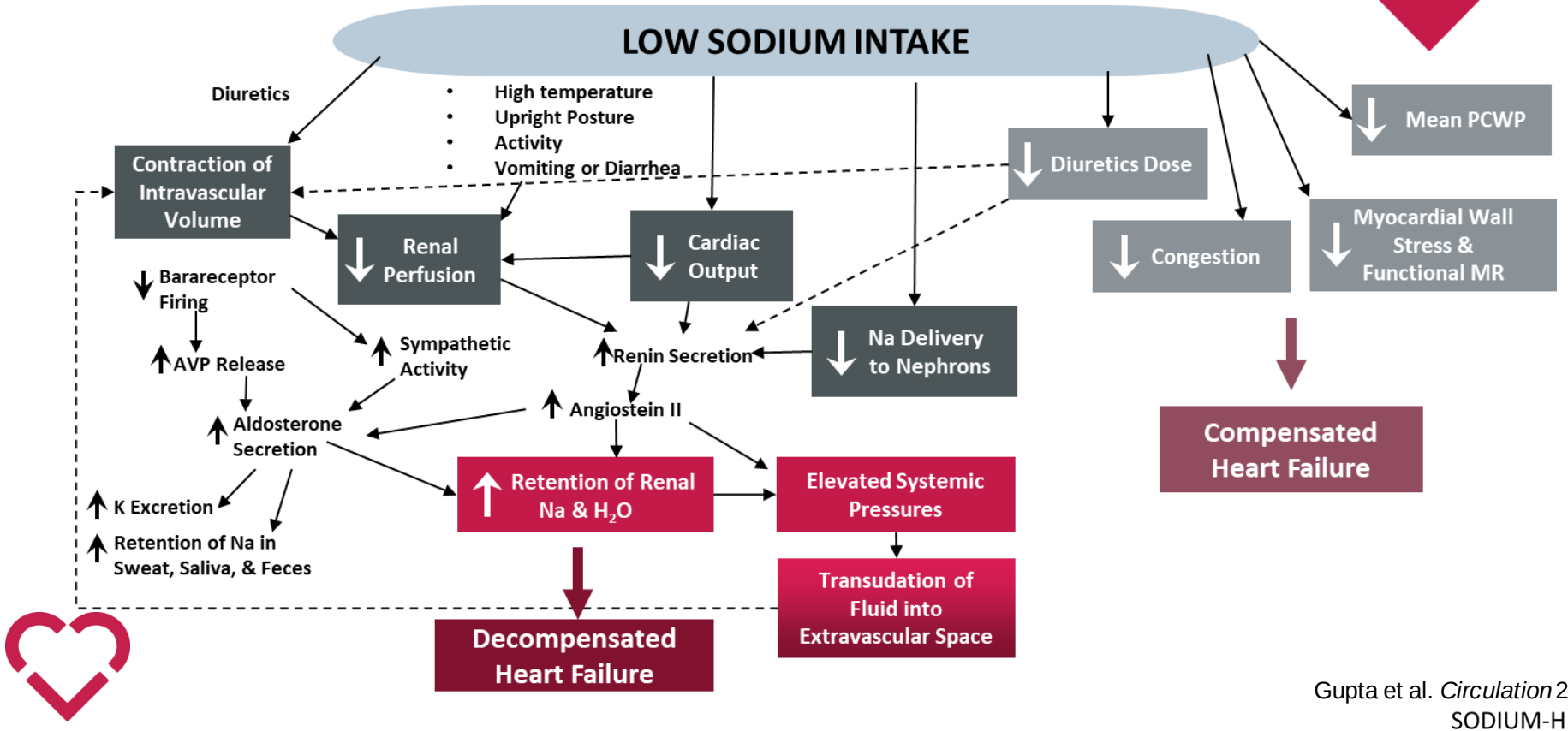
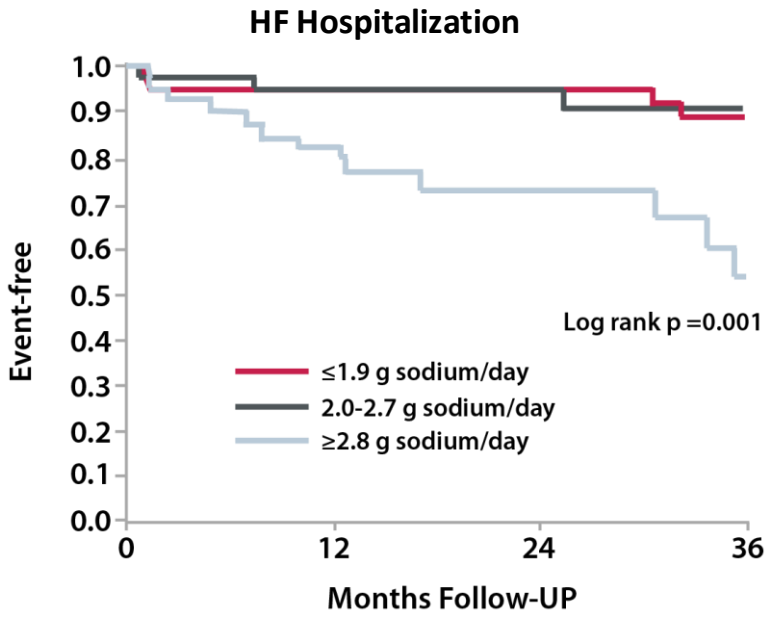
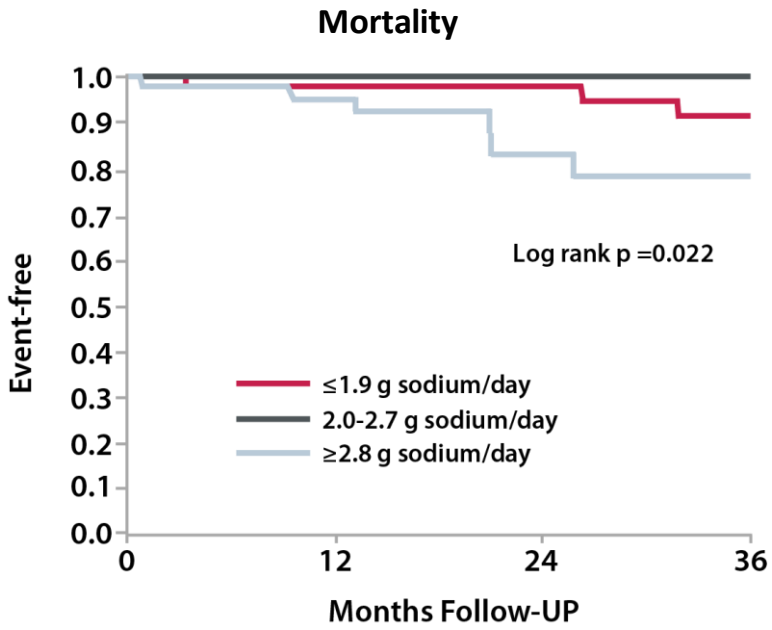
# Dietary Sodium Intake




Gupta et al. *Circulation* 2012

# Dietary sodium: Observational studies




**n= 123 patients with HF**

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

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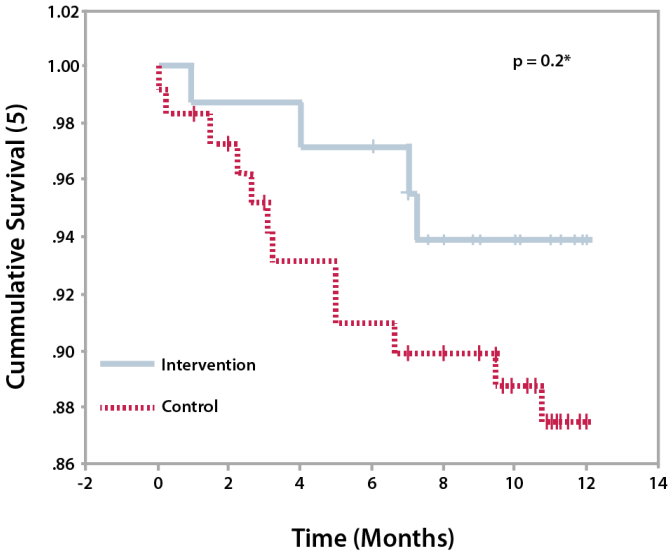
# Dietary sodium reduction: RCT

**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.

<u>Systematic review:</u>
9 studies
All < 100 patients
Mixed interventions

***No consistent results on any outcome***

Mahtani *JAMA: Internal Medicine* 2018

# 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

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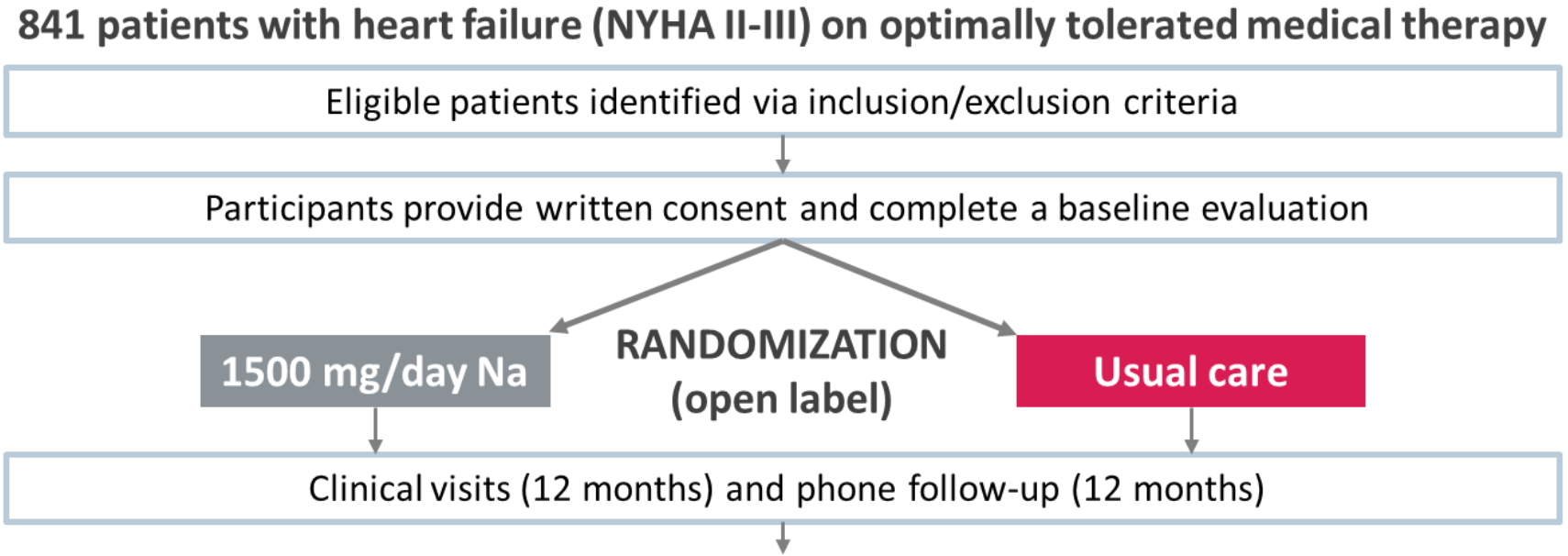
# SODIUM-HF: Trial Design




Colin-Ramirez, *AHJ*, 2018

# SODIUM-HF: Sites

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26 sites

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

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# SODIUM-HF: In/Exclusion criteria

**SODIUM Inclusion Criteria**

- ✓ 18 years or older and willing/able to sign informed consent.
- ✓ Confirmed diagnosis of HF (both reduced and preserved systolic function eligible)
- ✓ NYHA Class II-III
- ✓ On optimally tolerated medical therapy according to CCS guidelines

**SODIUM Exclusion Criteria**

- ✗ Patients with an average dietary intake of <1500 mg Na/day
- ✗ Serum sodium <130 mmol/L
- ✗ Hemodialysis-dependent chronic renal failure (or glomerular filtration rate <20 mL/min)
- ✗ Uncontrolled thyroid disorder or end-stage hepatic failure
- ✗ Cardiac device or revascularization procedure in previous month or planned in the next 3 months
- ✗ Hospitalization due cardiovascular causes in the previous 1 month
- ✗ Uncontrolled atrial fibrillation (resting heart rate >90 bpm)
- ✗ Active malignancy with an expected life expectancy <2 years
- ✗ Another comorbid condition or situation which could preclude compliance with the protocol
- ✗ Enrolled in another interventional research study

# SODIUM-HF: Intervention

Patients randomized to one of two study arms:

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

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

# 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

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

# SODIUM-HF: Sample Size / DMC

- Sample size:
  - Based on the primary composite outcome
  - Expected event rate of 25% in usual care arm
  - **30%** reduction in the primary outcome
  - **80%** power, two-sided type I error rate of 0.05
  - Total enrollment of **992** patients

- The Data Monitoring Committee
  - Reviewed data from the first **500** participants with complete 12-month follow-up
  - Mandate was to advise on *futility* (if conditional power was <20%) or *efficacy* (two-sided p-value <0.001).
  - This review, in addition to an assessment of trial operational feasibility and the impact of the COVID-19 pandemic, led to an early stopping with the last patient enrolled on December 09, 2020 and complete 12 month follow-up in December 2021.

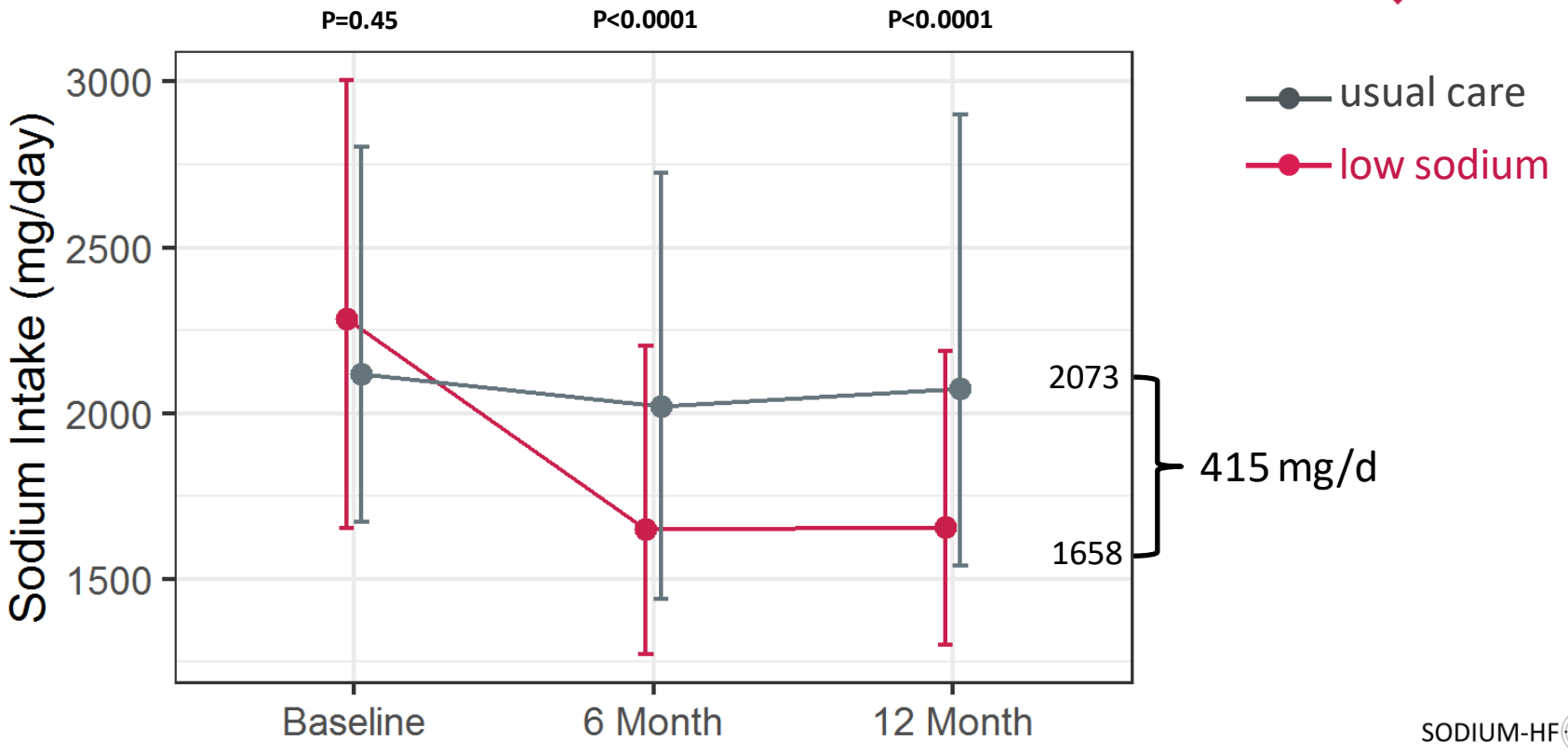
# SODIUM-HF: Baseline Characteristics

| | Low sodium diet group n=397 | Usual care group n=409 |
|---|---|---|
| **Age**, years | 66 (57–73) | 67 (58–75) |
| **Female Sex** | 127 (32%) | 141 (34%) |
| Geographical region | | |
| Canada | 230 (58%) | 241 (59%) |
| Australia and New Zealand | 79 (20%) | 78 (19%) |
| Mexico, Chile, and Colombia | 88 (22%) | 90 (22%) |
| Diagnosed with HF for ≥1 year | 269 (68%) | 282 (69%) |
| Hospitalised for HF in past 12 months | 129 (32%) | 141 (34%) |
| Ejection fraction | 36 (28–48) | 35 (27–50) |

# SODIUM-HF: Baseline Characteristics

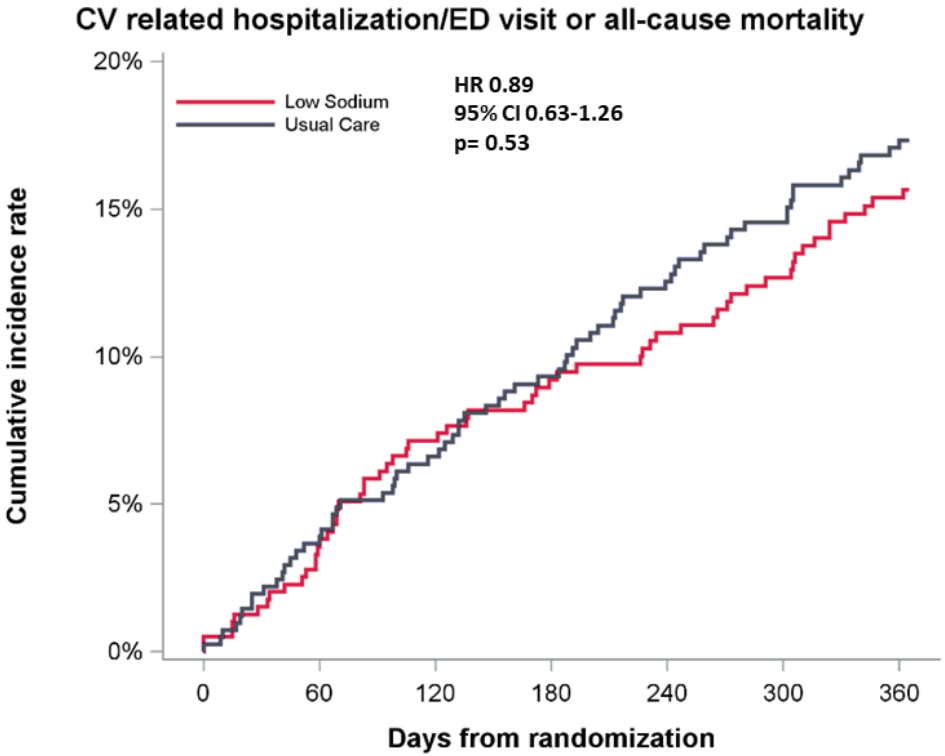
| | Low sodium diet group n=397 | Usual care group n=409 |
|---|---|---|
| **Medical history** | | |
| Coronary artery disease | 187 (47%) | 186 (45%) |
| Atrial fibrillation or flutter | 156 (39%) | 173 (42%) |
| Diabetes (type 1 or 2) | 132 (33%) | 156 (38%) |
| **Vital signs and physical findings** | | |
| BMI, kg/m² | 30 (26–35) | 31 (27–36) |
| Heart rate, beats per min | 69 (61–76) | 69 (61–77) |
| Systolic blood pressure, mm Hg | 118 (105–129) | 118 (104–130) |
| **Laboratory values** | | |
| eGFR, mL/min per 1·73m² | 61 (46–75) | 58 (42–71) |

# Dietary sodium intake



# Outcomes

# Primary Outcome

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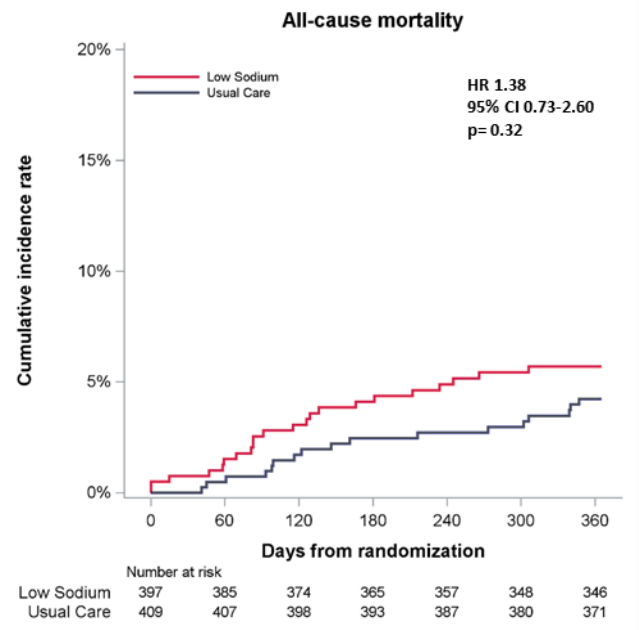
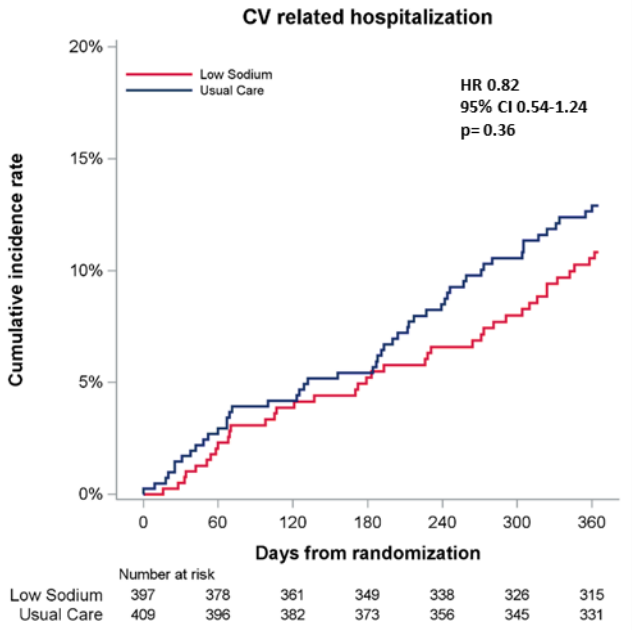
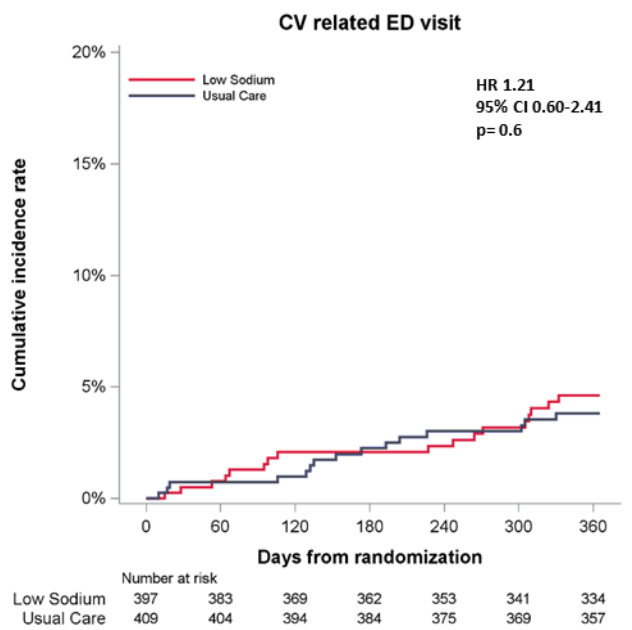
# Secondary Outcomes

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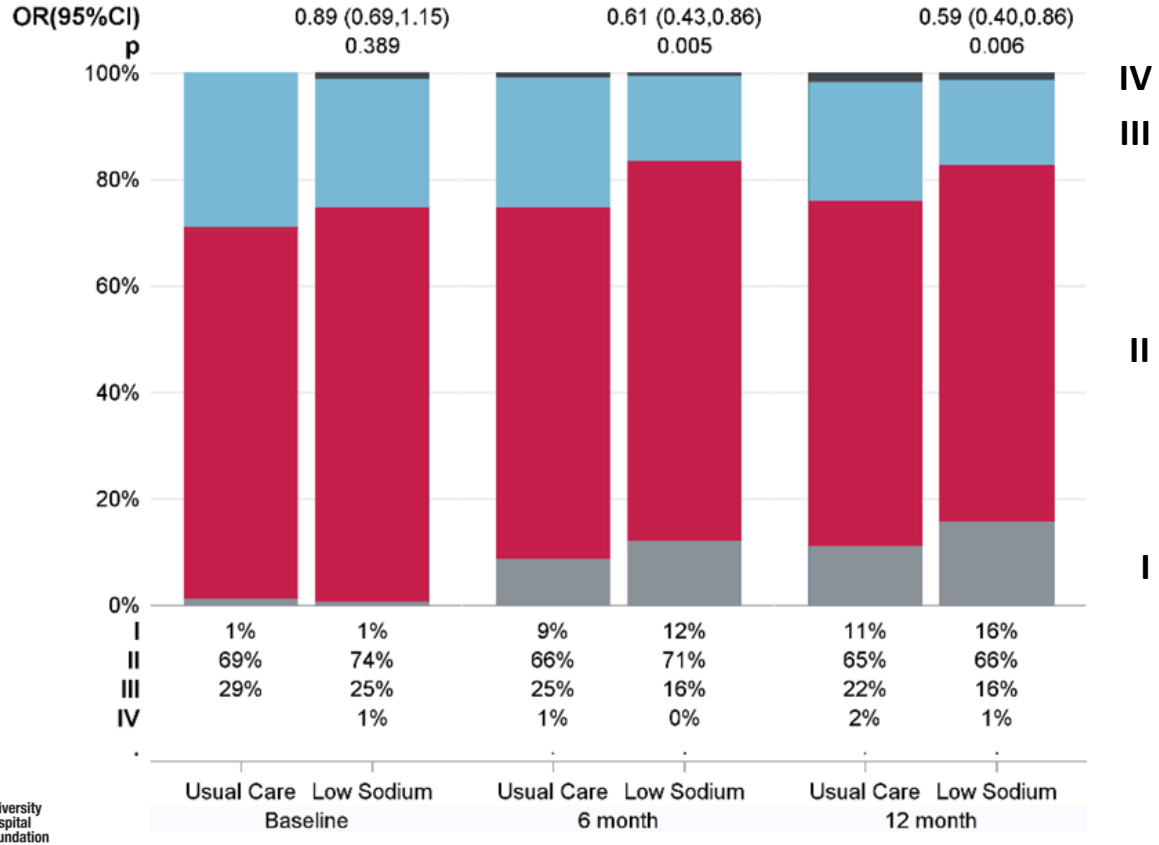
# Change in NYHA class

**NYHA class:**

- I
- II
- III
- IV

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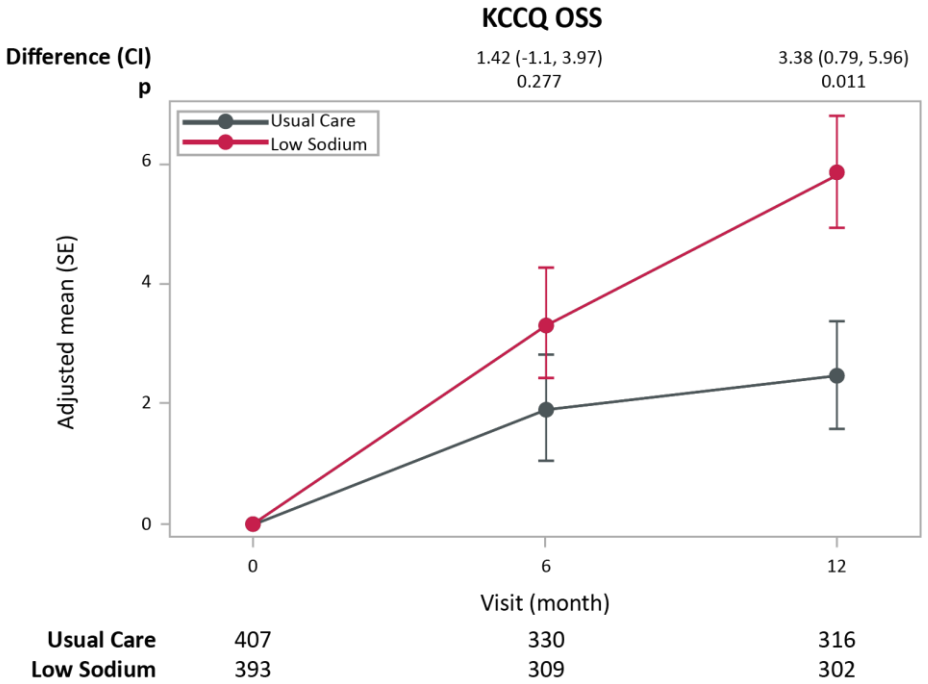
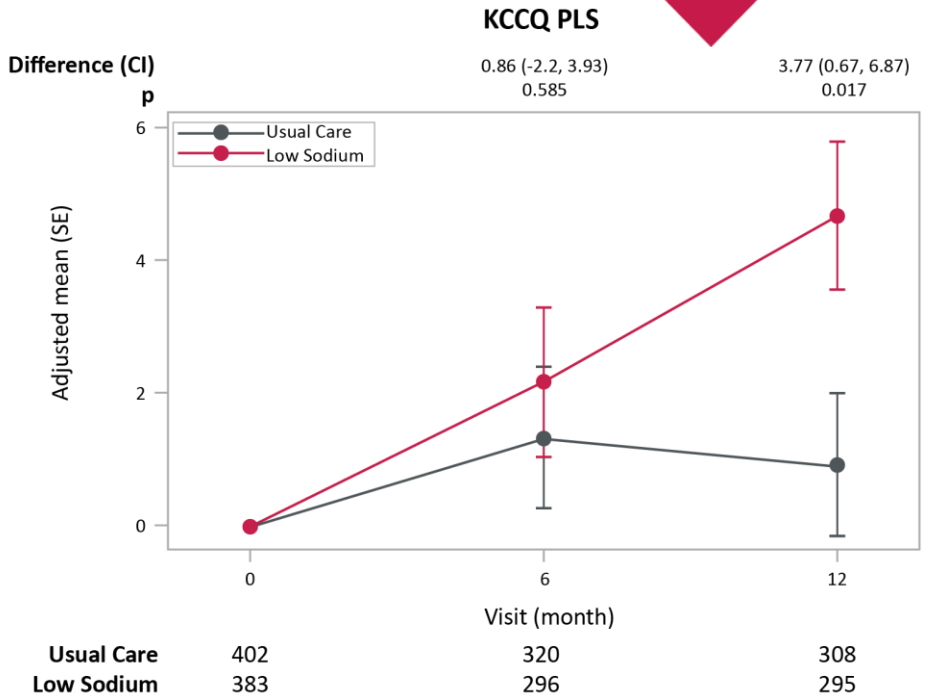
# Change in KCCQ score

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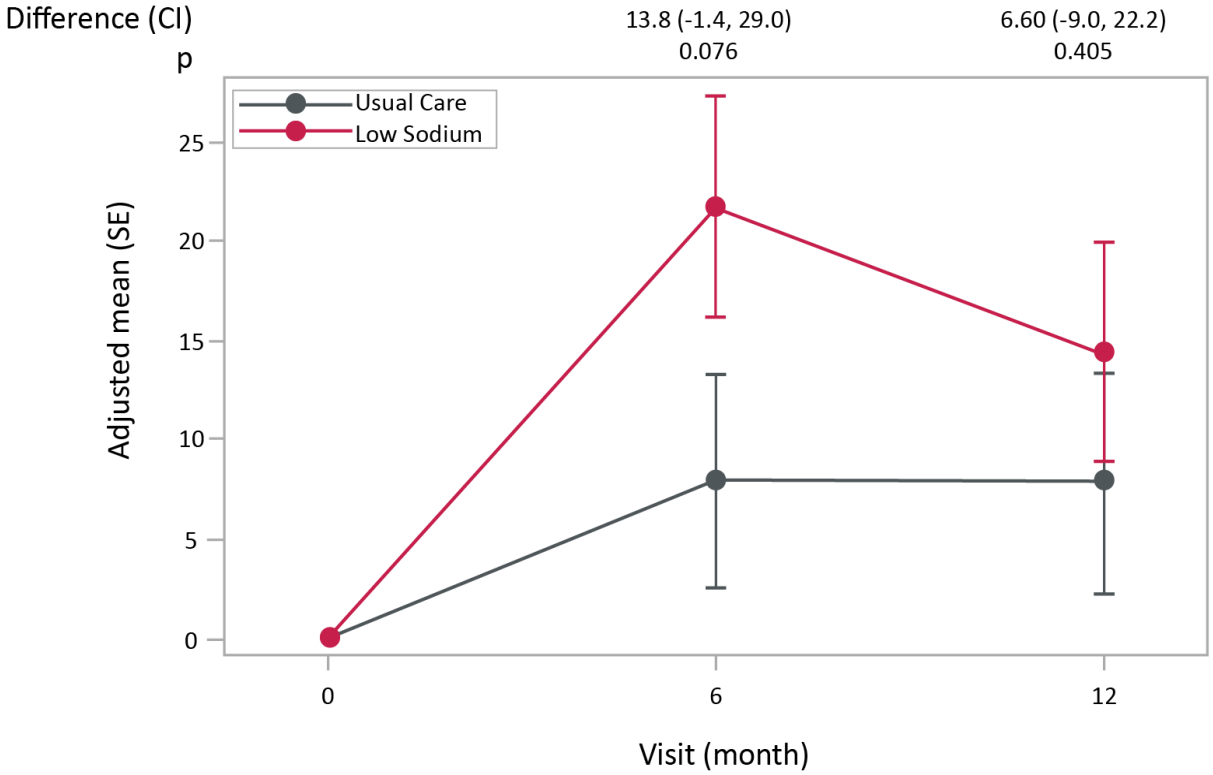
# Change in 6 min walk test distance




| | | | |
|---|---|---|---|
| **Usual Care** | 332 | 215 | 191 |
| **Low Sodium** | 328 | 204 | 199 |

# 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

# Conclusions

1. In ambulatory patients with HF, a dietary intervention to reduce sodium intake did not reduce clinical events.
2. There was a modest benefit on quality of life as measured by the KCCQ, and in NYHA class.
3. The 6-minute walk test was not statistically different between groups.

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# 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

# SODIUM-HF Participants

- A special thank you to those patients who volunteered their time and effort to participate in the SODIUM-HF trial