Evidence Synthesis Program

In-Hospital Sodium Intake for Acute Decompensated Heart Failure

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This report was prepared by the Evidence Synthesis Program Center located at the **VA Providence Health Care System,** directed by **Eric Jutkowitz, PhD and James Rudolph, MD** and funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development.

PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to conduct timely, rigorous, and independent systematic reviews to support VA clinicians, program leadership, and policymakers improve the health of Veterans. ESP reviews have been used to develop evidence-informed clinical policies, practice guidelines, and performance measures; to guide implementation of programs and services that improve Veterans' health and wellbeing; and to set the direction of research to close important evidence gaps. Four ESP Centers are located across the US. Centers are led by recognized experts in evidence synthesis, often with roles as practicing VA clinicians. The Coordinating Center, located in Portland, Oregon, manages program operations, ensures methodological consistency and quality of products, engages with stakeholders, and addresses urgent evidence synthesis needs.

Nominations of review topics are solicited several times each year and submitted via the ESP website. Topics are selected based on the availability of relevant evidence and the likelihood that a review on the topic would be feasible and have broad utility across the VA system. If selected, topics are refined with input from Operational Partners (below), ESP staff, and additional subject matter experts. Draft ESP reviews undergo external peer review to ensure they are methodologically sound, unbiased, and include all important evidence on the topic. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. In seeking broad expertise and perspectives during review development, conflicting viewpoints are common and often result in productive scientific discourse that improves the relevance and rigor of the review. The ESP works to balance divergent views and to manage or mitigate potential conflicts of interest.

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Operational Partners

Operational partners are system-level stakeholders who help ensure relevance of the review topic to the VA, contribute to the development of and approve final project scope and timeframe for completion, provide feedback on the draft report, and provide consultation on strategies for dissemination of the report to the field and relevant groups.

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Technical Expert Panel

To ensure robust, scientifically relevant work, the TEP guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked

areas of research; assures VA relevance; and provides feedback on work in progress. TEP members are listed below:

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Peer Reviewers

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence (see Appendix I for disposition of comments). Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center works to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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ABBREVIATIONS TABLE

ACC	American College of Cardiology
ADHF	Acute decompensated heart failure
BNP	Brain (or B-type) natriuretic peptide
BUN	Blood urea nitrogen
CI	Confidence interval
eGFR	Estimated glomerular filtration rate
ESC	European Society of Cardiology
ESP	Evidence Synthesis Program
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HF	Heart failure
HSS	Hypertonic saline solution
ICU	Intensive care unit
IQR	Interquartile range
IV	Intravenous
KQ	Key Questions
LVEDD	Left ventricle end-diastolic diameter
LVEF	Left ventricular ejection fraction
MD	Mean difference
NMD	Net mean difference
NR	Not reported
NRCS	Nonrandomized comparative study
NS	Not significant
NT-proBNP	N-terminal pro-brain (or B-type) natriuretic peptide
NYHA	New York Heart Association
PRA	Plasma renin activity
RCT	Randomized controlled trials
RD	Risk difference
RoB	Risk of bias
RR	Relative risk
SD	Standard deviation
TDS-HF	Thirst Distress Scale for Heart Failure
VAS	Visual analogue scale

EXECUTIVE SUMMARY

Key Findings

Five studies compared a lower sodium diet to a higher sodium diet (unrestricted in 4 studies); 15 studies compared supplemental sodium chloride (NaCl) with furosemide to furosemide alone in patients hospitalized with acute decompensated heart failure (ADHF). Of the 15 supplemental NaCl studies, 14 evaluated hypertonic saline solution (HSS) and 1 evaluated oral NaCl tablets.

- Adults hospitalized with ADHF consumed fewer calories on a restricted sodium diet compared to higher sodium diet. Sodium restriction did not differentially affect other intermediate, clinical, or health service use outcomes. Studies provided insufficient evidence for N-terminal pro-brain natriuretic protein (NT-proBNP), weight, and mortality. No study reported data on estimated glomerular filtration rate (eGFR) or serum cystatin C.
- Supplemental NaCl (mostly given as HSS) with furosemide significantly decreased serum creatinine, blood urea nitrogen (BUN), BNP, and weight and increased eGFR, urine output, and serum sodium. There were no significant differences in NT-proBNP, serum aldosterone, plasma renin activity (PRA), or cystatin C. Supplemental NaCl improved some clinical outcomes (New York Heart Association [NYHA] functional class and thirst symptoms) and reduced hospital length of stay, but did not affect intensive care unit admissions. No study reported data on clinical congestion score. Studies provided insufficient evidence on mortality and readmission outcomes.

INTRODUCTION

ADHF is a leading cause of hospitalization and rehospitalization in the United States (US). The goal of treatment for people hospitalized with ADHF is to reverse acute hemodynamic abnormalities and improve symptoms. In addition to pharmacological therapies (*eg,* diuretics and vasodilators), standard inpatient management of ADHF includes restricting dietary sodium. However, sodium restriction can negatively affect patients by activating antidiuretic and anti-natriuretic systems and reducing blood pressure, which can increase heart rate. There is also concern that patients find low-sodium food less flavorful, which could negatively affect nutrition intake and lead to poor adherence to a low-sodium diet.

Supplemental sodium (given as either HSS infusion or oral NaCl tablets) is proposed as an adjuvant therapy to loop diuretics in patients hospitalized with ADHF. This therapeutic approach is motivated by the observation that HSS causes volume expansion and mobilization of fluid to the intravascular compartment, which improves kidney function, urine output, and weight loss. Despite the potential clinical benefits, inpatient providers may be hesitant to adopt supplemental sodium given conceptual concerns that increased sodium intake may exacerbate HF symptoms.

The VA ESP was asked by the VA Office of Hospital Medicine for an evidence review on interventions affecting sodium intake patients hospitalized for ADHF. In collaboration with VA stakeholders, we developed the following Key Questions (KQs):

KQ1: Among adults hospitalized for decompensated heart failure, what is the comparative effectiveness of different prescribed sodium intake interventions?

KQ1a: Does effectiveness differ as a function of patient characteristics, including by age, comorbid conditions (kidney function, hypertension, diabetes, stroke, body mass index), existing versus new onset heart failure, preserved versus reduced ejection fraction or pre-hospitalization dietary sodium intake, sex, and race/ethnicity?

METHODS

We searched for peer-reviewed articles in Medline (via PubMed), Embase, ClinicalTrials.gov, CINAHL, and the Cochrane Database of Systematic Reviews from inception to February 13, 2023. Eligible studies evaluated the effect of prescribed sodium intake interventions (*eg*, restricted dietary intake, intravenous HSS, oral NaCl supplementation) for people ≥18 years of age hospitalized and treated for ADHF. We excluded studies that evaluated sodium intake as a continuous exposure (*ie*, not prescribed), that were conducted in the emergency department (without an inpatient component) or in an outpatient setting, that did not report patient-level interventions (*eg*, if they compared hospital policies that were not explicitly uniformly applied), or that did not include a comparison group. We included randomized controlled trials (RCT) and nonrandomized (observational) comparative studies (NRCS), whether prospective or retrospective and regardless of whether they were adjusted for potential confounders. Prioritized outcomes included intermediate (serum creatinine, brain [or B-type] natriuretic peptide [BNP], N terminal-proBNP [NT-proBNP], and caloric intake), clinical (clinical congestion score, weight loss, and 30-day all-cause mortality), and health service use measures (length of hospital stay and 30-day readmission). We analyzed all outcomes (except post-hospitalization outcomes) from the first in-hospital measurement to the end of the intervention or discharge. Where there were at least 3 studies reporting results from sufficiently similar analyses (based on population, interventions, comparators, and outcomes), we conducted meta-analyses using random-effects models. Using GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology, we determined certainty of evidence for each prioritized outcome (but not other outcomes). The review protocol was registered in PROSPERO (CRD42023410146).

RESULTS

Twenty studies reported the effectiveness of prescribed sodium for patients hospitalized with ADHF. Five studies (4 RCTs and 1 NRCS) evaluated the effectiveness of restricted dietary sodium intake interventions (with 381 analyzed patients), and 15 studies (13 RCTs and 2 NRCSs) evaluated the effectiveness of HSS with furosemide (14 studies) or oral NaCl with furosemide (1 study) (with 3,483 analyzed patients). The majority of the studies were conducted in Europe ($N = 9$), followed by South America ($N = 5$), Asia ($N = 3$), the Middle East ($N = 2$), and US ($N = 1$). ES Table shows the summary results for prioritized outcomes.

ES Table. Summary of Findings for Prioritized Outcomes

	Dietary Sodium Interventions			Supplemental Sodium Interventions*		
Outcome	**Studies (Patients); Design**	**Overall Confidence**	**Summary of Findings**	**Studies (Patients); Design**	**Overall Confidence**	**Summary of Findings**
Creatinine	3 (159); RCT	Moderate	Pooled NMD = 0.08 mg/dL, 95% CI (−0.08, 0.23)	11 (2,766); RCT	Moderate	**Pooled NMD = −0.38 mg/dL, 95% CI (−0.54, −0.22)**
BNP	2 (128); RCT	Low	Net *median* difference = 525 and −13 pg/mL	7 (2,848); 6 RCT and 1 NRCS	Low	**Pooled NMD = −62.84 pg/mL, 95% CI (−103.61, −22.08)**
NT-pro BNP	1 (31); RCT	Insufficient	No conclusion	3 (235); RCT	Low	Pooled NMD = −1614.17 pg/mL, 95% CI (−3581.66, 353.31)
Caloric Intake	2 (243); RCT, NCRS	Low	**Consume <20 kcal/kg/day RR = 3.4, 95% CI [1.70, 6.86])** **MD = −4.4 kcal/kg/day, 95% CI (−7.26, −1.53)** **MD in percent estimate of daily requirement: −16, 95% CI (−6.6, −25.4)**	0	NA	No evidence
Clinical Congestion Score	2 (128); RCT	Moderate	NMD = −0.5, 95% CI (−1.76, 0.76) and 0.4, 95% CI (−1.6, 2.4)	0	NA	No evidence
Weight Change	4 (191); RCT	Insufficient	No conclusion	14 (3,333); 13 RCTs and 1 NCRS	Moderate	**Pooled NMD = −2.66 kg, 95% CI (−4.70, −0.62)**
Mortality (All Cause)	4 (191); RCT	Insufficient	No conclusion	4 (2,317); RCT	Insufficient	No conclusion
Readmission	3 (159); RCT	Low	Pooled RR = 1.07, 95% CI (0.68, 1.69)	2 (159); RCT	Insufficient	No conclusion
Length of Hospital Stay	3 (159); RCT	Low	Pooled NMD = 3.1 days, 95% CI (−0.6, 6.7)	11 (3,243); 9 RCTs and 2 NRCS	Moderate	**Pooled NMD = −2.90 days, 95% CI (−4.02, −1.79)**

Notes. Statistically significant summary findings are in bold font.
*14 studies evaluated HSS and 1 study evaluated oral NaCl.
Abbreviations. BNP=brain (or B-type) natriuretic peptide; CI=confidence interval; MD=mean difference; NA=not applicable; NMD=net mean difference; NRCS=non-randomized controlled study; NT-proBNP=N-terminal pro-brain (or B-type) natriuretic peptide; RCT=randomized controlled trial; RR=relative risk.

Effect of Dietary Sodium Intake Restriction

Five studies conducted between 2008 and 2016 (that analyzed 381 participants) compared a low sodium diet to a higher sodium diet (unrestricted in 4 studies). Four RCTs were conducted in Brazil and 1 NRCS was conducted in Japan. Two RCTs had methodological concerns due to missing outcome data, not following intent-to-treat principles, or randomized patients based on medical record number and not concealing allocation. The NRCS was presented in a conference abstract and reported minimal methodological details. Prescribed sodium intake in the intervention groups ranged from 0.8 g/day (in 3 RCTs) to 2.4 g/day (in the NRCS). Sodium intake in the control groups ranged from 2.8 g/day to 3-5 g/day. Four studies also restricted fluid in the intervention group (800 to 1000 mL/day), 2 studies restricted fluid intake in the higher sodium diet groups (800 mL/day and 1000 mL/day), and 2 did not indicate any fluid restriction in the higher sodium diet groups. Three studies restricted diet until discharge, hospital day 7, or if there was a clinical indication to end it early (whichever came first). The other 2 studies did not report the duration of the intervention.

Intermediate Measures

In summary, there were no significant differences in serum creatinine (in 3 studies) and BNP (2 studies) between a low sodium diet and higher sodium diet (ES Table). Fewer calories were consumed by patients on a low sodium diet compared with a higher sodium diet (2 studies). There is insufficient evidence for the effect of dietary intervention on NT-proBNP or weight loss (due to imprecise estimates and methodological limitations).

Other specific findings included no significant difference in BUN (3 studies), urine output (1 study), proportion of patients prescribed diuretics or dose of diuretics (3 studies), serum sodium (3 studies), aldosterone (1 study), or plasma renin activity (PRA;1 study). Certainty of evidence was not assessed for these outcomes. No study reported eGFR or serum cystatin C.

Clinical Measures

There was no significant difference in clinical congestion score (ES Table). Studies provided insufficient evidence for mortality (no conclusion).

A low sodium diet combined with fluid intake restrictions significantly increased thirst (2 studies) but there was no significant difference in shortness of breath (1 study), well-being (1 study), or days to compensation (1 study). Certainty of evidence was not assessed for these outcomes.

Health Service Use

There was no difference in 30-day readmission or length of stay between a low sodium diet and higher sodium diet (ES Table). Patients consumed significantly less sodium (*ie*, were adherent to their prescribed diet) on a low sodium diet compared to higher sodium diet (2 studies).

Effect of Supplemental Sodium (and Diuretics)

Fifteen studies conducted between 1996 and 2022 analyzed 3,483 participants and evaluated the effectiveness of HSS ($N = 14$) or oral NaCl ($N = 1$) with diuretics in patients hospitalized with ADHF. Nine studies were conducted in Europe, 2 in Asia, 2 in the Middle East, 1 in the US, and

1 in South America. In 1 RCT, an independent physician assigned patients to treatment groups, and 1 RCT had major discrepancies within the text and poor methodological reporting of outcome definitions (therefore, high risk of bias). Three RCTs had methodological concerns related to allocation concealment and blinding (*ie*, moderate risk of bias). Two NRCSs either conducted crude unadjusted analyses or did not report a method to address confounding (therefore, high risk of bias). Seven studies described tailoring the concentration of HSS (between 1.4% and 4.6% NaCl) based on the patients' serum sodium levels, 6 studies evaluated a fixed HSS concentration (between 1.7% and 7.5% NaCl), and 1 study did not report concentration of HSS. Total sodium intake (calculated from both HSS and dietary intake) ranged from 0.7 to 8.1 g/day. One study used oral NaCl formulation to replicate neurohormonal effects of HSS intervention and for easy administration. Fourteen studies combined HSS or oral NaCl with intravenous furosemide, and 1 NRCS did not report information on diuretics usage in the conference abstract.

Intermediate Measures

The studies found statistically significant net decreases in serum creatinine (11 studies), BNP (7 studies), and weight (14 studies) from admission to last in-hospital measurement for patients administered sodium supplementation with furosemide compared to furosemide alone (ES Table). There was no significant difference in NT-proBNP (3 studies) or serum aldosterone (3 studies).

Other specific findings included significant net decreases in BUN (12 studies) and significant net increases in eGFR (6 studies), urine output (12 studies), and serum sodium (13 studies); and PRA (1 study) or cystatin C (2 studies). Certainty of evidence was not assessed for these outcomes. No study reported caloric intake.

Clinical Measures

There is insufficient evidence for the effect of sodium supplementation with furosemide on mortality (ES Table). No study reported clinical congestion score. Other nonprioritized outcomes for which certainty of evidence was not assessed included an increased likelihood of improving 2 NYHA functional classes for HSS with furosemide (3 studies). There is a reduction of thirst symptoms (1 study) but no evidence of a difference in a composite measure of HF symptoms (2 studies) or other symptoms of HF including shortness of breath (2 studies).

Health Service Use Measures

Hospital length of stay was shorter for patients who received sodium supplementation with furosemide compared to furosemide alone (ES Table). There was no significant difference in intensive care unit admissions (1 study). There is insufficient evidence on readmission (2 studies; 1 small study with serious methodological limitations, and conflicting results among 2 studies).

DISCUSSION

ADHF is a leading cause of hospitalization, rehospitalization, and morbidity in the US and in the VA system. Although a restricted sodium diet with diuretic therapy is standard practice for patients hospitalized with ADHF, we identified only 5 relatively small studies (total $N = 381$) that have evaluated this strategy. Restricting sodium in ADHF patients is hypothesized to reduce fluid retention and congestion. However, the evidence does not support that weight change, urine

output, and clinical congestion score differed between patients who received restricted or higher sodium diets. Importantly, about 16% fewer calories were consumed by patients who received a restricted diet (in 2 studies), and 2 studies reported increased thirst for patients who received a restricted sodium diet combined with fluid restriction. While the clinical implications of short-term reduced caloric intake and thirst are unclear, it may lead to poor experience of care and create unnecessary friction with clinical staff. No study reported data on quality of life or patient experience of care.

A larger evidence base evaluated the effect of combining HSS (or oral sodium supplementation) with furosemide (15 studies, total $N = 3,483$), which is hypothesized to reduce hyperactivation of the renin-aldosterone-angiotensin pathway and reduce the sodium-avid state of the kidneys. Consistent with this hypothesis, we found that sodium supplementation with furosemide compared to furosemide alone significantly improved kidney function, increased urine output, and reduced weight. No sodium supplementation study evaluated caloric intake, but there is no reason to believe this strategy would affect food consumption. Sodium supplementation with furosemide also reduced hospital length of stay by 3 days, which is large and meaningful for patients and health systems; although the 1 study conducted in US found no significant difference in hospital length of stay between oral NaCl with furosemide and furosemide alone. Therefore, the magnitude of any reduction in length of stay in the VA is unclear. Variation across studies in the duration of intervention and diuretic dose makes it challenging to identify the best sodium supplementation with diuretic strategy. Despite the apparent beneficial effect of this intervention, providers may still have concerns about administering sodium to people with ADHF, which is counter to conventional practice.

No study reported differences in effectiveness by patient characteristics (age, sex, or race/ethnicity), comorbid conditions, community dietary sodium intake, existing versus new onset heart failure, or preserved versus reduced ejection fraction. Finally, no study compared a dietary sodium restriction to sodium supplementation with furosemide.

Implications for VA Policy

All dietary sodium RCTs were conducted in Brazil and most HSS studies were conducted in Europe. The majority of European studies were conducted by 3 different author groups. Despite this, the overall findings (particularly for intermediate and clinical outcomes) likely translate to the VA, since the underlying biology and mechanisms are not likely different by country. As noted, the magnitude of changes in length of stay found in studies conducted in mostly Europe may not apply to the VA, and the 1 study conducted in the US (oral NaCl) found no significant difference in length of stay. Any potential effect on length of stay is dependent on typical length of stay for ADHF admissions at individual institutions and health care systems. Our findings call for VA Medical Centers to review the routine practice of severely restricting sodium intake for patients admitted with ADHF. However, sodium supplementation with loop diuretics to augment diuresis shows promise as a strategy to improve inpatient management of ADHF. In addition to evaluating the clinical data, VA decision makers will need to consider implementation needs and barriers. Providers and systems may be reluctant to change practice since the use of sodium in HF is counterintuitive and discussed in medical curricula as something to be avoided. Sodium supplementation and intravenous diuretic protocols may require additional resources for patient monitoring and safety protocols. Lastly, training medical staff will be critical to promote the safe use of HSS in selected patients with ADHF. To evaluate needs and barriers, VA can apply

implementation science methods. This can include interviews with Veterans, providers, and Medical Center leadership and using the VA medical record to monitor safety of patients who receive sodium supplementation.

Research Gaps/Future Research

The evidence base on restricting dietary sodium was small and had several addressable limitations: missing outcome data, failure to follow intent-to-treat analysis, or randomizing patients based on medical record number. Thus, there is a need for a well-designed, adequately powered RCT of pragmatic design to assess the effectiveness of HSS infusion for patients admitted with ADHF. The absence of adequately powered RCT data from North America presents an opportunity for the VA to conduct its own effectiveness and implementation study of this strategy. For sodium supplementation, comparative effectiveness studies of different dosing strategies (durations and concentrations) are needed to identify the optimal approach. The effect of sodium supplementation on length of stay in the US also needs to be addressed. Studies need to examine differences in effectiveness by patient demographics, heart failure phenotypes, chronicity of heart failure, and comorbid conditions. It is likely feasible to evaluate differences in effectiveness using robust quasi-experimental methods or conducting *post hoc* analyses of existing RCTs. No study evaluated patient quality of life or satisfaction with care, which may be especially important for interventions that restrict dietary sodium.

Limitations

This evidence review has several limitations. We were unable to compare effects by intervention dosing or duration. Outcomes of 30-day mortality and 30-day readmission may be affected by care after discharge, and we did not evaluate corresponding outpatient care protocols. Studies examining dietary interventions in outpatient settings can be difficult to conduct since patients often self-report sodium consumption and adherence is more challenging. We focused on studies conducted in an inpatient setting where diet can be controlled by providers and patients are likely to be more compliant with treatment.

Conclusions

Although restricting dietary sodium is standard practice for patients admitted with ADHF, only a few small studies have examined this approach. There is no difference in BNP, clinical congestion score, 30-day readmission, and length of stay between low sodium and higher sodium diets. Importantly, fewer calories are consumed by patients on low sodium diets compared to higher sodium diets. Studies provide insufficient evidence for the effect of dietary sodium interventions on NT-pro BNP and weight loss. In contrast, serum creatinine, BNP, and weight, but not mortality, decreased for patients administered sodium supplementation with furosemide compared to furosemide alone. Importantly, length of hospital stay was shorter for patients who received sodium supplementation with furosemide. Sodium supplementation studies provide insufficient evidence for mortality and 30-day readmission. There is a need for well-designed RCTs to assess the effectiveness of sodium restriction for the inpatient management of ADHF and for more US-based RCTs of HSS (or oral sodium) with furosemide.

EVIDENCE REPORT

INTRODUCTION

PURPOSE

The Evidence Synthesis Program (ESP) was asked by the Veterans Health Administration (VHA) Hospital Medicine for an evidence review on interventions affecting sodium intake (*eg*, dietary sodium restriction and supplemental sodium chloride [NaCl] given as either hypertonic saline solution [HSS] infusion or oral NaCl tablets) for adults ≥18 years of age hospitalized for acute decompensated heart failure (ADHF). For decades, standard non-pharmacologic inpatient care for people with ADHF has included restricting dietary sodium intake. However, evidence on the benefit of sodium restriction in the inpatient setting is mixed and there are concerns of harms, particularly related to antidiuretic effects and poor nutritional intake. In contrast, several studies suggest that the use of supplemental sodium in combination with an intravenous diuretic regimen may improve kidney function and reduce mortality in patients with ADHF. Veterans and providers could benefit from clear guidance on the use of sodium intake interventions to manage ADHF in an inpatient setting. VHA Hospital Medicine intends to use this ESP review to inform national clinical guidance on sodium restriction during acute care for patients with ADHF.

BACKGROUND

Heart failure (HF) affects around 26 million people worldwide,[1] 6.2 million people in the United States (US) alone, and 5% of Veterans.[2,3] HF is also a leading cause of hospitalization and rehospitalization in the US.[4] Despite progress in evidence-based pharmacotherapies and device interventions, most HF patients are hospitalized within 5 years of a diagnosis.[5,6] Approximately 38% of hospitalizations of people with HF are for ADHF,[5] which is characterized by sudden or gradual onset of signs and symptoms of HF with pulmonary and/or systemic congestion related to increased left- and right-heart filling pressures (*eg*, dyspnea, orthopnea, weight gain, and lower limb swelling). People experiencing ADHF require immediate hospitalization or unplanned office or emergency room visits to stabilize their symptoms.[7,8]

The goal of treatment for patients hospitalized with ADHF is to reverse acute hemodynamic abnormalities and improve symptoms.[9] This is predominantly achieved by using diuretics (*eg,* loop diuretics) and vasodilators that decrease venous congestion and volume overload.[9] In addition to pharmacological therapies, for decades the standard inpatient management of ADHF has included restricting dietary sodium.[10] However, there is no consensus in clinical guidelines on the threshold of sodium intake per day. For example, the 2022 American Heart Association/American College of Cardiology/Heart Failure Society of America (AHA/ACC/HFSA) Guideline for the Management of Heart Failure recommends a daily sodium intake of <2.3 g/day, and the 2021 European Society of Cardiology (ESC) guidelines recommend sodium intake of <5 g/day.[11,12]

The motivation to restrict dietary sodium is based on the clinical observation that excess sodium contributes to fluid retention.[13] However, sodium restriction can also have a negative effect by activating antidiuretic and anti-natriuretic systems, which leads to further development of congestion.[14] There is also concern that patients find low-sodium food less flavorful, which could negatively affect nutrition intake and lead to poor adherence to a low-sodium diet. Low

sodium intake may also reduce blood pressure that in turn increases heart rate and negates the effects of beta-blockers.[14] Most data on restricted dietary sodium come from studies conducted in outpatient settings.[15] Few studies have formally evaluated the effect of sodium restriction in inpatient settings.

Conversely, supplemental sodium (either HSS infusion or oral NaCl tablets) has been proposed as an adjuvant therapy to loop diuretics to improve diuretic efficacy in patients hospitalized with ADHF.[16] This therapeutic approach is motivated by the observation that volume expansion by HSS as a resuscitation fluid leads to the mobilization of fluid to the intravascular compartment, which is followed by increased urine output.[18] Randomized controlled trials (RCTs) conducted in inpatient and outpatient settings found that HSS with loop diuretics improved kidney function, urine output, weight loss, and electrolyte abnormalities, in addition to decreased plasma renin activity (PRA), inflammatory markers, and biomarkers including brain (or B-type) natriuretic peptide (BNP) levels.[17-19] Despite the potential clinical benefits, inpatient providers may be hesitant to adopt HSS given conceptual concerns that increased sodium intake may exacerbate HF symptoms.[18]

To date, most systematic reviews on sodium intake interventions have included studies combining data from both inpatient and outpatient settings.[20,21] We, therefore, conducted a systematic review on comparative effectiveness of various oral and/or intravenous prescribed sodium intake interventions in the treatment for ADHF patients during hospitalization.

METHODS

TOPIC DEVELOPMENT

We worked with representatives from VHA Hospital Medicine and our Technical Expert Panel (TEP) to refine the review scope and develop the key questions (KQ). We focus on studies that report on prescribed sodium intake to manage ADHF in an inpatient setting (*eg,* restricted dietary sodium intake or HHS). We excluded studies that did not prescribe sodium intake (*eg*, epidemiologic evaluation where daily sodium intake was evaluated as a continuous measure). We evaluated the effect that prescribed sodium intake had on intermediate measures (*eg,* neurohormonal activation and weight), clinical outcomes (*eg,* time to clinical stability and clinical congestion score), and health service use outcomes (*eg,* length of hospital stay and 30-day rehospitalization).

KEY QUESTIONS

KQ1: Among adults hospitalized for decompensated heart failure, what is the comparative effectiveness of different prescribed sodium intake interventions?

KQ1a: Does effectiveness differ as a function of patient characteristics, including by age, comorbid conditions (kidney function, hypertension, diabetes, stroke, body mass index), existing versus new onset heart failure, preserved versus reduced ejection fraction or pre-hospitalization dietary sodium intake, sex, and race/ethnicity?

PROTOCOL

A preregistered protocol for this review can be found on the PROSPERO international prospective register of systematic reviews (http://www.crd.york.ac.uk/PROSPERO/; registration number CRD42023410146).

DATA SOURCES AND SEARCHES

We searched Medline (via PubMed), Embase, ClinicalTrials.gov, CINAHL, and the Cochrane Database of Systematic Reviews from inception to February 13, 2023. We used Medical Subject Headings (MeSH) and free text terms for *decompensated heart failure* and related terms, *prescribed sodium intake*, and *inpatient*, together with filters for primary studies (see Appendix A for complete search strategies). We ensured that known relevant publications were captured by our searches. Additional citations were sought from hand-searching reference lists of relevant systematic reviews and consultation with content experts.

STUDY SELECTION

Citations were uploaded into EndNote, where duplicates were removed. We screened citations in Abstrackr (http://abstrackr.cebm.brown.edu),[22] which has machine learning algorithms to prioritize relevant citations. To ensure a common understanding of the eligibility criteria, we ran pilot rounds of 100 citations at a time, where all team members screened the same citations, until we achieved acceptable agreement. Subsequently, we screened citations in duplicate with conflicts adjudicated during team meetings or by a third senior researcher. Based on empirical evidence, we stopped screening when all remaining unscreened abstracts had a prediction value of <0.40 (on a 0–1 scale) and subsequently 400 abstracts in a row were rejected.[22] Accepted

abstracts underwent full-text review using an evidence mapping process independently by 1 researcher with confirmation of excluded articles by a second researcher. When necessary, the reviewers consulted a third senior researcher. A list of studies excluded at full-text review, with rejection reasons, is provided in Appendix B.

Eligibility criteria are listed in Table 1. In brief, eligible study participants were ≥18 years of age, hospitalized and treated for ADHF. Eligible studies evaluated the effect of prescribed sodium intake interventions, including restricted dietary sodium intake and supplemental sodium intake. We included any dietary sodium restriction, any concentration of intravenous supplemental NaCl (including HSS, half-normal saline, *etc*), and any prescribed supplemental oral NaCl intake. Studies were excluded if they were conducted in the emergency department (without an inpatient component) or outpatient setting, if they did not report patient-level interventions (*eg*, comparison of hospital policies that were not explicitly uniformly applied), or did not include a comparison group. We included RCT, nonrandomized comparative studies (NRCS), and other comparative observational studies, whether prospective or retrospective, and regardless of whether they were adjusted for potential confounders. We analyzed laboratory or intermediate measures, clinical outcomes, and health care utilization. We analyzed all outcomes except 30-day rehospitalization and 30-day mortality from the first in-hospital measurement to the end of the intervention or discharge.

Table 1. Inclusion and Exclusion Criteria

	Inclusion Criteria	Exclusion Criteria
Population	Adults ≥18 years of age hospitalized for treatment of decompensated HF, including for exacerbation of a chronic condition or new onset or previously undetected heart failure	• Advanced HF requiring mechanical support or heart transplant • Patients in cardiogenic shock • Patients undergoing surgery • Patients on dialysis
Intervention	Prescribed sodium intake • Restricted dietary sodium intake • Increased oral sodium intake (*eg*, NaCl tablets) • Intravenous saline (hypertonic saline, normal saline, hypotonic [half normal] saline, other saline)	• Patients not prescribed sodium intake (*eg*, a hospital policy without explicit implementation in individuals) • Sodium intake evaluated as a continuous variable • Subgroups of patients based on average sodium intake or hospital policy
Comparator	• More (including normal/typical) sodium intake (as a comparator of restricted dietary sodium intake) • Less oral sodium intake (as comparator of sodium tablets) • Other intravenous saline regimen (including none)	
Outcomes	• Laboratory/Intermediate measures o RAAS activation o Neurohormonal activation o Kidney function (*eg,* serum creatinine, eGFR) o BNP / NT-proBNP o Urine output o Weight loss o Nutritional intake (calories and fluid)	

	Inclusion Criteria	Exclusion Criteria

	• Clinical outcomes
	  ○ Clinical congestion score
	  ○ Supplemental oxygen levels
	  ○ Duration or timing of IV diuretics
	  ○ Time to clinical stability (as defined by study)
	  ○ Mortality (inpatient and 30 days)
	  ○ Quality of life (generic or HF-specific)
	  ○ HF-related symptoms (*eg,* thirst, shortness of breath)
	  ○ Prescribed guideline recommended therapy after discharge (*eg,* ACE inhibitors)
	• Adherence to prescribed diet in the inpatient setting.
	• Discharge location (*eg,* home, skilled nursing, cardiac rehab)
	• Health care utilization
	  ○ Length of hospital stay
	  ○ Hospital readmission related to HF within 30 days
	  ○ Cardiovascular related ED visit within 30 days
	  ○ Transfer to ICU (proxy for clinical deterioration)
	  ○ Mechanical ventilation (proxy for clinical deterioration)	

Timing	• In-hospital (preferentially end-of-treatment or hospital discharge) for all except 30-days post discharge for hospital readmission and mortality	
Setting	• Inpatient	• Emergency department only • Outpatient
Study Design	• RCT • Nonrandomized comparative study, prospective or retrospective	• Single group (noncomparative) studies • Association between sodium as a continuous measure (not a prescribed intervention) and outcomes
Other	• No language restriction • No country restriction	

Abbreviations. ACE inhibitors=angiotensin converting enzyme inhibitors; BNP=brain (or B-type) natriuretic peptide; ED=emergency department; eGFR=estimated glomerular filtration rate; HF=heart failure; ICU=intensive care unit; NT-proBNP=N-terminal pro-brain (or B-type) natriuretic peptide; NRCS=nonrandomized comparative study; RAAS=renin-angiotensin-aldosterone system; RCT=randomized controlled trial.

DATA EXTRACTION AND ASSESSMENT

We created a data extraction form in the Systematic Review Data Repository-Plus (SRDR+) online system (https://srdrplus.ahrq.gov). We extracted the following data from eligible studies: study design, setting, baseline population characteristics, amount, and duration of sodium intake (intervention and comparator), and intermediate, clinical, and health service use outcomes. All data extraction was first completed by 1 reviewer and then checked by a second reviewer. Disagreements were resolved by consensus or discussion with a third reviewer.

Study risk of bias was independently assessed by 2 reviewers using questions derived from the Cochrane Risk of Bias and the ROBINS-I (Risk Of Bias In Non-randomized Studies – of Interventions) tools (Appendix C).[23,24] For all study designs, we also evaluated whether the article was free of discrepancies, and reporting of patient eligibility criteria, protocols, setting,

and outcome assessments were sufficiently clear. For RCTs, we evaluated the method of randomization, allocation concealment, and whether intention-to-treat analysis was used. For NRCSs, we evaluated whether patients in the treated and comparison groups were similar and what strategies were used to deal with potential confounders.

SYNTHESIS AND CERTAINTY OF EVIDENCE

For both KQs, we compared results in study groups using relative risks (RR) for dichotomous outcomes. When a study had no events in 1 group, we calculated risk differences (RD). We compared continuous data using net mean differences (NMD; *ie*, difference-in-differences or between-intervention comparisons of within-intervention changes from baseline to follow-up) or mean differences (MD) between interventions for outcomes evaluated only post-intervention (*eg,* length of stay). When necessary, we estimated NMDs or MDs and their standard deviations from reported data, including from reported medians and ranges.[25,26] Adjusted analyses were preferentially extracted over unadjusted (crude) comparisons. Where there were at least 3 studies reporting results from sufficiently similar analyses (based on population, interventions, comparators, and outcomes), we conducted meta-analyses using the restricted maximum-likelihood estimation (REML) random-effects models in the "meta" package for R version 4.3.0 (2023-04-21). Statistical heterogeneity was estimated using the I^2 statistic, which estimates the percentage of heterogeneity ascribed to statistical heterogeneity (not ascribed to random chance).

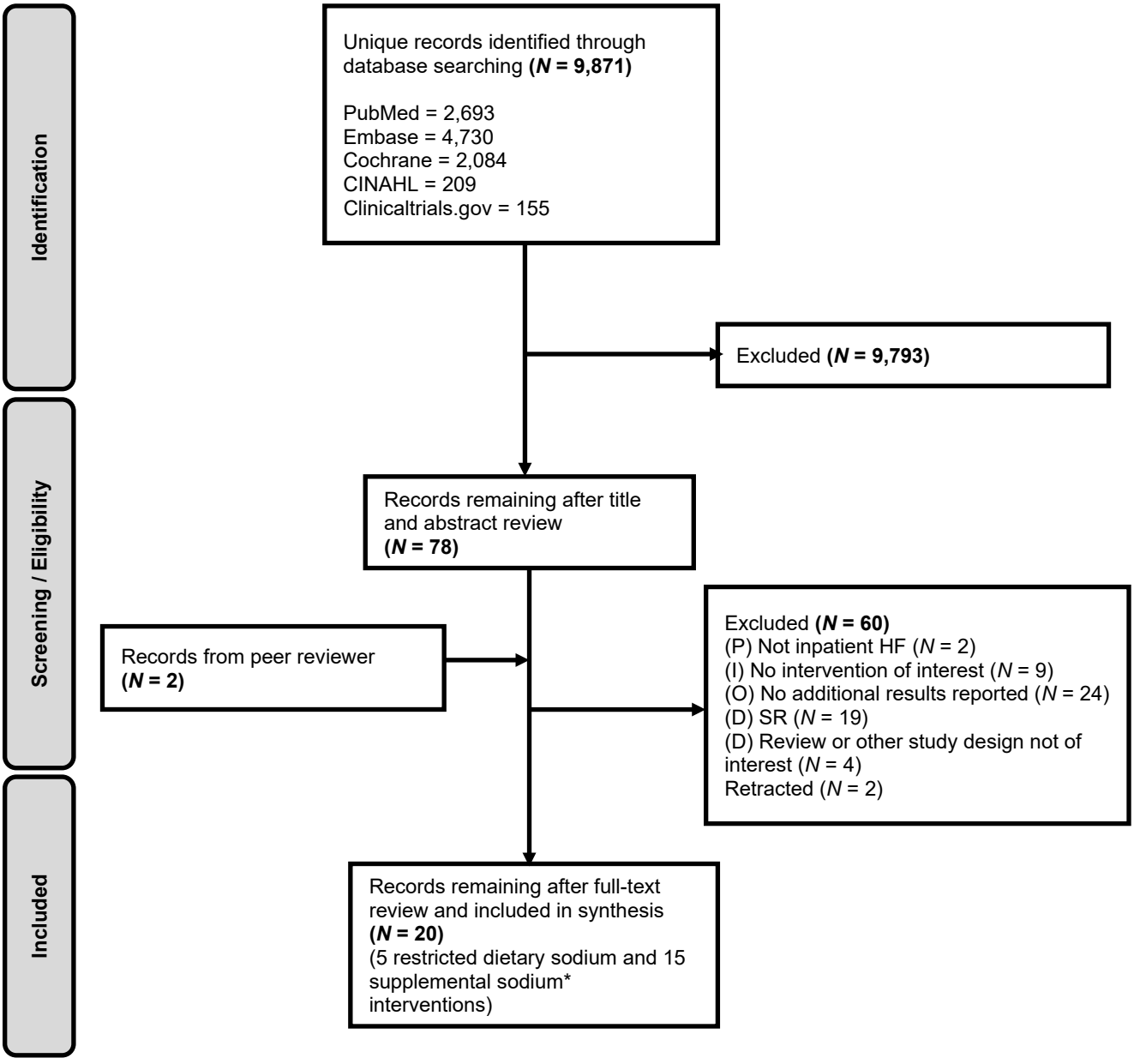
We assessed the certainty of evidence following the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach.[27] We compiled key study findings in evidence profiles, which provide the basis for determination of certainty of evidence and summarize conclusions for outcomes prioritized by the stakeholders: serum creatinine, BNP, NT-pro BNP, caloric intake, clinical congestion score, weight loss, 30-day all-cause mortality, 30-day readmission, and length of hospital stay. Within each priority outcome, we considered the study design, the number of studies (and participants), methodological limitations (*ie,* risk of bias), directness of the evidence, precision of the findings, consistency across studies, and other issues. Based on these, we determined certainty of evidence, which could be high, moderate, or low. Where we found few or no comparable studies, we report that there is insufficient evidence to draw conclusions. We did not determine certainty of evidence for non-prioritized outcomes.

RESULTS

LITERATURE FLOW AND OVERVIEW

Of 9,871 unique records screened, 78 studies were accepted for full-text review. Upon reviewing these, 20 studies[28-47] were eligible (Figure1). The most common reasons for exclusion included records without additional outcomes of interest (*N* = 24), systematic reviews (*N* = 19), and not an intervention of interest (*N* = 9). We found no additional studies from the existing systematic reviews.

Figure 1. Literature Flowchart



Notes. *14 studies evaluated HSS and 1 study evaluated supplemental oral NaCl.
Abbreviations. D=design; HF=Heart failure; HSS=hypertonic saline solution; I=intervention; NaCl=sodium chloride; O=outcome; P=population; SR=systematic review.

Twenty studies were included and reported the effectiveness of dietary sodium intake[28,29,31,32 30] (*N* = 5), intravenous HSS with furosemide[33-46] (*N* = 14), or oral NaCl supplementation[47] (*N* = 1*)* for patients hospitalized with ADHF. Table 2 shows the summary characteristics of the eligible studies, Appendix D presents design details, and Appendix E presents baseline characteristics. There were 17 RCTs[28,29,31-33,35,37-43,45-47] and 3 NRCSs.[30,36,44] The 5 studies that evaluated the effectiveness of restricted dietary sodium intake intervention included 381 patients total (4 RCTs *N* = 191[28,29,31,32] and 1 NRCS *N* = 190[30]). Fourteen studies that evaluated the effectiveness of HSS with furosemide included 3,483 patients (13 RCTs *N* = 3,166[33-35,37-43,45-47] and 2 NRCSs *N* = 317[36,44]). One RCT evaluating HSS with furosemide conducted in Italy was large (*N* = 1,927).[37] One RCT (*N* = 65) compared oral NaCl with furosemide to furosemide alone and was included in the synthesis of the HSS studies.[47] Two studies[30,44] were published as conference abstracts. The majority of the studies were conducted in Europe (*N* = 9),[33-39,44,45] followed by South America (N = 5),[28,29,31,32,40] Asia (*N* = 3),[30,41,43] the Middle East (*N* = 2),[42,46] and the US (*N* = 1).[47]

Appendix F.1 describes the dietary sodium restriction interventions and Appendix F.2 describes the sodium supplementation with furosemide interventions. Appendix G presents categorical outcomes and Appendix H presents continuous outcomes.

Table 2. Summary Characteristics of Eligible Studies

Characteristics	Restricted Dietary Sodium Intake (*N* = 5)	Supplemental Sodium Intake[a] (*N* = 15)
Design		
RCT (*N* = 16)	4	13
NRCS (*N* = 3)	1	2[b]
Risk of Bias		
Low (*N* = 9)	2	8
Moderate (*N* = 4)	1	3
High (*N* = 6)	2	4
Countries		
Brazil (*N* = 5)	4	1
China (*N = 1)*	--	1
France (*N* = 1)	--	1
Italy (*N = 8*)	--	8
Iran (*N* = 1)	--	1
Japan (*N* = 2)	1	1
Turkey (*N* = 1)	--	1
United States (*N* = 1)	--	1
Interventions		
Restricted prescribed sodium diet (*N* = 5)	5	--
Hypertonic saline solution with IV furosemide (*N* = 14)	--	14
Oral NaCl tablets with IV furosemide (*N* = 1)	--	1
Intermediate Measures		
Aldosterone (*N* = 4)	1	3
BNP (*N* = 9)	2	7

Characteristics	Restricted Dietary Sodium Intake (*N* = 5)	Supplemental Sodium Intake[a] (*N* = 15)
Caloric intake[c] (*N* = 2)	2	--
Diuretics dose during hospitalization (*N* = 4)	3	1
Fluid intake (*N* = 1)	1	--
Kidney function (creatinine[d]) (*N* = 14)	3	11
Kidney function (blood urea nitrogen) (*N* = 15)	3	12
Kidney function (eGFR) (*N* = 6)	--	6
Kidney function (serum cystatin C) (*N* = 2)	--	2
NT-proBNP (*N* = 4)	1	3
Plasma renin activity (*N* = 2)	1	1
Renin (*N* = 1)	--	1
Serum sodium (*N* = 16)	3	13
Clinical Outcomes		
Clinical congestion score (*N* = 2)	2	--
Composite HF-related symptoms[e] (*N* = 1)	--	1
HF-related symptom (change in NYHA functional class) (*N* =3)	--	3
HF-related symptom (general well-being) (*N* = 1)	1	--
HF-related symptom (shortness of breath[f]) (*N* = 3)	1	2
HF-related symptom (thirst[g]) (*N* = 3)	2	1
All-cause mortality[h] (*N* = 8)	4	4
Percent of patients received diuretics in hospital (*N* = 2)	2	NA
Time on IV diuretics[i] (*N* = 2)	2	NA
Time to clinical stability (*N* = 1)	1	--
Urine output (*N* = 13)	1	12
Weight change (*N* = 18)	4	14
Adherence Outcomes		
Adherence to prescribed interventions (*N* = 2)	2	NA
Health Service Utilization Outcomes		
Length of hospital stay (*N* = 14)	3	11
Readmission (HF-related or all-cause) (*N* = 5)	3	2
Transfer to ICU (*N* = 1)	--	1

Notes. [a] 14 studies evaluated HSS and 1 study evaluated supplemental oral NaCl; [b] One retrospective and 1 prospective NRCS; [c] One NRCS reported the incidence of low caloric intakes (caloric intakes less than 20 kcal/kg per day); [d] One NRCS reported worsening of renal function, represented by an increase in serum creatinine ≥0.3 mg/dL; [e] Composite includes dyspnea, lower edema, weakness, palpitation and fatigue; [f] One RCT reported perceived dyspnea using visual analogue scale in dietary sodium interventions; [g] Perceived thirst using visual analogue scale or Thirst Distress Scale for Heart Failure (TDS-HF); [h] Reported in-hospital and at 30-day follow up; [i] The time to transition from IV to oral diuretic therapy.
Abbreviations. BNP=brain (or B-type) natriuretic peptide; eGFR=Estimated Glomerular Filtration Rate; HF=heart failure; HSS=hypertonic saline solution; ICU=intensive care unit; IV=intravenous; N=number; NA=not applicable (not an outcome of interest for supplemental NaCl interventions), NRCS=non-randomized comparative studies; NT-proBNP=N-terminal pro-brain (or B-type) natriuretic peptide; RCT=randomized clinical trials.

RESTRICTED DIETARY SODIUM INTAKE

Five studies (4 RCTs and 1 NRCS) conducted between 2008 and 2016 involving 381 analyzed participants (243 intervention, 138 control) compared a low sodium diet to higher sodium diet

(unrestricted in 4 studies).[28-32] All 5 studies had similar inclusion and exclusion criteria (Appendix D).

The 4 RCTs were all conducted in Brazil in a single-center hospital setting.[28,29,31,32] Patients in the RCTs were, on average, from 54 to 72.3 years old (Appendix E).[28,29,31,32] Most participants (in 3 of the 4 RCTs with data) were male (56.3–69%).[28,29,32] Only 2 RCTs reported data on race/ethnicity, with White participants making up 81% and 84% of the study samples (no data on other patients).[29,31] Three of the RCTs reported patient HF classification at baseline on the New York Heart Association (NYHA) scale, with 9.5% of patients being classified as NYHA Class II in 1 study,[31] 47% and 50.9% as NYHA Class III in 2 studies,[29,31] and 39.6% and 45% as NYHA Class IV in 2 studies.[29,31] One RCT reported baseline NYHA classification for patients randomized to the low sodium group only, with 28.6% and 71.4% of participants classified as NYHA Classes III and IV, respectively.[28] Three RCTs reported mean (SD) of left ventricular ejection fraction (LVEF) at baseline from 26.0% (8.7) to 60.9% (7.5),[29,31,32] and 1 study reported mean (SD) of left ventricle end-diastolic diameter (LVEDD) 63.2% (12.2).[32]

The single NRCS ($N = 190$) was conducted in Japan, included participants with a median age of 79 years, did not report information on race/ethnicity, and 100% of participants were classified as NYHA II-IV at baseline.[30]

Although it was not possible to blind participants or personnel, all the RCTs studies had independent outcome assessors. One of the RCTs was, in fact, "quasi-randomized" in that it allocated patients based on medical record number. It was downgraded for high risk of bias randomization and allocation concealment (Appendix C).[28] Another RCT was also judged to be at high risk of bias because of incomplete outcome data due to missing follow-up data.[32] The NRCS was presented in a conference abstract,[30] reported minimal methodological details, and was at moderate risk of bias.

Appendix F.1 describes the dietary sodium interventions. Prescribed sodium intake in the intervention groups ranged from a maximum of 0.8 g/day (in 3 studies) to 2.4 g/day (the NRCS). Sodium intake in higher sodium groups (*ie*, control) ranged from 2.8 g/day to 3-5 g/day. Two studies restricted fluid intake in both intervention and higher sodium diet groups (ranging from 800 mL/day and 1000 mL/day),[28,32] and 2 studies did not indicate any fluid restriction in both intervention and higher sodium diet groups.[29,31] In 2 studies, fluid intake did not differ between the intervention and control groups.[28,32] Two studies described implementing a restricted diet until discharge or hospital day 7 (whichever came first),[29,31] and in 1 study, patients received a restricted diet until hospital day 7 unless there was a clinical indication to end it early.[32] Two of the studies did not report the duration of the intervention.[28,32]

EFFECT OF RESTRICTED DIETARY SODIUM

In summary (Table 3), there was no statistically significant difference in serum creatinine (moderate confidence) or BNP (low confidence) between a low sodium and a higher sodium diet. Fewer calories were consumed by patients on a low sodium diet compared with a higher sodium diet (low confidence). There were no significant differences in clinical congestion score (moderate confidence), 30-day readmission, and length of stay between a low sodium diet and higher sodium diet (low confidence). Studies provided insufficient evidence (no conclusion) for

effects on NT-pro BNP, weight loss, and mortality, due to imprecise estimates and very serious methodological limitations.

Other findings (certainty of evidence not assessed) included no statistically significant difference in blood urea nitrogen, urine output, prescribed diuretics or dose of diuretics, serum sodium, aldosterone, or PRA for patients on a low sodium diet compared to a higher sodium diet. There was an increase in thirst but no difference in shortness of breath and general well-being for patients on a low sodium diet compared to a higher sodium diet. There was no difference in days to compensation. Patients were adherent to the prescribed sodium diet. No study reported data on estimated glomerular filtration rate (eGFR) or serum cystatin C.

Table 3. Summary of Findings for Restricted Dietary Sodium Interventions

Outcome	Studies (Patients); Design	Methodological Limitations	Indirectness	Imprecision	Inconsistency	Other Issues	Overall Confidence	Summary of Findings
Creatinine	3 (159); RCT[29,31,32]	Serious[a]	Direct	Precise	Consistent	None	Moderate	Pooled NMD = 0.08 mg/dL, 95% CI (−0.08, 0.23)
BNP	2 (128); RCT[29,31]	No limitations	Direct	Not precise[c]	Consistent	Sparse data	Low	Net *median* difference = 525 and −13 pg/mL
NT-pro BNP	1 (31); RCT[32]	Very serious[a]	Direct	Not precise[d]	NA	Single Study	Insufficient	No conclusion
Caloric intake	2 (243); RCT[30,31] NCRS[30]	Serious[b]	Direct	Precise	Consistent	Sparse data	Low	Consume <20 kcal/kg/day RR = 3.4, 95% CI [1.70, 6.86]) MD = −4.4 kcal/kg/day, 95% CI (−7.26, −1.53). MD in percent estimate of daily requirement: −16, 95% CI (−6.6, −25.4)
Clinical congestion score	2 (128); RCT[29,31]	No limitations	Direct	Precise	Consistent	Sparse data	Moderate	NMD = −0.5, 95% CI (−1.76, 0.76) and 0.4, 95% CI (−1.6, 2.4)
Weight change	4 (191); RCT[28,29,31,32]	Serious[a,b]	Indirect[e]	Not precise[f]	Serious[g]	None	Insufficient	No conclusion
Mortality (All cause)	4 (191); RCT[28,29,31,32]	Serious[a,b]	Indirect[e]	Not precise[h]	Consistent	Sparse data[i]	Insufficient	No conclusion
Readmission	3 (159); RCT[28,29,31,32]	Serious[a]	Direct	Precise	Serious[j]	None	Low	Pooled RR = 1.07, 95% CI (0.68, 1.69)
Length of hospital stay	3 (159); RCT[29,31,32]	Serious[a]	Direct	Not precise[k]	Consistent	None	Low	Pooled NMD = 3.06 days, 95% CI (−0.61, 6.72)

Notes. [a] One study was high risk of bias due to incomplete outcome data and no intent to treat analysis; [b] One study was moderate risk of bias due to uncertainty about the completeness of the outcome data and selective reporting; [c] One study had a wide IQR at baseline and follow-up for both groups; [d] Wide IQR at baseline and follow-up measures for both groups; [e] Data reported at different time points; [f] At least 1 study had a large SD; [g] Two of 4 studies reported a decrease in weight for higher diet and 2 reported a decrease for low sodium diet; [h] At least 1 study had a wide confidence interval; [I] Only 5 events per group (total events for all participants = 10) across all of the included studies; [j] Two studies reported a lower risk for low sodium diet, and 1 study reported a higher risk for low sodium diet; [k] At least 1 study had a wide confidence interval.

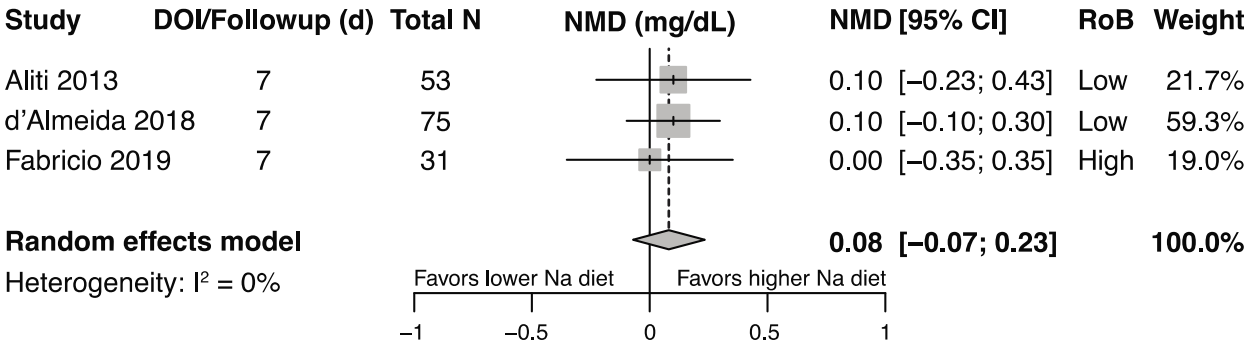
Abbreviations. BNP=brain (or B-type) natriuretic peptide; CI=confidence interval; MD=mean difference; NA=not applicable; NMD=net mean difference; NRCS=non-randomized controlled study; NT-proBNP=N-terminal pro-brain (or B-type) natriuretic peptide; RCT=randomized controlled trial; RR=relative risk.

Intermediate Outcomes

Serum Creatinine

Three RCTs found no significant difference in serum creatinine from baseline to 7 days between the diet intervention arms (pooled NMD = 0.08 mg/dL, 95% CI [−0.07, 0.23]; Figure 2).[29,31,32] The duration of intervention was 7 days in all studies. One RCT (Fabricio et al) yielded a highly imprecise estimate regarding difference in the likelihood that serum creatinine would increase by ≥0.3 mg/dL over 7 days between patients randomized to a low sodium diet of 1.2 g/day Na compared to a higher sodium diet of 2.8 g/day Na (RR = 0.94, 95% CI [0.43, 2.04]).[32] (Note that we use the abbreviation for sodium, Na, when reporting a dose or serum level.)

Figure 2. Serum Creatinine: Low Sodium versus Higher Sodium Diet

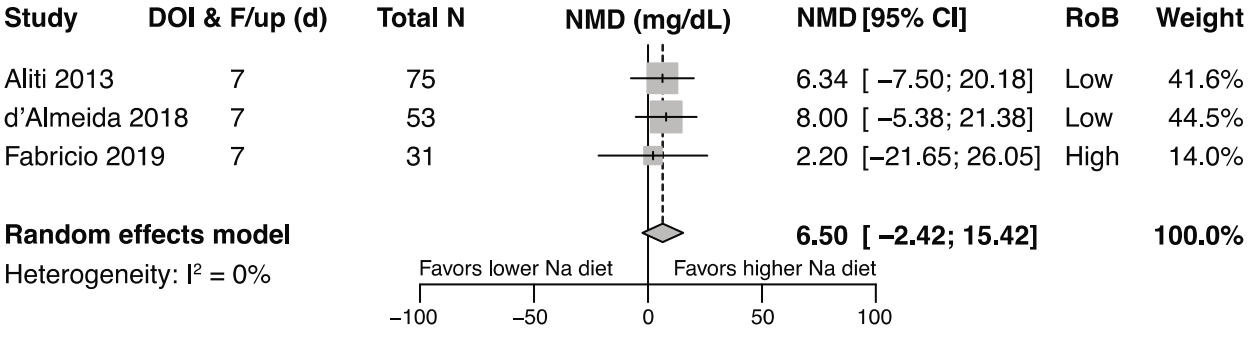


Notes. Net reduction in serum creatinine is considered to be a favorable outcome.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; N=sample size; Na=sodium; NMD=net mean difference; RoB=risk of bias.

Blood Urea Nitrogen (BUN)

Three studies found no significant difference in BUN from baseline to 7 days (the duration of the intervention and follow-up) for patients who received a low sodium diet compared to higher sodium diet (pooled NMD = 6.5 mg/dL, 95% CI [−2.4, 15.4]; Figure 3),[29,31,32] although all 3 studies found a small net increase in BUN among patients on low sodium diets compared with higher sodium diets.

Figure 3. Blood Urea Nitrogen (BUN): Low Sodium versus Higher Sodium Diet



Notes. Net reduction in BUN is considered to be a favorable outcome.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; N=sample size; Na=sodium; NMD=net mean difference; RoB=risk of bias.

Estimated Glomerular Filtration Rate (eGFR) and Serum Cystatin C

No study reported data on eGFR or serum cystatin C.

Natriuretic Proteins (BNP and NT-proBNP)

Two RCTs reported change in BNP from baseline to 7 days or discharge and 1 study reported change in NT-proBNP. One RCT found no significant difference in median BNP from baseline to 7 days between patients on a low sodium diet (0.8 g/day Na) compared to higher sodium diet (~3-5 g/day Na; net *median* difference = 525 pg/mL, $p = 0.51$).[29] A second RCT found no significant difference in median BNP between intervention (0.8 g/day Na) and control arms (~4 g/day Na) from baseline to 7 days (net *median* difference = −13 pg/mL, $p = 0.85$).[31] Finally, 1 RCT found no significant difference in change in serum NT-proBNP between a low (1.2 g/day Na) and higher sodium diet (2.8 g/day Na) groups from baseline to 7 days (net *median* difference = 139 pg/mL, NS).[32]

Weight Change

Four RCTs reported no significant difference in change in weight from baseline to 3 or 7 days.[28,29,31,32] We did not meta-analyze these studies because of the inconsistent time points when weight was reported. One RCT found no significant difference in change in weight from baseline to the primary end point of 3 days (middle of intervention) between the low sodium diet (0.8 g/day Na) and higher sodium diet (~3-5 g/day Na; NMD = 0.3 kg, 95% CI [−1.9, 2.4]).[29] The same study reported no significant difference in weight change from baseline to 7 days (means not reported, $p = 0.12$).[29] A second RCT found no significant difference in mean change in weight from baseline to 3 days and baseline to 7 days ($p > 0.99$ and $p = 0.49$, respectively) between a low sodium diet (0.8 g/d Na) and higher sodium diet (~4 g/day Na).[31] A third RCT found no significant difference in mean change in weight from baseline to 7 days between a low sodium diet (1.2 g/day Na) and higher sodium diet (2.8 g/day Na; NMD = −1.0 kg, 95% CI [−18.2, 16.2]).[32] Finally, the fourth RCT found no significant difference in percent change in weight from baseline to time of compensation (the study did not clearly report mean days to compensation) between patients on a low sodium diet of 0.8 g/day compared to higher sodium diet of 4 g/day (MD = 2.2%, 95% CI [−3.5, 7.9]).[28]

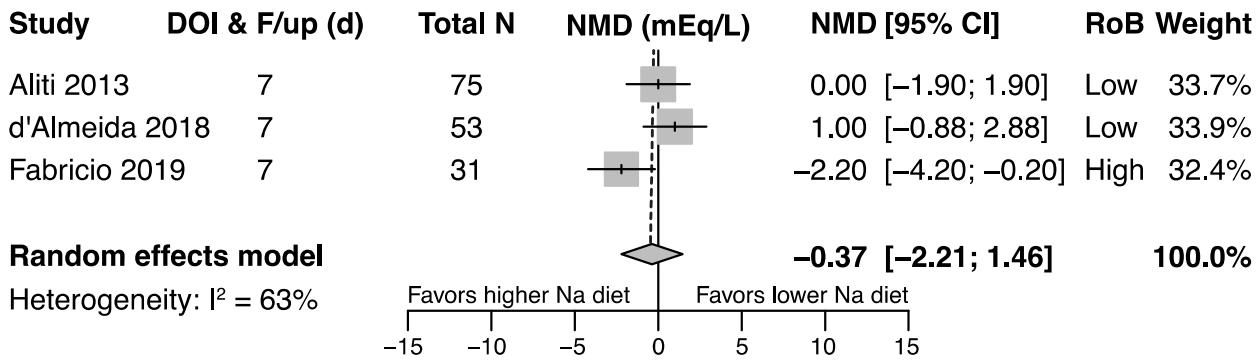
Urine Output

One RCT found no significant difference in urine output between the low sodium diet (1.2 g/day Na) and higher sodium diet (2.8 g/day Na) groups from baseline to 7 days (MD = 1.4 L/24 hr, 95% CI [−0.6, 3.4]).[32]

Serum Sodium

Three RCTs, overall, found no significant difference in serum sodium from baseline to day 7 (duration of intervention and follow-up) between the low and higher sodium arms (pooled NMD = −0.4 mEq/L, 95% CI [−2.2, 1.5]; Figure 4).[29,31,32] One study found a statistically significant, but clinically small, net *decrease* (*ie*, worsening) in serum sodium in the patients given the low sodium diet.[32] The authors hypothesize that the effect of natriuresis caused by the loop diuretics and the restricted sodium intake combined to lower serum sodium levels.

Figure 4. Serum Sodium: Low Sodium versus Higher Sodium Diet



Notes. Net increase in serum sodium is considered to be a favorable outcome.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; N=sample size; Na=sodium; NMD=net mean difference; RoB=risk of bias.

Prescribed Diuretics

Two RCTs reported no significant difference in the proportion of patients who received diuretics while hospitalized between the low sodium diet and higher sodium diet (RR = 0.97, 95% CI [0.89, 1.07] and 1.00, 95% CI [0.83, 1.20]).[29,32]

Three RCTs reported prescribed diuretic dose during the hospitalization.[28,31,32] One RCT reported no significant difference in change in diuretic (furosemide) dose from baseline to 7 day between the low sodium diet of 0.8 g/day Na and higher sodium diet of ~4 g/day Na (NMD = 4.3 mg/day, 95% CI [−12.0, 20.6]).[31] One RCT found no difference in cumulative loop diuretic dose during hospitalization between the low sodium (1.2 g/day Na) and higher sodium diet groups (2.8 g/day Na; MD = 103.5 mg/day, 95% CI [−14.2, 221.2]).[32] One RCT found no difference in daily and cumulative diuretic (furosemide) dose during the compensation period between the low sodium diet 0.8 g/day Na and higher sodium diet of 4 g/day Na (MD = −0.2 mg/day, 95% CI [−0.6, 0.3] and −31.0 mg/day, 95% CI [−265.7, 203.7], respectively).[28] Finally, 2 RCTs found no significant difference in the time to transition from an intravenous to an oral diuretic administration (median difference = 0 days and MD = 0.3 days, 95% CI [−0.86, 1.46]).[29,31]

Nutritional Intake

One NRCS found that the risk of consuming fewer calories (defined as <20 kcal/kg/day) was significantly greater for people who received a low sodium diet (2.4 g/day Na) compared to higher sodium diet (4 g/day Na; RR = 3.4, 95% CI [1.70, 6.86]).[30] The NRCS and an RCT also reported calorie intake as a continuous measure. The NRCS found fewer calories (defined as the percent of estimated daily requirement) were consumed by patients prescribed a low sodium diet compared to those prescribed a higher sodium diet (MD = −16.0%, 95% CI [−6.6, −25.4]).[30] Similarly, an RCT found fewer calories were consumed by patients on a restricted sodium diet (0.8 g/day Na) compared to those on a higher sodium diet (~4 g/day Na; MD = −4.4 kcal/day, 95% CI [−7.3, −1.5]).[31] This RCT also found fewer liquids were consumed over 7 days in the low sodium diet group which also restricted fluids to 800 mL/day compared to those in the higher sodium diet group which did not restrict fluid intake (median difference = −312.7 mL/day, $p < 0.001$).[31]

Other Intermediate Measures

One RCT found no significant difference in aldosterone from baseline to day 7 of admission or discharge between those on a low sodium diet (0.8 g/day Na) compared to higher sodium diet (~4 g/day Na; NMD = 11 pg/mL, $p = 0.85$).[31] Similarly, 1 RCT reported no difference in PRA from baseline to day 7 or discharge in patients on a low sodium diet (0.8 g/day Na) compared to patients on a higher sodium diet (~4 g/day Na; NMD = −0.9 ng/mL/h, $p = 0.42$).[31]

Clinical Outcomes

Clinical Congestion Score

Two RCTs reported clinical congestion scores between the low sodium and higher sodium diet groups from baseline to 3 or 7 days.[29,31] One RCT found no significant difference in scores between the low sodium (0.8 g/day Na) and higher sodium (~3-5 g/day Na) groups from baseline to 3 and 7-days (NMD = −0.6, 95% CI [−2.1, 0.9] at 3 days and −0.5, 95% CI [−1.8, 0.8] at 7 days).[29] A second RCT reported no significant difference in scores from baseline to day 7 of the intervention between the low sodium diet of 0.8 g/day Na and higher sodium diet of ~4 g/day Na (NMD = 0.4, 95% CI [−1.6, 2.4]).[31]

Heart Failure Related Symptoms

Two RCTs evaluated thirst via a 10-point visual analogue scale.[29,31] In both studies, patients randomized to the low sodium diet compared to higher sodium diet reported greater feelings of thirst from baseline to 7-day follow-up.[29,31] An RCT found a significant increase in thirst for patients in the low sodium diet (0.8 g/day Na) compared to higher sodium diet group (~3 to 5 g/day Na; NMD = 1.5, 95% CI [0.4, 2.7], $p = 0.01$).[29] In this study, fluid intake was limited to a maximum of 800 mL/day in the intervention group, while liberal fluid intake of ≥2500 mL/day was allowed in the higher sodium group. Similarly, 1 RCT reported significantly greater perceived thirst during the study period for patients on a diet of 0.8 g/day Na and a restriction of 800 mL/day fluid compared to a diet of ~4 g/day Na and unlimited fluid intake ($p = 0.03$).[31]

One study found no significant difference in shortness of breath and general well-being, both measured by a 10-point visual analogue scale, for patients randomized to a low sodium diet (1.2 g/day Na) compared to higher sodium diet (2.8 g/day Na) from baseline to day 7 (NMD = 0.8, 95% CI [−0.3, 1.9] and 0.6, 95% CI [−0.9, 2.1], respectively).[32]

Mortality

Four studies reported all-cause mortality at different time points.[28,29,31,32] Two RCTs reported no deaths in either group during the 7-day intervention period[29] or during hospitalization.[30] Two RCTs reported 30-day mortality outcomes. The event rates were low in both studies, yielding very imprecise estimates (RR = 0.93, 95% CI [0.15, 5.84][32] and RR = 0.77, 95% CI [0.12, 5.04][31]). One RCT also reported a highly imprecise estimate of mortality *not* related to HF (RR = 1.29, 95% CI [0.09, 18.8], time frame unclear).[28]

Other Clinical Outcomes

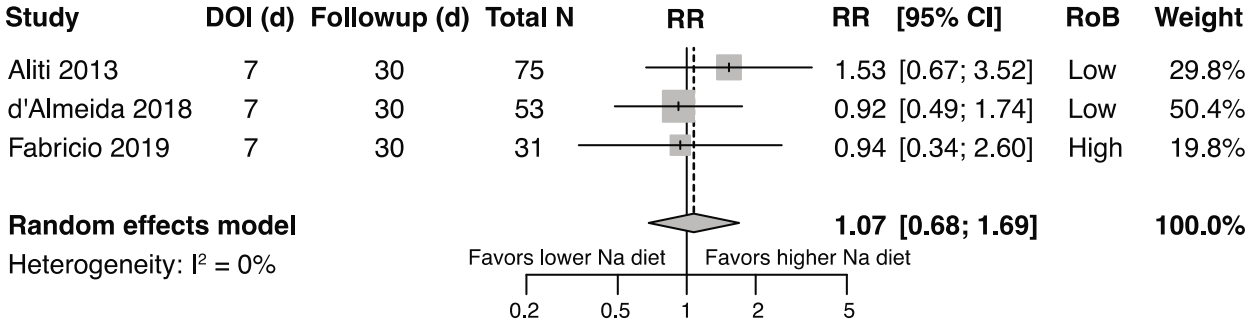
One RCT found no significant difference in days to compensation between a low sodium (0.8g/day Na) and higher sodium diet (4 g/day Na; MD = 0.9, 95% CI [−0.3, 2.1]).[28]

Health Service Utilization Outcomes

Readmission

Three RCTs reported no significant difference in 30-day readmission between patients on a low sodium diet compared to higher sodium diet (pooled RR = 1.07, 95% CI [0.68, 1.69]; Figure 5).[29,31,32] One RCT reported 30-day readmission due to HF,[29] while the other 2 RCTs[31,32] reported all-cause 30-day readmission.

Figure 5. 30-Day Readmission: Low Sodium versus Higher Sodium Diet

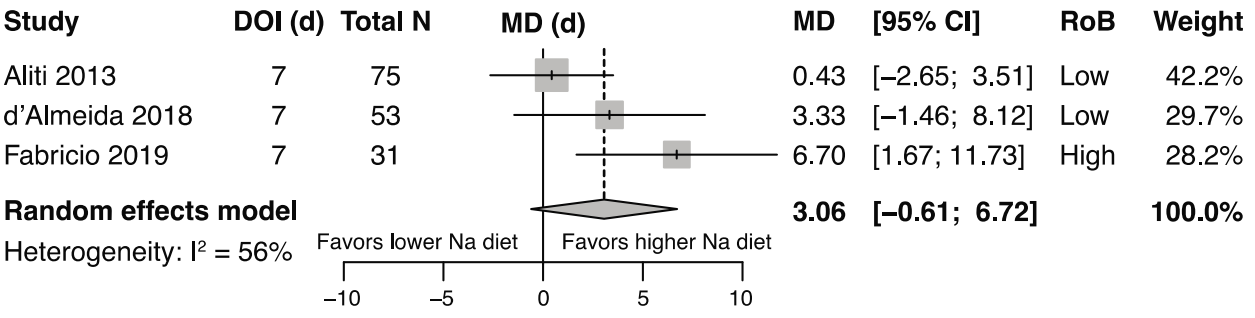


Notes. Lower rate of readmission is considered to be a favorable outcome.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; N=sample size; Na=sodium; RoB=risk of bias; RR=risk ratio.

Length of Hospital Stay

Three RCTs reported a nonsignificant longer length of stay for patients on a low sodium diet compared to the higher sodium diet (pooled MD = 3.1 days, 95% CI [−0.6, 6.7]; Figure 6).[29,31,32] None of the studies, though, provided a hypothesis for why a low sodium diet would increase length of stay. There was a moderate degree of heterogeneity across studies, with differences ranging from 0.4 to 6.7 days.

Figure 6. Length of Hospital Stay: Low Sodium versus Higher Sodium Diet



Notes. Shorter hospital stay is considered to be a favorable outcome.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; N=sample size; Na=sodium; MD=mean difference; RoB=risk of bias.

Adherence

Two RCTs evaluated adherence to the hospital diet by measuring the amount of sodium consumed.[31,32] The 2 RCTs found significantly less sodium was consumed over 7 days by patients who received a low sodium diet compared to higher sodium diet (median difference = −1.3 g/day Na, $p < 0.001$ and MD = −1.5 g/day, 95% CI [−1.7, −1.2]).[31,32] A third RCT found no significant difference in the acceptance of the hospital diet defined as consuming 80% of the entire meal between the low (1.2 g/day Na) and higher sodium diet (2.8 g/day Na; mean 79.6% [14.3] vs 88.1% [12.3], $p = 0.08$).[32]

SUPPLEMENTAL SODIUM INTERVENTIONS (WITH DIURETICS)

Fifteen studies[33-47] including 13 RCTs[33-35,37-39,41-43,45-47] and 2 NRCSs[36,44] (conducted between 1996 and 2022) involving 3,483 participants (1,707 intervention, 1,776 control) evaluated the effectiveness of HSS with diuretics ($N = 14$) or oral NaCl with diuretics ($N = 1$) in patients hospitalized with ADHF. Appendix D shows the design details and Appendix E shows the baseline characteristics of the studies. Nine studies were conducted in Europe,[33-40,44,45] 2 in Asia,[41,43] 2 in the Middle East,[42,46] 1 in the US,[47] and 1 in South America.[40] Most studies were conducted in single-center hospitals,[34,36-46] but 2 studies did not report the hospital settings.[33,35] The mean age of patients ranged from 47 to 76 years. The percentage of male population ranged from 38.3% to 81.3% and males were the minority in only 2 studies. Only 1 study, which was conducted in the US, reported data on race/ethnicity (86% White and 14% Black or African American). In 11 studies,[33-35,37-40,42,43,45] mean (SD) of left ventricular ejection fraction (LVEF) at baseline ranged from 23.9% (6.3) to 56.4% (10.6), and 2 studies[36,41] reported median (IQR) of LVEF at baseline [(34.5) (26.5, 41) and 37 (28.5, 42.5)]. Mean (SD) of LVEDD 71.6 mm (9.7) was reported in 1 study.[40]

In 1 RCT, an independent physician assigned patients to treatment groups, and 1 RCT had major discrepancies within the text and poor methodological reporting of outcome definitions (therefore both are high risk of bias).[35,43] Three RCTs had moderate risk of bias due to concerns over the method of allocation concealment and blinding.[33,45,46] Finally, 2 NRCSs had high risk of bias because they either conducted crude unadjusted analyses or did not report a method to address confouding.[36,44]

Appendix F.2 describes the sodium supplementation interventions including saline solution, sodium dose, diuretics, fluid intake, other intervention (*eg*, dietary sodium), and duration of interventions. In 7 studies, the concentration of HSS (between 1.4% and 4.6% NaCl) was tailored based on the patients' serum sodium levels.[33-37,39,45] In 6 studies,[38,40-42,46] HSS concentration was fixed (ranging from 1.94% to 7.5% NaCl). One study used compound HSS (NaCl 2.8%, KCl 0.2%, and $MgSO_4$ 0.9%)[43] and 1 study did not report concentration of HSS.[44] One study (conducted in the US) used an oral NaCl formulation to replicate neurohormonal effects of HSS intervention and for easy administration to the study population.[47] Dietary sodium intake was reported in 11 studies during the intervention period.[33-39,41,43,45,47] Total sodium intake (calculated by the research team from all sources including diet) in the supplemental sodium arms ranged from 1.15 to 8.1 g/day, and in furosemide alone arms ranged from 0.7 g/d to 2.9 g/d. All but 1 study (a conference abstract) explicitly noted that HSS or oral sodium was combined with furosemide. In 9 studies sodium supplementation was combined with a conventional dose of furosemide (≤250 mg/d),[37-39,41-43,45-47] in 3 studies HSS was combined with high doses of furosemide (500-1000 mg/d),[33-35] and 1 study combined HSS with 125-1000 mg of furosemide.[36]

Ten studies compared supplemental sodium with furosemide to furosemide alone,[33-37,39,42,43,45,47] 3 studies compared HSS with furosemide to furosemide with normal saline,[38,40,46] 1 study compared HSS with furosemide to furosemide with glucose (5%),[41] and 1 study did not report whether patients in the comparison arm received furosemide.[44] Intervention durations varied across the studies (ranging from 1 day to 12 days), and 3 studies did not clearly define or report the duration of intervention period.[37,39,44]

In summary (Table 4), there were significant net decreases in creatinine, BNP, and weight from admission to last in-hospital measurement for patients administered supplemental sodium and furosemide compared to furosemide alone (low confidence for BNP and moderate confidence for others). Hospital length of stay was shorter for patients who received supplemental sodium (moderate confidence). There was no significant difference in NT-pro BNP (low confidence). Studies provide insufficient evidence (no conclusion) for mortality and 30-day readmission, and the studies did not report calorie intake or clinical congestion score.

For other outcomes (certainty of evidence not assessed), there was a significant net decrease in BUN; a significant net increase in eGFR, urine output, and serum sodium; and no significant difference in cystatin C, aldosterone, or PRA for patients administered supplemental sodium and furosemide compared to furosemide alone. Patients who received supplemental sodium with furosemide had a greater likelihood of improving on the NYHA functional class from admission to discharge. Two studies had conflicting findings related to dyspnea. Two RCTs found that fewer patients who were administered HSS and furosemide experienced dyspnea. One RCT, though, found no difference in a composite measure of clinical symptoms (dyspnea, lower limb edema, weakness, palpitations, and fatigue) at discharge between groups. One RCT found a reduction in thirst at the end of the 4 day intervention. Finally, 1 RCT found no difference in intensive care unit admissions.

Table 4. Summary of Findings for Supplemental Sodium Interventions

Outcome	Studies (Patients); Design	Methodological Limitations	Indirectness	Imprecision	Inconsistency	Other Issues	Overall Confidence	Summary of Findings
Creatinine	11 (2,766); RCT[33-35,37-42,46,47]	No limitations	Indirect[a]	Precise	Consistent	None	Moderate	Pooled NMD = −0.38 mg/dL, 95% CI (−0.54, −0.22)
BNP	7 (2,848); 6 RCT[35,37-40,43] and 1 NRCS[36]	Serious limitations[b,c,d]	Indirect[a]	Precise	Consistent	Sparse data	Low	Pooled NMD = −62.84 pg/mL, 95% CI (−103.61, −22.08)
NT-pro BNP	3 (235); RCT[41,45,47]	Serious limitations[e]	Indirect[a]	Imprecise[f]	Consistent	Sparse data[g]	Low	Pooled NMD = −1614.17 pg/mL, 95% CI (−3581.66, 353.31)
Caloric intake	0	NA	NA	NA	NA	NA	NA	No evidence
Clinical congestion score	0	NA	NA	NA	NA	NA	NA	No evidence
Weight change	14 (3,333); 13 RCTs[33-35,37-43,45-47] and 1 NCRS[44]	No limitations	Indirect[a]	Precise	Consistent[h]	None	Moderate	Pooled NMD = −2.66 kg, 95% CI (−4.70, −0.62)
Mortality (all cause)	4 (2,317); RCT[35,37,40,43]	Serious limitations[b]	Indirect[a]	Imprecise	Inconsistent[i]	Sparse data	Insufficient	No conclusion
Readmission	2 (159); RCT[35,47]	Serious limitations[b]	Direct	Precise	Inconsistent[j]	None	Insufficient	No conclusion
Length of hospital stay	11 (3,243); 9 RCTs[33-35,37-39,42,44,47] and 2 NRCS[36,44]	Serious limitations[b, c, k]	Direct	Precise	Consistent	Large effect[l]	Moderate	Pooled NMD = −2.90 days, 95% CI (−4.02, −1.79

Notes. [a] Studies reported outcomes at different time points; [b] One RCT was high risk of bias due to randomization decided by an independent physician and no allocation concealment, [c] One RCT was high risk of bias due to outcome not clearly being defined and uncertainty about blinding; [d] One NRCS was high risk of bias because treatment and comparison groups were matched by age and sex and no adjusted comparisons; [e] One RCT was moderate risk of bias due to no blinding of participants and personnel and unclear allocation concealment; [f] One RCT reported significant net decrease in NT-proBNP and 2 RCTs reported non-significant decrease in outcome result; [g] Two RCTs reported outcome in median (IQR) and 1 RCT reported outcome in mean (SD); [h] One RCT reported a small weight gain (0.12 kq) in HSS group after 24-hr HSS intervention compared to furosemide alone while the remaining RCTs reported weight loss; [I] Two RCTs reported no death during hospitalization, 1 RCT reported greater mortality risk in HSS group during hospitalization, and 1 RCT reported higher mortality risk in control group at 30-day follow-up; [j] 1 RCT found reduction in 30-day readmission and another RCT found no difference in 30-day readmission outcome; [k] 1 RCT was moderate risk of bias due to no blinding and incomplete outcome data; [l] 1 NRCS being an outlier of longer length of stay in HSS group after the intervention.
Abbreviations. BNP=brain (or B-type) natriuretic peptide; CI=confidence interval; kg=kilogram; NA=not applicable; NMD=net mean difference; NRCS=non-randomized controlled trial; NT-proBNP=N-terminal pro-brain (or B-type) natriuretic peptide; RCT=randomized controlled trial; RR=relative risk.

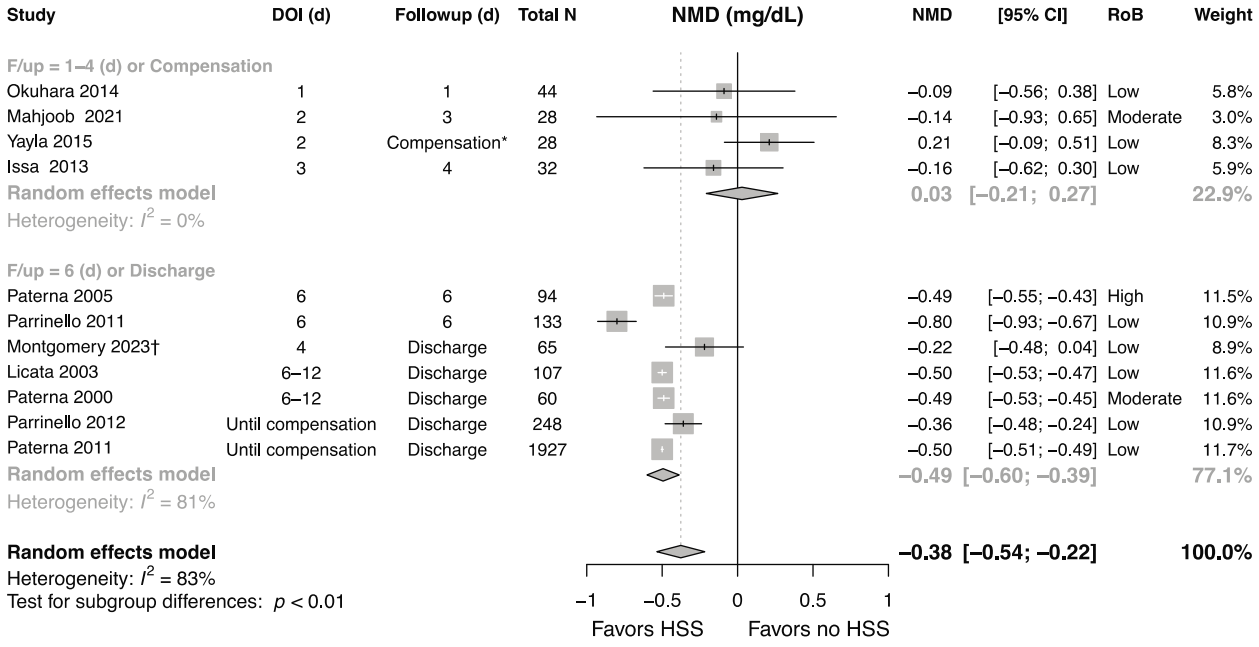
Intermediate Outcomes

Serum Creatinine

Eleven RCTs[33-35,37-42,46,47] found a significant net decrease in serum creatinine from baseline to the last in-hospital measurement for patients randomized to HSS or oral NaCl with furosemide compared to furosemide alone (pooled NMD = −0.38 mg/dL, 95% CI [−0.54, −0.22]; Figure 7). Duration of intervention varied among studies (from 1 to 6 or more days, or until compensation), as did the timing of the last in-hospital measurement (24 hours to 6 days or discharge).

Meta-analysis revealed statistical heterogeneity in NMDs across studies. As shown in Figure 7, studies with shorter durations of intervention (1-3 days), which also had shorter duration of follow-up (1 to 4 days or compensation), found no difference in NMD for serum creatinine (pooled NMD = 0.03 mg/dL, 95% CI [−0.21, 0.27]), but after about 4 or 6 or more days of treatment and follow-up, serum creatinine levels were significantly lower in the sodium supplementation group (pooled NMD = −0.49 mg/dL, 95% CI [−0.60, −0.39]). The NMD was significantly greater in longer duration studies than shorter duration studies ($p < 0.001$).

Figure 7. Serum Creatinine: Supplemental Sodium (With Furosemide) versus Furosemide



Notes. Net reduction in serum creatinine is considered to be a favorable outcome.
* Time to compensation; † Compared oral NaCl with furosemide to furosemide alone.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; N=sample size; NMD=net mean difference; RoB=risk of bias.

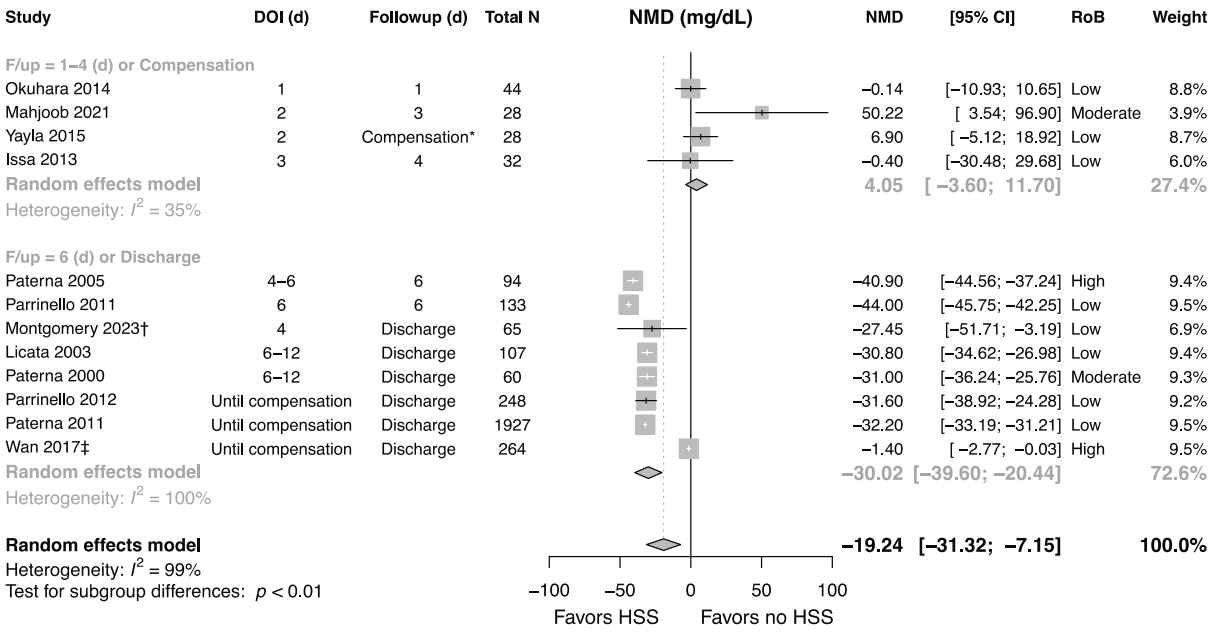
Blood Urea Nitrogen (BUN)

Twelve RCTs found a significant net decrease in BUN from baseline to last reported in-hospital measurement (24 hours or 6 days or discharge) for patients randomized to supplemental sodium with furosemide compared to furosemide alone (pooled NMD = −19.2 mg/dL, 95% CI [−31.3, −7.2]; Figure 8).[33-35,37-43,46,47] Mahjoob et al was the only study to report a large, statistically

significant effect that favored furosemide alone (NMD = 50.2 mg/dL, 95% CI [3.5, 96.9]).[46] In this study, patients were randomized to either HSS with furosemide or furosemide alone for 48 hours. The study did not offer an explanation for why BUN may have risen to such a degree. A *post hoc* sensitivity analysis excluding Mahjoob et al did not alter the conclusion (pooled NMD = −22.3 mg/dL, 95% CI [−33.2, −11.3]).

Meta-analysis revealed statistical heterogeneity in NMDs across studies. As shown in Figure 8, similar to serum creatinine, studies with shorter durations of intervention (1-3 days), which also had shorter duration of follow-up (1 to 4 days or compensation), found no difference in NMD for BUN levels (pooled NMD = 4.1 mg/dL, 95% CI [−3.6, 11.7]), but after about 4 or 6 or more days of treatment and follow-up, BUN levels were significantly lower in the sodium supplementation group (pooled NMD = −30.0 mg/dL, 95% CI [−39.6, −20.4]). Excluding the 1 outlier longer-term study with no effect (Wan et al) in a post hoc sensitivity analysis yielded an even greater, more precise NMD (pooled NMD = −21.2 mg/dL, 95% CI [−33.8, −8.5]). With or without Wan et al, the NMD was significantly greater in longer duration studies than shorter duration studies ($p < 0.01$).

Figure 8. Blood Urea Nitrogen (BUN): Supplemental Sodium (With Furosemide) versus Furosemide



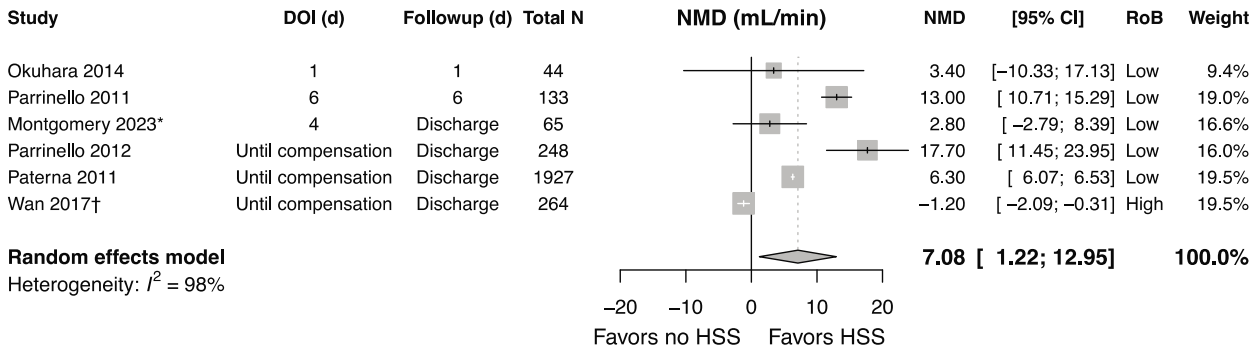
Notes. Net reduction in serum BUN is considered to be a favorable outcome.
* Time to compensation. † Compared oral NaCl with furosemide to furosemide alone; ‡ Potential outlier among longer-duration studies; excluded in a post hoc sensitivity analysis of the subgroup.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; N=sample size; NMD=net mean difference; RoB=risk of bias.

Estimated Glomerular Filtration Rate (eGFR)

Six RCTs reported a significant net increase in eGFR from baseline to last in-hospital measurement (24 hours to 6 days or discharge) for patients randomized to HSS or oral NaCl with furosemide compared to furosemide alone (pooled NMD = 7.1 mL/min, 95% CI [1.2, 13.0]; Figure 9).[37-39,41,43,47] Statistical heterogeneity was very large across studies, but no clear

explanation was found. The single short duration study (1 day) did not differ from longer duration studies. Wan et al was the only study to report a small and significant net decrease in eGFR for patients who received HSS with furosemide compared to furosemide alone (NMD = −1.2 mL/min, 95% CI [−2.1, −0.3). This study had major discrepancies between text and tables and unclear outcome definitions (high risk of bias). A post hoc sensitivity analysis excluding Wan et al yielded a larger and more precise effect relative to the main analysis (pooled NMD = 9.2 mL/min, 95% CI [3.7, 14.7]; I^2 = 91%), although heterogeneity remained comparable to the main analysis.

Figure 9. Estimated Glomerular Filtration Rate (eGFR): Supplemental Sodium (With Furosemide) versus Furosemide



Notes. Net increase in eGFR is considered to be a favorable outcome.
* Compared oral NaCl with furosemide to furosemide alone; † Wan 2017 was excluded in post hoc sensitivity analysis.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; HSS=hypertonic saline solution (or oral sodium with furosemide); N=sample size; NMD=net mean difference; RoB=risk of bias.

Serum Cystatin C

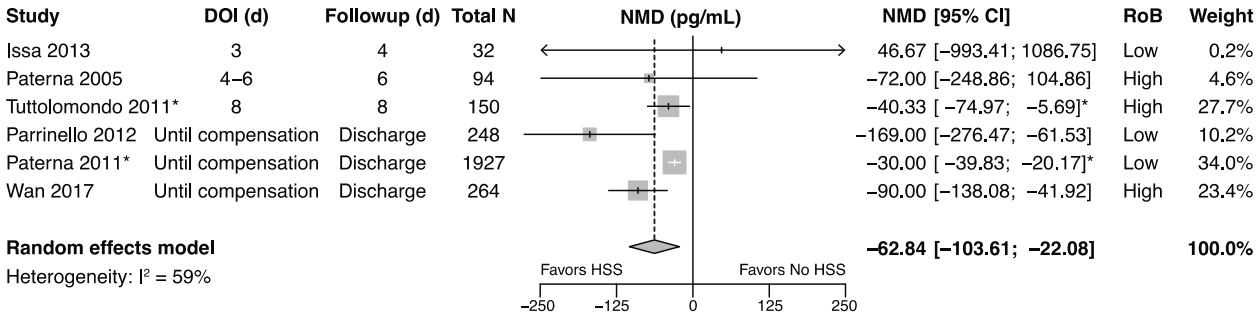
Two RCTs found no significant difference in serum cystatin C between HSS and furosemide from baseline to last in-hospital measurement.[40,41] One RCT found no significant difference in serum cystatin C between HSS with furosemide and furosemide alone from baseline to day 4, which was 24 hours after the intervention period (NMD = −0.15 mg/L, 95% CI [−0.50, 0.20]).[40] Similarly, a second RCT found no significant difference in serum cystatin C between HSS with furosemide to furosemide with glucose (5%) from baseline to the end of 24-hour intervention (NMD = −0.10 mg/L, 95% CI [−0.65, 0.45]).[41]

Natriuretic Proteins (BNP and NT-proBNP)

Seven studies in total reported on BNP; however, only 4 reported BNP at baseline and follow-up,[35,39,40,43] while 2 studies only reported BNP at follow-up[36,37] and 1 study graphically reported BNP (means were not extracted).[38] Across 6 studies reporting extractable data, there was a significant net decrease in BNP among patients who received HSS with furosemide compared to furosemide alone (pooled NMD = −62.8 pg/mL, 95% CI [−103.6, −22.1]; Figure 10).[35-37,39,40,43] One RCT graphically reported a decrease in BNP from baseline to 6 days for patients who received HSS with furosemide compared to furosemide alone ($p < 0.001$). In a post hoc sensitivity analysis with the 4 studies reporting baseline and follow-up data, the net effect was greater and remained statistically significant (pooled NMD = −103.3 pg/mL, 95% CI [−151.8,

−54.8]; I^2 = 0%). The shorter duration studies were imprecise and thus did not clearly differ in findings from longer duration studies.

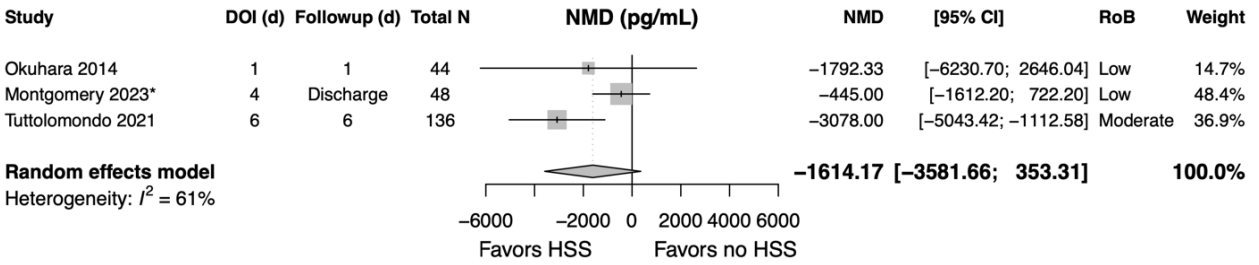
Figure 10. BNP: Supplemental Sodium (With Furosemide) versus Furosemide



Notes. Net reduction in BNP is considered to be a favorable outcome.
* Mean difference at follow-up time point (no baseline data reported). Excluded from post hoc sensitivity analysis.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; N=sample size; NMD=net mean difference; RoB=risk of bias.

Three RCTs found no significant difference in NT-proBNP from baseline to last in-hospital measurement (pooled NMD = −1614.2 pg/mL, 95% CI [−3581.7, 353.3]; Figure 11).[41,45,47] The last in-hospital measurement varied between 1 to 6 days or discharge. One RCT found a significant net decrease in NT-pro BNP between HSS with furosemide compared to furosemide alone from baseline to the end of 6-day intervention period (NMD = −3078.0 pg/mL, 95% CI [−5043.4, −1112.6]).[45] The remaining 2 RCTs found nonsignificant net decreases in NT-pro BNP between either HSS or oral NaCl and furosemide compared to furosemide alone.[41,47]

Figure 11. NT-proBNP: Supplemental Sodium (With Furosemide) versus Furosemide



Notes. Net reduction in NT-proBNP is considered to be a favorable outcome.
* Compared oral NaCl with furosemide to furosemide alone.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; HSS=hypertonic saline solution (or oral sodium with furosemide); N=sample size, NMD=net mean difference, RoB=risk of bias.

Weight

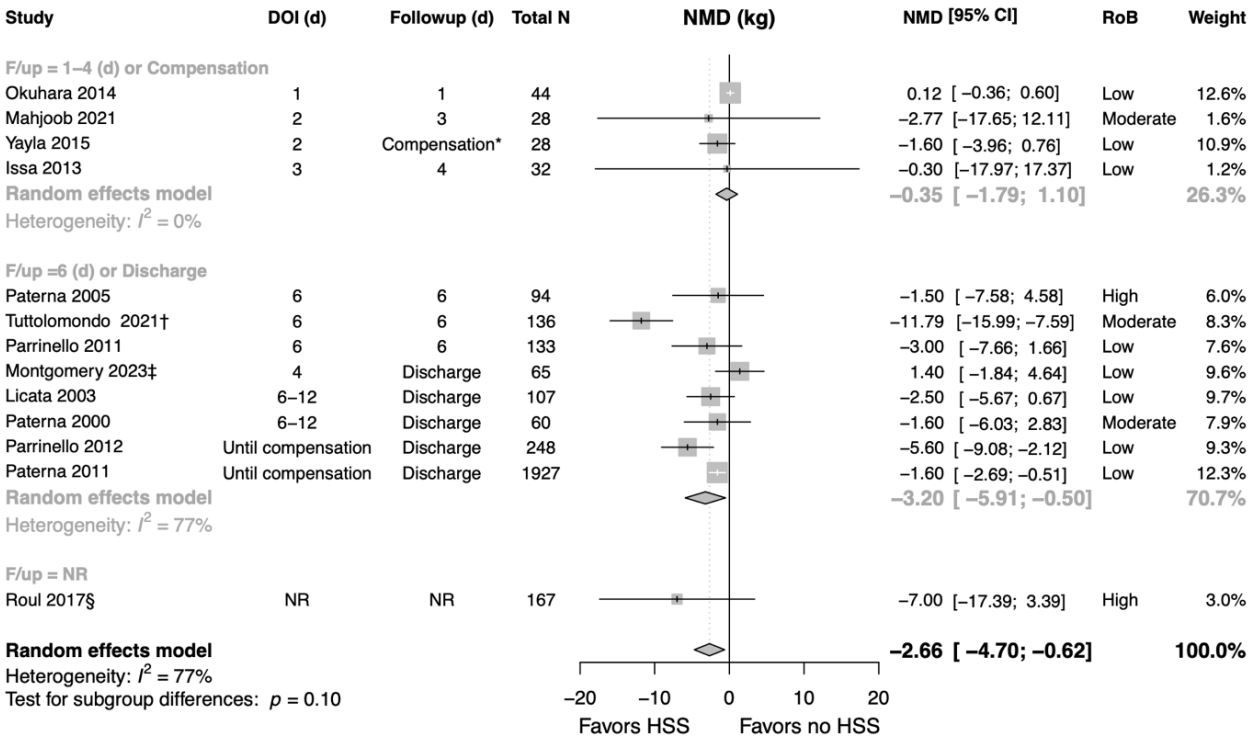
Fourteen studies (13 RCTs[33-35,37-43,45-47] and 1 NRCS[44]) reported change in body weight from baseline to in-hospital follow up (3 to 6 days or discharge). Wan et al presented weight data that was inconsistent with adult patients (*eg*, 23.44 kg mean weight at baseline) and was excluded from meta-analyses.[43] Roul et al reported median weight without data to allow an estimate of variance (net median difference = −7 kg), so we used the median SD from the other 11 RCTs in

the meta-analysis. In pooled data from 13 studies,[33-35,37-42,45-47] there was a significant net decrease in weight from baseline to last in-hospital measurement for patients who received supplemental sodium with furosemide compared to furosemide alone (pooled NMD = −2.7 kg, 95% CI [−4.7, −0.6]; Figure 12).

Meta-analysis revealed statistical heterogeneity in NMDs across studies. As shown in Figure 12, studies with shorter durations of intervention (1-3 days), which also had shorter duration of follow-up (1 to 4 days or compensation), found no difference in NMD for weight (pooled NMD = 0.4 kg, 95% CI [−1.8, 1.1]), but after about 4 or 6 or more days of treatment and follow-up, weight changes were significantly greater in the sodium supplementation group (pooled NMD = −3.2 kg, 95% CI [−5.9, −0.5]). The NMD was not significantly greater in longer duration studies than shorter duration studies ($p = 0.10$).

Montgomery et al compared oral NaCl with furosemide to furosemide alone and was the only study to report an increase in weight, but the effect size was small and nonsignificant. In a post hoc sensitivity analysis, we excluded Roul et al (for which we estimated the SD) and the pooled NMD was minimally changed (pooled NMD = −2.5 kg, 95% CI [−4.6, −0.5]). In another post hoc sensitivity analysis, we excluded Tuttolomondo 2021 et al, which reported a much larger reduction in weight than the other studies. The net effect remained statistically significant, but with a substantially smaller effect size (pooled NMD = −1.5 kg, 95% CI [−2.7, −0.3]; $I^2 = 56\%$).

Figure 12. Weight: Supplemental Sodium (With Furosemide) versus Furosemide

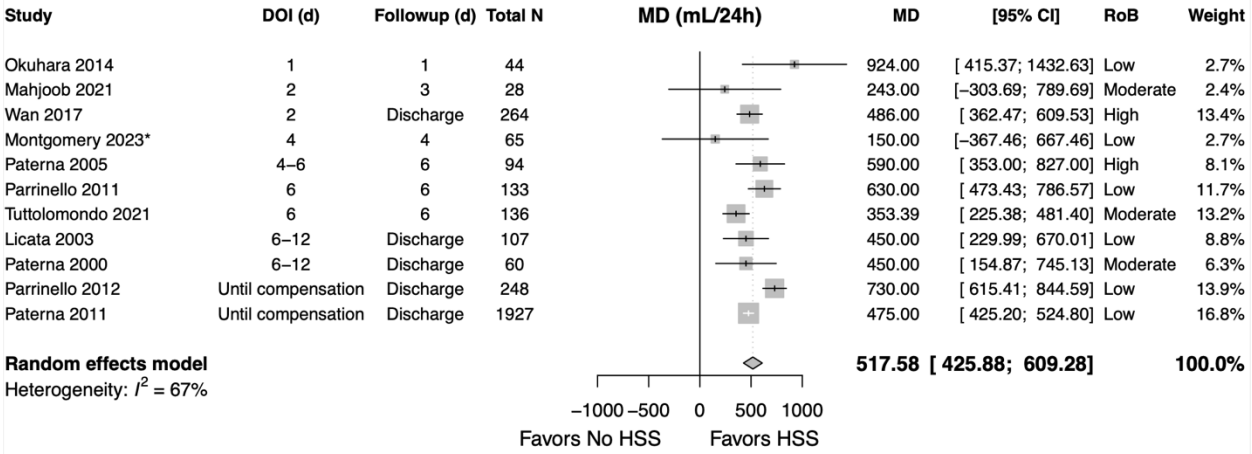


Notes. Net reduction in weight is considered to be a favorable outcome.
* Time to compensation; † Compared oral NaCl with furosemide to furosemide alone; ‡ Potential outlier. Excluded in a post hoc sensitivity analysis; § NMD and 95% CI estimated from reported median data. Excluded in a post hoc sensitivity analysis.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; HSS=hypertonic saline solution (or oral sodium with furosemide); N=sample size; NMD=net mean difference; RoB=risk of bias.

Urine Output

Twelve RCTs reported urine output at various periods of follow-up (24 hours to 4 days or 6 days or discharge).[33-35,37-41,43,45-47] Most reported average daily (24 hour) urine output for the duration of follow-up. One study (Issa et al) reported only urine output (per kg per hour) on selected days and was excluded from meta-analyses.[40] Meta-analysis of the 11 RCTs that reported average daily urine output (or equivalent data) found a clinically large, statistically significant greater urine output in the sodium supplementation with furosemide groups (pooled MD = 517.6 mL/24 hr, 95% CI [425.9, 609.3]; Figure 13). Although there was some heterogeneity in the estimate of the MD, the studies were consistent in finding favorable effects of sodium supplementation with furosemide, which were mostly clinically large and statistically significant. The study by Issa et al, which reported day-specific data for 3 days plus 24 hours post-intervention, in contrast found a nonsignificant, small effect ($p = 0.07$). If we assume that their reported data represent the full duration of follow-up for all patients, then the estimated MD was 43.6 mL/24 hr (95% CI [−3.6, 90.8]). Including this in the meta-analysis would reduce the pooled MD to 459.4 mL/24 hr (95% CI [327.0, 591.8]).

Figure 13. Urine Output: Supplemental Sodium (With Furosemide) versus Furosemide



Notes. Net increase in urine output is considered to be a favorable outcome. * Compared oral NaCl with furosemide to furosemide alone.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; N=sample size; NMD=net mean difference; RoB=risk of bias.

Caloric Intake

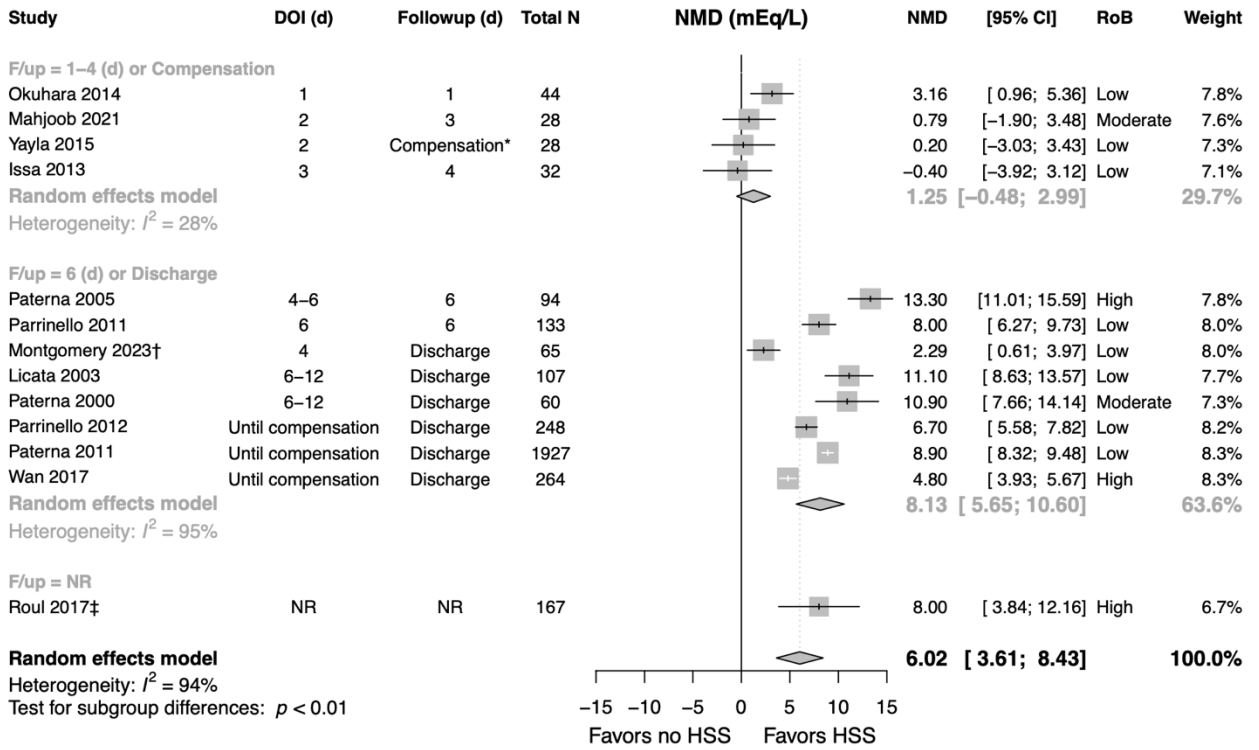
No study reported data on caloric or fluid intake.

Serum Sodium

Thirteen studies (12 RCTs[33-35,37-43,46,47] and 1 NRCS[44]) evaluated serum sodium at baseline and at the end of intervention or discharge. Pooled data from 13 studies found a significant net increase in serum sodium from baseline to last in-hospital measurement (24 hours to 6 days or discharge) for patients who received sodium supplementation with furosemide compared to furosemide alone (pooled NMD = 6.0 mEq/L, 95% CI [3.6, 8.4]; Figure 14**)**. Results remained consistent in a post hoc sensitivity analysis that excluded data from the NRCS that only reported serum sodium at follow-up (pooled NMD = 5.9 mEq/L, 95% CI [3.4, 8.5].[44]

Meta-analysis revealed large statistical heterogeneity in NMDs across studies (I^2 = 94%). As shown in Figure 14, studies with shorter durations of intervention (1-4 days), which also had shorter duration of follow-up (1 to 4 days or compensation), mostly found no difference for serum sodium (pooled NMD = 1.3 mg/dL, 95% CI [-0.5, 3.0]), but after about 4-6 or more days of treatment and follow-up, NMD for serum sodium was larger (pooled NMD = 8.1 mg/dL, 95% CI [5.7, 10.6]). The NMD was significantly greater in longer duration studies than short duration studies ($p < 0.01$). While the statistical heterogeneity across the longer duration studies remained high, they all consistently found a relatively large, statistically significant improvement with sodium supplementation.

Figure 14. Serum Sodium: Supplemental Sodium (With Furosemide) versus Furosemide

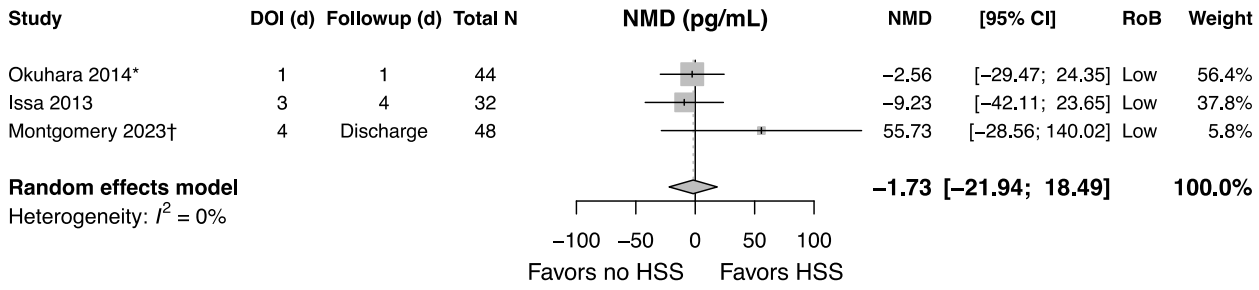


Notes: Net increase in serum sodium is considered to be a favorable outcome.
* Time to compensation. † Compared oral NaCl with furosemide to furosemide alone. ‡ NMD and 95% CI estimated from reported median data. Excluded in a post hoc sensitivity analysis.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; N=sample size, NMD=net mean difference; RoB=risk of bias.

Serum Aldosterone

Three RCTs found no significant difference in serum aldosterone from baseline to end of intervention (1 day to discharge) for patients who received HSS or oral NaCl with furosemide compared to furosemide alone (pooled NMD = −1.7 pg/mL, 95% CI [−21.9, 18.5]; Figure 15).[40,41,47] Montgomery et al reported a nonsignificant net increase in aldosterone, but the estimate was imprecise with a large confidence interval.

Figure 15. Serum Aldosterone: Supplemental Sodium (With Furosemide) versus Furosemide



Notes. Net decrease in serum aldosterone is considered to be a favorable outcome.
* Unit used for aldosterone was not reported; † Compared oral NaCl with furosemide to furosemide alone.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; HSS=hypertonic saline solution (or oral sodium with furosemide); N=sample size; NMD=net mean difference; RoB=risk of bias.

Plasma Renin Activity (PRA)

One RCT found no significant difference in PRA from baseline to at the end of 24-hr intervention in patients who received HSS with furosemide compared to furosemide alone (net *median* difference = −0.1 ng/mL/hr).[41] One study reported no significant difference in renin levels from baseline to in-hospital follow-up (4 days) for patients who received HSS with furosemide intervention compared to furosemide alone (net *median* difference = 2.2, unit not reported).[40]

Clinical Outcomes

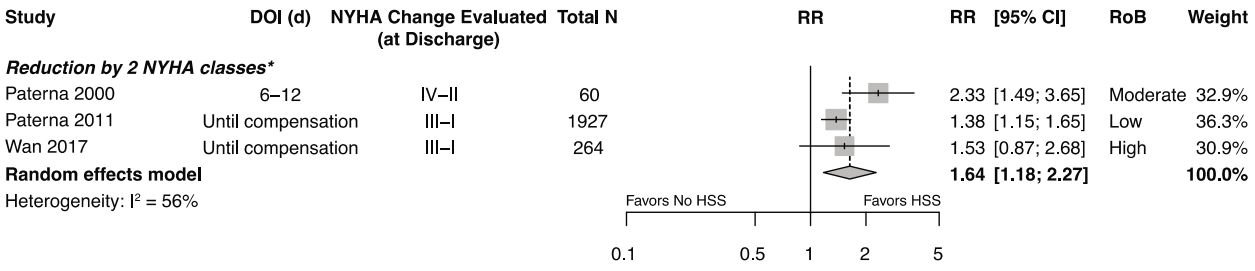
Clinical Congestion Score

No study reported data on a clinical congestion score.

Heart Failure–Related Symptoms

Three RCTs reported the change in NYHA functional class from admission to discharge.[33,37,43] In 2 studies (Paterna 2000 and Paterna 2011), all patients had a reduction in NYHA class prior to discharge (by 1 or 2 classes); in Wan et al, 88% had improvement. Pooling data from the 3 studies found that those randomized to HSS and furosemide were more likely to *improve* by 2 NYHA functional classes (*eg*, from class IV to II or from class III to I) than those on furosemide only (pooled RR = 1.64, 95% CI [1.18, 2.27]; Figure 16).[33,37,43] In the study by Wan et al (where 12% of patients did not improve in NYHA class), the RR for improving by 1 *or* 2 classes was not statistically significant (RR = 1.42, 95% CI [0.68, 2.96]).

Figure 16. NYHA Functional Class, Change in Class: Supplemental Sodium (With Furosemide) versus Furosemide



Notes. The analyzed outcome is an improvement (in NYHA class). Thus, RR > 1 favors HSS (improved heart function is more likely with HSS).
* All patients improved by 1 or 2 NYHA classes in Paterna 2000 and Paterna 2011.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention; RoB=risk of bias; RR=relative risk.

Thirst

One RCT reported reduction in symptoms of thirst (TDS-HF score) from baseline to the end of 4-day intervention among patients randomized to oral NaCl with furosemide compared to furosemide alone. The score ranged from −1.2 to 0.11, with higher scores indicating greater thirst symptoms. No significant difference was found (NMD = −1.3 unit, 95% CI [−4.2, 1.5]).[47]

Shortness of Breath

Two RCTs reported data on shortness of breath.[41,45] One RCT reported fewer patients experienced dyspnea and systematic venous congestion 24 hours after treatment among patients randomized to HSS with furosemide compared to furosemide with 5% glucose (RR = 1.73, 95% CI [1.10, 2.71]).[41] A second RCT reported no significant difference in resting dyspnea and work effort dyspnea between the groups at the end of the intervention (RR = 0.46, 95% CI [0.1, 2.03] and RR = 0.52, 95% CI [0.278, 0.99], respectively).[45]

Composite Clinical Parameters

One RCT[43] found no significant difference in a composite measure of clinical symptoms (dyspnea, lower limb edema, weakness, palpitations, and fatigue) at discharge for patients administered HSS with furosemide or furosemide alone (RR = 0.99, 95% CI [0.92, 1.07]).

Mortality (All-Cause)

Four RCTs reported all-cause mortality.[35,37,40,43] Two RCTs reported no deaths in both groups during hospitalization.[37,43] One RCT (Issa et al) reported an atypically large number of in-hospital deaths compared with other studies. They reported 10 (50%) in-hospital deaths among patients randomized to HSS with furosemide and 4 (33.3%) in-hospital deaths for patients randomized to furosemide alone (RR = 1.5, 95% CI [0.60, 3.74]).[40] The fourth RCT reported 3 deaths during 30-day follow-up in patients treated with furosemide alone (0 vs 3 deaths, RD = −0.065, 95% CI [−0.145, 0.015].[35]

Health Service Utilization Outcomes

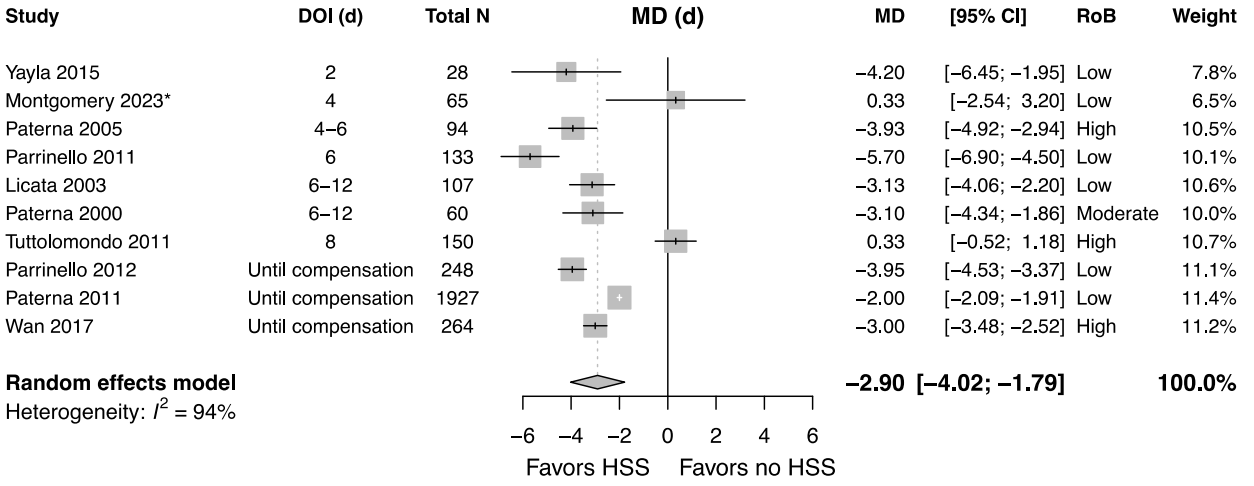
Readmission

One RCT[35] found a decrease in 30-day heart failure–related readmission for HSS with furosemide compared to furosemide alone (0 vs 12 events; RD = −0.26, 95% CI [−0.39, −0.13]). Another RCT found no significant difference in 30-day readmissions for oral NaCl with furosemide compared to furosemide alone (RR = 0.91, 95% CI [0.36, 2.31]).[47]

Length of Stay

Eleven studies (9 RCTs[33-35,37-39,42,43,47] and 2 NRCSs[36,44]) reported hospital length of stay. One NRCS[44] reported a longer median length of stay for patients who received HSS compared to no HSS (median difference = 11 days). This study did not report data to estimate a variance between groups and thus was excluded from meta-analysis. Of note, this study was an outlier both in direction and magnitude of difference in length of stay. The pooled estimate of the 10 remaining RCTs showed a shorter length of stay for sodium supplementation with furosemide compared to furosemide alone (pooled MD = −2.9 days, 95% CI [−4.0, −1.8]; Figure 17).[33-39,42,43] Among these 9 RCTs, there were 2 outlier studies that found no difference (Tuttolomondo 2011 et al and Montgomery 2023 et al). Excluding these studies in a post hoc sensitivity analysis yielded a slightly greater effect, with greater precision (pooled MD = −3.5 days, 95% CI [−4.3, −2.7], I^2 = 94%). Of note, Montgomery 2023 et al was the only study conducted in the US, and it found no significant difference between oral NaCl with furosemide compared to furosemide alone (MD = 0.3 days, 95% CI [-2.5, 3.2]).

Figure 17. Length of Hospital Stay: Supplemental Sodium (With Furosemide) versus Furosemide



Notes. Shorter length of stay is considered to be a favorable outcome.
* Compared oral NaCl with furosemide to furosemide alone.
Abbreviations. CI=confidence interval; d=day; DOI=duration of intervention N=sample size; MD=Mean difference; RoB=risk of bias.

Transfer to Intensive Care Unit (ICU)

One US-based RCT found no significant difference in intensive care unit admission during hospitalization for oral NaCl with furosemide compared to furosemide alone (RR = 0.56, 95% CI [0.15, 2.15]).[47]

DISCUSSION

We identified 5 studies (4 RCTs and 1 NRCS) that compared a low sodium diet to higher sodium diet, and 15 studies (13 RCTs and 2 NRCSs) that compared HSS with furosemide or, in 1 instance, oral NaCl with furosemide, to furosemide alone. The most frequently evaluated outcomes for dietary sodium interventions were weight loss, diuretic dose during hospitalization, and all-cause mortality. For sodium supplementation studies, weight was the most frequently reported outcome followed by urine output, serum sodium, serum creatinine, and length of hospital stay. Only 1 study was conducted in the US and was not in the VA system. Key findings include the following:

Dietary Sodium Interventions

Intermediate Outcomes

- There is no evidence of a difference in serum creatinine (moderate confidence), BNP (low confidence) or BUN, urine output, serum Na, aldosterone, PRA, prescribed diuretics, or dose of diuretics between a low sodium and higher sodium diet (certainty of evidence not assessed).
- It is unknown if a low sodium diet affects NT-pro BNP (insufficient evidence).
- Fewer calories may be consumed by patients on a low sodium diet (low confidence).
- The studies did not evaluate eGFR or serum cystatin C.

Clinical Outcomes

- There is no evidence of a difference in clinical congestion score between a low sodium diet compared to higher sodium diet (moderate confidence).
- Perceived thirst, but not other HF symptoms (shortness of breath or general well-being), may be greater for patients who receive a low sodium diet compared to higher sodium diet (certainty of evidence not assessed).
- It is unknown if a low sodium diet affects weight loss or mortality (insufficient evidence).
- Patients were adherent to the prescribed sodium diet (certainty of evidence not assessed).

Health Service Utilization Outcomes

- There were no significant differences in 30-day readmission or length of stay between a low sodium diet compared to higher sodium diet (low confidence).

Sodium Supplementation With Furosemide

Intermediate Outcomes

- Sodium supplementation with furosemide may decrease serum creatinine (moderate confidence) and BNP (low confidence), but not NT-proBNP (low confidence).

- Sodium supplementation with furosemide may increase urine output, serum sodium, and eGFR, and may decrease BUN. There is no evidence of differences in cystatin C, serum aldosterone, or PRA (certainty of evidence not assessed).
- The studies did not evaluate caloric intake.

Clinical Outcomes

- Sodium supplementation with furosemide may decrease weight (moderate confidence), reduce thirst symptoms (certainty of evidence not assessed), and improve NYHA functional class from admission to discharge (certainty of evidence not assessed).
- There may be no difference in shortness of breath or a composite measure of HF symptoms (certainty of evidence not assessed).
- It is unknown if sodium supplementation with furosemide affects mortality (insufficient evidence).
- The studies did not evaluate a clinical congestion score.

Health Service Utilization Outcomes

- Sodium supplementation with furosemide may reduce length of hospital stay (moderate confidence).
- It is unknown whether sodium supplementation with furosemide reduces 30-day readmission or intensive care unit admission during hospitalization (insufficient evidence).

SUMMARY

ADHF is 1 of the leading causes of hospitalization and rehospitalization in the US.[4] For decades, patients hospitalized with ADHF have been prescribed a restricted sodium diet with diuretic therapy. One surprising finding from this review was that only 5 relatively small studies, with only 381 analyzed patients, evaluated the effect of restricting dietary sodium in an inpatient setting. The goal of restricting sodium in ADHF patients is to reduce fluid retention and congestion. Yet there were no significant differences in weight change, urine output, and clinical congestion score from baseline to last in-hospital measurement between patients who received restricted or higher sodium diets. Furthermore, for most prioritized intermediate, clinical, and health service utilization outcomes, there was no significant difference between patients who received a restricted or higher sodium diet. Importantly, restricting dietary sodium may be associated with harms. Fewer calories were consumed by patients who received a restricted diet (presumably because they did not like the taste of their food), and 2 studies reported increased thirst for patients who received a restricted sodium diet combined with fluid restriction.[29,31] It is possible that this may partially explain why this strategy did not reduce hospital length of stay or other HF symptom metrics. Based on these data, the results suggest that a restricted sodium diet may *not* improve inpatient outcomes and may potentially result in poor experience with care. Unfortunately, these additional outcomes were not reported in all the included studies. Also, these findings are based on only small studies, mostly conducted in Brazil.

Unlike the restriction of dietary sodium, there is a larger evidence base evaluating the effect of combining furosemide with bolus sodium in the form of HSS or oral NaCl (15 studies and total analyzed $N = 3,483$). HSS is hypothesized to ameliorate diuretic resistance by shifting water from interstitial compartment, thus restoring effective intravascular volume and improving renal blood flow. In addition, HSS is expected to reduce hyperactivation of the renin-aldosterone-angiotensin pathway and help reduce the sodium-avid state of the kidneys.[18] Consistent with this hypothesis, we found that HSS (or in 1 instance oral NaCl tablets) and furosemide compared to furosemide alone yielded a significant net improvement in kidney function (net reductions in serum creatinine and BUN and a net increase in eGFR), increased urine output, and reduced weight. Indirect evidence (across studies) suggests that improvements in kidney function and serum sodium become evident after about 4 to 6 days of treatment.

Despite evidence to suggest the efficacy of sodium supplementation as an adjuvant therapy for loop diuretics, providers may still have concerns that administering sodium to people with ADHF can lead to sodium overcorrection or pulmonary edema. Notably, though, the average sodium increase in these interventions was ~6 mEq/L, which is lower than the maximum of 8 mEq/L per 24 hour change in sodium that is deemed safe in acute correction. There were no reports of worsening pulmonary edema or hypoxia with administration of sodium supplementation in these studies, while shortness of breath symptoms and NYHA class improved across studies.

STRENGTHS AND LIMITATIONS OF THE EVIDENCE BASE

The evidence base on restricting dietary sodium has several important limitations. First, only 5 small studies evaluated restricted dietary sodium interventions in an inpatient setting. Second, 2 of the 4 RCTs had major methodological limitations due to missing outcome data, not following an intent-to-treat analysis, or using hospital record number to randomize patients. Third, 2 studies did not clearly define how long patients were administered a restricted diet, which we assumed was for the duration of their hospitalization.[28,30] Lastly, the few, small studies combined with heterogeneity in maximum sodium consumption (range 0.8 g/day to 2.4 g/day) makes it challenging to know whether outcomes may differ by the amount of prescribed sodium.

Most studies evaluating HSS (or oral sodium) and furosemide had low risk of bias (*ie*, no major methodological weaknesses). We synthesized data based on the last in-hospital measurement; however, there was meaningful variation across studies in the timing of outcome assessment. Some studies evaluated outcomes immediately after the intervention and others at discharge. At a minimum, future studies should report outcomes at admission, after the intervention, and at discharge. In addition, studies inconsistently reported whether they restricted dietary sodium. Lastly, variation across studies in the duration of intervention (24 hours to 12 days) and dose of furosemide (conventional or high dose) makes it challenging to identify the best sodium supplementation with diuretic strategy.

Although of importance to stakeholders, studies were inconsistent in whether they reported HF-related symptoms (and which symptoms), and none of the diet studies reported change in NYHA class. Of crucial importance to determine who might benefit most (or least) from the interventions, the studies did not report differences in effectiveness by patient characteristics (age, sex, or race/ethnicity), comorbid conditions, or community dietary sodium intake. Only 2 dietary studies reported baseline data on race/ethnicity[29,31] (only reporting the proportion of

White participants), and only the US-based sodium supplementation study (or oral sodium) reported data by race/ethnicity (only reporting the proportion of White and Black participants). The studies did not report outcomes by existing versus new-onset HF or preserved versus reduced ejection fraction. However, 3 studies found that HSS and furosemide resulted in meaningful improvements in NYHA functional class from admission to discharge. Finally, no study compared a dietary sodium restriction to HSS and furosemide.

IMPLICATIONS FOR VA POLICY AND PRACTICE

HF is highly prevalent among the Veteran population and is an important cause of hospitalization, morbidity, and mortality in the VA.[3] Providing the best care to Veterans hospitalized with decompensated heart failure is paramount to the VA's mission. No study was conducted in the VA and only 1 study (oral sodium tables) was conducted in the US. All 4 dietary sodium RCTs were conducted in Brazil and most HSS studies were conducted in Europe. Two separate author groups each conducted 2 of the European studies,[36,38,39,45] and a third author group conducted 3 of the European studies.[33,35,37] Men were the majority in most studies (range 32%–81%; the VA population is 89% male) and no study reported effectiveness by sex. Despite these differences, the main overall findings likely translate to the VA population, as the underlying biology and pathophysiologic mechanisms are not likely different by country. It is also reasonable to hypothesize that the finding of a reduction in length of stay for sodium supplementation with diuretics may be reproduced in the VA, but it is likely that the magnitude of change in length of stay (a measure particularly sensitive to a health system's characteristics) may be substantially different than found in mostly European studies. Veterans Integrated Services Networks with strong transitional care programs (*eg,* Hospital in Home and Cardiac Rehabilitation programs) are likely in the best position to leverage the observed reductions in length of stay for sodium supplementation. However, the single US study found no significant difference in hospital length of stay between oral sodium tablets with furosemide compared to furosemide alone.

As a high reliability organization, the VA should consider adapting and implementing the best evidence for Veterans with ADHF within its care delivery system. Our findings call for the careful review of the routine inpatient practice of severely restricting sodium intake for patients admitted with ADHF. While physiologic measures were largely unchanged with low sodium diets, the reduction in calories is a serious concern for the Veteran population who may be fluid overloaded ("overweight") and malnourished. The use of HSS (or oral sodium supplementation) with loop diuretics to augment diuresis deserves consideration for inclusion in hospital protocols as a strategy for ADHF.

As VA Medical Centers and providers evaluate the merits of sodium supplementation, they will also need to consider broader implementation needs and barriers. Providers and systems may be reluctant to change practice. The pathophysiology of sodium in HF is generally discussed in medical curricula as something to be avoided. The counterintuitive nature of administering a high-sodium solution to patients in ADHF, concerns of over-correction or precipitation of pulmonary edema, and limited experience of providers will require education, partnership with cardiovascular and renal specialists, buy-in from leadership, and clear protocols. In addition, HSS will require greater utilization of clinical resources for patient monitoring with an appropriate safety protocol in place. Furthermore, clinical experience with the use of HSS for

ADHF likely varies between facilities, and training of medical staff will be critical to promote the safe use of HSS in selected patients with ADHF.

Limited evidence of RCT data from North America suggests a unique opportunity for VA hospitals to evaluate effectiveness and implementation of this strategy in the US and to fill the gaps in evidence for VA providers and policy makers. Conducting studies in the US would be particularly informative to understand the effect of intervention on health system outcomes pertinent to the US (such as length of hospital stay), which are likely to differ substantially across different health systems and countries. In addition, interviews with Veterans, providers, and Medical Center leadership can identify barriers and facilitators to implementation of clinical interventions employing sodium supplementation with loop diuretic protocols. After systems adopt these protocols, effectiveness and safety measures can be evaluated by using the VA data.

RESEARCH GAPS/FUTURE RESEARCH

Despite millions of people affected by HF worldwide, there is limited evidence on the effect of prescribed sodium interventions in an inpatient setting. Fewer than 400 people contributed data to the dietary sodium intake studies and fewer than 3,500 people contributed data to the sodium supplementation studies. There is a need for a well-designed, adequately powered RCT of pragmatic design to assess the effectiveness of HSS infusion (and possibly separately oral supplementation) for patients admitted with ADHF. There was variation in HSS administration (concentration ranged from 1.15% to 7.5%), tailoring dosage (tailoring or fixed), and duration of treatment. There are several broader research needs. Future studies should focus on examining differences in effectiveness by patient characteristics (age, sex, or race/ethnicity), HF phenotypes, chronicity of HF, and comorbid conditions. There is also a need to understand patient quality of life, experience, and satisfaction with care. As protocols are translated into practice, there will be a need to evaluate implementation efforts which can be incorporated into the pragmatic research design.

The evidence regarding restricted in-hospital dietary sodium is small. Future, well-conducted, larger studies would be needed to effectively evaluate the dietary sodium restriction. However, given the reluctance of patients to have their dietary sodium restricted (as evidenced by decreased caloric intake), the lack of evidence of a beneficial effect of restricted dietary sodium (to date), and the apparent effectiveness of sodium supplementation with furosemide treatment, it is unclear whether future studies of restricted in-hospital dietary sodium are warranted.

STRENGTHS AND LIMITATIONS OF THE SYSTEMATIC REVIEW PROCESS

Our review represents the most up-to-date report evaluating the evidence the practice of dietary sodium restriction and the use of HSS (or oral sodium supplementation) with furosemide among hospitalized patients with ADHF. This evidence review has several limitations. There was variation in the dietary sodium intake and sodium supplementation administration strategies, and we were unable to compare effects by dosing or duration. Outcomes of 30-day mortality and 30-day readmission may be affected by care after discharge, but we were unable to evaluate corresponding outpatient care protocols. We were likewise unable to investigate potential sources of heterogeneity of treatment effects (explanations for differences across studies) because of small numbers of studies and lack of reporting on many characteristics of interest or

of subgroup analyses. A strength of our review was the focus on hospitalized patients. Studies examining dietary interventions in outpatient settings are challenging to conduct because sodium consumption is documented via patient reported diaries. Documenting (and managing) sodium consumption in an inpatient setting is likely easier, and thus reported intakes are likely more accurate. While we did not define a priori sensitivity analyses, the post hoc sensitivity analyses based on removing substantive outliers provide important supportive evidence.

CONCLUSIONS

Findings from this review call into the question the conventional practice of restricting dietary sodium for managing ADHF in an inpatient setting. Only a few studies examined the effect of restricting dietary sodium, and these studies had important methodological limitations. There was no evidence of differences in most intermediate, clinical, or health service use outcomes for patients prescribed a restricted sodium diet compared to a higher sodium diet, but patients consumed fewer calories on a low sodium diet compared to a higher sodium diet. Studies provide insufficient evidence for the effect of numerous outcomes, including mortality. Patients who received HSS (or in 1 instance, oral sodium supplementation) and furosemide, compared to furosemide alone, had clinical improvements in intermediate, clinical, and health service use outcomes, particularly related to effective diuresis and length of hospital stay, without evidence of deleterious kidney or HF effects. The effects of sodium supplementation and furosemide therapy may not become evident until at least 4 to 6 days of treatment. However, especially since little research has been conducted in the US, there is a need for well-designed and large RCTs to further assess the effectiveness of sodium supplementation and furosemide treatment for inpatients with ADHF. There is a particular need for future research to examine heterogeneity of treatment effects based on patient characteristics and to identify the optimal duration, dose, and protocol of sodium supplementation treatment. While more rigorous trials would be needed to determine whether restricted dietary sodium is effective in the inpatient setting, the apparent benefit of sodium supplementation and furosemide treatment may preclude the need for additional dietary studies.

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APPENDIX A. SEARCH STRATEGIES

MEDLINE

(((“Heart Failure”[Mesh] or ((heart failure[tiab] or cardiac failure[tiab] or myocardial failure[tiab] or CHF[tiab]) AND (hospital* OR inpatient OR “Acute Disease”[Mesh] or acute[tiab] or decompensated[tiab])) OR heart decompensation[tiab]) AND ("Saline Solution, Hypertonic"[Mesh] OR Hypertonic Saline OR Hypertonic sodium chloride OR HSS OR salt hypertonic OR Sodium tablets OR "Saline Solution"[Mesh] OR Intravenous saline OR Normal saline OR Hypotonic saline OR Saline solution OR Lactate* ringer's OR "Ringer's Lactate"[Mesh] OR “Diet, Sodium-Restricted”[Mesh] or sodium-restrict* or salt-restrict* or sodium-free or salt-free or low-salt or low-sodium or reduced-salt or reduced-sodium or ((sodium[tiab] or salt[tiab]) AND (restrict*[tiab] or reduc*[tiab] or low[tiab] or free[tiab])))) NOT (“address”[pt] OR “autobiography”[pt] OR “bibliography”[pt] OR “biography”[pt] OR “case reports”[pt] OR “comment”[pt] OR “congress”[pt] OR “dictionary”[pt] OR “directory”[pt] OR “festschrift”[pt] OR “government publication”[pt] OR “historical article”[pt] OR “interview”[pt] OR “lecture”[pt] OR “legal case”[pt] OR “legislation”[pt] OR “news”[pt] OR “newspaper article”[pt] OR “patient education handout”[pt] OR “periodical index”[pt] OR "comment"[ti] OR "Editorial"[Publication Type] OR "ephemera"[pt] OR "in vitro techniques"[mh] OR "introductory journal article"[pt] OR ("Animals"[Mesh] NOT "Humans"[Mesh]) OR (child[Mesh] NOT adult[Mesh]) OR rats[tw] OR rat[tw] OR cow[tw] OR cows[tw] OR chicken*[tw] OR horse[tw] OR horses[tw] OR mice[tw] OR mouse[tw] OR bovine[tw] OR sheep[tw] OR ovine[tw] OR murinae[tw] OR cats[tw] OR cat[tw] OR dog[tw] OR dogs[tw] OR rodent[tw])) AND ("Cohort Studies"[Mesh] OR cohort OR "Clinical Trial" [Publication Type] OR (follow-up OR followup) OR longitudinal OR "Placebos"[Mesh] OR placebo* OR "Research Design"[Mesh] OR "Evaluation Study" [Publication Type] OR "Comparative Study" [Publication Type] OR ((comparative OR Intervention) AND study) OR pretest* OR posttest* OR prepost* OR “before and after” OR interrupted time* OR time serie* OR intervention* OR ((quasi-experiment* OR quasiexperiment* OR quasi OR experimental) AND (method OR study OR trial OR design*)) OR “real world” OR “real-world” OR "Case-Control Studies"[Mesh] OR (case AND control) OR "Random Allocation"[Mesh] OR "Clinical Trial" [Publication Type] OR "Double-Blind Method"[Mesh] OR "Single-Blind Method"[Mesh] OR random* OR "Placebos"[Mesh] OR placebo OR ((clinical OR controlled) AND trial*) OR ((singl* OR doubl* OR trebl* OR tripl*) AND (blind* OR mask*)) OR rct OR crossover OR cross-over OR cross-over OR "treatment switching" OR "Treatment Switching"[Mesh] OR RCT OR "Randomized Controlled Trial" [Publication Type] OR systematic[sb] OR meta-analysis[pt] OR meta-analysis as topic[mh] OR meta-analysis[mh] OR meta analy* OR metanaly* OR metaanaly* OR met analy* OR (systematic AND (review* OR overview*)) OR "Review Literature as Topic"[Mesh] OR cochrane[tiab] OR embase[tiab] OR (psychlit[tiab] or psyclit[tiab]) OR (psychinfo[tiab] or psycinfo[tiab]) OR (cinahl[tiab] or cinhal[tiab] OR “cumulative index to nursing and allied health”) OR science citation index[tiab] OR ibids[tiab] OR “international bibliographic information on dietary supplements” OR cancerlit[tiab] OR reference list*[tiab] OR bibliograph*[tiab] OR hand-search*[tiab] OR relevant journals[tiab] OR manual search*[tiab] OR ((selection OR inclusion OR exclusion) AND criteria[tiab]) OR data extraction[tiab] OR relevant journals OR "Systematic Review" [Publication Type] OR "Comparative Effectiveness Research"[Mesh] or "Comparative Effectiveness")

EMBASE

No.	Query	Results
#64	#45 AND #55 AND #62 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim	5643
#63	#45 AND #55 AND #62	13088
#62	#56 OR #59 OR #60 OR #61	627326
#61	'ringer lactate solution'	9234
#60	(((((((hypertonic AND saline OR hypertonic) AND sodium AND chloride OR hss OR salt) AND hypertonic OR sodium) AND tablets OR intravenous) AND saline OR normal) AND saline OR hypotonic) AND saline OR saline) AND solution OR lactate*) AND ringer*	12542
#59	'sodium chloride'	238797
#58	#45 AND #55 AND #56 AND ([article]/lim OR [article in press]/lim) AND [humans]/lim	4882
#57	#45 AND #55 AND #56	11117
#56	#51 OR #52 OR #53 OR #54	472391
#55	#46 OR #47 OR #48 OR #49 OR #50	10320989
#54	(sodium OR salt) AND (restrict* OR reduc* OR low OR free)	472391
#53	'sodium free' OR 'salt free' OR 'low salt' OR 'low sodium' OR 'reduced salt' OR 'reduced sodium'	14002
#52	'salt restrict'	2
#51	'sodium restriction'	11815
#50	heart AND decompensation	7940
#49	decompensated	32589
#48	acute AND disease	1098740
#47	inpatient	191126
#46	'hospital'	9716334
#45	#41 OR #42 OR #43 OR #44	713122
#44	chf	30735
#43	myocardial AND failure	136191
#42	cardiac AND failure	315468
#41	('heart'/exp OR heart) AND ('failure'/exp OR failure)	686908

COCHRANE

#1	MeSH descriptor: [Heart Failure] explode all trees	12328
#2	heart failure or cardiac failure or myocardial failure or CHF	48961
#3	#1 OR #2	48982
#4	hospital* OR inpatient OR decompensated OR heart decompensation	407267
#5	MeSH descriptor: [Acute Disease] explode all trees	10838
#6	#4 OR #5	413481

#7	sodium-restrict* or salt-restrict* or sodium-free or salt-free or low-salt or low-sodium or reduced-salt or reduced-sodium	2215
#8	MeSH descriptor: [Diet, Sodium-Restricted] explode all trees	701
#9	(sodium or salt) AND (restrict* or reduc* or low or free)	24630
#10	MeSH descriptor: [Saline Solution, Hypertonic] explode all trees	584
#11	MeSH descriptor: [Saline Solution] explode all trees	284
#12	MeSH descriptor: [Ringer's Lactate] explode all trees	281
#13	Hypertonic Saline OR Hypertonic sodium chloride OR HSS OR salt hypertonic OR Sodium tablets OR Intravenous saline OR Normal saline OR Hypotonic saline OR Saline solution OR Lactate* ringer*	32690
#14	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13	53612
#15	#3 AND #6 AND #14	2096

CINAHL

((heart failure or cardiac failure or myocardial failure or CHF) AND (hospital OR inpatient or acute or decompensat*)) AND (Hypertonic Saline OR Hypertonic sodium chloride OR HSS OR salt hypertonic OR Sodium tablets OR Intravenous saline OR Normal saline OR Hypotonic saline OR Saline solution OR Lactate* ringer's OR sodium-restrict* or salt-restrict* or sodium-free or salt-free or low-salt or low-sodium or reduced-salt or reduced-sodium OR ((sodium or salt) AND (restrict* or reduc* or low or free)))

CLINICALTRIALS.GOV

Condition: ((heart failure OR cardiac failure OR myocardial failure OR CHF) AND (acute OR decompensat*)) AND

Other terms: (Saline OR Hypertonic sodium chloride OR HSS OR salt OR Sodium OR Lactate ringer)

APPENDIX B. EXCLUDED STUDIES

1. Abshire M, Xu J, Baptiste D, et al. Nutritional interventions in heart failure: a systematic review of the literature. *Journal of Cardiac Failure*. 2015;21(12):989-999. *Systematic Review.*
2. Biao F, Huang L. GW27-e1005 Liberal versus restricted fluid administration in heart failure patients: a meta-analysis of 6 randomized trials. *Journal of the American College of Cardiology*. 2016;68(16_Supplement):C149-C149. doi:doi:10.1016/j.jacc.2016.07.561. *Systematic Review.*
3. Biegus J, Zymlinski R, Siwolowski P, et al. Controlled decongestion by Reprieve therapy in acute heart failure: results of the TARGET-1 and TARGET-2 studies. *European Journal of Heart Failure*. 2019;21(9):1079-1087. *Not sodium intake.*
4. Bikdeli B, Strait KM, Dharmarajan K, et al. Intravenous fluids in acute decompensated heart failure. *JACC: Heart Failure*. 2015;3(2):127-133. *Not sodium intake.*
5. Bocchi E. Hypertonic saline solution in heart failure. 2008. ClinicalTrials identifier: NCT00555685. https://clinicaltrials.gov/study/NCT00555685. *No additional results reported.*
6. Castro-Gutiérrez V, Rada G. Should sodium intake be restricted in chronic heart failure? *Medwave*. 2016;16(Suppl5). *Other; not hospitalized only/This is not primary study but literature review for SRs.*
7. Chimparlee N. Effects of salt and fluid restriction on dyspnea in patients with acute decompensated heart failure. 2020. ICTRP identifier: TCTR20200508002. https://trialsearch.who.int/Trial2.aspx?TrialID=TCTR20200508002. *No additional results reported.*
8. Colin-Ramirez E, Sepehrvand N, Rathwell S, et al. Sodium restriction in patients with heart failure: A systematic review and meta-analysis of randomized clinical trials. *Circulation: Heart Failure*. 2023;16(1):e009879. *Systematic Review.*
9. Covic A, Copur S, Tapoi L, et al. Efficiency of hypertonic saline in the management of decompensated heart failure: a systematic review and meta-analysis of clinical studies. *American Journal of Cardiovascular Drugs*. 2021;21:331-347. *Systematic Review.*
10. Crane C, Hertel A, Hobza C, Menard JR. Does hypertonic saline infusion with furosemide improve outcomes for patients with acute CHF exacerbation? *Evidence-Based Practice*. 2018;21(2):E5-E6. *Other; help desk answer.*
11. d'Almeida KSM, Trojahn MM, Barilli SLS, et al. Preliminary results of a randomized clinical trial on the effect of fluid and dietary sodium restriction in the management of patients with heart failure and preserved ejection fraction. *Journal of Cardiac Failure*. 2016;22(8):S63. *No additional results reported.*
12. da Silva E. Effect of dietary sodium restriction in the management of patients with heart failure and diastolic dysfunction. 2013. ClinicalTrials.gov identifier: NCT01896908. https://clinicaltrials.gov/show/NCT01896908. *No additional results reported.*
13. d'Almeida KS, Rabelo-Silva ER, Souza GC, et al. Effect of fluid and dietary sodium restriction in the management of patients with heart failure and preserved ejection fraction: study protocol for a randomized controlled trial. *Trials*. 2014;15:1-6. *No additional results reported.*
14. De Vecchis R, Baldi C, Cioppa C, Giasi A, Fusco A. Effects of limiting fluid intake on clinical and laboratory outcomes in patients with heart failure. *Herz*. 2016;41(1):63. *Systematic* Review.

15. De Vecchis R, Esposito C, Ariano C, Cantatrione S. Hypertonic saline plus iv furosemide improve renal safety profile and clinical outcomes in acute decompensated heart failure. *Herz*. 2015;40(3):423. *Systematic Review.*
16. De Vecchis R, Paccone A, DiMaio M. Effects of a restricted water intake on various clinical and laboratory outcomes in patients with heart failure: a meta-analysis of randomized controlled trials. *Minerva Cardioangiologica. Retracted.*
17. DiNicolantonio JJ, Di Pasquale P, Taylor RS, Hackam DG. Low sodium versus normal sodium diets in systolic heart failure: systematic review and meta-analysis. *Heart*. 2012. *Systematic Review.*
18. DiNicolantonio JJ, Pasquale PD, Taylor RS, Hackam DG. Low sodium versus normal sodium diets in systolic heart failure: Systematic review and meta-analysis. *Heart. Retracted.*
19. Engelmeier R. Safety and efficacy of low dose hypertonic saline solution and high dose furosemide for congestive heart failure (REaCH). 2009. ClinicalTrials.gov identifier: NCT01028170. https://clinicaltrials.gov/show/NCT01028170. *No additional results reported.*
20. Engelmeier RS, Le TT, Kamalay SE, et al. Randomized trial of high dose furosemide-hypertonic saline in acute decompensated heart failure with advanced renal disease. *Journal of the American College of Cardiology*. 2012;59(13S):E958-E958. *Not sodium intake.*
21. Fabrício CG, Gentil JR, Amato CA, Marques F, Schwartzmann PV, Simões MV. Prospective, randomized and blinded clinical study testing two levels of dietary sodium intake in patients with acute decompensated heart failure. *Journal of Cardiac Failure*. 2016;22(8):S55. *No additional results reported.*
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26. Guglin M. Low sodium vs. regular diet in patients admitted for heart failure (SALT). 2016. Clinicaltrials.gov identifier: NCT02689635. https://clinicaltrials.gov/show/NCT02689635. *No additional results reported.*
27. He L, Sun L, Yang Y, et al. Clinical experience of supplying sodium chloride for the treatment of patients with severe heart failure. *Zhonghua xin xue Guan Bing za zhi*. 2012;40(9):766-769. *Not sodium intake.*
28. Ingrassia O. Sodium management in acute and chronic heart failure (SMAC-HF). 2000. ClinicalTrials.gov identifier: NCT01156337. https://ClinicalTrials.gov/show/NCT01156337. *No additional results reported.*

29. Inuzuka Y, Kishimori T, Inoue T, et al. Sodium restriction in Japanese patients hospitalized with acute decompensated heart failure. *Journal of Cardiac Failure*. 2015;21(10):S183. *No additional results reported.*
30. Issa V, Ayub-Ferreira S, Bacal F, et al. Prevention of renal dysfunction with hypertonic saline solution in patients with decompensated heart failure: a prospective, double blind, randomized, placebo-controlled trial. *European Heart Health.* 2011:162-163. *No additional results reported.*
31. Issa VS, Ayub-Ferreira S, Bacal F, et al. Hypertonic saline solution for prevention of renal dysfunction in patients with decompensated heart failure (HYSS-HF STUDY): A double-blind, randomized controlled trial. *Journal of the American College of Cardiology*. 2011;57(14S):E218-E218. *No additional results reported.*
32. Issa VS, Bacal F, Mangini S, et al. Hypertonic saline solution for renal failure prevention in patients with decompensated heart failure. *Arquivos Brasileiros de Cardiologia*. 2007;89:251-255. *No additional results reported.*
33. Issa VS, Bacal F, Mangini S, et al. Hypertonic saline solution for renal failure prevention in patients with decompensated heart failure. *Arquivos Brasileiros de Cardiologia*. 2007;89:251-255. *Other; pre-post (N=9).*
34. Issa VS, Ayub-Ferreira S, Bacal F, et al. Hypertonic saline solution for prevention of renal dysfunction in patients with decompensated heart failure-prospective, double blind, randomized, placebo-controlled trial. *European Heart Health*. *No additional results reported.*
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36. Lee Y-W, Huang L-H, Ku C-H. Use of dietary sodium intervention effect on neurohormonal and fluid overload in heart failure patients: Review of select research based literature. *Applied Nursing Research*. 2018;42:17-21. *Systematic Review.*
37. Li Z, Wang Z, Liu N, Li H. Effect of hypertonic saline solution combined with furosemide on acute heart failure: A meta-analysis. *Computational and Mathematical Methods in Medicine*. 2022: 5728967. *Systematic Review.*
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APPENDIX C. CRITERIA USED IN QUALITY ASSESSMENT

Question	Yes	No	Unclear
Clarity			
1. Clear reporting with no discrepancies (Y/N)			
2. Were eligibility criteria clear? (Y/N)			
3. Were interventions adequately described? (Y/N)			
4. Were the outcomes fully defined? (Y/N)			
Bias Assessment			
5. Random sequence generation: Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence.			
6. Allocation concealment: Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.			
7. Blinding of participants and personnel: Performance bias due to knowledge of the allocated interventions by participants during the study.			
8. Blinding of outcome assessor (detection bias): Detection bias due to knowledge of the allocated interventions by outcome assessors.			
9. Incomplete outcome data (attrition bias): Attrition bias due to amount, nature or handling of incomplete outcome data.			
10. Selective Reporting (reporting bias): Reporting bias due to selective outcome reporting.			
11. Intention-to-treat-analysis: Bias due to incomplete reporting and analysis according to group allocation.			
12. If observational study, comparator group was sufficiently similar (and selected patients were all included or a random sample were included).			
13. If observational study, Adjustment for confounders. a. Crude analysis (unadjusted comparison between ADP and no ADP) [High RoB] b. Regression adjustment or patient-matching (accounting for at least age, sex, and symptom duration OR a risk score) [Low RoB] c. Regression adjustment or patient-matching (not accounting at least one of for age, sex, symptom duration, or risk score) [Moderate RoB] d. Propensity score analysis (or equivalent) [Low RoB]			

Author, Year, PMID, Design	Free of Discrepancies	Eligibility Clear	Intervention Clear	Outcomes Adequately Defined	Blinding		Incomplete Outcome Data	Selective Reporting	RCT			NRCS		Overall RoB
					Participants and Personnel	Outcome Assessor			Random Sequence Generation	Allocation Concealment	ITT	Comparator Group Similar	Confounder Adjustment	
Dietary Interventions														
Aliti, 2013, 23689381, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	N/A	N/A	Low RoB (RCT)
Fabricio, 2019, 31221280, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)	Yes (low concern)	Yes (high concern)[a]	No (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	N/A	N/A	High RoB (RCT)
D'Almeida, 2018, 29793053, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	N/A	N/A	Low RoB (RCT)
Velloso, 1991, 1824218, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)	Yes (low concern)	Unclear	Unclear	No (high concern)[b]	No (high concern)[b]	Unclear	N/A	N/A	High RoB (RCT)
Inuzuka, 2016, NRCS[c]	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)	N/A	Unclear	Unclear	Unclear	N/A	N/A	N/A	Yes (low concern)	Yes (low concern)	Moderate RoB (NRCS)
Saline Solution Interventions														
Issa, 2013, 22243938, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	N/A	N/A	Low RoB (RCT)
Paterna, 2005, 15963399, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low concern)	No (low concern)	No (high concern)[d]	No (high concern)[d]	Yes (low concern)	N/A	N/A	High RoB (RCT)
Wan, 2017, 28701670, RCT	No (high concern)[e]	Yes (low concern)	Yes (low concern)	No (high concern)[f]	No (high concern)	No (high concern)	No (low concern)	No (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	N/A	N/A	High RoB (RCT)
Mahjoob, 2021, 34903983, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Unclear	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Unclear	Yes (low concern)	N/A	N/A	Moderate RoB (RCT)
Tuttolomondo, 2011, 20346637, NRCS	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Unclear	Yes (low concern)	No (low concern)	No (low concern)	N/A	N/A	N/A	Yes (low concern)	No (high concern)[g]	High RoB (NRCS)
Licata, 2003, 12660669, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	N/A	N/A	Low RoB (RCT)
Paterna, 2000, 10938493, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)	Yes (low concern)	Unclear	No (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	N/A	N/A	Moderate RoB (RCT)

Author, Year, PMID, Design	Free of Discrepancies	Eligibility Clear	Intervention Clear	Outcomes Adequately Defined	Blinding		Incomplete Outcome Data	Selective Reporting	RCT			NRCS		Overall RoB
					Participants and Personnel	Outcome Assessor			Random Sequence Generation	Allocation Concealment	ITT	Comparator Group Similar	Confounder Adjustment	
Paterna, 2011, 21701268, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	N/A	N/A	Low RoB (RCT)
Parrinello, 2012, 22980301, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Unclear	Yes (low concern)	N/A	N/A	Low RoB (RCT)
Yayla, 2015, 26135463, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)[h]	Yes (low concern)	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	N/A	N/A	Low RoB (RCT)
Parrinello, 2011, 21440872, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	N/A	N/A	Low RoB (RCT)
Tuttolomondo, 2021, 34288546, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Unclear	Yes (low concern)	N/A	N/A	Moderate RoB (RCT)
Okuhara, 2014, 24462960, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Unclear	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Unclear	Yes (low concern)	N/A	N/A	Low RoB (RCT)
Roul, NRCS[c]	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (high concern)	Unclear	Yes (low concern)	Unclear	Unclear	N/A	N/A	N/A	No (high concern)	No (high concern)	High RoB (NRCS)
Montgomery, 2023, 37044281, RCT	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	Yes (low concern)	No (low concern)	No (low concern)	Yes (low concern)	Unclear	Yes (low concern)	N/A	N/A	Low RoB (RCT)

Notes. [a] 30% of participants had missing outcome data; [b] Randomization based on odd or even of medical record number; [c] Conference abstract with limited methodological details; [d] assignment of patient was decided by an independent physician; [e] Sample sizes and outcome events in the table are different than in text; [f] Outcomes not clearly defined in the methods section; [g] Match treatment and comparison group by age and sex and then conducted unadjusted comparisons; [h] For outcomes reported once patients reach compensated state; unclear when this occurred.
Abbreviations. ITT=intention to treat; NRCS=nonrandomized comparative study; RCT=randomized controlled trial.

APPENDIX D. DESIGN DETAILS

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Study Location Details (Hospital Type, Centers)	Inclusion Criteria	Exclusion Criteria
Aliti, 2013, 2368938, NCT01133236, Brazil	RCT	2009-2012	Academic, Single center	Boston criteria ≥ 8, (LV)EF ≤ 45% Length of stay of no more than 36 hours after hospital admission, ≥ 18 yo	Cardiogenic shock, endogenous creatinine clearance rate of 30 mL/min/1.73m^2, survival compromised due to other underlying disease or hinder treatment adherence (*eg*, dementia, cognitive deficits)
Fabricio, 2019, 31221280, NCT03722069, Brazil	RCT	2014-2016	Academic, Single center	Framingham, ≥ 18 yo	ACS, ADHF secondary to acute renal failure, creatinine clearance <30 ml/ min/1.73 m², stroke, dementia, severe cognitive impairment, cancer, decompensated DM, severe liver disease, septic shock, acute or chronic primary disease of the renal parenchyma, cerebrovascular accident, nutritional disorders or unable to ingest food by mouth, vomiting, dysphagia, or gastroenteritis
d'Almeida, 2018, 29793053, NCT01896908, Brazil	RCT	2013-2016	Academic, Single center	(LV)EF ≥50%, ≥18 yo, Overt clinical signs of congestion, dyspnea, orthopnea in the week before hospitalization, BNP >100 pg/mL	Cardiogenic shock, eGFR ≤ 30 mL/min, HF due to severe valvular disease, difficulty in adhering to treatment (*eg*, dementia or cognitive deficits)
Inuzuka, 2016, Japan	NRCS	2011-2012	Not reported	NYHA: II-IV, median BNP 856 pg/mL	NR
Velloso, 1991, 1824218, Brazil	RCT	NR	Academic, Single center	NYHA: III or IV	Systemic arterial hypertension (upper DBP to 110mmHg), significant pulmonary arterial hypertension, renal insufficiency (serum creatinine > 2mg%), restrictive syndrome cases
Issa, 2013, 22243938 NCT00555685 Brazil	RCT	2008-2010	Academic[a], Single center	≥18 yo, diagnosed DHF with congestive phenomena, (LV)EF: < 40%	Patient refusal, signs of hypoperfusion, alcohol abuse, primary valvular disease, MI or unstable angina within 6 months, cardiac surgery or angioplasty, restrictive cardiomyopathy, COPD, immunosuppressive therapy, malignant tumors, acute pulmonary embolism, surgical

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Study Location Details (Hospital Type, Centers)	Inclusion Criteria	Exclusion Criteria
					intervention or infections in last 30 days, serum creatinine > 3.0 mg/dL, serum potassium > 5.5 mg/dL, severe systemic disease expected to impair survival, pregnancy or childbearing potential, no clinical parameters of hypoperfusion at the time of enrollment
Licata, 2003, 12660669 Italy	RCT	1996-1999	Single center	Refractory CHF according to Framingham criteria and NYHA, uncompensated CHF (dyspnea, weakness, lower limb edema, or anasarca) of NYHA IV, unresponsive to treatment with high oral doses of furosemide and/or combinations of diuretics (thiazide, loop diuretic, and spironolactone), ACEIs, digitalis, nitrates, and receiving this therapy at least 2 weeks before the study and hospitalization. Patients being unresponsive when they showed with a reduction of urine volume and a constant increase of body weight (BW) and the impairment of clinical signs of CHF despite the increase of furosemide and the combination of other diuretics. LV(EF) < 35%, serum creatinine < 2 mg/dL, BUN ≤ 60 mg/dL, a reduced urinary volume, and a low natriuresis. None of the patients had to take non-steroid anti-inflammatory drugs.	NR
Mahjoob, 2021, 34903983 IRCT20200812048380N1 Iran	RCT	2018-2019	Academic, Single center[b]	≥18 yo with diffuse peripheral edema with no response to oral furosemide (80 mg), patients with proteinuria and edema resistant to treatment and nephrotic syndrome	Candidate for hemodialysis, pacemaker implantation, SBP ≤ 80 mmHg, GFR ≤ 15 mL/min, serum albumin ≤ 2.5 g/dL, serum potassium ≥ 5.5 mEq/L, serum sodium > 145 mEq/L, urine volume ≤ 100 mL/ d, dementia, cerebral vascular disease, substance or alcohol addiction, receiving mineralocorticoids, inability to give informed consent

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Study Location Details (Hospital Type, Centers)	Inclusion Criteria	Exclusion Criteria
Okuhara, 2014, 24462960 Japan	RCT	2011-2012	Academic, Single center[c]	ADHF with symptoms of NYAH III/IV and SBP > 80 mmHg, eGFR > 15 mL/min/1.73 m^2, serum sodium < 148 mmol/L	Use of inotropic agents, carperitide, hemodiafiltration or noninvasive positive pressure ventilation (NPPV), complicated by systemic infection, ACS, or distinct endocrine diseases (*eg*, syndrome of inappropriate secretion of antidiuretic hormone)
Paterna, 2000, 10938493 Italy	RCT	1996-1998	NR	Refractory CHF according to Framingham criteria and NYHA, DCHF (dyspnea, weakness, lower limb edema, or anasarca) of NYHA IV, unresponsive to treatment with high oral doses of furosemide and/or combinations of diuretics (thiazide, loop diuretic, and spironolactone), ACEIs, digitalis, nitrates, and receiving this therapy at least 2 weeks before the study and hospitalization. Patients being unresponsive with a reduction of urine volume and a constant increase of body weight and impairment of clinical signs of CHF despite the increase of furosemide and the combination of other diuretics. LV(EF) < 35%, serum creatinine < 2 mg/dL, BUN ≤ 60 mg/dL, a reduced urinary volume, and a low natriuresis. None of the patients had to take non-steroid anti-inflammatory drugs.	NR
Paterna, 2005, 15963399, Italy	RCT	2000-2002	NR	Refractory CHF according to Framingham criteria and NYHA, DCHF (dyspnea, weakness, lower limb edema, or anasarca) of NYHA IV, unresponsive to treatment with high oral doses of furosemide and/or combinations of diuretics (thiazide, loop diuretic, and spironolactone), ACEIs, digitalis, nitrates for at least 2 weeks before the study and hospitalization. Patients being unresponsive with a reduction of urine volume and a constant increase of body weight and impairment of clinical signs of CHF despite the increase of furosemide and the combination of other diuretics.	NR

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Study Location Details (Hospital Type, Centers)	Inclusion Criteria	Exclusion Criteria
				LV(EF) < 35%, serum creatinine < 2 mg/dL, BUN ≤ 60 mg/dL, a reduced urinary volume (<500 ml/24 h), and a low natriuresis. None of the patients had to take non-steroid anti-inflammatory drugs	
Paterna, 2011, 21701268 NCT01156337 Italy	RCT	2000-2007	Academic, Single center[d]	DHF by chronic ischemic or nonischemic cardiomyopathy, > 18 years, Framingham criteria and NYHA functional classification for HF, uncompensated HF (dyspnoea, weakness and lower limb edema), in NYHA III functional class, was unresponsive to treatment with oral high doses of furosemide, spironolactone, ACEIs, digitalis nitrates at least 4 weeks before the study and before hospitalization. Patients were judged unresponsive with a reduction of urine volume, a constant increase of body weight and an impairment of clinical HF despite the increase of furosemide. LV(EF) < 40%, serum creatinine < 2.5 mg/dL, BUN < 60 mg/dL and reduced urinary volume (800 mL/d) despite the established treatments. No patients received NSAIDs.	NYHA class < III or > III on admission or with NYHA class III at discharge, with concomitant main comorbidities, cerebral vascular disease, dementia, cancer, uncompensated diabetes, severe hepatic disease, inability to give informed consent, requiring pacemaker implantation and those with an alcoholic habit, declined to take part in the study protocol, patients with side effects for ACEI treatment (cough), patients who did not follow the assigned treatment, did not attend the scheduled clinical visits, did not adhere to prescribed diet and the fluid intake of 1000 mL/day or had a reduction or discontinuation of prescribed treatments during follow-up.
Parrinello, 2011, 21440872 Italy	RCT	2007-2008	Academic, Single center	Framingham criteria, NYHA functional classification for CHF; DCHF (dyspnea, weakness, lower limb edema or anasarca), NYHA functional class IV, unresponsive to treatment with oral high doses of furosemide and combinations of diuretics (thiazide, furosemide, and spironolactone), ACEIs, digitalis, beta-blockers, nitrates for at least 2 weeks before the study and hospitalization. Patients being unresponsive with reduction in urine volume, a constant increase in body weight, and an impairment in the clinical signs of HF, despite the increase in furosemide and its combination with other diuretics. LV(EF) < 40%; serum creatinine < 2.0 mg/d; BUN < 60 mg/dL; reduced urinary volume (<500 mL/24 h); low natriuresis (< 60 mEq/24	Patients unable to provide informed consent; those with cardiac resynchronization therapy (to avoid interference with echocardiographic measurements); patients with concomitant important comorbidities, such as end-stage of renal insufficiency or those on dialysis; uncompensated diabetes; cerebral vascular disease; dementia; cancer; liver cirrhosis or other edematous syndromes; patients being treated with steroids or nonsteroidal antiinflammatory drugs (NSAIDs) or who were alcohol dependent; and those who did not follow the treatment protocol (a fluid intake of 1,000 mL day and prescribed sodium diet). In addition, patients with side effects for ACE inhibitors (a cough), even if

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Study Location Details (Hospital Type, Centers)	Inclusion Criteria	Exclusion Criteria
				h), despite having received the established treatments and no cardiac resynchronization therapy. None of the patients had taken NSAIDs.	these patients were taking angiotensin-2 blockers, were excluded from the study to maximize the homogeneity of the treatments.
Parrinello, 2012, 22980301 NCT01419132 Italy	RCT	2011	Academic, Single center	ADHF according to the AHA/ ESC guidelines and who met criteria on hospital admission as follows; signs/symptoms of HF; NYHA functional class III or IV on admission due to an exacerbation of symptoms with at least 1 class deterioration; evidence of systolic dysfunction on echocardiographic examination on admission ([EF] < 45%); BNP levels on admission > 100 pg/mL. 18-95 yo	NYHA class < III on admission; patients with ASC, pulmonary thromboembolism, cardiac tamponade, pericarditis, renal insufficiency (serum creatinine > 2.5 mg/dL, BUN > 60 mg/dL), dialysis, chronic liver disease, pleuropneumonia, blood and autoimmune diseases, concomitant other important comorbidity, cerebral vascular disease, dementia, cancer, or uncompensated diabetes; decline to provide informed consent, patients requiring pacemaker implantation and those with issues of excessive alcohol consumption. None of the patients took NSAIDS.
Roul, 2017 France	NRCS, Retrospective	2013-2015	Single center	Patients admitted for heart failure with low plasma sodium level at entry or treated with hypertonic saline solution during hospitalization	NR
Tuttolomondo, 2011, 20346637 Italy	NRCS, Prospective	2005-2009	Single center	Patients admitted with heart failure according to ESC or NYHA functional class II or worse plus objective evidence of cardiac dysfunction (LV)EF: < 30% or abnormal diastolic function echocardiographically detected, normal systolic function at rest without signs of CHF	Acute myocarditis, active pulmonary and liver disease, autoimmune disorders, infections, malignant diseases, muscle diseases, renal insufficiency (serum creatinine ≥ 2.5 mg/dL), chronic inflammatory diseases, rheumatological diseases, hematological disease, regular treatment with anti-inflammatory drugs
Tuttolomondo, 2021, 34288546 NCT04628325 Italy	RCT	2017-2019	Single center[e]	ADHF due to HFrEF according to the European Society of Cardiology (ESC) criteria or NYHA functional class II or worse plus objective evidence of cardiac dysfunction (LV)EF < 40%, >18 yo	Acute myocarditis, active pulmonary and liver disease, autoimmune disorders, infections, malignant diseases, muscle disorders, renal insufficiency (serum creatinine ≥ 2.5 mg/dL), chronic inflammatory diseases, rheumatological diseases, hematological diseases, regular treatment with anti-inflammatory drugs.

Author, Year, PMID, Protocol Number, Country	Study Design	Study Dates	Study Location Details (Hospital Type, Centers)	Inclusion Criteria	Exclusion Criteria
Wan, 2017, 28701670 China	RCT	2017	Single center	DHF (dyspnoea, weakness, lower limb edema or anasarca) and chronic ischemic or nonischemic cardiomyopathy according to the definition of HF, Framingham criteria, and NYHA functional classification for HF; unresponsive to treatment with high doses of furosemide, spironolactone, ACEIs, digitalis, and nitrates (reduction of urine volume, a constant increase of body weight, and impairments caused by clinical HF as reported above, in spite of an increase in furosemide and a combination of other diuretics; had started this therapy at least 6 months before hospitalization. LV(EF) < 40%, serum creatinine < 1.73 mg/dL, BUN < 60 mg/dL, urinary volume < 500 mL/d.	Age < 18 years; plasma albumin < 30 g/L; cancer, severe diabetes, cerebral vascular disease, dementia, or severe hepatic disease; NYHA class > III or < III on admission or with NYHA class III at discharge; failure to follow the assigned treatment; did not attend scheduled clinical visits, did not follow the prescribed diet, or serious water or activity restrictions.
Yayla, 2015, 26135463 Turkey	RCT	2011-2012	Academic, Single center	ADHF with reduced or preserved LVEF, Patients who were admitted to the emergency department within the previous 24 h with diagnosis of ADHF, pro-BNP > 300 pg/ml	IV diuretic use before admission to hospital, serum creatinine levels > 2.0 mg/dl, SBP < 90 mmHg; requiring IV vasodilators or inotropic agents other than digoxin, patients with suspected ACS
Montgomery, 2023, 37044281 United States	RCT	2020-2022	Academic, Single center	≥ 18 yo, admitted to cardiology floor (non-ICU) with primary diagnosis of DHF, NT-proBNP >1000 ng/L, Initiation of continuous furosemide infusion of ≥ 10 mg/hr	Renal replacement therapy, ultrafiltration, eGFR < 15mL/min/1.73m2, average SBP > 180mmHg, DBP > 100mmHg for 24 h, serum sodium concentration <120mEq/L or >145mEq/L, admission with intention to undergo open heart surgery, inability to swallow or absorb oral medications, diagnosis of diabetes insipidus, use of IV inotropes, vasopressors or vasodilators at enrollment, anticipated stay of fewer than 72 h, use of intravenous radiocontrast in the prior 72 h or anticipated use during current hospitalization, current use of NaCl tablets or vasopressin antagonist medication.

Notes. [a] Tertiary hospital dedicated to cardiology; [b] Patients admitted to post CCU ward; [c] Patients admitted to Division of Cardiovascular Medicine; [d] Patients admitted to Emergency Medicine and Cardiology Department; [e] Patients admitted to Internal Medicine ward.
Abbreviations. ACE=angiotensin converting enzyme; ACEI= angiotensin converting enzyme inhibitor; ACS=acute coronary syndrome; ADHF=acute decompensated heart failure; AHA=American Heart Association; BNP=brain (or B-type) natriuretic peptide; BP=blood pressure; BUN=blood urea nitrogen;

CCU=critical care unit; COPD=chronic obstructive pulmonary disease; DBP=diastolic blood pressure; DHF=decompensated heart failure; DM=diabetes mellitus; ED=emergency department; eGFR=estimated glomerular filtration rate; ESC=European Society of Cardiology; GFR=glomerular filtration rate; h=hour; HF=heart failure; ICU=intensive care unit; IV=intravenous; LVEF=left ventricular ejection fraction; m=meter; MI=myocardial infraction; min=minute; mL=milliliter; mmHg= millimeters of mercury; NR=not reported; NRCS=nonrandomized comparative studies; NSAIDs=non-steroidal anti-inflammatory drugs; NT-proBNP=N-terminal pro-brain (or B-type) natriuretic peptide; NYHA= New York Heart Association; pro-BNP= pro B-type Natriuretic Peptide; RAAS= renin-angiotensin-aldosterone system; RCT=randomized controlled trial; SBP=systolic blood pressure; yo=years old.

APPENDIX E. BASELINE CHARACTERISTICS

Author, Year, PMID	N Analyzed	Race/Ethnicity, %	Age, Mean (SD) or %	Male, %	Clinical Features, Mean (SD) or %	Heart Failure Classification, Mean (SD) or %	Medication History, %
Aliti, 2013, 23689381	75	White, 84 Other races, NR	60 (11.0)	69	NR	LVEF (%), 26.0 (8.7) NYHA III, 47 NYHA IV, 45	Metoprolol tartrate, 56 Carvedilol, 3 Captopril, 48 Enalapril maleate, 29 ARBs, 11 Spironolactone, 51 Hydralazine, 29 Furosemide, 81 Hydrochlorothiazide, 12
Fabricio, 2019, 31221280	44	NR	57.9 (12.0)	59.1	Weight, 77.1 (23.7) SBP, 109.2 (23.1) DBP, 70.8 (18.2) MAP, 83.7 (19.5) HR, 73.6 (12.2) Serum Na, 135.3 (4.9)	LVEDD (mm), 63.2 (12.2) LVEF (%), 28.9 (12.6)	β-blockers, 79.5[a] ACEIs, 43.2[a] ARBs, 20.5[a] Hydralazine, 29.5[a] Furosemide, 88.6[a] Nitrate, 29.5[a]
d'Almeida, 2018, 29793053	53	White, 81.1 Other races, NR	72.3 (11.7)	32.1	SBP, 127.0 (25.9) DBP, 70.5 (12.9)	LVEF (%), 60.9 (7.5) NYHA II, 9.5 NYHA III, 50.9 NYHA IV, 39.6	β-blockers, 75.5 ACEIs, 64.2 ARBs, 17 Spironolactone, 26.4 Hydralazine, 18.9 Furosemide, 83 Hydrochlorothiazide, 11.3
Inuzuka, 2016	190	NR	79 (Med)	NR	BNP, 856 (Med)	NYHA II-IV, 100	NR
Velloso, 1991, 1824218	32	NR	54	56.3	NR	NYHA III, 28.6% in low sodium diet group NYHA IV, 71.4% in low sodium diet group	Furosemide, 100 Hydrochlorothiazide, 100 Digitalis, 100 Amiloride, 100

Author, Year, PMID	N Analyzed	Race/Ethnicity, %	Age, Mean (SD) or %	Male, %	Clinical Features, Mean (SD) or %	Heart Failure Classification, Mean (SD) or %	Medication History, %
Issa, 2013, 22243938	32	NR	47.4 (13.1)	81.3	BMI, 27.7 (6.1) SBP, 101.6 (15.5) DBP, 65.2 (9.1) Serum Na, 136.7 (3.5)	LVEDD (mm), 71.6 (9.7) LVEF (%), 23.9 (6.3)	β-blockers, 78.1 ACEIs, 56.4 Spironolactone, 43.8 Hydralazine, 56.3 Digoxin, 28.1 Dobutamine, 34.4
Licata, 2003, 12660669	107	NR	74.6 (7)	63.6	SBP, 143.5 (23.5) DBP, 81 (13.5) HR, 83.5 (14) Serum Na, 135.3 (7.5)	LVEF (%), 30.4 (4) NYHA IV, 100	NR[b]
Mahjoob, 2021, 34903983	28	NR	65.1(12.9)	53.6	Weight, 83.2 (20.5) SBP, 123.3 (19.7) DBP, 72.5 (8.7) HR, 80.3 (72-110) [Med (full range)] Serum Na, 135.1 (4.1)	NR	NR
Okuhara, 2014, 24462960	44	NR	72 (10.5)	68.2	NR	LVEF (%), 34.5 (26.5,41) [Med (IQR)] NYHA III, 54.5 NYHA IV, 45.5	ACEIs/ ARBs, 65.9 Loop diuretics, 68.2 Aldosterone antagonists, 40.9 Thiazide diuretics, 15.9 β-blockers, 65.9
Paterna, 2000, 10938493	60	NR	73.9 (6.9) 65-90 yo (Range)	65	Weight, 73.4 (9.2) SBP, 143.5 (25.7) DBP, 81.4 (14.1) HR, 83.3 (14.6) Serum Na, 135.3 (7.4)	LVEF (%), 30.3 (4.3) NYHA IV, 100	NR
Paterna, 2005, 15963399	94	NR	74.6 (7)	63.8	Weight, 75.9 (15.5) SBP, 145.5 (21.5) DBP, 81 (13.5) HR, 83 (13.5) Serum Na, 134.4 (6.5)	LVEF (%), 30.2 (3) NYHA IV, 100	NR

Author, Year, PMID	N Analyzed	Race/Ethnicity, %	Age, Mean (SD) or %	Male, %	Clinical Features, Mean (SD) or %	Heart Failure Classification, Mean (SD) or %	Medication History, %
Paterna, 2011, 21701268	1927	NR	74.1(12)	62.9	Weight, 83.6 (14) SBP, 135.5 (15.5) DBP, 76 (7.5) HR, 89 (19.5) Serum Na, 138.3 (7.5)	LVEF (%), 34.1 (4.5) NYHA III, 100	Carvedilol, 69.4 Captopril, 100 Spironolactone, 84.9 Furosemide, 100 Digitalis, 11.5
Parrinello, 2011, 21440872	133	NR	76.0 (8) 65-82 yo (range)	64.7	Weight, 75.9 (15.5) SBP, 134 (23) DBP, 80.5 (12.5) HR, 81.5 (12) Serum Na, 135.5 (5)	LVEF<40%, 100 NYHA IV, 100	NR[b]
Parrinello, 2012, 22980301	248	NR	73.5 (9.7)	59.7	SBP, 143.5 (23) DBP, 81.0 (12) HR, 84.0 (11) Serum Na, 138.8 5.2)	LVEF<45%, 100 NYHA III or IV, 100	β-blockers, 46 ACEIs, 100 Spironolactone, 64.9 Furosemide, 62.9 Digitalis, 40.3
Roul, 2017	167	NR	78	55	NR	NR	NR
Tuttolomondo, 2011, 20346637	150[c]	NR	65 (61.5, 80.5) [Med (IQR)]	54	Weight, 73.5 (69.5, 83) [Med (IQR)][a] SBP, 142.5 (134, 150) [Med (IQR)][a] DBP, 80.5 (77.5, 95) [Med (IQR)][a] HR, 84 (80, 97) [Med (IQR)] Serum Na, 138 (129.5, 140.5) [Med (IQR)][a]	LVEF (%), 37 (28.5, 42.5) [Med (IQR)] NYHA II, 40 NYHA III, 34.7 NYHA IV, 25.3	NR

Author, Year, PMID	N Analyzed	Race/Ethnicity, %	Age, Mean (SD) or %	Male, %	Clinical Features, Mean (SD) or %	Heart Failure Classification, Mean (SD) or %	Medication History, %
Tuttolomondo, 2021, 34288546	136	NR	76.2 (7.7)	49.3	Weight, 78.1 (14.2) SBP, 127.1 (17.5) DBP, 70.4 (10.5)	LVEF (%), 56.4 (10.6) NYHA II, 16.9 NYHA III, 66.2 NYHA IV, 16.9	β-blockers, 61 ACEIs, 73.5 ARBs, 13.2 Mineralocorticoid receptor antagonists, 18.4
Wan, 2017, 28701670	264	NR	60.9 (10.1)	38.3	SBP, 143 (17.5 DBP, 67 (10.5) Serum Na: 135.7 (3.6	LVEF (%), 38.3 (1.6) NYHA III, 100	β-blockers, 39.4 ACEIs, 85.2 Spironolactone, 91.7 Digitalis, 77.7 Furosemide, 100
Yayla, 2015, 26135463	28[d]	NR	69.2 (10.4)	56	Weight, 81 (17.5) Serum Na, 137.4 (4.8)	LVEF (%), 42.1 (14.2)	β-blockers, 55.8 ACEIs or ARB, 60.5 Aldosterone antagonist, 25.6 Furosemide, 65.1
Montgomery, 2023, 37044281	65	White 86 Black 14	70 (12)	63	Weight, 100 (29) SBP, 113 (17) DBP, 62 (7.9) HR, 76 (14) Serum Na, 140 (3.4)	LVEF (%), 45 (16)	β-blockers, 72.3 ACEIs or ARB, 32.3 Spironolactone, 52.3 Hydralazine, 52.3 Furosemide, 100

Notes. [a] Calculated by the research team based on data of low sodium and normal sodium diet groups; [b] Patients received medications (*eg*, ACEIs, digitalis, nitrates) during the study period; did not report the % of patients; [c] NRCS, prospective study with 4 arms (furosemide with HSS group [N=120], furosemide group [N=30], asymptomatic group [N=30], healthy group [N=30]); we included furosemide with HSS group and furosemide group in the analysis; [d] Furosemide with HSS (N=14) and furosemide bolus (N=14) groups were included in the analysis.

Abbreviations. ACE=angiotensin converting enzyme; ACEIs= angiotensin converting enzyme inhibitors; ARB=angiotensin receptor blockers; BMI=body mass index; BNP=brain (or B-type) natriuretic peptide; DBP=diastolic blood pressure; LVEDD=left ventricle end-diastolic diameter; LVEF=left ventricular ejection fraction; mm=millimeters; Na=sodium; NR=not reported; NRCS=nonrandomized comparative studies; NYHA= New York Heart Association; SBP=systolic blood pressure; yo=year.

APPENDIX F. DESCRIPTION INTERVENTIONS

Table F.1. Description of Dietary Sodium Interventions

Author, Year, PMID	Arm	Sodium Intake	Fluid Intake	Duration of Interventions
Aliti, 2013, 23689381	Low sodium diet	0.8g/d Na	Maximum intake, 800 mL/d	Until hospital day 7 or until discharge in patients whose length of stay was less than 7 days
	Unrestricted sodium diet	Standard hospital diet, 3-5 g/d Na	Liberal fluid, at least 2500 mL/d	Until hospital day 7 or until discharge in patients whose length of stay was less than 7 days
Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na	1000 mL/d	7 days (or less based on clinical indication[a])
	Unrestricted sodium diet	2.8 g/d Na	1000 mL/d	7 days (or less based on clinical indication[a])
d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na	800 mL/d	Until day 7 of admission or at hospital discharge, whichever came first
	Unrestricted sodium diet	Standard hospital diet, ~4 g/d Na	Unlimited fluid intake	Until day 7 of admission or at hospital discharge, whichever came first
Inuzuka, 2016	Low sodium diet	2.4 g/d Na	NR	NR[b]
	Unrestricted sodium diet	4 g/d Na	NR	NR[b]
Velloso, 1991, 1824218	Low sodium diet	0.8 g/d Na	800 mL/d	NR[b]
	Unrestricted sodium diet	4 g/d Na	800 mL/d	NR[b]

Notes. [a] Clinical indication defined by the medical team responsible for the treatment of the patient based on the occurrence of hypotension, hyponatremia, or worsening of renal function, the intervention could be stopped before the 7th day of hospitalization; [b] The study did not clearly define the duration of intervention.
Abbreviations. d=day; g=gram; mL=milliliter; Na=sodium; NR=not reported.

Table F.2. Description of Hypertonic Saline Solution Interventions

Author, Year, PMID	Arm	Saline Solution	Fluid Intake	Diuretic	Other interventions	Sodium Intake via Saline Solution[a]	Sodium Intake from Diet[b]	Total Sodium Intake[c]	Duration of Interventions
Issa, 2013, 22243938	Furosemide with HSS	100 mL of HSS[d] (7.5% NaCl) twice daily	NR	IV furosemide[e] Bolus per day	NR	5.9 g/d	NR	5.9 g/d	3 (d)
	Furosemide without HSS	100 mL of NS[d] (0.9% NaCl) twice daily	NR	IV furosemide[e] Bolus per day	NR	0.7 g/d	NR	0.7 g/d	3 (d)
Licata, 2003, 12660669	Furosemide with HSS	150 mL of HSS[f] (1.4%-4.6% NaCl) twice daily	1000 mL/d	IV furosemide[g,h] (500-1000 mg) 30-min infusion twice daily	Sodium diet (2.76 g/d Na)	1.65 g/d – 5.43 g/d	2.76 g/d	4.41– 8.1 g/d	6-12 (d)
	Furosemide without HSS	NR	1000 mL/d	IV furosemide[g,h] (500-1000 mg) bolus twice daily	Sodium diet (1.84 g/d Na)	NR	1.84 g/d	1.84 g/d	6-12 (d)
Mahjoob, 2021, 34903983	Furosemide with HSS	150 mL of HSS (5% NaCl) twice daily	NR	IV furosemide (250 mg) per day	NR	5.9 g/d	NR	5.9 g/d	48 (h)
	Furosemide without HSS	150 mL of NS every 12 h	NR	IV furosemide (250 mg) per day	NR	1.06 g/d	NR	1.06 g/d	48 (h)
Okuhara, 2014, 24462960	Furosemide with HSS	500 mL of HSS (1.7% NaCl) per day	500 mL/d	IV furosemide (40 mg) per day	Sodium diet (2.4 g/d Na)	3.34 g	2.4 g/d	5.7 g/d	24 (h)
	Furosemide with glucose	500 mL of glucose (5%) per day	500 mL/d	IV furosemide (40 mg) per day	Sodium diet (2.4 g/d)	0 g/d	2.4 g/d	2.4 g/d	24 (h)
Paterna, 2000, 10938493	Furosemide with HSS	150 ml of HSS[f] (1.4-4.6% NaCl) twice daily	1000 mL/d	IV furosemide[g,h] (500-1000 mg) 30-min infusion twice daily	Sodium diet (2.76 g/d Na)	1.65 g/d – 5.42 g/d	2.76 g/d	4.41– 8.1 g/d	6-12 (d)
	Furosemide without HSS	NR	1000 mL/d	IV furosemide[g,h] (500-1000 mg) bolus twice daily	Sodium diet (2.76 g/d Na)	NR	2.3 g/d	2.3 g/d	6-12 (d)

Author, Year, PMID	Arm	Saline Solution	Fluid Intake	Diuretic	Other interventions	Sodium Intake via Saline Solution[a]	Sodium Intake from Diet[b]	Total Sodium Intake[c]	Duration of Interventions
Paterna, 2005, 15963399	Furosemide with HSS	150 ml of HSS[f] (1.4%- 4.6%) NaCl twice daily	1000 mL/d	IV furosemide[h] (500-1000 mg) 30-min infusion twice daily	Sodium diet (2.76 g/d Na)	1.65 g/d – 5.42 g/d	2.76 g/d	4.41– 8.1 g/d	4-6 (d)
	Furosemide without HSS	NR	1000 mL/d	IV furosemide[h] (500-1000 mg) bolus twice daily	Sodium diet (1.84 g/d Na)	NR	1.84 g/d	1.84 g/d	4-6 (d)
Paterna, 2011, 21701268	Furosemide with HSS	150 ml of HSS[f] (1.4%–4.6% NaCl) twice daily	1000 mL/d	IV furosemide[h] (250 mg) 30-minute infusion twice daily	Sodium diet (2.76 g/d Na)	1.65 g/d – 5.42 g/d	2.76 g/d	4.41 – 8.1 g/d	NR
	Furosemide without HSS	NR	1000 mL/d	IV furosemide[h] (500-1000 mg) bolus twice daily	Sodium diet (1.84 g/d Na)	NR	1.8 g/d	1.8 g/d	NR[1]
Parrinello, 2011, 21440872	Furosemide with HSS	150 ml of HSS (3% NaCl) twice daily	1000 mL/d	IV furosemide (250 mg) twice daily	Sodium diet (2.76 g/d Na)	3.54 g/d	2.76 g/d	6.3 g/d	6 (d)
	Furosemide without HSS	150 mL of NS (0.9% NaCl) twice daily	1000 mL/d	IV furosemide (250 mg) twice daily	Sodium diet (1.84 g/d Na)	1.06 g/d	1.84 g/d	2.9 g/d	6 (d)
Parrinello, 2012, 22980301	Furosemide with HSS	HSS[f] (1.4%–4.6% NaCl) twice daily	1000 mL/d	IV furosemide (250 mg) 30-min infusion twice daily	Normal sodium diet	NR	NR	NR	NR
	Furosemide without HSS	NR	1000 mL/d	IV infusion furosemide (250 mg) twice daily	NR	NR	NR	NR	NR
Roul, 2017	HSS	HSS	NR	NR	NR	NR	NR	NR	NR
	Without HSS	NR	NR	NR	NR	NR	NR	NR	NR

Author, Year, PMID	Arm	Saline Solution	Fluid Intake	Diuretic	Other interventions	Sodium Intake via Saline Solution[a]	Sodium Intake from Diet[b]	Total Sodium Intake[c]	Duration of Interventions
Tuttolomondo, 2011, 20346637	Furosemide with HSS	150 mL of HSS[i,k] (1.4-4.6% NaCl) twice daily	NR	IV infusion furosemide[g, h] (125-1000 mg) 30-min infusion twice daily	Sodium diet (1.61 g/d Na)	1.65 g/d – 5.43 g/d	1.61 g/d	3.3 g/d – 7 g/d	8 (d)
	Furosemide without HSS	NR	NR	IV infusion furosemide[g,h] (125-1000 mg) 30-min infusion twice daily	Sodium diet (1.61 g/d Na)	NR	1.61 g/d	1.61 g/d	8 (d)
Tuttolomondo, 2021, 34288546	Furosemide with HSS	150 ml of HSS[j, k] (1.4-4.6% NaCl) twice daily	NR	IV infusion furosemide[g,h] (120–250 mg) 30-min infusion twice daily	Sodium diet (1.61 g/d Na)	1.65 g/d – 5.43 g/d	1.61 g/d	3.3 g/d – 7 g/d	6 (d)
	Furosemide without HSS	NR[k]	NR	IV infusion furosemide (120–250 mg) 30-min infusion twice daily	Sodium diet (1.61 g/d Na)	NR	1.61 g/d	1.61 g/d	6 (d)
Wan, 2017, 28701670	Furosemide with HSS	100 ml of c-HSS[l] twice daily	< 500 mL	IV furosemide (100 mg) 1 h infusion twice daily	Normal sodium diet (2.76 g/d Na)	2.2 g/d	2.76 g/d	4.96 g/d	Until compensated[m]
	Furosemide without HSS	NR	< 500 mL	IV furosemide (100 mg) 1 h infusion twice daily	Normal sodium diet (2.76 g/d Na)	NR	2.76 g/d	2.76 g/d	Until compensated[m]

Author, Year, PMID	Arm	Saline Solution	Fluid Intake	Diuretic	Other interventions	Sodium Intake via Saline Solution[a]	Sodium Intake from Diet[b]	Total Sodium Intake[c]	Duration of Interventions
Yayla, 2015,[n] 26135463	Furosemide with HSS	150 ml of HSS (1.95% NaCl) in 30 min once daily	NR	IV furosemide (160 mg) in 30 min once daily	NR	1.15 g/d	NR	1.15 g/d	48 (h)
	Furosemide (cIV) without HSS	NR	NR	IV furosemide (160 mg) continuous infusion in 16h/ d	NR	NR	NR	NR	48 (h)
	Furosemide (bI) without HSS	NR	NR	IV furosemide (80 mg) bolus twice daily	NR	NR	NR	NR	48 (h)
Montgomery, 2023, 37044281 United States	Furosemide with oral NaCl	NR	Unlimited	IV furosemide	2 g Oral NaCl thrice per day + Restricted Na diet (~0.8 g/d Na)	NR	3.2 g/d	3.2 g/d	4 (d)
	Furosemide without oral NaCl	NR	Unlimited	IV furosemide	Restricted Na diet (~0.8 g/d Na)	NR	0.8 g/d	0.8 g/d	4 (d)

Notes. [a] Calculated by the research team based on sodium intake from IV HSS if reported; [b] Calculated by the research team based on oral sodium intake from diet if reported; [c] Calculated by the research team based on combined sodium intake from IV HSS and oral diet if reported; [d] 100 mL of solution was infused during 1 h; [e] Initial dose of furosemide was estimated based on the dose previously administered to patient, renal function and body weight, and initial dose could be modified according to the initial patient response with pre-established objective to achieve a weight loss of 500-1000 g/d; [f] The dose of HSS was determined according to serum Na (HSS 4.6%, 3.5%, between 1.4% and 2.4% were administered for patients with serum Na < 125 mEq/L, between 126 and 135 mEq/L, > 135 mEq/L respectively); [g] Daily dosage of furosemide was defined considering diuretics, urinary volume, BP, severity of signs of symptoms of congestion; [h] Once the clinically compensated state was reached, IV furosemide and HSS were stopped and replaced with oral furosemide and oral KCl supplementation, and the best therapy continued without changes after discharge with the standard therapy (*eg*, ACEIs, digitalis, and nitrates) in both groups; [i] The dose of HSS was determined in each patient according to these schedules: for serum Na values <125 mEq/L, the HSS concentration was 3.5% and for serum Na values >135 mEq/L, the HSS concentration varied between 1.4% and 2.4%; [j] The dose of HSS was determined in each patient as follows: the HSS concentration 3.5% for serum Na values < 135 mEq/L and between 1.4% and 2.4% for serum Na values > 135 mEq/L; [k] All patients underwent an acute saline load with 15 mL/kg of 0.9% NaCl (over 60 min) on the day after the end of the treatment period (6 days); [l] Compound hypertonic saline solution: the concentrations of NaCl, KCl, and MgSO4 were 2.8%, 0.2%, and 0.9% respectively; [m] Did not clearly define the duration of intervention; [n] Furosemide with HSS (N=14) and furosemide bolus (N=14) groups were included in the analysis.
Abbreviations. bI=bolus IV; cIV=continuous intravenous infusion; d=day; g=gram; HSS=hypertonic saline solution; h=hour; IV=intravenous; kg=kilograms; mg=milligram; min=minute; mL=milliliter; Na=sodium; NaCl=sodium chloride; NR=not reported.

APPENDIX G. CATEGORICAL OUTCOMES

Outcome	Study Year PMID	Arm	Total Sodium Intake[1]	Fluid Intake	Time	Outcome Definition	n/N (%)	Effect Size (95% CI)[2]	Reported P value
Clinical Outcomes									
Mortality	*Diet (g/d Na)*								
	Aliti, 2013, 23689381 RCT	Low sodium diet	Max 0.8 g/d Na for 7 days or less	Max 800 mL/d	7 (d)	All-cause mortality	0/38 (0)	RD 0.0 (-0.051, 0.051)	-
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less	≥2500 mL/d			0/37 (0)		
	d'Almeida, 2018, 29793053 RCT	Low sodium diet	0.8 g/d Na for 7 days or less	800 mL/d	30 (d) after discharge	All-cause mortality	2/30 (6.7)	RR 0.77 (0.12, 5.04)	> 0.99
		Unrestricted sodium	~4 g/d Na for 7 days or less	Unlimited fluid intake			2/23 (8.7)		
	Fabricio, 2019, 31221280 RCT	Low sodium diet	1.2 g/d Na for 7 days	1000 mL/d	During hospitalization	All-cause mortality	0/16 (0)	RD 0.0 (-0.117, 0.117)	-
		Unrestricted sodium diet	2.8 g/d Na for 7 days	1000 mL/d			0/15 (0)		
		Low sodium diet	1.2 g/d Na for 7 days	1000 mL/d	30 (d) after discharge	All-cause mortality	2/16 (12.5)	RR 0.93 (0.15, 5.84)	1.0
		Unrestricted sodium diet	2.8 g/d Na for 7 days	1000 mL/d			2/15 (13.3)		
	Velloso, 1991, 1824218 RCT	Low sodium diet	0.8 g/d Na for NR days[3]	800 mL/d	NR	Mortality not directly related to congestive heart failure (one a sudden death and one septic shock due to lung disease)	1/14 (7.1)	RR 1.29 (0.09,18.8)	NR
		Unrestricted sodium diet	4 g/d Na for NR days[3]	800 mL/d			1/18 (5.6)		
	HSS (%NaCl)								
	Issa, 2013, 22243938 RCT	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 (d) Total Na 5.9 =~6 g/d[4]	NR	During hospitalization	All-cause mortality	10/20 (50)	RR 1.5 (0.60, 3.74)	NR
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 (d) Total Na 0.7 g/d[4]	NR			4/12 (33.3)[5]		
	Paterna, 2005, 15963399 RCT	Furosemide with HSS	150 mL of HSS (1.4%-4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	30 (d)	Death during the 30-day study period, all-cause (2 sudden death and 1 irreversible HF)	0/48 (0)	RD -0.065 (-0.145, 0.015)	NR
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			3/46 (6.5)		
	Paterna, 2011,	Furosemide with	150 mL of HSS	1000 mL/d	During	Mortality from cardiac	0/953 (0)		-

Outcome	Study Year PMID	Arm	Total Sodium Intake[1]	Fluid Intake	Time	Outcome Definition	n/N (%)	Effect Size (95% CI)[2]	Reported P value
	21701268 RCT	HSS	(1.4%–4.6% NaCl) twice daily until compensation[6] (1.65-5.42 g/d Na) Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d		hospitalization	cause during hospitalization		RD 0.0 (-0.002, 0.002)	
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[6] Total Na 1.8 g/d	1000 mL/d			0/974 (0)		
	Wan, 2017, 28701670, RCT	Furosemide with compound HSS	100 mL c-HSS[7] (2.8% NaCl) twice daily until clinical compensation[8] (2.2 g/d Na) Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	During hospitalization	All-cause mortality	0/132 (0)	RD 0.0 (-0.015, 0.015)	-
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d Na until clinical compensation[8] Total Na 2.76 g/d = ~2.8 g/d	< 500 mL/d			0/132 (0)		
HF-Related Symptom	*HF-Related Symptom (Change in NYHA Functional Class)*								
	HSS (% NaCl)								
	Paterna, 2000, 10938493	Furosemide with HSS	150 mL of HSS (1.4%-4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Number of patients who had their NYHA changed from IV to III at discharge	2/30 (6.67)	RR 0.11 (0.03, 0.44)	< 0.05
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			18/30 (60)		
		Furosemide with HSS	150 mL of HSS (1.4%-4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d		Number of patients who had their NYHA changed from IV to IIa or IIb at discharge	28/30 (93.33)	RR (2.42) (1.55, 3.76)	-
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			12/30 (40)		
	Paterna, 2011, 21701268 RCT	Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl) twice daily until compensation[6]	1000 mL/d	Discharge	Number of patients who had their NYHA changed from III to II at discharge	736/953 (77.2)	RR 0.93 (0.89, 0.97)	

Outcome	Study Year PMID	Arm	Total Sodium Intake[1]	Fluid Intake	Time	Outcome Definition	n/N (%)	Effect Size (95% CI)[2]	Reported P value
			(1.65- 5.42 g/d Na) Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d						<0.29[9]
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[6] Total Na 1.8 g/d	1000 mL/d			813/974 (83.5)		
		Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl) twice daily until compensation[6] (1.65- 5.42 g/d Na) Moderate sodium diet 2.76 g/d Na Total Na ~4.5-8.2 g/d	1000 mL/d	Discharge	Number of patients who had their NYHA changed from III to I at discharge	217/953 (22.8)	RR 1.38 (1.15, 1.65)	<0.006
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[6] Total Na 1.8 g/d	1000 mL/d			161/974 (16.5)		
	Wan, 2017, 28701670 RCT	Furosemide with compound HSS	100 mL c-HSS[7] (2.8% NaCl) twice daily until clinical compensation[8] (2.2 g/d Na) Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Discharge	Number of patients who had their NYHA change from NYHA class III to II at discharge	92/132[10] (69.7), 89/132 (67.4)	RR 0.96 (0.82, 1.12) RR (second data) 0.93 (0.79, 1.09)	>0.05
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d Na until clinical compensation[8] Total Na 2.76 g/d = ~2.8 g/d	< 500 mL/d			96/132 (72.7)		
		Furosemide with compound HSS	100 mL c-HSS[7] (2.8% NaCl) twice daily until clinical compensation[8] (2.2 g/d Na) Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Discharge	Number of patients who had their NYHA class change from III to I at discharge	26/132[10] (19.7), 43/132 (32.6)	RR 1.53 (0.87, 2.68) RR (second data) 1.19 (0.82, 1.73)	<0.05
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d Na until clinical compensation[8] Total Na 2.76 g/d = ~2.8 g/d	< 500 mL/d			17/132[10] (12.9) 36/132 (27.3)		

Outcome	Study Year PMID	Arm	Total Sodium Intake[1]	Fluid Intake	Time	Outcome Definition	n/N (%)	Effect Size (95% CI)[2]	Reported P value
	HF-Related Symptom (Shortness of Breath)								
	HSS (%NaCl)								
	Okuhara, 2014, 24462960 RCT	Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) for 24 hs (3.34 g/d Na) Restricted sodium to 2.4 g/d Na Total Na 5.7 g/d = ~6 g/d	500 mL/d	24 (h)	Rapid relief from dyspnea[11] and systemic venous congestion provided by HSS infusion (duration of intervention = 24 hours)	19/22 (86)	RR 1.73 (1.10, 2.71)	0.01
		Furosemide with glucose (5%)	500 mL/d 5% glucose Restricted sodium to 2.4 g/d Na for 24 hs Total Na 2.4 g/d	500 mL/d			11/22 (50)		
	Tuttolomondo, 2021, 34288546 RCT	Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 6 days (1.65-5.42 g/d Na) 15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 3.3-7 g/d[12]	NR	Baseline	Resting dyspnea (not specified how it was assessed or what was score or scale used)	12/68 (17.6)	-	0.97
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 1.61 g/d[12]	NR			11/68 (16.2)		
	Tuttolomondo, 2021, 34288546, RCT	Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 6 days (1.65-5.42 g/d Na) 15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 3.3-7 g/d[12]	NR	6 (d)	Resting dyspnea (not specified how it was assessed or what was score or scale used) at the end of the first phase of the therapy.	2/12[13] (16.7)	RR 0.46 (0.1, 2.03)	0.24
		Furosemide Without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 1.61 g/d[12]	NR			4/11[13] (36.4)		
	Tuttolomondo, 2021,	Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 6 days (1.65-5.42	NR	Baseline	Work/effort dyspnea (not specified how it was assessed or what was	61/68 (89.7)	-	

Outcome	Study Year PMID	Arm	Total Sodium Intake[1]	Fluid Intake	Time	Outcome Definition	n/N (%)	Effect Size (95% CI)[2]	Reported P value
	34288546, RCT		g/d Na) 15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 3.3-7 g/d[12]			score or scale used)			1.0
		Furosemide Without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 1.61 g/d[12]	NR			61/68 (89.7)		
	Tuttolomondo, 2021, 34288546, RCT	Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 6 days (1.65-5.42 g/d Na) 15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 3.3-7 g/d[12]	NR	6 (d)	Work/effort dyspnea (not specified how it was assessed or what was score or scale used) at the end of the first phase of the therapy.	11/61[13] (18.0)	RR 0.52 (0.278, 0.99)	0.044
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 1.61 g/d[12]	NR			21/61[13] (34.4)		
	HF-Related Symptom (Clinical Parameter Indicates Dyspnea, Lower Edema, Weakness, Palpitation and Fatigue)								
	HSS (%NaCl)								
	Wan, 2017, 28701670, RCT	Furosemide with compound HSS	100 mL c-HSS[7] (2.8% NaCl) twice daily until clinical compensation[8] (2.2 g/d Na) Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	At discharge	Improvement in clinical symptoms after treatment (clinical parameter indicates dyspnea, lower edema, weakness, palpitation and fatigue), compensated state (discharge).	119/132 (90.33)	RR 0.99 (0.92, 1.07)	>0.05
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d Na until clinical compensation[8] Total Na 2.76 g/d= ~2.8 g/d	< 500 mL/d			120/132 (91.2)		

Outcome	Study Year PMID	Arm	Total Sodium Intake[1]	Fluid Intake	Time	Outcome Definition	n/N (%)	Effect Size (95% CI)[2]	Reported P value
Patients Received Diuretic in Hospital	*Diet (g/d Na)*								
	Aliti, 2013, 23689381 RCT	Low sodium diet	Max 0.8 g/d Na for 7 days or less	Max 800 mL/d	3 (d)	Patients administered IV furosemide during the first 3 days of hospitalization	36/38 (94.7)	RR 0.97 (0.89, 1.07)	>0.99
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less	≥2500 mL/d			36/37 (97.3)		
	Fabricio, 2019, 31221280 RCT	Low sodium diet	1.2 g/d Na for 7 days	1000 mL/d	During hospitalization	Patients administered furosemide (route not specified)	15/16 (94)	RR 1.0 (0.83, 1.20)	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days	1000 mL/d			14/15 (93)		
Utilization Measure									
30-Day Readmission	*Diet (g/d Na)*								
	Aliti, 2013, 23689381 RCT	Low sodium diet	Max 0.8 g/d Na for 7 days or less	Max 800 mL/d	30 (d)	Readmission because of heart failure	11/38 (29)	RR 1.53 (0.67, 3.52)	0.41
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less	≥2500 mL/d			7/37 (19)		
	d'Almeida, 2018, 29793053 RCT	Low sodium diet	0.8 g/d Na for 7 days or less	800 mL/d	30 (d)	Readmission	12/30 (40)	RR 0.92 (0.49, 1.74)	> 0.99
		Unrestricted sodium	~4 g/d Na for 7 days or less	Unlimited fluid intake			10/23 (43.5)		
	Fabricio, 2019, 31221280 RCT	Low sodium diet	1.2 g/d Na for 7 days	1000 mL/d	30 (d)	Readmission	5/16 (31)	RR 0.94 (0.34, 2.6)	1.0
		Unrestricted sodium diet	2.8 g/d Na for 7 days	1000 mL/d			5/15 (33)		
	HSS (%NaCl)								
	Paterna, 2005, 15963399 RCT	Furosemide with HSS	150 mL of HSS (1.4%-4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	30 (d)	Readmissions in the 30-day follow-up for clinical signs of HF[14]	0/48 (0)	RD -0.261 (-0.39, -0.13)	<0.05
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			12/46 (26.1)		
	Montgomery, 2023, 37044281 RCT	Furosemide with oral NaCl	2 g oral NaCl three times per day for 4 days. Restricted sodium diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	30 (d)	Readmissions	7/34 (21)	RR 0.91 (0.36, 2.31)	NR

Outcome	Study Year PMID	Arm	Total Sodium Intake[1]	Fluid Intake	Time	Outcome Definition	n/N (%)	Effect Size (95% CI)[2]	Reported P value
		Furosemide without oral NaCl	Restricted sodium diet ~0.8 g/d Na	No restriction			7/31 (23)		
Transfer to ICU (Proxy for Clinical Deterioration)	*HSS (%NaCl)*								
	Montgomery, 2023, 37044281 RCT	Furosemide with oral NaCl	2 g oral NaCl three times per day for 4 days. Restricted sodium diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	During hospitalization	ICU stay during hospitalization	3/ 34 (9)	RR 0.56 (0.15, 2.15)	NR
		Furosemide without oral NaCl	Restricted sodium diet ~0.8 g/d Na	No restriction			5/31 (16)		
Laboratory/Intermediate Measures									
Kidney Function (Creatinine)	*Diet (g/d Na)*								
	Fabricio, 2019, 31221280 RCT	Low sodium diet	1.2 g/d Na for 7 days	1000 mL/d	7 (d)	Worsening of renal function, represented by an increase in serum creatinine ≥ 0.3 mg/dL	7/16 (43.8)	RR 0.94 (0.43, 2.04)	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days	1000 mL/d			7/15 (46.7)		
Calorie Intake	*Diet (g/d Na)*								
	Inuzuka, 2016 NRCS	Low sodium diet	Max 2.4 g/d Na for NR days[15]	NR	Time point was not explicitly reported	The incidence of low caloric intakes (caloric intakes less than 20 kcal/kg per day)	77/145 (53)	RR 3.4 (1.7, 6.86) OR 6.15 (2.58, 14.67)	0.02
		Unrestricted sodium diet	4 g/d Na for NR days[15]	NR			7/45 (15)		

Notes. [1] Review team calculated based on IV and oral sodium intake if reported; [2] Review team calculated effect size and 95% CI; [3] The duration of intervention was not reported; however, most outcomes were reported at compensation which was defined as return to functional classes 1 or II and without edema; [4] Total sodium per day provided by IV fluid only, sodium diet was not reported; [5] Percentage has been corrected from the one reported in the text (33.3 instead of 30); [6] Defined as dry status, change in NYHA functional class to at least II on clinical judgment and the accomplishment of ideal body weight, as calculated by the Lorenz formula and detected by bioimpedance vector analysis; [7] c-HSS contains, additional to the 2.8% NaCl, 0.2% KCl, 0.9% MgSO4; [8] Patients were considered clinically compensated when they achieved an improved NYHA classification and appropriate body weight calculated by the Lorenz formula and bioelectrical impedance measurement; [9] Adjusted for multiple comparison; [10] Discrepancy between the data in the table and the text – we report data from the table; [11] Using 5-point Likert scale (patients with worse dyspnea and no change of score between baseline and 24 hours after initiation of the treatment were categorized as ‘‘no dyspnea improvement,’’ and those with improved dyspnea score were categorized as “dyspnea improvement"); [12] Total sodium per day during the 6 days of intervention (first phase of therapy), not including the sodium from the 0.9% NaCl (second phase of therapy); [13] The denominator is the number of patients who had dyspnea at admission (baseline) and not the sample (group) size; [14] They presented, at entry, higher functional class than at discharge (NYHA functional class III), while the remaining patients maintained the same NYHA functional class achieved at the time of hospital discharge; [15] Intervention duration was not reported.
Abbreviations. C-HSS=Compound hypertonic saline solution; d=day; HF=heart failure; HSS=hypertonic saline solution; IV=intravenous; Max=maximum; Na=sodium; NaCl=sodium chloride; n/N=n number of event; N sample size; NR=not reported; NYHA=New York Heart Association; OR=odds ratio; RD=risk difference; RR=risk ratio.

APPENDIX H. CONTINUOUS OUTCOMES

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
Lab/Intermediate Measures										
Weight	*Diet (g/d Na)*									
	Aliti, 2013, 23689381	Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	Baseline	Weight (kg)	38	78 (14.6)	-	0.29
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	82.4 (21.5)		
		Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	3 (d)	Weight change (kg) from baseline to day 3 (primary end point).	38	−4.42 (2.85)	NMD 0.25 (-1.9, 2.4)[3]	P value (NMD) 0.82
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	−4.67 (5.6)		
		Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	7 (d)	Weight change from baseline to day 7	38	NR	-	P value (NMD) 0.12
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	NR		
	d'Almeida, 2018, 2979305	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Baseline	Weight (kg)	30	80.5 (17.8)	-	0.58
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	77.6 (16.1)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	3 (d)	Weight (kg) change from baseline to day 3 (primary end point).	30	NR	NR	P value (NMD) >0.99
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	NR		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	7 (d)[#]	Weight (kg) change from baseline to day 7	30	-1.6 (2.2)	NMD 0.2 (-0.36, 0.77)[3]	P value (NMD) 0.49
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	-1.8 (2.1)		
	Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	Baseline	Weight (kg)	16	80.9 (32.7)	-	
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	68.5 (13)		
		Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	7 (d)	Weight (kg) at day 7	16	76.2 (31.8)	11.4 (-5.7, 28.5)	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	64.8 (14.0)	NMD -1	

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
									(-18.2, 16.2)	
	Velloso, 1991, 1824218	Low sodium diet	0.8 g/d Na for NR days[4]	800 mL/d	Uncompensated and vs. compensated	Percentage change in weight	14	12.2 (9.2)	2.2 (-3.5, 7.9)[3]	0.45
		Unrestricted sodium diet	4 g/d Na for NR days[4]	800 mL/d			18	10.0 (5.9)		
	HSS (% NaCl)									
	Issa, 2013, 22243938	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 (d) Total Na 5.9 =~6 g/d[5]	NR	Baseline	Weight (kg)	20	83.8 (18.4)	-	P interaction 0.62
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 (d) Total Na 0.7 g/d[5]	NR			12	79.0 (28.0)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 (d) Total Na 5.9 =~6 g/d[5]	NR	1 (d)	Weight (kg)	20	82.8 (18.0)	4.6 (-13.8, 23.0)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 (d) Total Na 0.7 g/d[5]	NR			12	78.2 (27.7)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 (d) Total Na 5.9 =~6 g/d[5]	NR	2 (d)	Weight (kg)	20	82.0 (17.8)	3.4 (-12.93, 19.73)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 (d) Total Na 0.7 g/d[5]	NR			12	78.6 (27.6)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 (d) Total Na 5.9 =~6 g/d[5]	NR	3 (d)	Weight (kg)	20	81.3 (17.6)	3.4 (-12.9, 19.2) NMD (Baseline-3 d) -1.4 (-19.05, 16.25)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 (d) Total Na 0.7 g/d[5]	NR			12	77.9 (27.8)		
	Issa, 2013, 22243938	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 (d) Total Na 5.9 =~6 g/d[5]	NR	4 (d) which is 24 h after intervention	Weight (kg)	20	80.9 (18.3)	4.5 (-12.0, 21.0) NMD -0.3	

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 (d) Total Na 0.7 g/d[5]	NR			12	76.4 (27.6)	(-17.97, 17.37)	
	Paterna, 2005, 15963399	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Weight (kg)	48	76.0 (16)	-	NR
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	75.8 (15)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	6 (d)	Weight (kg)	48	65.8 (15)	-1.3 (-7.2, 4.6) NMD -1.5 (-7.58, 4.58)	NR
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	67.1 (14)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline-6 d	Weight (kg)	48	-10.9 (4.1)	NMD (Baseline-6 d) -2.8 (-4.15, -1.44)	<0.0001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	-8.1 (2.4)		
	Wan, 2017, 28701670	Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Baseline	Weight (kg)	132	23.4 (9)[10]	-	NR
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[9] Total Na ~2.8 g/d	< 500 mL/d			132	24.2 (11)[10]		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Discharge	Weight (kg)	132	21.7(70)[10]	-	
		Without c-HSS Furosemide	Normal sodium diet 2.76 g/d until clinical compensation[9] Total Na ~2.8 g/d	< 500 mL/d			132	22.0 (01)[10]		
	Mahjoob, 2021, 34903983	Furosemide with HSS	150 mL (5% NaCl) twice daily for 48 (h) Sodium diet NR Total Na 5.9=~6 g/d[5]	NR	Baseline	Weight (kg)	14	84.71 (21.11)	-	0.7[11]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	81.74 (19.82)		
		Furosemide with HSS	150 mL (5% NaCl) twice daily for 48 (h) Sodium diet NR Total Na 5.9=~6 g/d[5]	NR	3 (d)	Weight (kg)	14	78.3 (20.26)	0.2 (-14.4,14.8) NMD -2.77 (-17.65, 12.11)	0.98[12]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	78.1 (19.04)		
		Furosemide with HSS	150 mL (5% NaCl) twice daily for 48 (h) Sodium diet NR Total Na 5.9=~6 g/d[5]	NR	Baseline-3 (d)	Weight change from baseline to day 3	14	-6.38 (2.17)	NMD (Baseline-3 d) -2.79 (-4.5, -1.0)[3]	0.002[12]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	-3.59 (2.12)		
	Licata, 2003, 12660669	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 (d) Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na 4.41-8.1 g/d	1000 mL/d	Baseline	Weight (kg)	53	74.5 (9)	-	NR

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 (d) Total Na 1.8 g/d	1000 mL/d			54	72.7 (9)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 (d) Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na 4.41-8.1 g/d	1000 mL/d	Discharge	Weight (kg)	53	63.6 (8)	-0.7 (-3.9, 2.2) NMD -2.5(-5.67, 0.67)	
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 (d) Total Na 1.8 g/d	1000 mL/d			54	64.3 (7)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 days Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na 4.41-8.1 g/d	1000 mL/d	Baseline-Discharge	Weight change from baseline to discharge, kg.	53	-9.9 (4.15)	NMD (Baseline-Discharge) -1.4 (-2.7, -0.08)	NS
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 days Total Na 1.8 g/d	1000 mL/d			54	-8.5 (2.6)		
	Paterna, 2000, 10938493	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Weight (kg)	30	73.8 (9.1)	-	NR
		Furosemide Without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	72.9 (9.3)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Weight (kg)	30	63.8 (8.8)	-0.7 (-4.8, 3.4) NMD -1.6 (-6.03, 2.83)	NR

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	64.5 (7.5)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline-Discharge	Weight change from baseline to discharge, kg.	30	-9.9 (4.14)	NMD (Baseline-Discharge) -1.43 (-3.18, 0.32)	NS
		Furosemide Without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	-8.47 (2.61)		
	Paterna, 2011, 21701268	Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Weight (kg)	953	82.7 (13)	-	NR
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	84.5 (15)		
		Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Weight (kg)	953	73.2 (6)	-3.4 (-3.99, -2.80) NMD (Baseline-Discharge) -1.6 (-2.69, -0.51)	<0.0001
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	76.6 (7)		
	Parrinello, 2012, 22980301	Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Baseline	Weight (kg)	122	75.8 (15)	-	0.72
		Furosemide without HSS	NR	1000 mL/d			126	76.5 (16)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Discharge	Weight (kg)	122	64.4 (5)	-5.6 (-9.08, -2.12)[3]	P value between-group: Discharge 0.0001
		Furosemide without HSS	NR	1000 mL/d			126	70.7 (3)		
		Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Baseline-Discharge	Weight change from baseline to discharge	122	-11.4 (1.43)[16]	NMD -5.6 (-5.96, -5.23)	<0.001
		Furosemide without HSS	NR	1000 mL/d			126	-5.8 (1.45)[16]		
	Yayla, 2015, 26135463	Furosemide with HSS	150 mL HSS (1.95% NaCl) once daily for 48 (h) Sodium Diet NR Total Na 1.15 g/d[5]	NR	Baseline-Discharge	Weight change from baseline to discharge	14	-5.7 (3.6)	NMD (HSS vs bIV)[17] (Baseline-Discharge) -1.6 (-3.96, 0.76)	0.66
		Furosemide (continuous) cIV without HSS	Sodium Diet NR	NR			15	-4.6 (5.2)		
		Furosemide (bolus) bIV	Sodium Diet NR	NR			14	-4.1 (2.7)		
	Parrinello, 2011, 21440872	Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	Baseline	Weight (kg)	66	75.8 (15)	-	NS
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	76.0 (16)		
		Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	6 (d)	Weight (kg)	66	64.8 (5)	-3.2 (-6.1, -0.30) NMD (Baseline-6 d) -3 (-7.66, 1.66)	P value between-group at discharge <0.033
		Furosemide	150 mL of 0.9%	1000 mL/d			67	68.0 (11)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		without HSS	NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d							
	Tuttolomondo, 2021, 34288546	Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 6 days 15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 3.3-7 g/d[18]	NR	Baseline	Weight (kg)	68	82.9 (14.5)	-	<0.0005
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 1.61 g/d[18]	NR			68	73.3 (13.8)		
	Tuttolomondo, 2021, 34288546	Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 6 days 15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 3.3-7 g/d[18]	NR	6 (d)	Weight (kg)	68	67.50 (5.32)	-2.19 (-3.78, -0.59) NMD (Baseline-6 d) -11.79 (-15.99, -7.59)	NR
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 1.61 g/d[18]	NR			68	69.69 (4.08)		
	Okuhara, 2014, 24462960	Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	24 h	Weight (kg) change from baseline to 24 h, median (IQR)	22	-1.1 (0.725, 1.475)	Net Median Difference -0.71	P value (Net Median Difference) 0.05
		Furosemide with Glucose (5%)	500 mL/d 5% glucose per day	500 mL/d			22	-0.39 (-0.05, 1.20)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d							
	Roul, 2017	HSS	HSS (NaCl% NR) Sodium diet NR[19]	NR[19]	After intervention	Weight (kg)	11	73 (NR)	-7	<0.008
		without HSS	NR[19]	NR[19]			156	80 (NR)		
	Montgomery, 2023, 37044281	Furosemide With Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	4 (d)	Weight change from enrollment to day 4, (kg)	34	-4.0 (4.3)	Cohen d[a] 0.14 (-0.35, 0.63) NMD 0.6 (-1.468, 2.668)	0.57
		Furosemide without Oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	-4.6 (4.2)		
		Furosemide With Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	Discharge	Weight change from enrollment to discharge, (kg)	34	-6.3 (6.4)	Cohen d[a] 0.22 (-0.30, 0.74) NMD 1.4 (-1.845, 4.645)	0.41
		Furosemide without Oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	-7.7 (6.9)		
Kidney Function	*Kidney function (Creatinine, mg/dL)*									
	Diet (g/d Na)									
	Aliti, 2013, 23689381	Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	Baseline	Serum creatinine (mg/dL)	38	1.3 (0.5)	-	0.86
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	1.3 (0.6)		
		Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	7d	Serum creatinine (mg/dL)	38	1.3 (0.5)	0.1 (-0.08, 0.28) NMD (Baseline-7 d) 0.1 (-0.22, 0.42)[3]	P group * time (baseline – day 7) 0.44[20] P group * time (baseline-discharge) 0.55[21]
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	1.2 (0.3)		
	Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	Baseline	Serum creatinine (mg/dL)	16	1.5 (0.5)	-	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	1.5 (0.5)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	7 (d)	Serum creatinine (mg/dL)	16	1.7 (0.5)	0 (-0.35, 0.35) NMD (Baseline-7 d) 0 (-0.36, 0.36)	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	1.7 (0.5)		
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Baseline	Serum creatinine (mg/dL)	30	1.0 (0.3)	-	NR
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	1.2 (0.4)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	7 (d)#	Serum creatinine (mg/dL)	30	1.2 (0.7)	-0.1 (-0.44, 0.24) NMD (Baseline-7 d) 0.1 (-0.01, 0.30)[3]	P group * time (baseline - ≤ 7 days) 0.32[21]
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	1.3 (0.5)		
	HSS (% NaCl)									
	Issa, 2013, 22243938	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	Baseline	Serum creatinine (mg/dL)	20	1.72 (0.47)	-	P group * time interaction 0.004
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.58 (0.48)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	1 (d)	Serum creatinine (mg/dL)	20	1.71 (0.44)	-	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.81 (1.01)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	2 (d)	Serum creatinine (mg/dL)	20	1.65 (0.44)	-	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.96 (1.06)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice	NR	3 (d)	Serum creatinine (mg/dL)	20	1.66 (0.55)	-0.23	

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			daily for 3 days Total Na 5.9 =~6 g/d[5]						(-0.72, 0.26) NMD (Baseline-3 d)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.89 (0.77)	-0.37 (-0.81, 0.07)	
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	4 (d) which is 24 h after intervention	Serum creatinine (mg/dL)	20	1.88 (0.68)	-0.02 (-0.54, 0.50) NMD (Baseline-3 d)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.90 (0.76)		
	Paterna, 2005, 15963399	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Serum creatinine (mg/dl)	48	1.51 (0.1)	-	NR
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	1.55 (0.05)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	6 (d)	Serum creatinine (mg/dl)	48	1.45 (0.05)	-0.53 (-0.59, -0.47) NMD (Baseline-6 d) -0.49 (-0.55, -0.43)	P value between- group: At 6 days <0.0001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	1.98 (0.2)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Serum creatinine (mg/dl)	48	1.55 (0.05)	-0.42 (-0.48, -0.36) NMD (Baseline-Discharge) -0.42 (-0.48, -0.36)	<0.001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	1.97 (0.2)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
	Mahjoob, 2021, 34903983	Furosemide with HSS	150 mL (5% NaCl) twice daily for 48 (h) Sodium diet NR Total Na 5.9=~6 g/d[5]	NR	Baseline	Serum creatinine (mg/dL)	14	1.68 (0.81)	-	0.19[11]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	2.36 (1.22)		
		Furosemide with HSS	150 mL (5% NaCl) twice daily for 48 (h) Sodium diet NR Total Na 5.9=~6 g/d[5]	NR	3 (d)	Serum creatinine (mg/dL)	14	1.74 (0.75)	-0.82 (-1.64, 0.21)[3] NMD (Baseline-3 d)	0.12[11]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	2.56 (1.38)	-0.14 (-0.93, 0.65)	
	Licata, 2003, 12660669	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 ds Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na= ~4.5-8.2 g/d	1000 mL/d	Baseline	Serum creatinine (mg/dL)	53	1.6 (0.05)	-	NR
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 days Total Na 1.8 g/d	1000 mL/d			54	1.65 (0.05)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 ds Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na= ~4.5-8.2 g/d	1000 mL/d	Discharge	Serum creatinine (mg/dL)	53	1.4 (0.05)	-0.55 (-0.58, -0.52) NMD (Baseline-Discharge) -0.5 (-0.53, -0.47)	P value between groups: (Discharge) <0.001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 days Total Na 1.8 g/d	1000 mL/d			54	1.95 (0.1)		
	Paterna, 2000, 10938493	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12	1000 mL/d	Baseline	Serum creatinine (mg/dL)	30	1.6 (0.05)	-	NR

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			(d) Total Na 4.4-8.1 g/d							
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	1.65 (0.07)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Serum creatinine (mg/dL)	30	1.4 (0.07)	-0.54 (-0.58, -0.49) NMD (Baseline-Discharge) -0.49 (-0.53, -0.45)	P value between-group at discharge <0.001
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	1.94 (0.1)		
	Paterna, 2011, 21701268	Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Serum creatinine (mg/dL)	953	1.65 (0.05)	-	NR
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	1.61 (0.05)		
		Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Serum creatinine (mg/dL)	953	1.45 (0.05)	-0.46 (-0.47, -0.45) NMD (Baseline-Discharge) -0.5 (-0.51, -0.49)	NR
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	1.91 (0.1)		
	Parrinello, 2012, 22980301	Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Baseline	Serum creatinine (mg/dL)	122	1.22 (0.4)	-	0.53

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide without HSS	NR	1000 mL/d			126	1.18 (0.6)		
		Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Discharge	Serum creatinine (mg/dL)	122	1.28 (0.48)	-0.32 (-0.48, -0.16) NMD (Baseline-Discharge) -0.36 (-0.48, -0.24)	P value between-group At Discharge 0.0001
		Furosemide without HSS	NR	1000 mL/d			126	1.6 (0.32)		
	Yayla, 2015, 26135463	Furosemide with HSS	150 mL HSS (1.95% NaCl) once daily for 48 (h) Sodium Diet NR Total Na 1.15 g/d[5]	NR	Baseline	Serum creatinine (mg/dL)	14	0.96 (0.29)	-	P values between-group 0.27
		Furosemide (continuous) clV without HSS	Sodium Diet NR	NR			15	1.10 (0.26)		
		Furosemide (bolus) blV without HSS	Sodium Diet NR	NR			14	0.93 (0.32)		
		Furosemide with HSS	150 mL HSS (1.95% NaCl) once daily for 48 (h) Sodium Diet NR Total Na 1.15 g/d[5]	NR	48 (h)	Serum creatinine (mg/dL)	14	1.17 (0.32)	0.2 (-0.12, 0.52)[3] NMD (HSS vs blV)[17] 0.17 (-0.05, 0.39)	P values between-group 0.04 HSS vs blV 0.22
		Furosemide (continuous) clV without HSS	Sodium Diet NR	NR			15	1.27 (0.31)		
		Furosemide (bolus) blV without HSS	Sodium Diet NR	NR			14	0.97 (0.27)		
		Furosemide with HSS	150 mL HSS (1.95% NaCl) once daily for 48 (h) Sodium Diet NR Total Na 1.15 g/d[5]	NR	Baseline-compensated	Serum creatinine (mg/dL)	14	1.27 (0.49)	NMD (HSS vs blV)[17] (Baseline-compensation) 0.24 (-0.09, 0.57)	0.09
		Furosemide (continuous) clV without HSS	Sodium Diet NR	NR			15	1.46 (0.60)		
		Furosemide (bolus) blV without HSS	Sodium Diet NR	NR			14	1.03 (0.40)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide with HSS	150 mL HSS (1.95% NaCl) once daily for 48 (h) Sodium Diet NR Total Na 1.15 g/d[5]	NR	Baseline-48 (h)	Change in serum creatinine from baseline to 48 hours.	14	0.20 (0.21)	NMD HSS vs bIV[17] (Baseline-48 h) 0.16 (0.03, 0.30)	0.08
		Furosemide (continuous) cIV without HSS	Sodium Diet NR	NR			15	0.16 (0.21)		
		Furosemide (bolus) bIV without HSS	Sodium Diet NR	NR			14	0.04 (0.15)		
		Furosemide with HSS	150 mL HSS (1.95% NaCl) once daily for 48 (h) Sodium Diet NR Total Na 1.15 g/d[5]	NR	Baseline-Compensation	Change in serum creatinine from baseline to compensation	14	0.30 (0.42)	NMD HSS vs bIV[17] (Baseline-compensation) 0.2 (-0.06, 0.46)	0.18
		Furosemide (continuous) cIV without HSS	Sodium Diet NR	NR			15	0.36 (0.42)		
		Furosemide (bolus) bIV without HSS	Sodium Diet NR	NR			14	0.10 (0.28)		
	Parrinello, 2011, 21440872	Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	Baseline	Serum creatinine (mg/dL)	66	1.5 (0.3)	--	NS
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	1.4 (0.5)		
		Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	6 (d)	Serum creatinine (mg/dL)	66	1.1 (0.3)	-0.7 (-0.80, -0.59) NMD (Baseline-6 d) -0.8 (-0.93, -0.67)	<0.0001
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	1.8 (0.3)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
	Okuhara, 2014, 24462960	Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	Baseline	Serum creatinine (mg/dL)	22	1.56 (0.85)	-	NR
		Furosemide with Glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	1.45 (0.77)		
		Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	24 (h)	Serum creatinine (mg/dL) at 24 hours (end of intervention)	22	1.55 (0.75)	0.02 (-0.45, 0.49) NMD (Baseline-24 h) -0.09 (-0.56, 0.38)	NR
		Furosemide with Glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	1.53 (0.81)		
	Montgomery, 2023, 37044281	Furosemide With Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	4 (d)	Serum creatinine change from enrollment to day 4, mg/dL (units determined from clinical trial.gov and baseline table)	34	0.04 (0.39)	Cohen d[a] -0.26 (-0.75, 0.23) NMD -0.11 (-0.313, 0.093),	0.30
		Furosemide without Oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	0.15 (0.44)		
		Furosemide With Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	Discharge	Serum creatinine change from enrollment to discharge, mg/dL	34	-0.04 (0.51)	Cohen d[a] -0.41 (-0.91, 0.09) NMD -0.22 (-0.479, 0.039),	0.11
		Furosemide without Oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	0.18 (0.55)		
	Kidney Function (Urea, mg/dL)									

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
	Diet (g/d Na)									
	Aliti, 2013, 23689381	Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	Baseline	Urea, median (IQR)	38	56 (48, 87)	-	P value between-group Baseline 0.38 7 (d) 0.06 group * time 0.32
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	58 (41, 83)		
		Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	7 (d)	Urea, median (IQR)	38	59 (43, 88)	Median Difference 10 Net Median Difference (Baseline-7 d) 12	
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	49 (42, 71)		
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Baseline	Urea, mg/dL	30	51(19)	-	NR
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	54 (21)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	≤7 (d)	Urea, mg/dL,	30	60 (33)	5 (-10.8, 20.8) NMD (Baseline-study end) 8 (-1.8, 17.8)[3]	P group * time (Baseline-study end) 0.11[21]
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	55 (21)		
	Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	Baseline	Urea, mg/dL	16	68.4 (40.2)	-	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	66.6 (30.2)		
		Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	7 (d)	Urea, mg/dL	16	76.9 (36.6)	4 (-19.3, 27.3) NMD (Baseline-7 d) 2.2 (-21.6, 26.0)	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	72.9 (27.2)		
	HSS (% NaCl)									
	Issa, 2013, 22243938	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days	NR	Baseline	Urea, mg/dL	20	80.8 (35.6)	-	P group * time interaction

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			Total Na 5.9 =~6 g/d[5]							0.66
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	83.7 (43.6)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	1 (d)	Urea, mg/dL	20	78.6 (33.3)	-	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	82.7 (43.6)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	2 (d)	Urea, mg/dL	20	77.6 (32.8)	-	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	85.9 (46.5)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	3 (d)	Urea, mg/dL	20	77.0 (38.6)	-8.7 (-37.8, 20.5) NMD (Baseline-3 d) -5.8 (-35.00, 23.40)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	85.7 (42.0)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	4 (d) which is 24 h after intervention	Urea, mg/dL	20	83.2 (45.2)	-3.3 (-34.4, 27.8) NMD	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	86.5 (42.3)		
	Licata, 2003, 12660669	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 ds Normal sodium diet	1000 mL/d	Baseline	Urea, mg/dL	53	62 (4)	-	

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			2.76 g/d= ~2.8 g/d Na Total Na= ~4.5-8.2 g/d							
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 days Total Na 1.8 g/d	1000 mL/d			54	58.2 (3.5)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 ds Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na= ~4.5-8.2 g/d	1000 mL/d	Discharge	Urea, mg/dL	53	70 (9.5)	-27 (-31.3, -22.7) NMD (Baseline-Discharge) -30.8 (-34.62, -26.98)	P value between- group: At Discharge <0.001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 days Total Na 1.8 g/d	1000 mL/d			54	97 (13)		
	Mahjoob, 2021, 34903983	Furosemide with HSS	150 mL (5% NaCl) twice daily for 48 (h) Sodium diet NR Total Na 5.9=~6 g/d[5]	NR	Baseline	Urea, mg/dL	14	76.21 (52.28)	-	0.3[12]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	101.32 (72.04)		
		Furosemide with HSS	150 mL (5% NaCl) twice daily for 48 (h) Sodium diet NR Total Na 5.9=~6 g/d[5]	NR	3 (d)	Urea, mg/dL	14	138.86 (2.35)	25.1 (-15.2, 65.4) NMD (Baseline-3 d) 50.2 (3.54, 96.90)	P value between group at day 3 0.31[11]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	113.75 (73.91)		
	Okuhara, 2014, 24462960	Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) for 24 (h) Restricted sodium to 2.4 g/d Na Total Na 5.7=~6 g/d	500 mL/d	Baseline	Urea, mg/dL	22	32.33 (21.26)	-	NR
		Furosemide with Glucose (5%)	500 mL/d 5% glucose Restricted sodium to	500 mL/d			22	29.76 (15.37)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			2.4 g/d Na for 24 (h) Total Na 2.4 g/d							
		Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	24 (h)	Urea, mg/dL	22	30.86 (20.03)	2.43 (-8.60, 13.5) NMD (Baseline-24 h) -0.14 (-10.93, 10.65)	NR
		Furosemide with Glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	28.43 (15.58)		
	Parrinello, 2011, 21440872	Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	Baseline	Urea, mg/dL	66	62 (4)	-	NS
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	59 (4)		
		Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	6 (d)	Urea, mg/dL	66	52 (4)	-41 (-43.0, -38.9) NMD (Baseline-6 d) -44 (-45.75, -42.25)	<0.0001
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	93 (7)		
	Parrinello, 2012, 22980301	Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Baseline	Urea, mg/dL	122	67.7 (32.0)	-	0.48
		Furosemide without HSS	NR	1000 mL/d			126	65 (28)		
		Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily	1000 mL/d	Discharge	Urea, mg/dL	122	78.1 (32.4)	-28.9	P value between-group

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]						(-36.0, -21.8) NMD (Baseline-Discharge)	Discharge 0.0001
		Furosemide without HSS	NR	1000 mL/d			126	107 (24)	-31.6 (-38.92, -24.28)	
	Paterna, 2000, 10938493	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Urea, mg/dL	30	62.1 (4.1)	-	-
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	58.1 (3.7)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Urea, mg/dL	30	70 (9.5)	-27 (-32.91, -21.09) NMD (Baseline-Discharge)	<0.001
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	97 (13.5)	-31 (-36.24, -25.76)	
	Paterna, 2005, 15963399	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Urea, mg/dL	48	62 (4)	-	NR
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	56.1 (3.5)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	6 (d)	Urea, mg/dL	48	64 (9.5)	-35 (-39.1, -30.8) NMD (Baseline-6 d) -40.9 (-44.56,	P value between-group: At 6 days <0.0001

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	99 (11)	-37.24)	
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Urea, mg/dL	48	65 (10)	-33 (-37.5, -28.5) NMD (Baseline-Discharge) -38.9 (-42.9, -34.9)	P value between-group: At discharge <0.0001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	98 (12)		
	Paterna, 2011, 21701268	Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Urea, mg/dL	953	58.2 (3.5)	-	NR
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	56 (4)		
		Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Urea, mg/dL	953	71 (13)	-30 (-31.1, -28.9) NMD (Baseline-Discharge) -32.2 (-33.19, -31.21)	P value between groups <0.0001
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	101 (12)		
	Wan, 2017, 28701670	Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Baseline	Urea, mg/dL	132	56.1 (2.3)	-	NR

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[9] Total Na ~2.8 g/d	< 500 mL/d			132	54.5 (4.7)		
		Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Discharge	Urea, mg/dL	132	50.4 (6.4)	0.2 (-1.34, 1.74) NMD (Baseline-Discharge) -1.4 (-2.77, -0.03)	NR
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[9] Total Na ~2.8 g/d	< 500 mL/d			132	50.2 (6.4)		
	Yayla, 2015, 26135463	Furosemide with HSS	150 mL HSS (1.95% NaCl) once daily for 48 (h) Sodium Diet NR Total Na 1.15 g/d[5]	NR	Baseline-to-compensation	Uea, mg/dL	14	37.9 (16.8)	NMD HSS vs bIV[17] (Baseline-compensation) 3.8 (-9.37, 16.97)	0.72
		Furosemide (continuous) cIV without HSS	Sodium Diet NR	NR			15	38.8 (15.3)		
		Furosemide (bolus) bIV without HSS	Sodium Diet NR	NR			14	34.1 (18.7)		
	Montgomery, 2023, 37044281	Furosemide With Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	4 (d)	Urea change from enrollment to day 4, mEq/L, mg/dL (1mg/dL= 0.357 mEq/L)	34	3.1 (13), 8.68 (36.41)[2]	Cohen d[a] -0.57 (-1.07, -0.07) NMD -7.9 (-14.754, -1.046), -22.1 (-41.32, -2.93)	0.025
		Furosemide without Oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	11 (15) 30.81 (42.01)[2]		
		Furosemide With Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	Discharge	Urea change from enrollment to discharge, mEq/L, mg/dL (1mg/dL = 0.357 mEq/L)	34	3.2 (15), 8.96 (42.02)[2]	Cohen d[a] -0.55 (-1.05, -0.05) NMD	0.036

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
									-9.8 (-18.460, -1.140), -27.5 (-51.7, -3.19)	
		Furosemide without Oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	13 (20), 36.42 (56.02)[2]		
	Kidney Function (eGFR, mL/min or mL/min/1.73 m²)									
	HSS									
	Paterna, 2011, 21701268	Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Creatinine clearance[##], x (Unit: NR)	953	52.5 (2.2)	-	NR
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	52.1 (2.3)		
		Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Creatinine clearance[##], x(Unit: NR)	953	55.4 (3.3)	6.7 (6.5, 6.9) NMD (Baseline-Discharge) 6.3 (6.07, 6.53)	P value between groups: Discharge <0.0001
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	48.7 (2.1)		
	Parrinello, 2012, 22980301	Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Baseline	MDRD GFR, mL/min/1.73 m²	122	58.8 (26.8)	-	0.84
		Furosemide without HSS	NR	1000 mL/d			126	59.4 (22.2)		
		Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Discharge	MDRD GFR, mL/min/1.73 m²	122	59.1 (31.9)	17.1 (11.06, 23.14) NMD (Baseline-Discharge)	P value between-group. At discharge 0.0001

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide without HSS	NR	1000 mL/d			126	42 (12)	17.7 (11.45, 23.95)	
	Parrinello, 2011, 21440872	Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	Baseline	GFR, mL/min	66	52 (8)	-	NS
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	51 (5)		
		Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	6 (d)	GFR, mL/min	66	58 (6)	14 (11.8, 16.2) NMD (Baseline-6 d) 13 (10.71, 15.29)	<0.0001
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	44 (7)		
	Okuhara, 2014, 24462960	Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	Baseline	GFR, mL min^{-1} 1.73 m^{-2}	22	42.9 (22.6)	-	NR
		Furosemide with Glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	44.3 (25.6)		
		Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	24 (h)	GFR, mL min^{-1} 1.73 $m^{-2,}$	22	43.1 (21.9)	2 (-11.1, 15.1) NMD (Baseline-24 h) 3.4 (-10.35, 17.15)	NR
		Furosemide with Glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h)	500 mL/d			22	41.1 (22.5)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			Total Na 2.4 g/d							
	Wan, 2017, 28701670	Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Baseline	Creatinine clearance[##]	132	56.5 (3.5)	-	-
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[9] Total Na ~2.8 g/d	< 500 mL/d			132	45.7 (2.4)		
		Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Discharge	Creatinine clearance[##]	132	53.8 (4.1)	MD 9.6 (8.71, 10.49) NMD (Baseline-Discharge) -1.2 (-2.02, -0.38)	-
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[9] Total Na ~2.8 g/d	< 500 mL/d			132	44.2 (3.2)		
	Montgomery, 2023, 37044281	Furosemide With Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	4 (d)	eGFR change from enrollment to day 4, mL/min/1.73 m^2, median	34	1.67 (-4.55, 4.11)	Rank Biserial[α] (r_{rb}) 0.17 (-0.11, 0.42) Net Median Difference 4.5	0.25
		Furosemide without Oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	-2.83 (-7.45, 3.13)		
		Furosemide With Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	Discharge	eGFR change from enrollment to discharge, mL/min/1.73 m^2	34	1.4 (12)	Rank Biserial[α] (r_{rb}) 0.24 (-0.25, 0.73) NMD 2.8 (-2.792, 8.392)	0.34
		Furosemide without Oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	-1.4 (11)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
	Kidney Function (Serum Cystatin c, mg/L)									
	HSS (% NaCl)									
	Issa, 2013, 22243938	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	Baseline	Cystatin C, mg/L###	20	1.53 (0.40)	-	P group * time interaction 0.03
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.45 (0.50)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	1 (d)	Cystatin C, mg/L###	20	1.49 (0.39)	-	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.73 (0.63)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	2 (d)	Cystatin C, mg/L###	20	1.43 (0.31)	-	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.65 (0.53)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	3 (d)	Cystatin C, mg/L###	20	1.47 (0.30)	-0.23 (-0.52, 0.06) NMD (Baseline-3 d) -0.31 (-0.63, 0.01)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.70 (0.46)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	4 (d) which is 24 h after intervention	Cystatin C, mg/L###	20	1.63 (0.46)	-0.07 (-0.4, 0.3) NMD -0.15 (-0.50, 0.20)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days	NR			12	1.70 (0.55)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			Total Na 0.7 g/d[5]							
	Okuhara, 2014, 24462960	Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	Baseline	Serum Cystatin C, mg/L	22	2.04 (0.98)	-	NR
		Furosemide with Glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	1.94 (0.90)		
		Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	24 (h)	Serum Cystatin C, mg/L	22	2.04 (0.92)	0 (-0.54, 0.54) NMD (Baseline-24 h) -0.1 (-0.65, 0.45)	
		Furosemide with Glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	2.04 (0.92)		
Urine Output (mL/24h)	*Diet (Na g/d)*									
	Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	Baseline-7 d	Urine output (water loss), L[†]	16	-4.3 (3.0)	NMD (Baseline-7 d) 1.4 (-0.58, 3.38)	P value (NMD) 0.17
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	-2.9 (2.1)		
	HSS (%NaCl)									
	Issa, 2013, 22243938	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	Baseline	Urine output (mL/kg/h), Urine output mL/24 h	20	0.93 (0.55), 1870 (1106. 1)[2]	-	P interaction 0.11
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	0.73 (0.33), 1384 (625.7)[2]		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	1 (d)	Urine output (mL/kg/h), Urine output mL/24 h	20	1.15 (0.44), 2285 (874.4)[2]	239.3 (-712.1, 1190.7)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days	NR			12	1.09 (0.82), 2045.7 (1539)[2]		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			Total Na 0.7 g/d[5]							
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	2 (d)	Urine output (mL/kg/h), Urine output mL/24 h	20	1.29 (0.46), 2539 (905.2)[2]	822.4 (215.7, 1429.1)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	0.91 (0.43), 1716.6 (811.2)[2]		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	3 (d)	Urine output (mL/kg/h), Urine output mL/24 h,	20	1.12 (0.41), 2185.3 (800)[2]	-151.7 (-1009.4, 706.0) NMD (Baseline-3 d) -637.7 (-1443.21, 167.81)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.25 (0.74), 2337 (1383.5)[2]		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	4 (d) which is 24 h after intervention	Urine output (mL/kg/h), Urine output mL/24 h	20	0.83 (0.32), 1611.5 (621.3)[2]	-736 (-1609.0, 138.0) NMD -1221.5 (-2056.65, -386.35)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1.28 (0.8), 2347 (1466.9)[2]		
	Paterna, 2005, 15963399	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Urine output, ml/24 h	48	410 (141)	-NR	NR
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	425 (129)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	6 (d)	Urine output, ml/24 h	48	2250 (652)	450 (154, 745)	P value between groups At day 6 <0.0001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d)	1000 mL/d			46	1660 (515)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			Total Na 1.8 g/d[7]							
	Wan, 2017, 28701670	Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Baseline	-Urine output, mL/24 h	132	737(298)	-	NR
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[7] Total Na ~2.8 g/d	< 500 mL/d			132	792 (201)		
		Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Discharge	Urine output, (mL/24 h)	132	2048 (471)	486 (362.5, 609.5) NMD (Baseline-Discharge) 541 (432.75, 649.25)	P value between groups NR
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[7] Total Na ~2.8 g/d	< 500 mL/d			132	1562 (550)		
	Mahjoob, 2021, 34903983	Furosemide with HSS	Normal sodium diet 2.76 g/d = ~2.8 g/d Na until clinical compensation[9] Total Na ~2.8 g/d	< 500 mL/d	Baseline	Urine Output, mL/24 h	14	1254 (321)	-	0.48[11]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	1450 (1100)		
		Furosemide with HSS	150 mL (5% NaCl) twice daily for 48 (h) Sodium diet NR Total Na 5.9=~6 g/d[5]	NR	3 (d)	Urine Output, mL/24 h	14	2282 (790)	243 (-303.7, 789.7) NMD (Baseline-3 d)	0.39[12]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	2039 (682)	439 (-180.43, 1058.43)	
	Licata, 2003, 12660669	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to	1000 mL/d	Baseline	Urine Output, mL/24 h	53	390 (151)	-	NR

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			12 (d) Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na= ~4.5-8.2 g/d							
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 (d) Total Na 1.8 g/d	1000 mL/d			54	435 (139)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 (d) Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na= ~4.5-8.2 g/d	1000 mL/d	Discharge	Urine Output, mL/24 h	53	2100 (622)	450 (230.3, 669.7) NMD (Baseline-Discharge) 495 (296.68, 693.32)	P value between groups At discharge <0.001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 (d) Total Na 1.8 g/d	1000 mL/d			54	1650 (535)		
	Okuhara, 2014, 24462960	Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) for 24 (h) Restricted sodium to 2.4 g/d Na Total Na 5.7=~6 g/d	500 mL/d	24 (h)	Urine Output, mL/24 h	22	2701 (920)	924 (415.37, 1432.63)	<0.001
		Furosemide wutg Glucose (5%)	500 mL/d 5% glucose Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	1777 (797)		
	Paterna, 2000, 10938493	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Urine Output, mL/24 h	30	390 (155)	-	NR
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	433 (141)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Urine Output, mL/24 h	30	2100 (626)	450 (154.9, 745.1) NMD (Baseline-Discharge) 493 (227.28, 758.72)	P value between groups At discharge <0.001
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	1650 (537)		
	Paterna, 2011, 21701268	Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Urine Output, mL/24 h	953	635 (145)	-	NR
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	690 (155)		
		Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Urine Output, mL/24 h	953	2150 (565)	475 (425.2, 524.8) NMD (Baseline-Discharge) 530 (485.36 574.64)	P value between- group: At discharge <0.0001
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	1675 (550)		
	Parrinello, 2012, 22980301	Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Baseline	Urine Output, mL/24 h	122	427 (128)	-	0.18
		Furosemide without HSS	NR	1000 mL/d			126	447 (106)		
		Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14]	1000 mL/d	Discharge	Urine Output, mL/24 h	122	2180 (545)	730 (362.2, 1097.8) NMD	P value between- group. Discharge 0.0001

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			Total Na: assumed at least 3.5-4.5 g/d[15]						(Baseline-Discharge)	
		Furosemide without HSS	NR	1000 mL/d			126	1450 (352)	750 (646.78, 853.22)	
	Parrinello, 2011, 21440872	Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	Baseline	Urine Output, mL/24 h	66	425 (129)	-	NS
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	410 (141)		
		Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	6 (d)	Urine Output, mL/24 h	66	2180 (545)	630 (473.4, 786.6) NMD (Baseline-6 d) 615 (474.79, 755.21)	P value between-group At 6 d <0.0001
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	1550 (355)		
	Tuttolomondo, 2021, 34288546	Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 6 days 15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 3.3-7 g/d[18]	NR	Baseline	Urine Output, mL/24 h	68	1031.62 (212.29)	-	NR
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 1.61 g/d[18]	NR			68	1001.47 (167.72)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 6 days 15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 3.3-7 g/d[18]	NR	6 (d)	Urine Output, mL/24 h	68	2260.74 (466.37)	353.4 (225.4, 481.4) NMD (Baseline-6 d) 323.20 (211.96, 434.44)	NR
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 1.61 g/d[18]	NR			68	1907.35 (269.36)		
	Montgomery, 2023, 37044281	Furosemide with Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	4 (d)	Urine output, total amount from enrollment to day 4, mean urine output per day, mL	34	10000 (4200), 2500 (1050)	Cohen d[α] 0.13 (-0.36, 0.61) MD 600 (-1469.89), 2669.89)	0.61
		Furosemide without Oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	9400 (4300), 2350 (1075)	MD 150 (-362.73, 662.73)	
		Furosemide with Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	4 (d)	Cumulative diuretic efficiency from enrollment to day 4 (urine output (L) per 40 mg oral FE), median (IQR)	34	0.17 (0.06, 0.24)	Rank Biserial[α] (r_{rb}) 0.11 (-0.17, 0.37) Median Difference 0.03	0.45
		Furosemide without Oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	0.14 (0.07, 0.21)		
BNP/NT-proBNP	*Diet (g/d Na)*									
	Aliti, 2013, 23689381	Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	Baseline	BNP, pg/mL, median (IQR),	38	1084 (608, 1820)	-	0.67
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	1425 (632, 2297)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	7 (d)	BNP, pg/mL, median (IQR),	38	954 (488, 1331)	Median Difference 184 Net Median Difference 525	P value between-group Study end 0.92[20] From baseline to study end 0.51[21]
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	770 (4485, 1400)		
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Baseline	BNP, pg/mL, median (IQR)	30	301 (215, 524)	-	NR
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	186 (100, 325)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	7 (d)[#]	BNP, pg/mL, median (IQR),	30	286 (161, 368)	Median Difference 102 Net Median Difference -13	P group * time = 0.85[21]
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	184 (113, 286)		
	Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	Baseline	NT-proBNP, pg/mL, median (IQR)	16	4733 (503, 25000)	-	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	4069 (1486, 25000)		
		Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	7 (d)	NT-proBNP. pg/mL, median (IQR)	16	3954 (273, 10816)	Median Difference 803 Net Median Difference 139	NS
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	3151 (282, 6157)		
	HSS (% NaCl)									
	Issa, 2013, 22243938	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	Baseline	BNP, median (IQR)[##]	20	2077 (1046, 3353)	-	No difference in baseline values between HSS and placebo.
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1219 (574, 2336)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	4 (d) which is 24 h after intervention	BNP, median (IQR)[##],	20	1728 (1067, 3574)	Median Difference 344	NR

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	1384 (682, 1816)	Net Median Difference -514	
	Okuhara, 2014, 24462960	Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	Baseline	NT-proBNP, pg/mL, median (IQR),	22	6776 (4341, 10079)	-	NR
		Furosemide with glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	6525 (3547, 16116)		
		Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	24 (h)	NT-proBNP, pg/mL, , median (IQR),	22	4913 (2818, 8667)	Median Difference -2280 Net Median Difference -2531	NR
		Furosemide with glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	7193 (3604, 15670)		
	Parrinello, 2011, 21440872	Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	6 (d)	BNP, pg/mL	66	NR	-	P value between-group at 6 d Significant but not reported (BNP plasma levels were significantly lower for the HSS group compared with those without HSS)
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	NR		
	Parrinello, 2012, 22980301	Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Baseline	BNP, pg/mL	122	1284 (515)	-	0.64
		Furosemide without HSS	NR	1000 mL/d			126	1255 (475)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Discharge	BNP, pg/mL	122	542 (285)	-140 (-210.5, -69.5)[3] NMD (Baseline-Discharge) -169 (-276.47, -61.53)	P value (MD) between-group At discharge 0.0001
		Furosemide without HSS	NR	1000 mL/d			126	682 (296)		
	Paterna, 2011, 21701268	Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	BNP, pg/mL	953	355 (105)	-30 (-39.8, -20.2)	<0.0001
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	385 (115)		
	Paterna, 2005, 15963399	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	BNP, pg/mL	48	1212 (491)	-	<0.6
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	1265 (515)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	6 (d)	BNP, pg/mL	48	343 (196)	-125 (-216.3, -33.7) NMD (Baseline-6 d) -72 (-248.86, 104.86)	P value (MD) between-group At 6 d <0.008
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	468 (251)		
	Tuttolomondo, 2011, 20346637	Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 8 (d) 15 mL/kg of 0.9% NaCl (over 60 min) after 8 (d) once only. Low sodium diet 1.61 g/d Na for 10	NR	Baseline	BNP, pg/mL, median (IQR)	120	215.5 (80.5, 487	-	NR

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			(d) Total Na 3.3-7 g/d[18]							
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 8 (d) once only. Low sodium diet 1.61 g/d Na for 10 (d) Total Na 1.61 g/d[18]	NR			30	NR		
		Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 8 (d) 15 mL/kg of 0.9% NaCl (over 60 min) after 8 (d) once only. Low sodium diet 1.61 g/d Na for 10 (d) Total Na 3.3-7 g/d[18]	NR	8 (d)	BNP, pg/mL, median (IQR)	120	87 (66, 141.5)	Median difference -48 Net Median Difference could not be calculated due to NR at baseline for the second group	NR
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 8 (d) once only. Low sodium diet 1.61 g/d Na for 10 (d) Total Na 1.61 g/d[18]	NR			30	135 (78.5, 202)		
	Tuttolomondo, 2021, 34288546	Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 6 days 15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 3.3-7 g/d[18]	NR	Baseline	NT-proBNP, pg/mL	68	7237 (7931)	-	0.102
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 1.61 g/d[18]	NR			68	5381 (4829)		
		Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 6 days 15 mL/kg of 0.9%	NR	6 (d)	NT-proBNP, pg/mL	68	3244 (4159)	-1222 (-2660.9, 216.9)[3] NMD	P value between-group at 6 d 0.096

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 3.3-7 g/d[18]						(Baseline-6 d) -3078 (-5043.5, -1112.5)	
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 6 days once only. Low sodium diet 1.61 g/d Na Total Na 1.61 g/d[18]	NR			68	4466 (4332)		
	Wan, 2017, 28701670	Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Baseline	BNP, pg/ml	132	859 (154)	-	NR
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[7] Total Na ~2.8 g/d	< 500 mL/d			132	911 (277)		
		Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Discharge	BNP, pg/ml	132	134 (56)	NMD (Baseline-Discharge) -90 (-138.08, -41.92)	NR
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[7] Total Na ~2.8 g/d	< 500 mL/d			132	276 (78)		
	Montgomery, 2023, 37044281	Furosemide With Oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	Enrollment	NT-proBNP at admission, pg/mL, median (IQR)	25	4540 (2690, 10700)	-	-
		Furosemide without oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			21	3550 (2350, 6490)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide With oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	≤ 5 (d)	NT-proBNP at the end of study visit (≤ 5 (d)), pg/mL, median (IQR)	26	2840 (1630, 4550)	Rank biserial[α] (r_{rb}) -0.16 (-0.46, 0.17) Median Difference -680	0.34
		Furosemide without oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			22	3520 (2430, 5980)		
		Furosemide With oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted Sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	Enrollment to ≤ 5 (d)	NT-proBNP change from enrollment to the end of study visit (≤ 5 (d)), pg/mL, median (IQR)	25	-1050 (-3050, 207)	Rank biserial[α] (r_{rb}) -0.11 (-0.41, 0.22) Net Median Difference -10	0.52
		Furosemide without oral NaCl	Restricted Sodium Diet ~0.8 g/d Na	No restriction			21	-1040 (-1730, 212)		
Serum Na (mEq/L)	*Diet (g/d Na)*									
	Aliti, 2013, 23689381	Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	Baseline	Sodium, mEq/L	38	139 (4)	-	NR
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	139 (5)		
		Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	≤ 7 (d)	Sodium, mEq/L	38	139 (4)	0 (-1.6, 1.6) NMD 0 (-1.90, 1.90)	P value between-groups Study end > 0.99[20] From baseline to the study end 0.48[21]
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	139 (3)		
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Baseline	Sodium, mEq/L	30	140 (4)	-	NR
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	141 (3)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	≤ 7 (d)	Sodium, mEq/L	30	140 (4)	0 (-1.89, 1.89) NMD 1 (-0.88, 2.88)	P value Between-group (Baseline vs study end) 0.64[21]
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	140 (3)		
	Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	Baseline	Sodium, mEq/L	16	136.3 (3.2)	-	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	136.5 (2.2)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	7 (d)		16	135.3 (3.7)	-2.4 (-4.45, -0.35) NMD (Baseline-7 d) -2.2 (-4.19, -0.20)	P value (MD) < 0.05
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	137.7 (1.9)		
	HSS (% NaCl)									
	Issa, 2013, 22243938	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	Baseline	Sodium, mEq/L	20	137.6 (3.5)	-	P interaction 0.92
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	134.4 (5.6)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	1 (d)	Sodium, mEq/L	20	138.7 (3.7)	-	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	135.0 (5.5)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	2 (d)	Sodium, mEq/L	20	139.1 (3.9)	-	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	134.9 (6.1)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	3 (d)	Sodium, mEq/L	20	139.5 (4.6)	3.5 (0.03, 6.97) NMD (Baseline-3 d) 0.3 (-3.22, 3.82)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	136.0 (5.0)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	4 (d) which is 24 h after intervention	Sodium, mEq/L	20	137.8 (4.3)	NMD (Baseline-24 h after intervention) -0.3 (-3.8, 3.2)	
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	134.9 (5.2)		
	Roul, 2017	HSS	HSS (NaCl% NR) Sodium diet NR[19]	NR[19]	In-hospital	Sodium, mEq/L	11	137 (7)	8 (2.1, 13.8)	0.007
		without HSS	NR[19]	NR[19]			156	129 (3)		
	Licata, 2003, 12660669	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 ds Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na= ~4.5-8.2 g/d	1000 mL/d	Baseline	Sodium, mEq/L	53	135.8 (7)	-	NR
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 days Total Na 1.8 g/d	1000 mL/d			54	134.8 (8)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 ds Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na= ~4.5-8.2 g/d	1000 mL/d	Discharge	Sodium, mEq/L	53	142.3 (3.9)	12.1 (10.6, 13.6) NMD (Baseline-Discharge) 11.1 (8.63, 13.57)	P value between-group (Discharge) <0.001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 days Total Na 1.8 g/d	1000 mL/d			54	130.2 (4)		
	Mahjoob, 2021, 34903983	Furosemide with HSS	150 mL (5% NaCl) twice daily for 48 (h) Sodium diet NR Total Na 5.9=~6 g/d[5]	NR	Baseline	Sodium, mEq/L	14	135.21 (4)	-	0.91[11]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	134.93 (4.2)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide with HSS	150 mL (5% NaCl) twice daily for 48 (h) Sodium diet NR Total Na 5.9=~6 g/d[5]	NR	3 (d)	Sodium, mEq/L	14	138.86 (2.35)	0.28 (-0.05, 0.61) NMD (Baseline-3 d)	0.10[11]
		Furosemide without HSS	150 mL (0.9% NaCl) twice daily for 48 (h) Sodium diet NR Total Na ~1.1 g/d[5]	NR			14	137.79 (3.14)	0.79 (-1.90, 3.48)	
	Okuhara, 2014, 24462960	Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	Baseline	Sodium, mEq/L, median (IQR)	22	138 (136, 141)	-	NR
		Furosemide with glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	140.5 (137.3, 142)		
		Furosemide with HSS	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	24 (h)	Sodium, mEq/L, at 24 h end of intervention, median (IQR)	22	140.5 (138, 142)	Median Difference 1 Net Median Difference (Baseline-24 h) 3.5	NR
		Furosemide with glucose (5%)	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	139.5 (135.3, 141)		
	Parrinello, 2011, 21440872	Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	Baseline	Sodium, mEq/L	66	136 (6)	-	NS
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	135 (4)		
		Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d)	1000 mL/d	6 (d)	Sodium, mEq/L	66	140 (5)	1 (-0.7, 2.7) NMD (Baseline-6 d)	<0.0001

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			Total Na 6.3 g/d						8 (6.27, 9.73)	
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	131 (5)		
	Parrinello, 2012, 22980301	Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Baseline	Sodium, mEq/L	122	139.5 (5.6)	-	0.12
		Furosemide without HSS	NR	1000 mL/d			126	138 (4.7)		
		Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Discharge	Sodium, mEq/L	122	140.2 (3.5)	8.2 (4.1, 12.3)[3] NMD (Baseline-Discharge)	P value between-group At discharge 0.0001
		Furosemide without HSS	NR	1000 mL/d			126	132 (2.5)	6.7 (5.58, 7.82)	
	Paterna, 2000, 10938493	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Sodium, mEq/L	30	135.9 (6.8)	-	NR
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	134.7 (7.9)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Sodium, mEq/L	30	142.2 (3.8)	12.1 (10.0, 14.2) NMD (Baseline-Discharge)	P value between-group At discharge <0.001
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	130.1 (4.3)	10.9 (7.66, 14.14)	

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
	Paterna, 2005, 15963399	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Sodium, mEq/L	48	133.8 (6)	-	NR
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	134.9 (7)		
		Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	6 (d)	Sodium, mEq/L	48	142.3 (3.4)	12.2 (10.9, 13.5) NMD (Baseline-6 d) 13.3 (11.01, 15.59)	P value between-group At 6 days <0.0001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	130.1 (3)		
	Paterna, 2011, 21701268	Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Baseline	Sodium, mEq/L	953	137.8 (8)	-	NR
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	138.8 (7)		
		Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Sodium, mEq/L	953	143.2 (4)	7.9 (7.5, 8.3) NMD (Baseline-Discharge) 8.9 (8.32, 9.48)	P value between-group At discharge <0.0001
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	135.3 (3.9)		
	Wan, 2017, 28701670	Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice	< 500 mL/d	Baseline	Sodium, mEq/L	132	135.2 (2.3)	-	NR

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d							
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[7] Total Na ~2.8 g/d	< 500 mL/d			132	136.1 (4.8)		
		Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Discharge	Sodium, mEq/L	132	137.5 (2.9)	3.9 (3.11, 4.68) NMD (Baseline-Discharge) 4.8 (3.93, 5.67)	NR
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[7] Total Na ~2.8 g/d	< 500 mL/d			132	133.6 (3.6)		
	Yayla, 2015, 26135463	Furosemide with HSS	150 mL HSS (1.95% NaCl) once daily for 48 (h) Sodium Diet NR Total Na 1.15 g/d[5]	NR	Baseline-to-compensated	Sodium, mEq/	14	136.7 (4.1)	NMD HSS vs bIV[17] (Baseline-to-compensation) 0.7 (-2.2, 3.6)	P value between-group 0.37
		Furosemide (continuous) cIV without HSS	Sodium Diet NR	NR			15	134.0 (7.2)		
		Furosemide (bolus) bIV without HSS	Sodium Diet NR	NR			14	136.0 (3.8)		
	Montgomery, 2023, 37044281	Furosemide with oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	4 (d)	Sodium change from enrollment to day 4, mEq/L	34	-0.03 (3.3)	Cohen d[a] 0.86 (0.35, 1.37) NMD 2.57 (1.109, 4.031)	<0.001
		Furosemide without oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	-2.6 (2.7)		
		Furosemide with oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium	No restriction	Discharge	Sodium change from enrollment to discharge, mEq/L	34	-0.91 (3.5)	Cohen d[a] 0.66 (0.16, 1.17)	0.010

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
			Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d						NMD 2.29 (0.612, 3.968)	
		Furosemide without oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	-3.2 (3.4)		
Aldosterone,pg/mL	**Diet (g/d Na)**									
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Baseline	Aldosterone, pg/mL, median (IQR)	30	65 (44, 159)	-	NR
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	61 (35, 126)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	at 7 days or at discharge which came first (study end)? (d)[#]	Aldosterone, pg/mL, median (IQR).	30	81 (58, 164)	Median Difference 15 Net Median Difference (Baseline-7 d) 11	P value Between-group (Baseline vs study end) 0.85[21]
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	66 (36, 129)		
	HSS (% NaCl)									
	Issa, 2013, 22243938	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	Baseline	Aldosterone, median (IQR)[##]	20	10 (3.7, 17.2)	-	P value between-group At baseline NS
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	9.7 (6.2, 41.6)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 days Total Na 5.9 =~6 g/d[5]	NR	4 (d) which is 24 h after intervention	Aldosterone, median (IQR)[##]. after intervention)	20	12 (4.6, 19.7)	Median Difference 4.4 Net Median Difference (Baseline-after-intervention) 4.1	NR
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 days Total Na 0.7 g/d[5]	NR			12	7.6 (3.1, 79.9)		
	Okuhara, 2014, 24462960	HSS Furosemide	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	Baseline	Plasma aldosterone, pg/mL, median (IQR).	22	71 (35.1, 112.0)	-	NR

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Glucose (5%) Furosemide	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	76.4 (42.6, 94.6)		
		HSS Furosemide	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	24 (h)	Plasma aldosterone, pg/mL, median (IQR).	22	42.7 (23.3, 68.3)	Median Difference (Baseline-24 h) -2.1 Net Median Difference (Baseline-24 h) 3.3	NR
		Glucose (5%) Furosemide	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	44.8 (26.5, 66.2)		
	Montgomery, 2023, 37044281	Furosemide with oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	Enrollment	Aldosterone, pd/mL, median (IQR)	25	280 (131, 585)	-	-
		Furosemide without oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			21	303 (230, 481)		
		Furosemide with oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	≤ 5 (d)	Aldosterone, pd/mL, median (IQR)	26	284 (194, 593)	Rank biserial[a] (r_{rb}) -0.03 (-0.35, 0.30) Median Difference -7	0.87
		Furosemide without oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			22	291 (159, 639)		
		Furosemide with oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	Enrollment to ≤ 5 (d)	Aldosterone change from enrollment to end of stud visit (≤ 5 (d)), pd/mL, median (IQR)	25	17.1 (-51.2, 123)	Rank biserial[a] (r_{rb}) 0.17 (-0.16, 0.47) Net Median Difference 64.5	0.32
		Furosemide without oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			21	-47.4 (-116, 85.1)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
Renin	*HSS (%NaCl)*									
	Issa, 2013, 22243938	Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 (d) Total Na 5.9 =~6 g/d[5]	NR	Baseline	Renin, median (IQR)	20	20.6 (5.4, 35.4)	-	No difference in baseline values between groups
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 (d) Total Na 0.7 g/d[5]	NR			12	32.9 (17.9, 42.6)		
		Furosemide with HSS	100 mL/d HSS (7.5% NaCl) twice daily for 3 (d) Total Na 5.9 =~6 g/d[5]	NR	4 (d) which is 24 h after intervention	Renin, median (IQR)	20	13.7 (5.6, 35.1)	Median Difference -10.1 Net Median Difference 2.2	NR
		Furosemide without HSS	100 mL (0.9% NaCl) twice daily for 3 (d) Total Na 0.7 g/d[5]	NR			12	23.8 (17.8, 45.1)		
PRA (ng/ml/h)	*Diet (g/d Na)*									
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Baseline	PRA, ng/mL/h, median (IQR)	30	2.4 (0.6–9.1)	-	NR
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	2.8 (0.4–6.4)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	≤ 7 (d)	PRA, ng/mL/h,median (IQR).	30	4.5 (2.3–22.1)	Median Difference -1.3 Net Median Difference (Baseline-7d or less) -0.9	P value Between-group (Baseline vs ≤ 7 (d)) 0.42[21]
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	5.8 (1.5–21.3)		
	HSS (% NaCl)									
	Okuhara, 2014, 24462960	HSS Furosemide	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	Baseline	Plasma renin activity, (ng/ml/h), median (IQR)	22	1.1 (0.5, 6.5)	-	NR
		Glucose (5%) Furosemide	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	0.7 (0.3, 5.2)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
	Okuhara, 2014, 24462960	HSS Furosemide	500 mL/d of HSS (1.7% NaCl) per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 5.7=~6 g/d	500 mL/d	24 (h)	Plasma renin activity, (ng/ml/h), at 24 h, end of intervention, median (IQR)	22	0.9 (0.4, 8.1)	Median Difference 0.3 Net Median Difference (Baline-24 h) -0.1	
		Glucose (5%) Furosemide	500 mL/d 5% glucose per day Restricted sodium to 2.4 g/d Na for 24 (h) Total Na 2.4 g/d	500 mL/d			22	0.6 (0.3, 4.1)		
Calorie intake (kcal/kg)/ Fluid intake	*Calorie Intake/Fluid Intake*									
	Diet (g/d Na)									
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	≤ 7d	Calorie intake (kcal/kg/d)	30	15.1 (5.1)	-4.4 (-7.26, -1.53)	0.01
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	19.5 (5.4)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	≤ 7d	Fluid intake, mL/d, median (IQR)	30	582.7 (496.9, 662.4)	Median Difference -312.7	<0.001[11]
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	895.4 (751.2, 1121.8)		
	Inuzuka, 2016	Low sodium diet	Max 2.4 g/d for NR days	NR	NR	Caloric intake represented as a percentage of estimated daily requirements (timepoint was not reported)	145	96% (25)	-16 (-6.6, -25.4)	<0.01
		Unrestricted sodium diet	~4 g/d for NR days	NR			45	112% (29)		
Clinical Outcomes										
Clinical congestion score (CCS)	*Diet (g/d Na)*									
	Aliti, 2013, 23689381	Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	Baseline	CCS[22]	38	12.6 (3.1)	-	0.67
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	12.8 (2.8)		
		Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	3 (d)	CCS change from baseline to day 3 (a primary end point)	38	-4.03 (3.3)	NMD -0.59 (-2.10, 0.92)[3]	0.47
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	-3.44 (3.35)		
		Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	7 (d)	CCS at study end	38	6.4 (3.0)	-0.7 (-1.97, 0.57) NMD -0.5 (-1.76, 0.76)	NR
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	7.1 (2.6)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Baseline	CCS[22]	30	12.2 (3.2)	-	0.36
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	11.4 (2.7)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	3 (d)	CCS change from baseline to day 3.	30	NR	-	0.1
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	NR		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	7 (d)	CCS change from baseline to day 7.	30	-3.4 (3.5)	NMD 0.4 (-1.6, 2.4)	0.70
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	-3.8 (3.4)		
HF-Related Symptom	*HF-Related Symptom (Thirst)*									
	Diet (g/d Na)									
	Aliti, 2013, 23689381	Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	Baseline	Perceived thirst using Visual analogue scale[26]	38	4.08 (2.6)		0.65
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	3.95 (2.5)		
		Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	7 (d)	Perceived thirst using Visual analogue scale[26]	38	5.1 (2.9)	0.67 (0.2-1.13) NMD (Baseline-7 d) 1.53 (0.38, 2.67)	Time x group P 0.01[27]
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	3.44 (2)		
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Baseline	Perceived thirst using Visual analogue scale[26]	30	4.2 (3.6)	-	0.14
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	5.8 (2.6)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	≤ 7 d	Perceived thirst using Visual analogue scale	30	NR	-	Time x group P 0.03
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	NR		
	HSS (% NaCl)									
	Montgomery, 2023, 37044281	Furosemide with oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	4 (d)	TDS-HF score change from enrollment to day 4	34	-1.2 (5.1)	Cohen d[a] -0.23 (-0.73, 0.28) NMD -1.31 (-4.169, 1.549)	0.39

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide without oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	0.11 (6.5)		
	HF-Related Symptom (Shortness of Breath)									
	Diet (g/d Na)									
	Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	Baseline	Perceived dyspnea using Visual analogue scale[28]	16	4.8 (1.6)	-	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	6.3 (1.8)		
		Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	7 (d)	Perceived dyspnea using Visual analogue scale[28]	16	8.5 (1.4)	-0.7 (-1.55, 0.15)	P between-group 0.3
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	9.2 (1.0)	NMD (Baseline-7 d) 0.8 (-0.28, 1.88)	
	HF-Related Symptom (General Well-Being)									
	Diet (g/d Na)									
	Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	Baseline	Perceived General well-being using Visual analogue scale[29]	16	5.0 (2.3)	-	-
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	5.7 (2.2)		
		Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	7 (d)		16	8.1 (1.9)	-0.1 (-1.47, 1.27)	P between-group 0.59
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	8.2 (2.0)	NMD (Baseline-7 d) 0.6 (-0.89, 2.09)	
Diuretics Dose During Hospitalization	*Diet (g/d Na)*									
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Baseline	Mean dose of loop diuretics (furosemide), mg/d	30	72.7 (29)	-	0.64
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	69 (26.9)		
		Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	3 (d)	Mean dose of loop diuretics (furosemide), mg/d.	30	74.7 (34.8)	-	0.36
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	66.1 (31.0)		
		Low sodium diet	0.8 g/d Na for 7 days ora less**	800 mL/d	≤7 (d)	Mean dose of loop diuretics (furosemide)	30	68 (34.3)	NMD 4.3 (-11.97, 20.57)	0.38
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	60 (29.5)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
						administered, mg/d				
	Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	7 (d)	Final dose of furosemide, mg/d	16	81.3 (36.6)	14.2 (-6.80, 35.20)	NS
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	67.1 (21.6)		
		Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	During hospitalization	Cumulative dose of diuretic during hospitalization, mg	16	517.5 (209.6)	103.5 (-14.25, 221.25)	NS
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	414.0 (113.8)		
	Velloso, 1991, 1824218	Low sodium diet	0.8 g/d Na for NR days[4]	800 mL/d	During compensation period	Cumulative dose of furosemide, mg.	14	568 (343)	-31 (-265.74, 203.74)	P value 0.80[25]
		Unrestricted sodium diet	4 g/d Na for NR days[4]	800 mL/d			18	599 (327)		
		Low sodium diet	0.8 g/d Na for NR days[4]	800 mL/d	During compensation period	Daily furosemide dose, mg/h/day	14	1.43 (0.74)	-0.15 (-0.64, 0.34)	P value 0.57[25]
		Unrestricted sodium diet	4 g/d Na for NR days[4]	800 mL/d			18	1.58 (0.62)		
	HSS (% NaCl)									
	Montgomery, 2023, 37044281	Furosemide with oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	4 (d)	Total oral furosemide equivalent (FE) dosage from enrollment to day 4, mg	34	1840 (915, 2810)	Rank Biserial[α] (r_{rb}) -0.02 (-0.29, 0.26) Median Difference 220	0.91
		Furosemide without oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	1620 (1070, 3080)		
Time on IV Diuretics	*Diet (g/d Na)*									
	Aliti, 2013, 23689381	Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	During hospitalization	The median days to transition from IV to oral diuretic therapy	38	4 (2.0, 7.2)	Median Difference 0	0.58
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*	≥2500 mL/d			37	4 (2.0, 7.0)		
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	≤ 7 (d)	The mean days to transition from IV to oral diuretic therapy .	30	3 (2.3)	0.3 (-0.86, 1.46)	0.63
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	2.7 (2)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
Time to Clinical Stability	*Diet (g/d Na)*									
	Velloso, 1991, 1824218	Low sodium diet	0.8 g/d Na for NR days[4]	800 mL/d	During compensation period	Days to compensation (d)	14	7.5 (1.9)	0.9 (-0.34, 2.14)[3]	P value 0.18[25]
		Unrestricted sodium diet	4 g/d Na for NR days[4]	800 mL/d			18	6.6 (1.6)		
Adherence to Prescribed Diet Inpatient Setting										
	Diet (g/d Na)									
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	≤ 7 (d)	Consumption of dietary Na g/d, median (IQR)	30	1.2 (1.1, 1.3)	Median Difference -1.3	<0.001[21]
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	2.5 (2.4, 2.8)		
	Fabricio, 2019, 31221280	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	7 (d)	Consumption of dietary Na g/d, g/d (through the 24-h dietary recall),	16	0.10 (0.17)	-1.47 (-1.70, -1.23)	NR
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	2.47 (0.43)		
		Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	7 (d)	Consumption of at least 80% of the entire meal	16	79.6 (14.3%)	-8.5 (-17.87, 0.87)[3]	0.08
		Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d			15	88.1 (12.3%)		
Utilization Measures										
Length of Hospital Stay	*Diet (g/d Na)*									
	Aliti, 2013, 23689381	Low sodium diet	Max 0.8 g/d Na for 7 days or less*	Max 800 mL/d	Discharge	The overall median length of stay (d)	38	7 (3.8, 13)	Median Difference 1	0.89
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less*.	≥2500 mL/d			37	6 (4, 12.5)		
		Low sodium diet	Max 0.8 g/d Na for 7 days or less	Max 800 mL/d	Discharge	The length of stay among patients remained hospitalized after day 7	NR	NR	-	0.9
		Unrestricted sodium diet	~3- 5 g/d Na for 7 days or less	≥2500 mL/d			NR	NR		
	d'Almeida, 2018, 29793053	Low sodium diet	0.8 g/d Na for 7 days or less**	800 mL/d	Discharge	The overall median length of stay (d)	30	6 (1, 17)	Median Difference 2	0.52
		Unrestricted sodium	~4 g/d Na for 7 days or less**	Unlimited fluid intake			23	4 (2, 8)		
	Fabricio, 2019,	Low sodium diet	1.2 g/d Na for 7 days***	1000 mL/d	Discharge		16	18.1 (9.6)	6.7	0.02

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
	31221280	Unrestricted sodium diet	2.8 g/d Na for 7 days***	1000 mL/d		Mean hospitalization duration (d)	15	11.4 (3.5)	(1.67, 11.73)[3]	
	HSS (% NaCl)									
	Licata, 2003, 12660669	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily for 6 to 12 ds Normal sodium diet 2.76 g/d= ~2.8 g/d Na Total Na= ~4.5-8.2 g/d	1000 mL/d	Discharge	Hospitalization (d)	53	8.57 (2.3)	-3.13 (-4.06, -2.20)	<0.001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 6 to 12 days Total Na 1.8 g/d	1000 mL/d			54	11.7 (2.6)		
	Parrinello, 2011, 21440872	Furosemide with HSS	150 mL of HSS (3% NaCl) twice daily Light sodium diet 2.76 g/d Na for 6 (d) Total Na 6.3 g/d	1000 mL/d	Discharge	Hospitalization (d)	66	6.3 (3)	-5.7 (-6.90, -4.50)	<0.0001
		Furosemide without HSS	150 mL of 0.9% NaCl twice daily Low sodium diet 1.8 g/d Na for 6 (d) Total Na 2.9 g/d = ~3 g/d	1000 mL/d			67	12 (4)		
	Parrinello, 2012, 22980301	Furosemide with HSS	HSS (1.4%-4.6% NaCl)[6] twice daily Normosodic diet until compensation[14] Total Na: assumed at least 3.5-4.5 g/d[15]	1000 mL/d	Discharge	Hospitalization (d)	122	6.25 (2.12)	-3.95 (-4.53, -3.37)	<0.0001
		Furosemide without HSS	NR	1000 mL/d			126	10.2 (2.54)		
	Paterna, 2000, 10938493	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Hospitalization (d)	30	8.57 (2.3)	-3.1 (-4.34, -1.86)[3]	0.001

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
		Furosemide without HSS	Sodium diet 2.76 g/d Na for 6 to 12 (d) Total Na ~2.8 g/d[7]	1000 mL/d			30	11.67 (2.6)		
	Paterna, 2011, 21701268	Furosemide with HSS	150 mL of HSS (1.4%–4.6% NaCl)[6] twice daily until compensation[13] Moderate sodium diet 2.76 g/d Na Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Hospitalization (d)	953	3.5 (1)	-2 (-2.09, -1.91)	<0.0001
		Furosemide without HSS	Low sodium diet 1.8 g/d Na until compensation[13] Total Na 1.8 g/d[7]	1000 mL/d			974	5.5 (1)		
	Paterna, 2005, 15963399	Furosemide with HSS	150 mL of HSS (1.4%- 4.6% NaCl)[6] twice daily Normal sodium diet 2.76 g/d for 4 to 6 (d) Total Na 4.4-8.1 g/d	1000 mL/d	Discharge	Hospitalization (d)	48	6.57 (2.3)	-3.93 (-4.92, -2.94)	<0.0001
		Furosemide without HSS	Iposodic diet 1.8 g/d Na for 4 to 6 (d) Total Na 1.8 g/d[7]	1000 mL/d			46	10.5 (2.6)		
	Roul, 2017	HSS	HSS (NaCl% NR) Sodium diet NR[19]	NR[19]	Discharge	Median length of stay (d)	11	21 (IQR: NR)	Median Difference 11	NR
		without HSS	NR[19]	NR[19]			156	10 (IQR:NR)		
	Tuttolomondo, 2011, 20346637	Furosemide with HSS	150 mL of HSS (1.4–4.6% NaCl) twice daily for 8 (d) 15 mL/kg of 0.9% NaCl (over 60 min) after 8 (d) once only. Low sodium diet 1.61 g/d Na for 10 (d) Total Na 3.3-7 g/d[18]	NR	Discharge	Hospitalization (d), median (IQR)	120	10 (9, 11)	Median Difference 0	NR
		Furosemide without HSS	15 mL/kg of 0.9% NaCl (over 60 min) after 8 (d) once only. Low sodium diet 1.61 g/d Na for 10 (d) Total Na 1.61 g/d[18]	NR			30	10 (8,11)		

Outcome	Study, Year, PMID	Arm	Total Sodium Intake/d[1]	Fluid Intake/d	Time	Outcome Definition	N	Mean (SD)/Median (IQR)	MD (95% CI)[2]	Reported P Value
	Wan, 2017, 28701670	Furosemide with compound HSS	100 mL c-HSS[8] (2.8% NaCl) twice daily until clinical compensation[9] Normal sodium diet 2.76 g/d Na Total Na 5 g/d	< 500 mL/d	Discharge	Hospitalization time (d)	132	4 (2)	-3 (-3.48, -2.52)	<0.01
		Furosemide without compound HSS	Normal sodium diet 2.76 g/d until clinical compensation[9] Total Na ~2.8 g/d	< 500 mL/d			132	7 (2)		
	Yayla, 2015, 26135463	Furosemide with HSS	150 mL HSS (1.95% NaCl) once daily for 48 (h) Sodium Diet NR Total Na 1.15 g/d[5]	NR	Until compensation	Hospitalization (d), from baseline to compensated state.	14	3.7 (1.3)	HSS vs bIV[17] -4.2 (-6.45, -1.95)	<0.01
		Furosemide (continuous) cIV without HSS	Sodium Diet NR	NR			15	6.6 (3.4)		
		Furosemide (bolus) bIV without HSS	Sodium Diet NR	NR			14	7.9 (4.1)		
	Montgomery, 2023, 37044281	Furosemide with oral NaCl	2 g Oral NaCl three times per day for 4 days. Restricted sodium Diet ~0.8 g/d Na. Total Na ~ 3.2 g/d	No restriction	Discharge	Time to discharge from enrollment (days), median (IQR)	34	8.0 (6.00, 12.5)	Median Difference 1.0	NR
		Furosemide without oral NaCl	Restricted sodium Diet ~0.8 g/d Na	No restriction			31	7.0 (5.00, 13.5)		

Notes. [1] Calculated by research team based on IV Na (saline) and oral sodium intake (diet Na) if reported; [2] Calculated by research team; [3] 95% CI was calculated based on p value reported in the study; [4] The duration of intervention was not reported; however, most outcomes were reported at compensation which was defined as return to functional classes 1 or II and without edema; [5] Total sodium per day provided by IV fluid Na only, sodium diet in both groups was not reported and we assume it was at least 2.8 g/d; [6] The dose of HSS was determined according to serum Na (HSS 4.6%, 3.5%, between 1.4% and 2.4% were administered for patients with serum Na < 125 mEq/L, between 126 and 135 mEq/L, > 135 mEq/L respectively). In Tuttolomondo 2011, it was reported that HSS 3.5%, and between 1.4% and 2.4% were administered to patients with serum Na <125 mEq/L, and > 135 mEq/L respectively. In Tuttolomondo 2021, it was reported that HSS 3.5%, and between 1.4% and 2.4% were administered to patients with serum Na <135 mEq/L, and > 135 mEq/L respectively; [7] Total sodium per day provided by oral sodium intake (diet only) as no IV Na (saline) was reported or administered;[8] c-HSS contains, additional to the 2.8% NaCl, 0.2% KCl, 0.9% MgSO4; [9] Did not clearly define the duration of intervention; however, it was mentioned that the intervention would stop once patients reached compensation. Patients were considered clinically compensable when they achieved an improved NYHA classification and appropriate BW calculated by the Lorenz formula and bioelectrical impedance measurement; [10] The reported weight was not consistent with adult weight and not corresponding to the mean age reported, and it was not the difference or BMI, we did not include these values in our analysis. We contacted the author for clarification, but there has been no response; [11] Based on Mann-Whitney U test; [12] Based on Independent Sample T-test; [13] Defined as dry status, change in NYHA functional class to at least II on clinical judgment and the accomplishment of ideal BW, as calculated by the Lorenz formula and detected by bioimpedance vector analysis; [14] Compensation was defined, when the NYHA functional class reached at least class II with the accomplishment of dry weight, as detected by bioimpedance vector analysis; [15] The study did not mention the amount of HSS per day, or the amount of normal sodium diet; we assumed that patients received at least 100 mL of

HSS per day and that normal sodium diet provided at least 2.8 g/d, based on the previous assumption the research team calculated the total sodium intake per day;[16] Weight change was reported here as (-) to denote the direction of change (reduction). SD was calculated by research team as it was not reported for weight change in the study; [17] We considered bIV group as reference to compare with HSS group; [18] We calculated here the total sodium per day during the 6 days of intervention (first phase of therapy), not including the sodium from the 0.9% NaCl loading (second phase of therapy); [19] Data about HSS concentration, amount, frequency, Na diet, total fluid per day was not reported in the abstract; [20] Multiple comparison test with Bonferroni correction; [21] Repeated-measures analysis (generalized estimating equations method) for the between-group difference from baseline to the end of the study period; [22] The CCS is an instrument composed of 7 items that assess clinical signs and symptoms of congestion, including presence of rales, a third heart sound, jugular venous distension, peripheral edema, hepatojugular reflux, orthopnea, paroxysmal nocturnal dyspnea, and New York Heart Association functional class. The score ranges from 1 to 22 points, with higher scores being directly indicative of increased clinical congestion; [23] Significance determined using multiple comparison test with Bonferroni correction; [24] Difference significant at P = .002; adjusted covariance matrix for correction of different CCS at hospital day 7; [25] Determined by Student's t test; [26] Assessment of perceived thirst was performed using a visual analog scale. In this setting, patients were asked to grade their thirst on a scale of 0 to 10; [27] By mixed-effects models; [28] With 0 corresponding to marked shortness of breath and 10 to no shortness of breath; [29] With 0 representing the greatest possible malaise and 10 the maximum sensation of well-being; * For 7 days or less until hospital day 7 or until discharge in patients whose length of stay was less than 7 days; ** For 7 days or less until day 7 of admission or at hospital discharge, whichever came first; *** For 7 days 7 days (or less based on clinical indication, a clinical indication defined by the medical team responsible for the treatment of the patient based on the occurrence of hypotension, hyponatremia, or worsening of renal function, the intervention could be stopped before the 7th day of hospitalization); [α] Reported in the study; [#] At day 7 or at discharge, whichever came first; [##] Unit was not reported; [###] Research team converted the data from ng/mL to mg/L. [†] Complete unit was not reported.

Abbreviations. BNP=brain (or B-type) natriuretic peptide; BUN=blood urea nitrogen; ccs=clinical congestion score; d=day; C-HSS=Compound hypertonic saline solution; dL=deciliter; eGFR=estimated glomerular filtration rate; g=gram; GFR=glomerular filtration rate; h=hour; HSS=hypertonic saline solution; IQR=interquartile range; IV=intravenous; L=liter; Max=maximum; MD= mean difference; MDRD=Modification of Diet in Renal Disease; mEq=milliequivalent; mg=milligram; NMD=net mean difference; mL=milliliter; min=minute; m=meter; N=sample size; Na=sodium; NaCl=sodium chloride; ng=nanogram; NR=not reported; NT-proBNP=N-terminal brain (or B-type) natriuretic peptide; NYHA=New York Heart Association; pg=picogram; SD=standard deviation; TDS-HF=Thirst Distress Scale for Heart Failure (higher scores indicates more thirst distress).

APPENDIX I. PEER REVIEW DISPOSITION

Comment #	Reviewer #	Comment	Author Response
Are the objectives, scope, and methods for this review clearly described?			
1	1	Yes	Thank you.
2	3	Yes	Thank you.
3	4	Yes	Thank you.
4	5	Yes	Thank you.
Is there any indication of bias in our synthesis of the evidence?			
5	1	No	Thank you.
6	3	No	Thank you.
7	4	No	Thank you.
8	5	No	Thank you.
Are you aware of any published or unpublished studies that we may have overlooked?			
9	1	No	Thank you.
10	3	No	Thank you.
11	4	Yes - This study was published in 2023 and is an RCT of oral sodium during acute heart failure. "Oral Sodium to Preserve Renal Efficiency in Acute Heart Failure: A Randomized, Placebo-Controlled, Double-Blind Study" PMID: 37044281 DOI: 10.1016/j.cardfail.2023.03.018	The identified study was published after our search date. We have added the study to the report and updated the results and text accordingly.
12	5	Yes - https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00369-5/fulltext	The suggested study was not conducted in hospitalized heart failure patients, and does not meet our review eligibility criteria.
Additional suggestions or comments can be provided below.			
19	1	Wow. This is just amazing. Thank you.	Thank you.
20	3	There not seem to have bias on the analysis of data itself. But there seems to have a clear indication, between the lines, that the studies are "not good enough" because are made "somewhere else" outside US.	Thank you. Our intent was to note that health system related outcomes may not generalize across countries. We revised the text to clarify that studies in the US are needed to evaluate outcomes in the US context. “Limited evidence of RCT data from North

Comment #	Reviewer #	Comment	Author Response
			America suggests a unique opportunity for VA hospitals to evaluate effectiveness and implementation of this strategy in the US and to fill the gaps in evidence for VA providers and policy makers. Conducting studies in the US would be particularly informative to understand the effect of intervention on health system outcomes pertinent to the US (such as length of hospital stay), which are likely to differ substantially across different health systems and countries."
21	4	The authors appropriately point out that the HSS/furosemide data largely comes from Europe and that the findings (particularly LOS) may not apply to VA. Would it be valuable to expand on this by noting that most of the European studies are from the same research group?	Thank you for this comment. We revised the Discussion to comment that 3 research groups were responsible for conducting the majority of the European studies.
22	4	Ezekowitz et al RCT form Lancet was missed it appears which I hope is because the data cut was before 2022 otherwise would be a major oversight. https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)00369-5/fulltext Otherwise reads well	Thank you for sharing this study. Upon review, we found that the suggested study was not conducted in *hospitalized* heart failure patients, and, thus, does not meet our review eligibility criteria.