237

Association Between Sodium Intake and Systolic and Diastolic Blood Pressure: A Systematic Literature Review and Meta-analysis

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Introduction

- Sleep disorders, such as narcolepsy and idiopathic hypersomnia, are associated with high cardiovascular comorbidity burden,[1,2] which may be exacerbated by excess sodium consumption
- United States (US) and international health organisations, including the US Department of Agriculture, American Heart Association, American College of Cardiology, and World Health Organization, recommend limiting dietary intake of sodium (<2300 mg/day for most adults) to protect cardiovascular health[3-9]
- Despite the well-established evidence that excess sodium intake is directly linked to increased blood pressure, the majority (≈90%) of US adults consume more sodium than the recommended limit[3,10-14]
  - Certain narcolepsy treatments contain up to 1640 mg of sodium per nightly 9 g dosage,[15,16] potentially contributing to chronic sodium overconsumption in this high-risk population

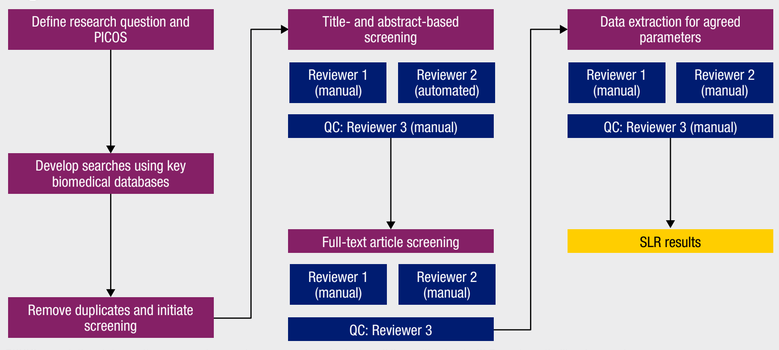
Objective

- This study aims to add to previous systematic literature reviews (SLRs) by using more expansive study eligibility criteria and providing an up-to-date meta-analysis to qualitatively and quantitatively evaluate the relationship between sodium intake and systolic and diastolic blood pressure (SBP; DBP)

Methods

- A comprehensive, gold-standard SLR was conducted using Embase®, MEDLINE®, CENTRAL®, conference proceedings, and clinical trial registries to identify studies published up to 7 December 2023
- Study selection, data extraction, and risk of bias assessments (Cochrane RoB 2.0,[17] Newcastle Ottawa Scale[18]) were conducted by 2 independent reviewers
  - For the title and abstract screening, 1 human reviewer was replaced with an artificial intelligence-based tool (GPT-4)
  - Any discrepancies were resolved by a third human reviewer
- Meta-analyses were conducted for studies meeting prespecified *Population, Intervention, Comparison, Outcomes, and Study design* (PICOS) criteria, including observational or interventional designs with ≥2 years of follow-up assessing the association between higher vs lower sodium levels (variably defined across studies) or per gram sodium increase and SBP/DBP in adults

Figure 1. SLR Process Overview



PICOS, population, intervention, comparison, outcomes, and study design; QC, quality check; SLR, systematic literature review.

Table 1. PICOS Criteria

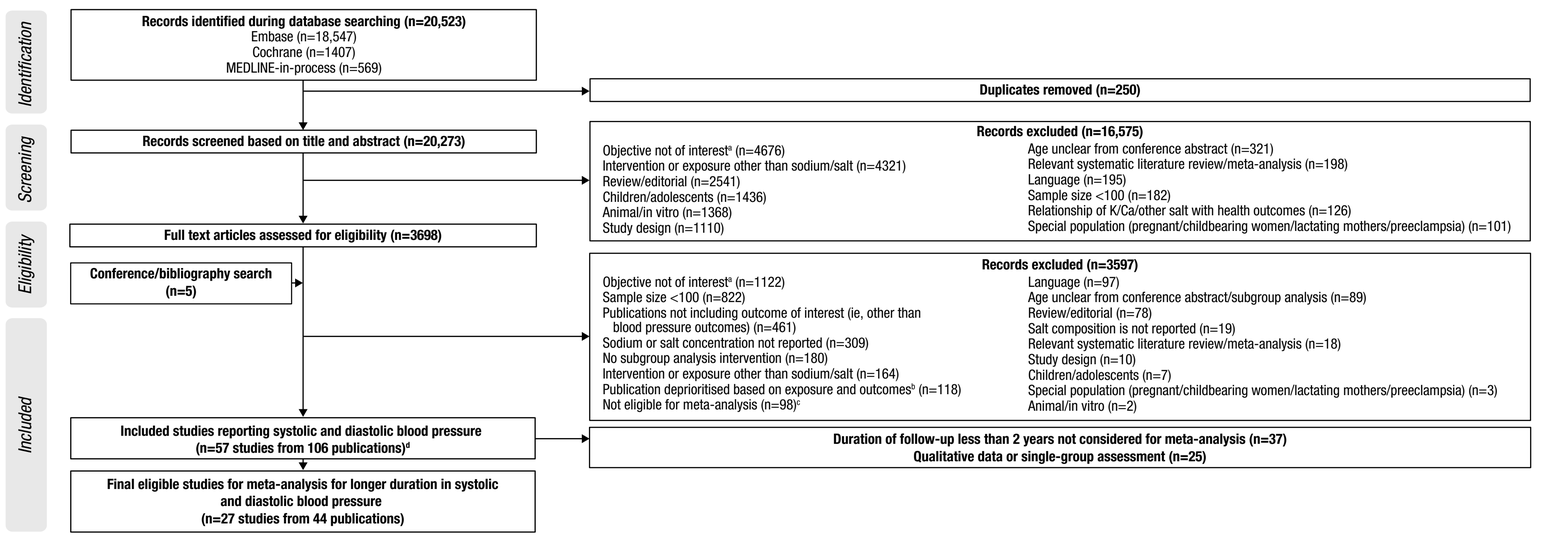
Inclusion Criteria	Exclusion Criteria
Population	
• Adults (≥18 years) with any condition or presentation, including individuals with and without pre-existing medical conditions, irrespective of gender, race, ethnicity, and region	• Individuals <18 years old • Studies for which outcomes for adults are not presented separately
Intervention/Exposure	
• No restriction on the type of intervention/exposure (eg, dietary or drugs), dose, or dosage form	• Sodium reduction beyond recommended limits (eg, 500 mg daily is the minimum body requirement according to AHA)
Comparator/Control	
• No restriction on the type of comparator/control; including studies that compare higher to lower/non-exposed sodium intake groups	• Sodium reduction beyond recommended limits (eg, 500 mg daily is the minimum body requirement according to AHA)
Outcomes	
• Diastolic and systolic blood pressure	• Studies that do not report a health outcome
Study design	
• Observational or interventional designs with ≥2 years of follow-up assessing the association between higher vs lower sodium levels or per gram sodium increase and SBP/DBP	

AHA, American Heart Association; DBP, diastolic blood pressure; PICOS, population, intervention, comparison, outcome, and study design; SBP, systolic blood pressure.

- Both fixed-effects and random-effects models were applied to primary analysis (all eligible studies with ≥2 years follow-up) and subgroup (studies where sodium levels were assessed via 24-hour urine collection to minimise bias and heterogeneity in sodium measurement) meta-analyses
  - Pooled effect estimates were derived using STATA v18.5-SE
- Statistical heterogeneity of effect estimates was assessed using the I^2 statistic
- Publication bias was evaluated using funnel plots, where asymmetry may indicate potential bias, such as selective reporting

Results

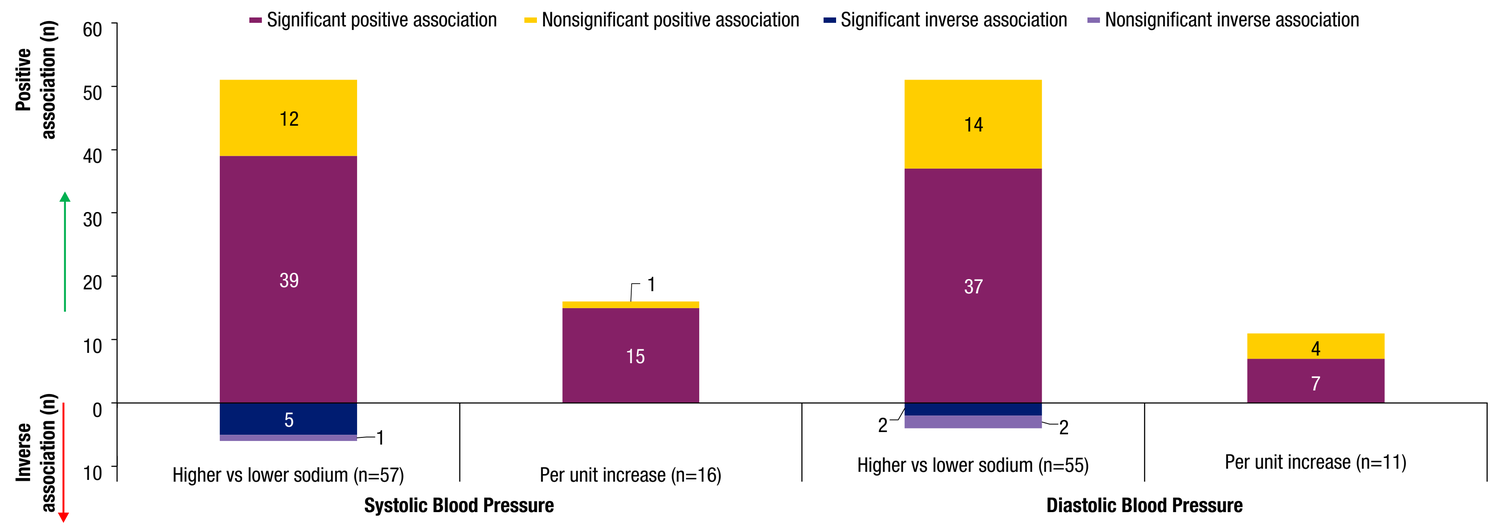
Figure 2. PRISMA Diagram



[a]Publications reporting associations of genetic variations with outcome response to salt; associations of outcomes with parameters other than salt intake; influence of sodium exposure on effectiveness of pharmacologic intervention; 0.9% sodium chloride as comparator; relationship of sodium/salt with minerals and hormones; adherence/preference data; or results from statistical modelling. [b]Publications reporting associations between sodium/potassium ratio, sodium/creatine ratio, sodium density, and outcome of interest; or outcomes such as DALY or annual percent change in prevalence rates across different years. [c]Fewer than 2 studies per outcome and analysis set; sample size not reported; sodium concentration <500 mg or <20 mmol; or other types of blood pressure outcomes reported (eg, home, ambulatory, office, supine, elevated, uncontrolled). [d]Eighteen studies reported the association of per gram sodium increase with blood pressure (16 reported only per gram increase, while 2 studies reported both comparisons between higher vs lower sodium and per gram increase).
Ca, calcium; DALY, disability-adjusted life-year; K, potassium; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses.

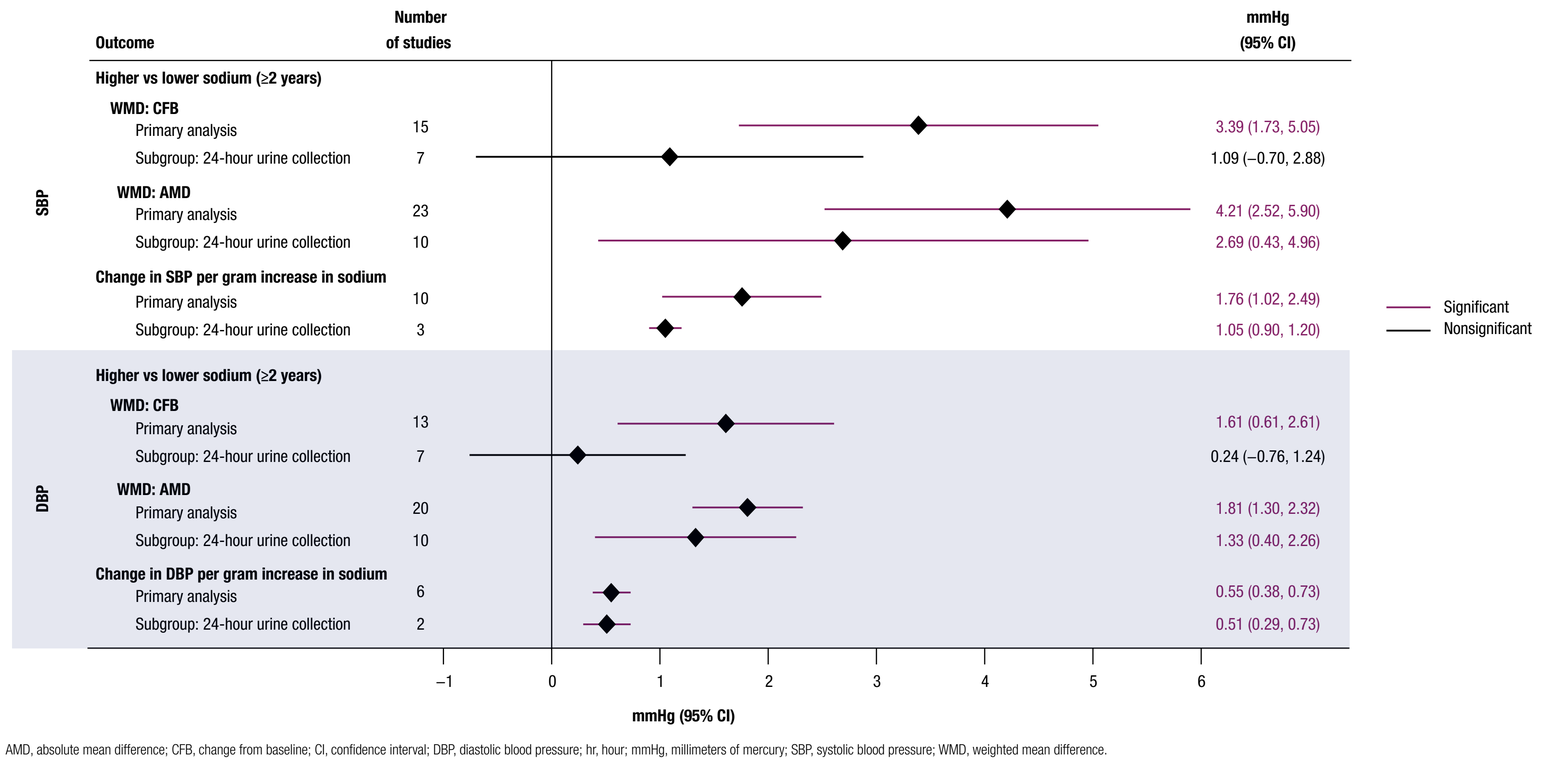
- Fifty-seven studies compared higher vs lower sodium intake and were included in the SLR irrespective of duration of follow-up; low risk of bias was observed in most studies (n=50, 87.7%)
  - Additionally, 18 studies reported results for per gram increase in sodium; low risk of bias was observed in each of these studies

Figure 3. Most Studies Reported That Higher Sodium/Salt Intake Was Significantly Associated With Increased SBP and DBP



- Higher sodium/salt intake was significantly associated with an increase in SBP (39/57 studies) and DBP (37/55 studies)

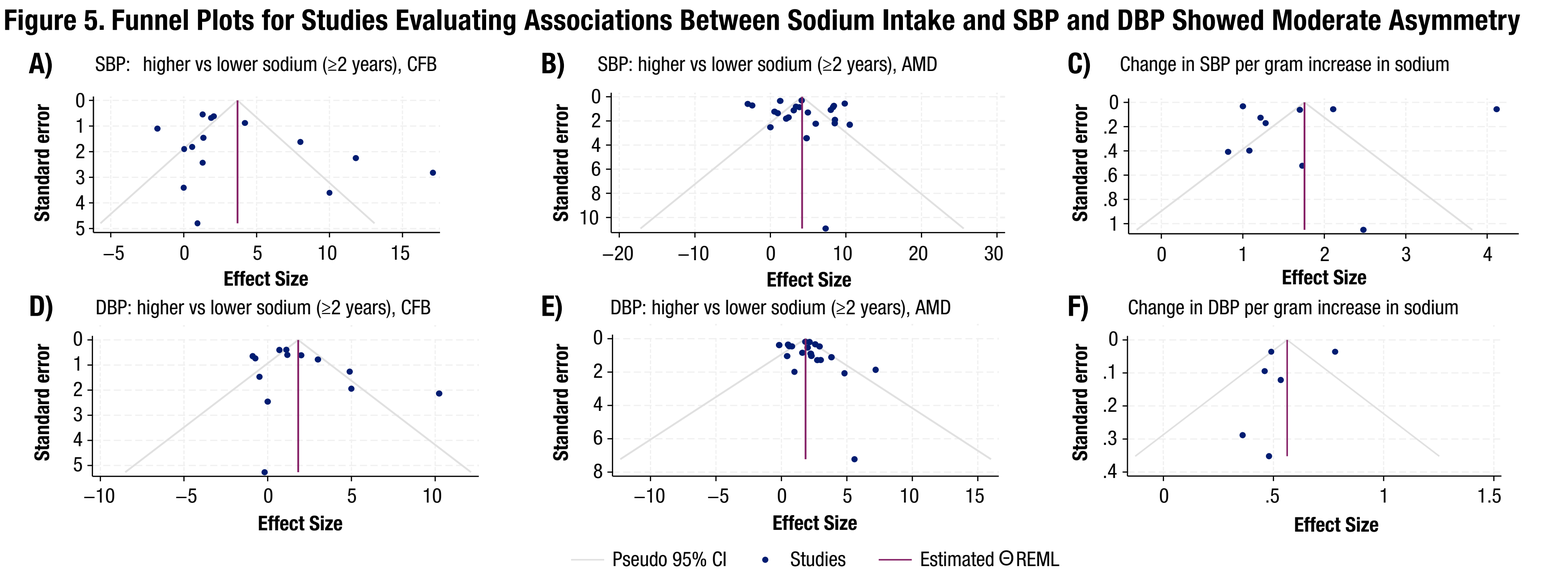
Figure 4. Higher Sodium Intake Was Significantly Associated With Increased SBP and DBP



AMD, absolute mean difference; CFB, change from baseline; CI, confidence interval; DBP, diastolic blood pressure; hr, hour; mmHg, millimeters of mercury; SBP, systolic blood pressure; WMD, weighted mean difference.

- Across studies with ≥2 years of follow-up eligible for meta-analysis (n=27), higher sodium intake was significantly associated with increases in SBP (weighted mean difference [WMD], change from baseline [CFB]: 3.39, 95% confidence interval [CI]: 1.73–5.05; WMD, absolute mean difference [AMD]: 4.21, 95% CI: 2.52–5.90) and DBP (WMD, CFB: 1.61, 95% CI: 0.61–2.61; WMD, AMD: 1.81, 95% CI: 1.30–2.32)
- Subgroup analyses of studies based on 24-hour urine collection also showed significant increases for AMD in SBP (WMD, AMD: 2.69, 95% CI: 0.43–4.96) and DBP (WMD, AMD: 1.33, 95% CI: 0.40–2.26), confirming the robustness of the findings
- Statistical heterogeneity was high for SBP and DBP

Figure 5. Funnel Plots for Studies Evaluating Associations Between Sodium Intake and SBP and DBP Showed Moderate Asymmetry



AMD, absolute mean difference; CFB, change from baseline; CI, confidence interval; DBP, diastolic blood pressure; REML, restricted maximum likelihood; SBP, systolic blood pressure.

- Funnel plots showed moderate asymmetry, suggesting potential publication bias

Conclusions

- This up-to-date and expansive SLR and meta-analysis confirm and further strengthen the evidence base for the relationship between higher sodium intake and increased blood pressure
- As with all SLRs and meta-analyses, these analyses relied on published literature, where studies with null or negative findings may be underrepresented
- Findings underscore the importance of reducing sodium consumption, as recommended by clinical and health authority guidelines, to manage blood pressure and protect cardiovascular health, particularly in populations at increased risk of cardiovascular morbidity and mortality

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