

**IAFNS Sodium in Foods and Health Implications Committee
Request for Proposals:**

Sodium/Potassium and CVD Risk

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Research Gap

This project addresses the question of whether modest reductions in sodium intake coupled with increases in potassium may achieve the public health goals of reduced hypertension and cardiovascular (CVD) risk more successfully than sodium reduction alone.

There is a well-established link between excess sodium intake, elevations in blood pressure and increased risk for hypertension and cardiovascular disease. There is also a substantial body of evidence that shows an inverse association between potassium intake and blood pressure, a key marker for cardiovascular health outcomes.

The 2019 Dietary Reference Intake did not give Potassium a Chronic Disease Risk Reduction Intake because the evidence did not support:

- 1) an intake-response relationship with blood pressure, (primary objective of this research); and
- 2) a strong relationship with actual CVD outcomes, beyond blood pressure reduction.

However, a moderate rating for strength of evidence was established for the relationship between increased potassium and decreased blood pressure. The DRI committee recommended that future research characterizes the relationship between potassium intake and CVD risk to determine if blood pressure qualifies as a surrogate marker in the context of potassium intake. Since 2019, there have been a number of trials that have looked at the benefits of potassium that need to be reviewed.

Project Overview:

This project has 2 potential phases:

Phase 1 is the development of an evidence map.

The evidence map should identify research that considers sources of potassium in potassium rich foods, supplements and potassium rich sodium substitutes.



Phase 2 is completion of a systematic review. The recipient of the funds to develop the evidence map will also be expected to have the capability, working capacity, and willingness to complete the systematic review if warranted. The systematic review will be launched if the evidence map suggests adequate new research on potassium has been generated since the full review was completed by the Dietary Reference Intakes for Sodium and Potassium Committee in 2019. If launched, Phase 2 will be funded separately.

This RFP is for Phase I only and seeks to address the research gap as suggested by the DRI committee by determining through knowledge mapping whether there is sufficient evidence to proceed to a systematic review to characterize the relationship between potassium (in foods, and different forms of potassium from supplements, and potassium rich sodium substitutes) and CVD risk, alone and in combination with sodium reduction.

If the knowledge map indicates sufficient evidence for a full systematic review, that systematic review is expected to bring credible weight to future deliberations about dietary guidance among authoritative bodies such as the National Academies of Science, Engineering and Medicine (NASEM) on dietary reference intakes and to inform the Dietary Guidelines Advisory Committee and other authoritative bodies.

Reference citations:

Sriperumbuduri S, Welling P, Ruzicka M, Hundemer GL, Hiremath S. Potassium and Hypertension: A State-of-the-Art Review. *Am J Hypertens*. 2024 Jan 16;37(2):91-100. doi: 10.1093/ajh/hpad094. PMID: 37772757.

Newberry SJ, Chung M, Anderson CAM, Chen C, Fu Z, Tang A, Zhao N, Booth M, Marks J, Hollands S, Motala A, Larkin J, Shanman R, Hempel S. Sodium and Potassium Intake: Effects on Chronic Disease Outcomes and Risks [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2018 Jun. Report No.: 18-EHC009-EF. PMID: 30125063.

Objective

- a. Identify research that quantifies the independent effect of added potassium (by dose and form from fortificants, supplements and potassium-rich sodium substitutes) on CVD risk directly. Relevant research using blood pressure (BP) as a marker of CVD may be included. Potassium sources would include potassium from added potassium chloride, potassium bicarbonate, potassium citrate and other organic anions- or supplements, not from adding potassium-rich foods to the diet.

Confounding variables of interest include, but are not limited to:

- Potassium level in baseline diet before supplementation
- Demographic and health-related characteristics of participants (normo-tensive, hypertensive, BMI, physical activity level, age, smoking status etc.)



- Level of dietary sodium intake
 - Blood pressure medication use. Other medication use.
- b. Identify research that quantifies any additive effect on CVD risk by increasing potassium in the diet (from dietary sources, supplements or KCl in foods) in combination with sodium reduction.

Questions to address: (identified research should address these questions)

1. Is there a dose-response relationship between added potassium and blood pressure? And does the form of added potassium matter?
2. Is the relationship affected by baseline potassium intake, particularly from fruits/vegetables/dairy?

Scope

In Scope:

Would include randomized clinical trials and other epidemiological studies of sufficient duration since 2018.

Measures and controls for measuring blood pressure meet accepted standards (see reference).

Out of Scope:

Mechanistic animal research.

Research that only considers naturally-occurring potassium in foods.

Deliverable

Primary deliverable: State-of-the-science knowledge map published in a peer-reviewed journal.

Additional deliverables:

- 1) Presentation to the funder at the project start on plans to include PICO criteria;
- 2) Interim report to the funder once papers to be included/excluded have been identified;
- 3) Final report and recommendations in the form of a presentation to the funder upon study completion.

Proposal Content

1. **Approach:** Please provide your approach to the research design elements. Identify key research questions, outcomes, methodology and an analysis plan. Where appropriate, please reference the validation of proposed methods.
2. **Anticipated challenges:** Please include proposed solutions to the anticipated challenges.



3. **Research Team:** Indicate the primary (and secondary) investigators, plus any additional contributors or collaborators. It is expected that content experts will be part of the review team.
4. **Investigator CV**
5. **Potential Conflicts of Interest:** List potential conflicts of interest for investigators, co-investigators and collaborators. We suggest using the [Elsevier Declaration Tool](#) to develop a declaration statement.
6. **Budget:** Provide a budget summary. IAFNS Sodium in Foods and Health Implications Committee will consider funding grants up to \$75k. IAFNS research grants typically are in the \$50-\$75k range and in exceptional cases go higher. Provide a strong rationale if your proposal exceeds this range, including for example an estimated number of studies to be extracted for the knowledge map. Publication fees at the lowest level needed to provide free access will be reimbursed to the PI if needed.
 - Indirect costs of up to 10% of the total direct costs will be considered for the management of the research project by the sponsoring institution and should be included in the total budget.
7. **Timeline of Key Deliverables:** IAFNS endeavors to complete projects in an aggressive yet timely manner. Ideally, the interim report would be completed within 4 months of signing a research agreement and the final presentation and manuscript completed in 7 months.
8. **Page Limit:** No more than 5 pages, single-spaced, excluding references and investigators' CVs.

Deadline: March 14, 2025, at 5:00 PM ET.

Submission Instructions: Please submit completed proposals to:

Trish Zecca

Sr. Nutrition Program Manager

tzecca@iafns.org

Proposal Review Process:

1. Proposals will be reviewed promptly by the Sodium in Foods and Health Implications Committee.
2. The review process will consider investigator credentials, fit with objectives, timeliness of deliverables, fit for budget and expected impact of research.



3. Applicants will be notified by email if additional information is needed.
4. Once the review process is over, all applicants will be notified of the disposition of their proposals in a timely manner. We do not provide individual feedback on specific proposals.
5. Upon initiation, the project summary and award institution will be published on our funded projects portal: <https://iafns.org/funded-projects/>

Critiques of individual proposals cannot be provided.

Use of Generative AI (GAI)

- Generative artificial intelligence (AI) is a type of AI which can be used to create new content (for example, text, code, images, video or music referred to as output).
 - If generative AI has been used, the Institution shall ensure that outputs from generative AI tools used in its applications are valid. This includes removing any false, misleading or hallucinated information.
 - For more information on the permissibility of specific case uses of GAI related to IAFNS-funded work, including in the development of a proposal, visit: <https://iafns.org/iafns-policies-on-generative-ai-use/>

References to consider:

In adults:

Muntner P, Einhorn PT, Cushman WC, Whelton PK, Bello NA, Drawz PE, Green BB, Jones DW, Juraschek SP, Margolis KL, Miller ER 3rd, Navar AM, Ostchega Y, Rakotz MK, Rosner B, Schwartz JE, Shimbo D, Stergiou GS, Townsend RR, Williamson JD, Wright JT Jr, Appel LJ; 2017 National Heart, Lung, and Blood Institute Working Group. Blood Pressure Assessment in Adults in Clinical Practice and Clinic-Based Research: JACC Scientific Expert Panel. *J Am Coll Cardiol*. 2019 Jan 29;73(3):317-335. doi: 10.1016/j.jacc.2018.10.069. PMID: 30678763; PMCID: PMC6573014