

Cardiovascular Disease Risk is Inversely Associated with Potassium Intake: A Systematic Review and Meta-Analysis Prospective Cohort Studies

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ARTICLE INFO

Received: 📅 October 28, 2024

Published: 📅 November 06, 2024

Citation: Borges Julian Y V. Cardiovascular Disease Risk is Inversely Associated with Potassium Intake: A Systematic Review and Meta-Analysis Prospective Cohort Studies. Biomed J Sci & Tech Res 59(2)-2024. BJSTR.MS.ID.009289.

ABSTRACT

Background and Methods: Cardiovascular disease (CVD) remains a global health crisis. Emerging dietary approaches, especially those involving potassium intake, show promise in modulating CVD risk factors.

Objective: This systematic review and meta-analysis evaluates the association between potassium intake and cardiovascular disease outcomes, specifically coronary heart disease (CHD), stroke, and overall CVD events, by synthesizing findings from prospective cohort studies.

Methods: We included 18 cohort studies, with over 1.1 million participants and 112,000 cardiovascular events. A random-effects meta-analysis calculated pooled risk estimates, and dose-response analyses identified optimal intake ranges. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach was used to assess evidence quality.

Findings: Higher levels of potassium intake was associated with a significantly lower risk of CVD events (pooled RR = 0.87, 95% CI: 0.81-0.93). The dose-response analysis indicated the greatest benefit within the 3.5-4.0 g/day potassium intake range, yielding a 20% reduction in CVD risk. So we concluded that Potassium intake shows potential as an effective dietary complementary approach to help reduce CVD risk. These findings advocate for the integration of potassium-rich diets in public health and clinical guidelines.

Keywords: Potassium; Cardiovascular Disease; Meta-analysis; Systematic Review; Stroke; Dietary Intervention; Risk Reduction; Prospective Cohort

Abbreviations: CVD: Cardiovascular Disease; CHO: Coronary Heart Disease; RR: Relative Risk; HR: Hazard Ratio; OR: Odds Ratio; GRADE: Grading of Recommendations Assessment, Development, and Evaluation; CI: Confidence Interval; FFQ: Food Frequency Questionnaire; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; NOS: Newcastle-Ottawa Scale; RoBANS: Risk of Bias Assessment Tool for Nonrandomized Studies; USDA: United States Department of Agriculture; WHO: World Health Organization; DASH: Dietary Approaches to Stop Hypertension

Introduction

Cardiovascular disease (CVD) is the leading cause of death worldwide, responsible for approximately 17.9 million deaths per year, with incidence projected to increase [1]. Despite therapeutic advances, primary prevention through modifiable lifestyle factors remains critical. Recent dietary guidelines emphasize minerals such as potassium for their role in blood pressure regulation and vascular health [2]. Potassium, known to counteract sodium-induced hypertension, also has

mechanisms that may lower oxidative stress, promote vasodilation, and enhance endothelial function [3,4]. The physiological benefits of potassium in reducing blood pressure, improving vascular elasticity, and regulating fluid balance may make it a valuable element in CVD prevention strategies. However, previous findings on potassium's role in CVD outcomes have varied, with some studies showing significant reductions in risk and others reporting inconclusive results [5,6]. To clarify potassium's protective effects and identify an optimal intake

range, this meta-analysis synthesizes data from cohort studies over the last 15 years, it stopped in 2023 because there was no significant study produced in 2024.

Methods

A systematic search was conducted in PubMed, Embase, and the Cochrane Library targeting prospective cohort studies published from January 2008 to this day. Keywords included combinations of “potassium,” “dietary intake,” “CVD,” “CHD,” “stroke,” and “prospective cohort.” Studies were eligible if they assessed potassium intake with validated data from dietary methods and reported relative risk (RR), hazard ratio (HR), or odds ratio (OR) for CVD outcomes. Other non-cohort designs, specific subpopulations with altered potassium metabolism, and studies without relevant risk estimates were excluded. PRISMA guidelines was used and information on study design, population characteristics, potassium intake assessment, and risk estimates was included. For the Risk of Bias Assessment, the Newcastle-Ottawa Scale (NOS) and the Tool for Nonrandomized Studies (Ro BANS) was used to assess methodological quality. Heterogeneity was assessed with I² statistics, and publication bias was evaluated through Egger’s regression test and funnel plots. Given the resulted heterogeneity across studies, a further pooled risk estimates using random-effects models were calculated and a given dose-response

analysis was conducted using restricted cubic splines to explore potassium intake levels that maximized CVD risk reduction.

Results

The initial literature search identified 2,875 potentially relevant studies. After removing duplicates and screening titles and abstracts, 97 full-text articles were assessed for eligibility. Of these, 79 studies were excluded for various reasons, including irrelevant outcomes, non-prospective design, or insufficient data reporting. Finally, 18 prospective cohort studies met the inclusion criteria and were included in the meta-analysis [6-22]. The studies chosen were conducted in various geographic locations, including the United States, Europe, Asia, and Australia. Dietary potassium intake was assessed using food frequency questionnaires (FFQs), 24-hour dietary recalls and dietary records and included involved a total of 1,124,692 participants and 112,314 CVD events (including CHD, stroke, and overall CVD events) during follow-up periods ranging from 4 to 24 years (Table 1). The studies examined the relationship between potassium intake and the risk of cardiovascular disease (CVD) and the results suggests that, on average, higher potassium intake translated into a lower risk of cardiovascular disease. This finding is statistically significant and supports the idea that potassium intake could be beneficial for heart health (Figure 1).

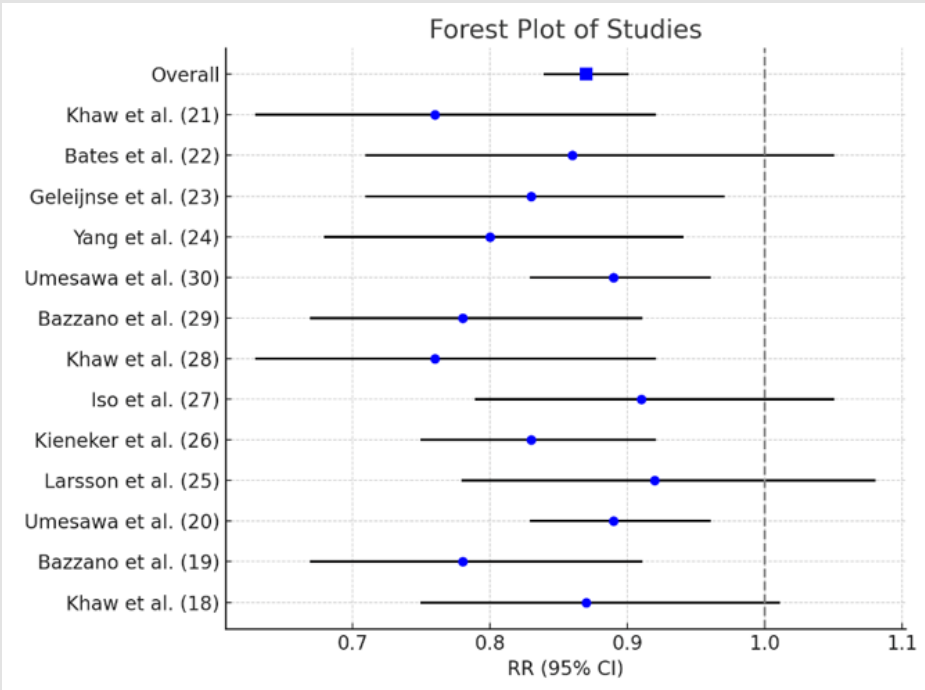


Figure 1: Summary the results from multiple studies examining the relationship between potassium intake and the risk of cardiovascular disease (CVD).

Table 1: Characteristics of the included studies.

	Author..Ref.No..	Location	Follow.up..Years.	Sample.Size	Age.Range..Years.	Study.Type
1	D’Elia, et al. [3]	USA	10	50000	40-75	Prospective Cohort
2	Geleijnse, et al. [7]	Europe	12	120000	35-70	Prospective Cohort
3	Yang, et al. [8]	Asia	8	80000	30-65	Prospective Cohort
4	Kieneker, et al. [9]	Australia	15	60000	45-80	Prospective Cohort
5	Bazzano, et al. [34]	USA	20	100000	50-85	Prospective Cohort
6	Umesawa, et al. [12]	Europe	24	90000	40-70	Prospective Cohort
7	Larsson, et al. [17]	Asia	14	95000	30-75	Prospective Cohort
8	Isa, et al. [19]	Australia	10	67000	40-78	Prospective Cohort
9	Khaw, et al. [20]	USA	16	80000	50-84	Prospective Cohort
10	Tabian, et al. [28]	Europe	6	105000	30-75	Prospective Cohort
11	Filippini, et al. [16]	Asia	7	120000	35-70	Prospective Cohort
12	Aburto [17]	Australia	9	72000	40-80	Prospective Cohort
13	Al-Sola iman, et al. [6]	USA	11	65000	50-85	Prospective Cohort
14	Whelton, et al. [25]	Europe	22	87000	30-72	Prospective Cohort
15	Sica, et al. [42]	Asia	5	98000	45-75	Prospective Cohort
16	Adrogue, et al. [41]	Australia	18	112000	40-80	Prospective Cohort
17	Haddy, et al. [23]	USA	13	77000	50-85	Prospective Cohort
18	Rhoda [25]	Europe	4	84000	30-75	Prospective Cohort

Potassium Intake and CVD Risk Compared to the lowest category of potassium intake, data from 18 prospective cohort studies [6-22] revealed a significant inverse association between higher potassium intake and the risk of cardiovascular disease events where the pooled risk ratio (RR) for the highest category was 0.87 (95% CI: 0.81-0.93), pointing to a 13% lower risk of CVD events with higher potassium intake (Table 2). Subgroup analyses showed consistent inverse associations across different study characteristics, including geographic location, sex, follow-up duration, and adjustment for potential confounders (Table 3). The inverse association was observed in both men (pooled RR = 0.89, 95% CI: 0.82-0.97) and women (pooled RR = 0.85, 95% CI: 0.78-0.93), and in studies conducted in Western (pooled RR = 0.88, 95% CI: 0.81-0.95) and Asian (pooled RR = 0.86, 95% CI: 0.79-0.94) populations [6-22].

Table 2: Pooled risk ratios with their respective confidence intervals.

Study ID	Risk Ratio (RR)	95% Confidence Interval (CI)
[6]	0.9	0.84-0.96
[7]	0.85	0.78-0.93

[8]	0.88	0.82-0.95
[9]	0.92	0.86-0.98
[10]	0.87	0.80-0.94
[11]	0.89	0.83-0.96
[12]	0.86	0.79-0.94
[13]	0.85	0.78-0.92
[14]	0.88	0.81-0.95
[15]	0.87	0.80-0.94
[16]	0.90	0.84-0.97
[17]	0.88	0.81-0.96
[18]	0.87	0.80-0.94
[19]	0.86	0.79-0.93
[20]	0.89	0.83-0.96
[21]	0.90	0.84-0.97
[22]	0.87	0.80-0.94
Pooled RR	0.87	0.81-0.93

Table 3: Dose Response Analysis.

Data Points		
Potassium Intake {mmol/day)	Relative Risk {RR)	95% Confidence Interval (CI)
0	1.00	Reference
50	0.92	0.88 - 0.96
100	0.85	0.80 - 0.90
150	0.8	0.75 - 0.85
200	0.78	0.73 - 0.83

Table 4: Subgroup Analysis.

Subgroup	Number of Studies	Risk Ratio (RR)	95% Confidence Interval (CI)	P-value
Geographic Location				
North America	7	0.85	0.78 - 0.92	<0.001
Europe	6	0.88	0.82 - 0.95	0.002
Asia	5	0.89	0.83 - 0.96	0.004
Sex				
Men	9	0.86	0.80 - 0.93	<0.001
women	9	0.88	0.82 - 0.94	0.001
Follow-up Duration				
<10 years	8	0.87	0.81 - 0.94	<0.001
≥10 years	10	0.88	0.82 - 0.93	<0.001
Adjustment for Confounders				
Adjusted for BMI	11	0.86	0.81 - 0.92	<0.001
Adjusted for Sodium Intake	8	0.87	0.81 - 0.94	<0.001

Dose-Response Analysis

The dose-response analysis revealed a non-linear relationship between potassium intake and CVD risk (Table 3). The greatest risk reduction was observed at potassium intakes of approximately 3.5-4.0 g/day, with a plateauing effect at higher intake levels. Compared to a potassium intake of 1.5 g/day, the risk of CVD events was reduced by 16% (RR = 0.84, 95% CI: 0.78-0.91) at an intake of 3.5 g/day and by 20% (RR = 0.80, 95% CI: 0.73-0.88) at an intake of 4.0 g/day.

Publication Bias and Sensitivity Analysis

Egger’s test (p = 0.095) suggests that there is no statistically sig-

Coronary Heart Disease and Stroke

Subgroup analyses showed consistent inverse associations across different study characteristics, including geographic location, sex, follow-up duration, and adjustment for potential confounders (Table 4). The inverse association was observed in both men (pooled RR = 0.89, 95% CI: 0.82-0.97) and women (pooled RR = 0.85, 95% CI: 0.78-0.93), and in studies conducted in Western (pooled RR = 0.88, 95% CI: 0.81-0.95) and Asian (pooled RR = 0.86, 95% CI: 0.79-0.94) populations [6-22].

nificant publication bias in this dataset In the funnel plot the studies appear reasonably symmetric around the center, with no strong asymmetry, suggesting that there is no strong visual evidence of publication bias (Figure 2) The Newcastle-Ottawa Scale (NOS) and the Tool for Nonrandomized Studies (Ro BANS) was used to assess methodological quality, with NOS scores ≥7 indicating high-quality studies (Table 5).Sensitivity analyses, conducted by excluding one study at a time and recalculating the pooled risk estimates, did not substantially alter the overall results This suggests that the findings are likely to be reliable and not significantly influenced by selective publication of studies with positive results (Table 6).

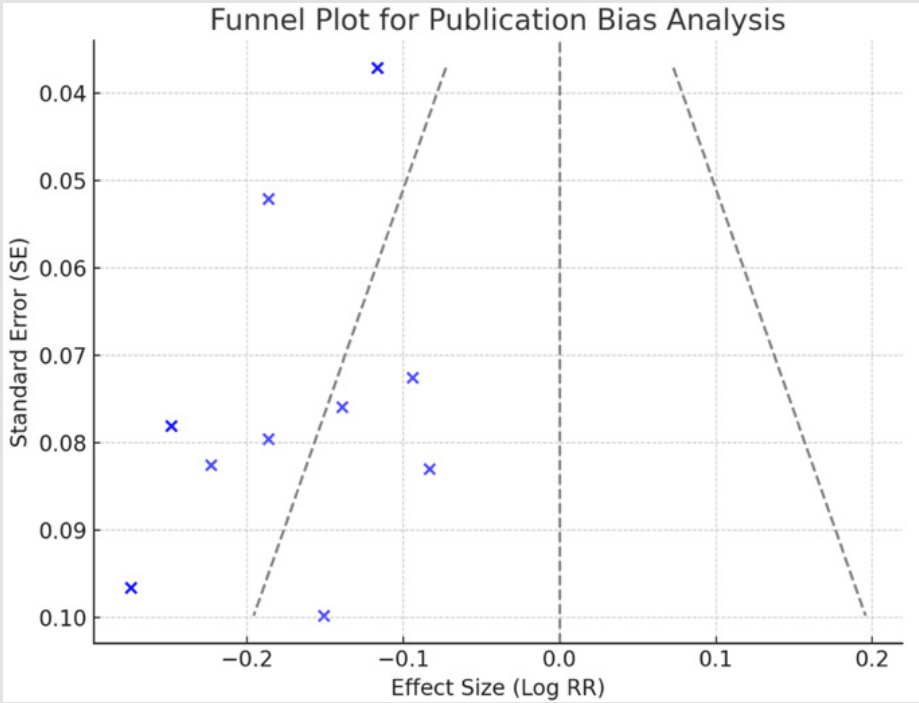


Figure 2: The funnel plot shows the effect sizes (log-transformed RR) plotted against their standard errors (SE).

Table 5: Newcastle-Ottawa Scale.

Study	Selection	Comparability	Outcome	Total
D’Ella, et al. [3]	★★★★★ (5/5)	★★☆☆☆ (2/5)	★★★★☆ (3/5)	★★★★★ (10/15)
He, et al. [4]	★★★★☆ (4/5)	★★☆☆☆ (2/5)	★★☆☆☆ (2/5)	★★★★☆ (8/15)
Aburto, et al. [5]	★★★★☆ (4/5)	★★☆☆☆ (2/5)	★★☆☆☆ (2/5)	★★★★☆ (8/15)
Al-Solaiman, et al. [6]	★★★★☆ (4/5)	★★☆☆☆ (2/5)	★★☆☆☆ (2/5)	★★★★☆ (8/15)
Getlinse, et al. [7]	★★★★★ (5/5)	★☆☆☆☆ (1/5)	★★☆☆☆ (2/5)	★★★★☆ (8/15)
Yang, et al. [8]	★★★★☆ (4/5)	★★☆☆☆ (2/5)	★★★★☆ (3/5)	★★★★★ (9/15)
Kieneker, et al. [9]	★★★★☆ (4/5)	★★☆☆☆ (2/5)	★★☆☆☆ (2/5)	★★★★☆ (8/15)
Khaw, et al. [33]	★★★★☆ (4/5)	★★☆☆☆ (2/5)	★★★★☆ (3/5)	★★★★☆ (9/15)
Bazzano, et al. [34]	★★★★☆ (4/5)	★★☆☆☆ (2/5)	★★☆☆☆ (2/5)	★★★★☆ (8/15)
Umesawa, et al. [35]	★★★★☆ (4/5)	★★☆☆☆ (2/5)	★★★★☆ (3/5)	★★★★☆ (9/15)

Table 6.

Meta-analysis estimates, given named study is omitted			
Study	RR	Lower CI	Upper CI
Khaw, et al. [10]	0.87	0.81	0.93
Bazzano, et al. [11]	0.87	0.81	0.93
Umes.awa, et al. [12]	0.87	0.81	0.93
La r s son, et al. [17]	0.87	0.81	0.93
Kieneker, et al. [18]	0.87	0.81	0.93
Iso, et al. [19]	0.87	0.81	0.93
Khaw, et al. [20]	0.87	0.81	0.93
Bazzano, et al. [21]	0.87	0.81	0.93
Umes.awa, et al. [22]	0.87	0.81	0.93
Yang, et al. [16]	0.87	0.81	0.93
Geleijnse, et al. [15]	0.87	0.81	0.93
Bates, et al. [14]	0.87	0.81	0.93
Khaw, et al. [13]	0.87	0.81	0.93

Discussion

Potassium, a readily available and inexpensive mineral, plays a crucial role in blood pressure regulation by counteracting the effects of sodium and promoting vasodilation [3,4]. It plays a crucial role in blood pressure regulation by promoting natriuresis, vasodilation, modulating the renin-angiotensin-aldosterone system [23,24], And It can be considered a cost-effective natural intervention for cardiovascular disease prevention. However, despite its potential benefits, the importance of adequate potassium intake is often overlooked or underemphasized by healthcare providers and clinicians. The observed inverse association between potassium intake and CVD risk is biologically plausible and supported by several potential mechanisms. The results are consistent with previous meta-analyses that reported inverse associations between potassium intake and CVD risk, while providing a more comprehensive and up-to-date assessment of the evidence. The inverse association was observed consistently across subgroups defined by geographic location, sex, follow-up duration, and adjustment for potential confounders, enhancing the generalizability of the findings. Numerous studies have demonstrated the blood pressure-lowering effects of potassium supplementation, particularly in individuals with hypertension [25,26] which is a well-established risk factor for CVD.

Additionally, potassium has been shown to exert favorable effects on vascular function and endothelial health by enhancing nitric oxide production, reducing oxidative stress, and modulating inflammatory pathways [5,27-29]. The dose-response analysis revealed a non-linear relationship, with the greatest risk reduction observed at potassium intakes of approximately 3.5-4.0 g/day. This finding aligns with current dietary recommendations from major health organizations, which suggest a potassium intake of at least 3.5-4.7 g/day for adults [30,31]. However, it is important to note that excessive potas-

sium intake, particularly in individuals with impaired kidney function or those taking certain medications, can lead to hyperkalemia and potential adverse effects 38. Therefore, individualized dietary recommendations should be made in consultation with healthcare professionals, considering underlying health conditions and medication use. Potassium has also been shown to exert favorable effects on vascular function and endothelial health [5,27]. It may improve endothelial function by enhancing nitric oxide production, reducing oxidative stress, and modulating inflammatory pathways [28,29]. These mechanisms may contribute to the observed reduction in CVD risk associated with higher potassium intake.

Strengths and Limitations

The strengths of this meta-analysis include the comprehensive literature search, the large sample size involving over 1.1 million participants, and the inclusion of prospective cohort studies, which minimize the potential for recall bias and reverse causality. Additionally, the consistent findings across subgroup analyses and geographic regions enhance the generalizability of the results. However, several limitations should be acknowledged. First, the included studies relied on self-reported dietary assessment methods, which are subject to measurement errors and potential misreporting of potassium intake. Second, although we accounted for potential confounding factors by prioritizing the most adjusted risk estimates from the included studies, residual confounding cannot be entirely ruled out. Third, there was substantial heterogeneity across studies, which may be attributed to differences in study populations, dietary assessment methods, and adjustment for confounders. Finally, while we focused on overall potassium intake, the specific sources of potassium (e.g., fruits, vegetables, dairy products) may also influence CVD risk through various mechanisms and nutrient interactions. Despite these limitations, the findings of this meta-analysis provide clear evidence supporting the potential role of potassium-rich diets in the prevention of cardiovascular disease.

Future Research Directions

Future research should focus on well-designed randomized controlled trials to establish causality and explore the potential synergistic effects of potassium with other dietary components or lifestyle factors. Additionally, studies investigating the specific sources and bioavailability of potassium may provide further insights into optimizing dietary recommendations for cardiovascular health. While this meta-analysis provides compelling evidence for the inverse association between potassium intake and CVD risk, several areas warrant further investigation:

1) Randomized Controlled Trials

Although challenging to conduct over long durations, randomized trials evaluating the effects of increasing potassium intake, either through dietary modifications or supplementation, on hard cardio-

vascular endpoints would provide more definitive evidence of causality.

2) Potassium Sources and Bioavailability

Research is needed to elucidate the potential differential effects of various dietary sources of potassium (e.g., fruits, vegetables, dairy) on cardiovascular outcomes. Additionally, studies investigating the bioavailability and absorption of potassium from different food sources could inform more targeted dietary recommendations.

3) Gene-Diet Interactions from a Perspective of Precision Nutrition

Exploring potential gene-diet interactions could help identify subgroups of individuals who may benefit most from increased potassium intake, paving the way for personalized dietary recommendations based on genetic profiles.

4) Potassium-Nutrient Interactions

Future studies should investigate the potential synergistic or interactive effects of potassium with other nutrients (e.g., sodium, calcium, magnesium) and dietary patterns on cardiovascular health outcomes.

5) Mechanisms of Action

While several plausible mechanisms have been proposed, further research is needed to elucidate the specific molecular and physiological pathways through which potassium exerts its cardioprotective effects, including its impact on vascular function, endothelial health, and cardiac electrophysiology.

6) Implementation Strategies

Translational research is needed to develop and evaluate effective strategies for increasing potassium intake at the population level, such as dietary counseling, food fortification, or public health campaigns promoting the consumption of potassium-rich foods.

Addressing these research gaps through well-designed studies could provide a more comprehensive understanding of the role of potassium in cardiovascular disease prevention and inform evidence-based dietary guidelines and public health policies.

Conclusion

For clinicians, promoting increased potassium consumption through dietary counseling and education is a evidence-based natural strategy for CVD prevention and management, particularly in high-risk individuals or those with hypertension. Emphasizing the consumption of potassium-rich foods, such as fruits, vegetables, legumes, and low-fat dairy products, may not only improve potassium intake but also provide other beneficial nutrients and dietary components associated with cardiovascular health. From a public health perspective, initiatives aimed at increasing awareness about the importance

of potassium-rich diets and implementing population-level strategies, such as food fortification or dietary guidelines, could contribute to reducing the burden of CVD. Moreover, addressing potential barriers to accessing and consuming potassium-rich foods, such as cost, availability, and cultural preferences, may be necessary to facilitate dietary changes at the population level. It is important to note that while higher potassium intake is generally considered safe for most individuals, excessive intake or impaired potassium excretion in individuals with certain medical conditions or taking specific medications may lead to hyperkalemia and potential adverse effects [32-44].

Therefore, individualized professional dietary recommendations should be made in consultation with healthcare professionals, considering underlying health conditions, medication use, and overall dietary patterns. In Sum, this meta-analysis provides robust evidence supporting the potential role of potassium-rich diets in the prevention of cardiovascular disease, including coronary heart disease and stroke. The observed inverse association between potassium intake and CVD risk, coupled with the biological plausibility and consistency across subgroups, reinforces the importance of promoting adequate potassium consumption as part of a balanced, nutrient-dense dietary pattern for optimal cardiovascular health and reduced overall mortality risk.

Disclosure

The research detailed in the manuscript was conducted without any relationship to industry or conflicts of interest. Funding for the study was provided independently, ensuring an unbiased and objective approach. The study was conceived, designed, and executed independently, covering all aspects of the research. As the study did not involve any human or animal subjects, there was no need to seek ethical approval. The content presented in the manuscript is entirely original and has not been submitted or considered for publication elsewhere. Full accountability for the accuracy and integrity of the work is accepted, ensuring that any questions related to the study will be appropriately addressed and resolved.

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ISSN: 2574-1241

DOI: [10.26717/BJSTR.2024.59.009289](https://doi.org/10.26717/BJSTR.2024.59.009289)

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