

Detailed Study Notes: Episode 451

Potassium & Blood Pressure: Influence of Sex & Sodium

Table of Contents

- [Introduction to this Episode](#)
- [Connection to Previous Episodes](#)
- [Background Context](#)
- [EPIC Cohort](#)
- [Study Design & Intake Assessment](#)
- [Results: Potassium & Sodium Intakes](#)
- [Results: Blood Pressure](#)
- [Results: Cardiovascular Disease](#)
- [Conclusions](#)
- [Practical Application](#)

Introduction to this Episode

It has been consistently shown in research that elevated dietary sodium consumption is associated with high blood pressure and an increased risk of cardiovascular disease. In addition, low levels of dietary potassium intake are associated with these same risks. However, there is some debate on how to characterize these relationships.

In a study published in European Heart Journal in July 2022, using data from the EPIC-Norfolk study, researchers attempted to answer whether the associations between potassium and both blood pressure and cardiovascular disease: 1) differ between men and women? and 2) depend on daily sodium intake.

In this episode Dr. Alan Flanagan and Danny Lennon discuss the details of this study and then link it to the overall evidence base and what this may mean for potassium (and sodium) intake considerations.

Connection to Previous Episodes

Episode [#375: Salt, Sodium & Health](#)

- Potassium can moderate the effect of sodium on BP and CVD, but not abolish an effect
- Stratifying by higher/lower potassium and higher/lower sodium, it seems higher potassium has large benefit at lower sodium intakes, but at higher sodium intakes people are still remaining at high-risk even when potassium is high

Episode [#415: Prof. Bruce Neal – Can Salt Substitutes Reduce Cardiac Events & Death?](#)

- (29.45 - 34.25): Prof. Neal addresses the claims that the BP lowering (and CV) effect is solely down to potassium, and not sodium
- BP reduction in [SSaSS](#) was likely due to a combination of sodium lowering and increasing potassium intake (baseline potassium was low)
- The reductions in CV could be for a variety of mechanisms BUT it still most likely that the majority of benefit is directly due to BP lowering

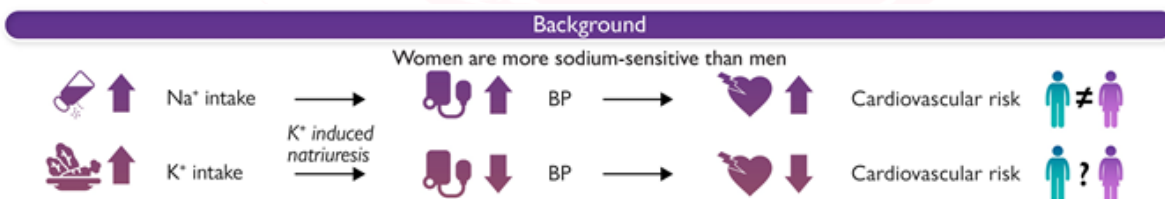
Background Context

The study:

- [Wouda et al., Eur Heart J. 2022 Jul 21;ehac313](#)
- Sex-specific associations between potassium intake, blood pressure, and cardiovascular outcomes: the EPIC-Norfolk study
- Published: 21 July 2022 - *European Heart Journal*
- From the lab of [Prof. Liffert Vogt](#) at University of Amsterdam & Amsterdam University Medical Center
 - Expertise in sodium homeostasis
 - Lead author is doctoral candidate Rosa Wouda

Why this trial? What's the evidence to date?

- [Elevated dietary sodium consumption](#), as well as [low levels of dietary potassium intake](#), is associated with high blood pressure and an increased risk of cardiovascular disease and premature death.
- RCTs of [dietary sodium reduction](#), as well as trials of [dietary potassium supplementation](#), have shown clear blood-pressure-lowering effects.
- And a potassium replete diet is associated with lower blood pressure (BP) and lower risk of cardiovascular disease (CVD).
- There is evidence that women are more sodium-sensitive than men.
- In this recent study by Wouda *et al.*, the researchers wanted to assess whether these associations between potassium and BP/CVD:
 - a) differ between men and women and
 - b) depend on daily sodium intake (i.e. is the association still present at increasing levels of sodium)



Adapted from: [Wouda et al., Eur Heart J, ehac313](#)

© The Author(s) 2022. Published by Oxford University Press on behalf of European Society of Cardiology.

EPIC Cohort

- The Wouda et al. study used data from the EPIC-Norfolk cohort.
- **European Prospective Investigation of Cancer (EPIC)** is a large multi-centre cohort study with participants enrolled from 23 centres across Europe. One of those locations is Norfolk, England.
- The [EPIC-Norfolk study](#) is a population-based prospective cohort study, co-ordinated by a team based at the University of Cambridge in the UK.
- EPIC-Norfolk recruited over 30,000 men and women aged 40-79 years at baseline in the mid-1990s from doctor’s practices in Norfolk, England.
- Participants have continued to provide follow up data and attend additional health checks over the past 25 years or so.

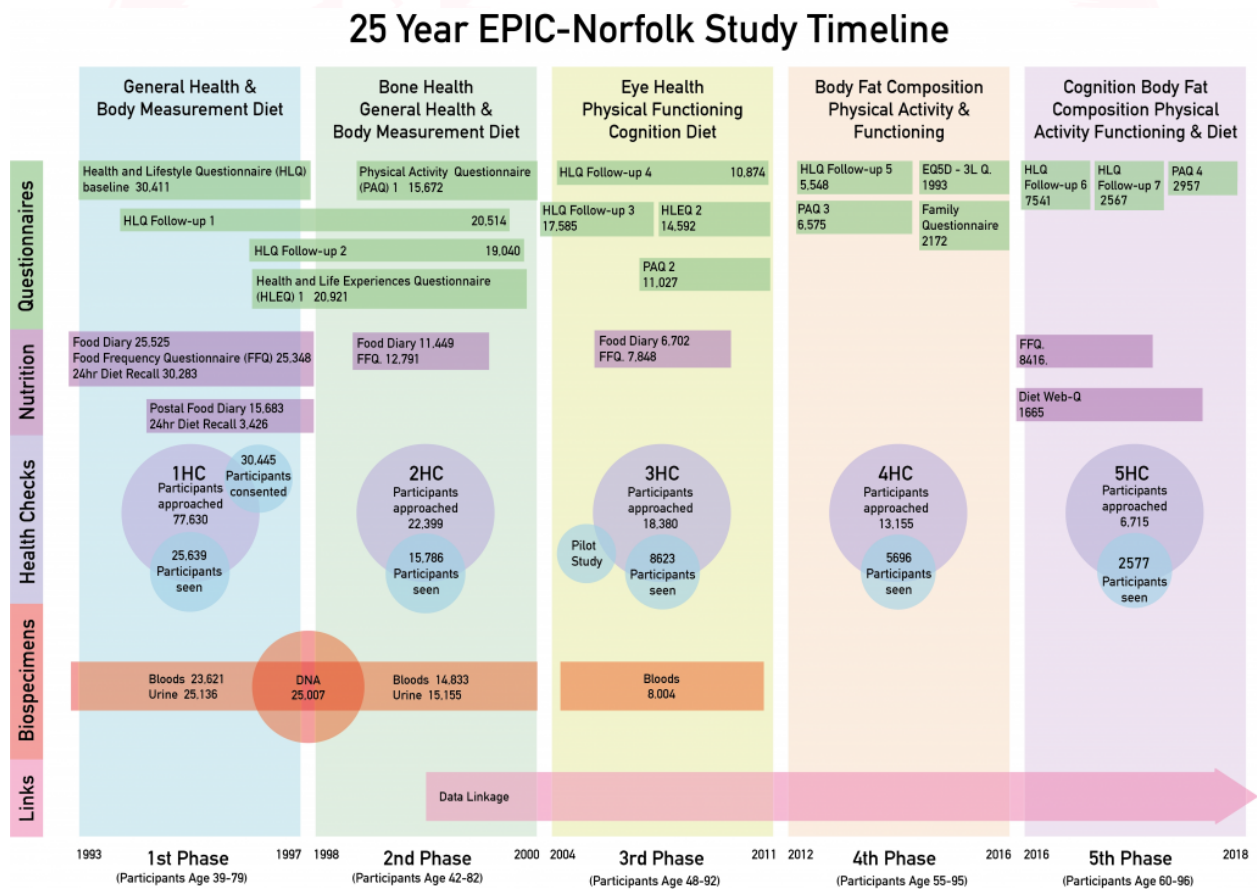
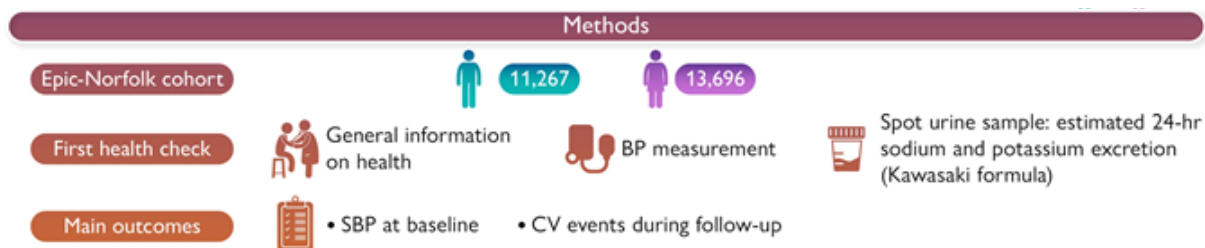


Image: [University of Cambridge](#)

Study Design & Intake Assessment



Adapted from: [Wouda et al., Eur Heart J, ehac313](#)

© The Author(s) 2022. Published by Oxford University Press on behalf of European Society of Cardiology.

- 24,963 participants (11,267 men & 13,696 women) from the EPIC-Norfolk cohort.
 - The mean age was 59 ± 9 years for men and 58 ± 9 years for women.
 - 18.5% of men and 18.6% of women used antihypertensive medication.
- On enrollment to this cohort study, general information on health and lifestyle was collected using a questionnaire, a physical examination was performed, blood was drawn, and a random spot urine sample was collected.
- Spot urine samples were stored until further analysis. Between 1998 and 2002, spot urine sodium and potassium concentrations were assayed.
- 24-hour sodium and potassium excretion were estimated from a single (spot) urine sample, using the Kawasaki formula.
- Estimated 24-h urine potassium and sodium excretion were considered to reflect daily intake.
- Actual daily potassium and sodium consumption are expected to be higher than 24-h urine potassium and sodium excretion, due to excretion of sodium and potassium through sweat and feces.
- The main outcomes were SBP at baseline (i.e. the day of spot urine collection) and the composite of hospitalization or mortality from CVD.
- Researchers performed a multivariable linear regression analysis stratified by sex to determine the association between potassium intake (g/day) and SBP.
- Adjustments were made for age, body mass index, sodium intake (tertiles), smoking status (never smoked, former smoker, current smoker), use of lipid-lowering drugs, alcohol use (g/day), a history of diabetes mellitus, and a history of CVD (stroke and/or myocardial infarction).
- To assess the effect of sodium intake on the association between potassium intake and SBP and CVD events, researchers performed analyses stratified by sodium intake tertile (thirds of intake for each of men and women).

Results: Potassium & Sodium Intakes

- **Estimated potassium intake:**
 - Men = 71 ± 16 mmol/day (2.8 ± 0.6 g/day)
 - Women = 66 ± 16 mmol/day (2.6 ± 0.6 g/day)
- **Estimated sodium intake:**
 - Men = 214 ± 62 mmol/day (4.9 ± 1.4 g/day)
 - Women = 183 ± 61 mmol/day (4.2 ± 1.4 g/day)

Breaking these average intakes in tertiles...

Potassium intake [mmol/day (g/day)] in Men

- Tertile 1 55 ± 6 (2.2 ± 0.2)
- Tertile 2 70 ± 4 (2.7 ± 0.1)
- Tertile 3 89 ± 11 (3.5 ± 0.4)

Potassium intake [mmol/day (g/day)] in Women

- Tertile 1 49 ± 6 (1.9 ± 0.2)
- Tertile 2 64 ± 4 (2.5 ± 0.1)
- Tertile 3 84 ± 12 (3.3 ± 0.5)

Sodium intake [mmol/day (g/day)] in Men

- Tertile 1 150 ± 28 (3.5 ± 0.7) 121 ± 26 (2.8 ± 0.6)
- Tertile 2 211 ± 14 (4.8 ± 0.3) 179 ± 14 (4.1 ± 0.3)
- Tertile 3 283 ± 41 (6.5 ± 0.9) 251 ± 43 (5.8 ± 1.0)

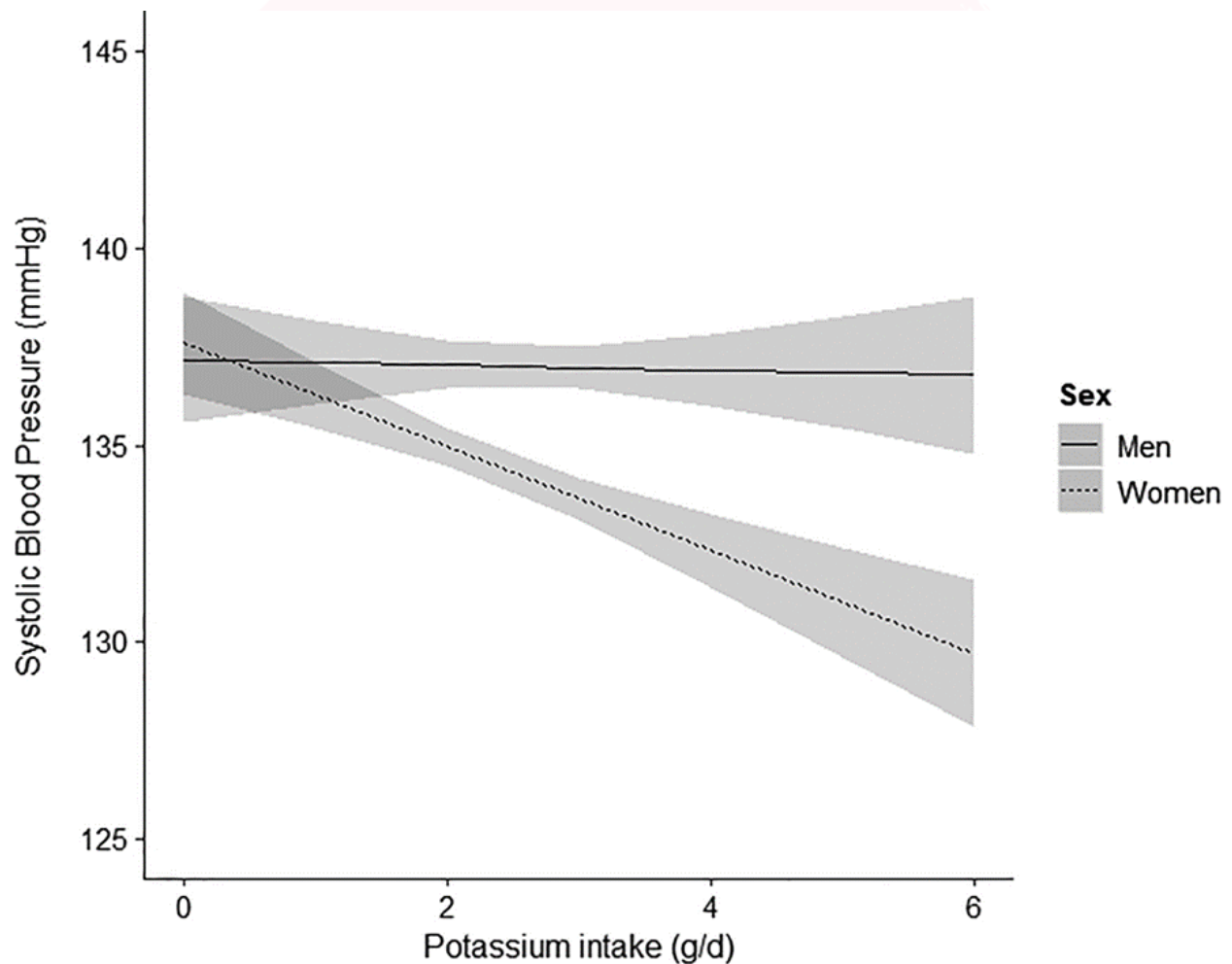
Sodium intake [mmol/day (g/day)] in Women

- Tertile 1 121 ± 26 (2.8 ± 0.6)
- Tertile 2 179 ± 14 (4.1 ± 0.3)
- Tertile 3 251 ± 43 (5.8 ± 1.0)

Results: Blood Pressure

Higher potassium intake = lower systolic blood pressure in women

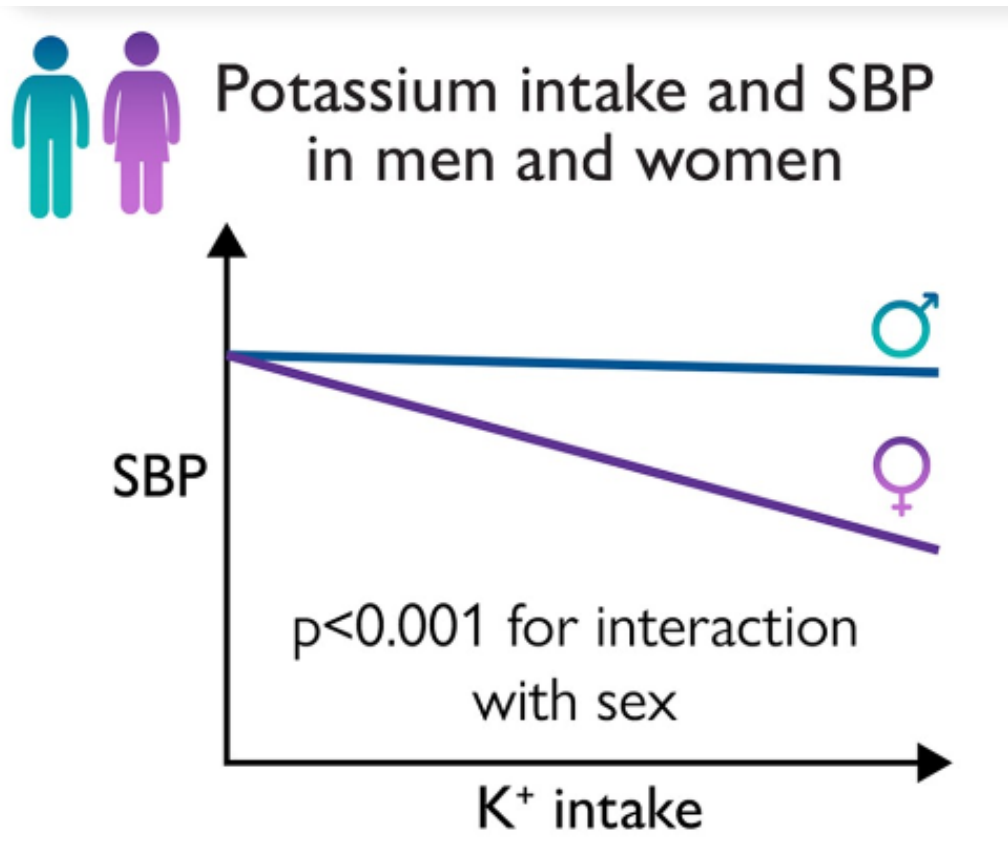
- After adjustments for sex, age and sodium intake (tertiles), potassium intake was significantly associated with SBP, with a significant interaction with sex.
 - So the relationship between potassium intake and systolic blood pressure lowering seems to be different between men and women (see graph below).



Interaction by sex for the association between potassium intake (g/day) and systolic blood pressure

Graph from: [Wouda et al., Eur Heart J, ehac313](#)

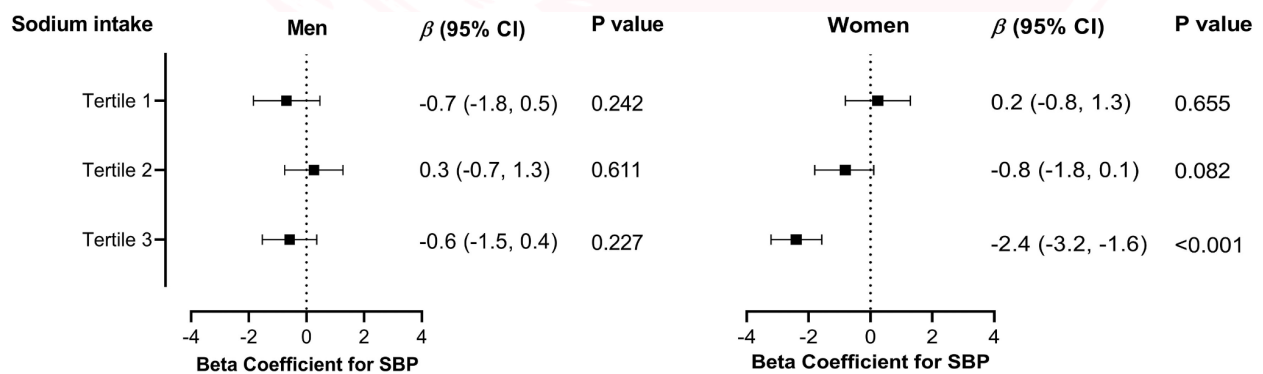
© The Author(s) 2022. Published by Oxford University Press on behalf of European Society of Cardiology.



Adapted from: [Wouda et al., Eur Heart J, ehac313](#)

© The Author(s) 2022. Published by Oxford University Press on behalf of European Society of Cardiology.

in women, a highly significant interaction by sodium intake (highest vs. lowest tertile) for the association between potassium intake and SBP was present (P < 0.001)



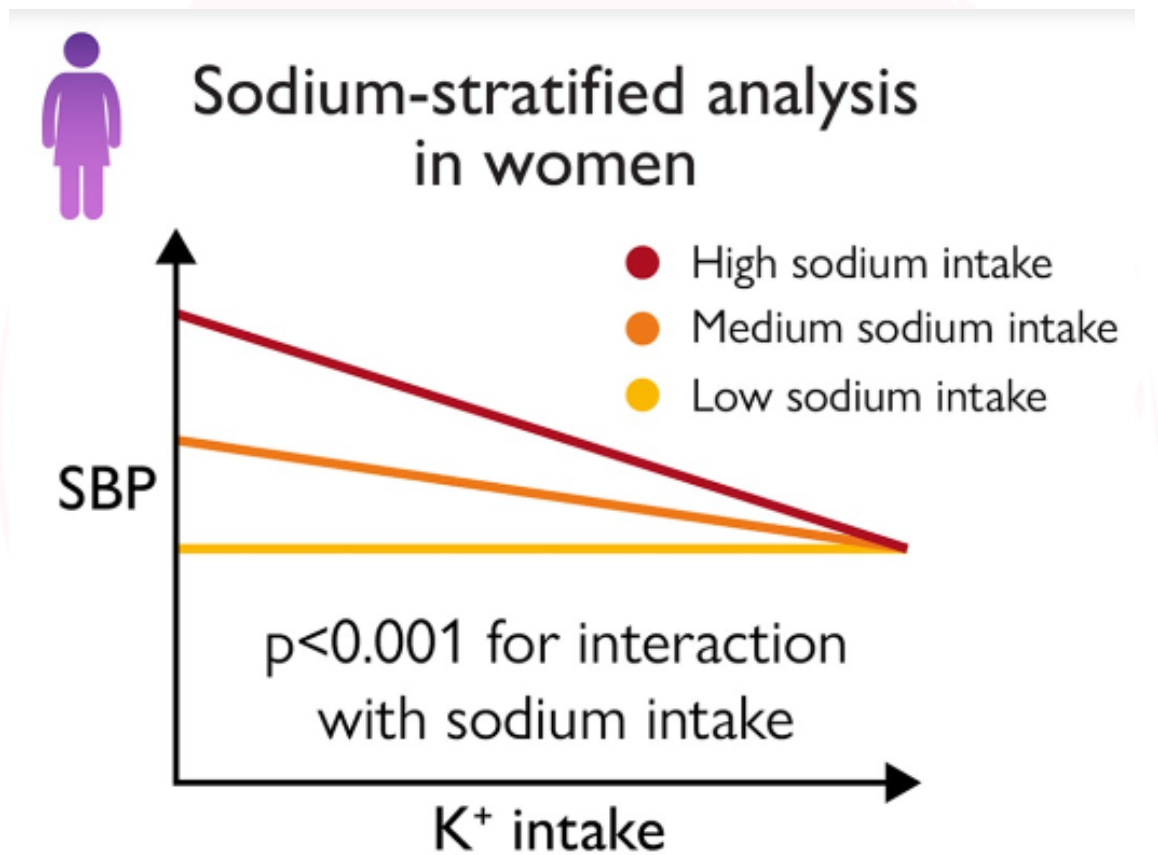
Association between potassium intake (g/day) and systolic blood pressure in men and women within every tertile of sodium intake.

Taken from: [Wouda et al., Eur Heart J, ehac313](#)

© The Author(s) 2022. Published by Oxford University Press on behalf of European Society of Cardiology.

in women within the highest tertile of sodium intake, every 1 g increase in daily potassium intake was associated with a 2.4 mmHg lower SBP.

the association between potassium intake (highest vs. lowest tertile) was stronger in women within the highest tertile of sodium intake compared with those within the lowest tertile of sodium intake



Adapted from: [Wouda et al., Eur Heart J, ehac313](#)

© The Author(s) 2022. Published by Oxford University Press on behalf of European Society of Cardiology.

Results: Cardiovascular Disease

- During a median follow-up time of 19.5 years, CVD events occurred in 13 596 (54.5%) participants:
 - Men: 6,705 CVD events (59.5% of male participants)
 - Women: 6,891 CVD events (50.3% of female participants)
- In the fully adjusted model, people within the highest tertile of potassium intake had a lower risk of CVD events, compared with those within the lowest tertile of potassium intake.
 - Highest vs. lowest = **HR of 0.87** (95% CI 0.82–0.93)
 - i.e. 13% risk reduction
- Both men and women within the highest tertile of potassium intake had a lower risk of CVD events compared with those within the lowest tertile of potassium intake.
- However, there was a significant interaction by sex for the association between potassium intake (highest vs. lowest tertile) and CVD events. With the hazard ratio (HR) associated with higher potassium intake being lower in women than in men (i.e. women have a greater reduction in risk):
 - **Women:** HR of 0.89 (95% CI 0.83-0.95)
 - **Men:** HR of 0.93 (95% CI 0.87-1.00)

Potassium intake and CV events

The association between potassium intake (highest vs. lowest tertile) and CVD events was stronger in women than in men ($p=0.033$ for interaction)



HR 0.89

95% CI 0.83-0.95



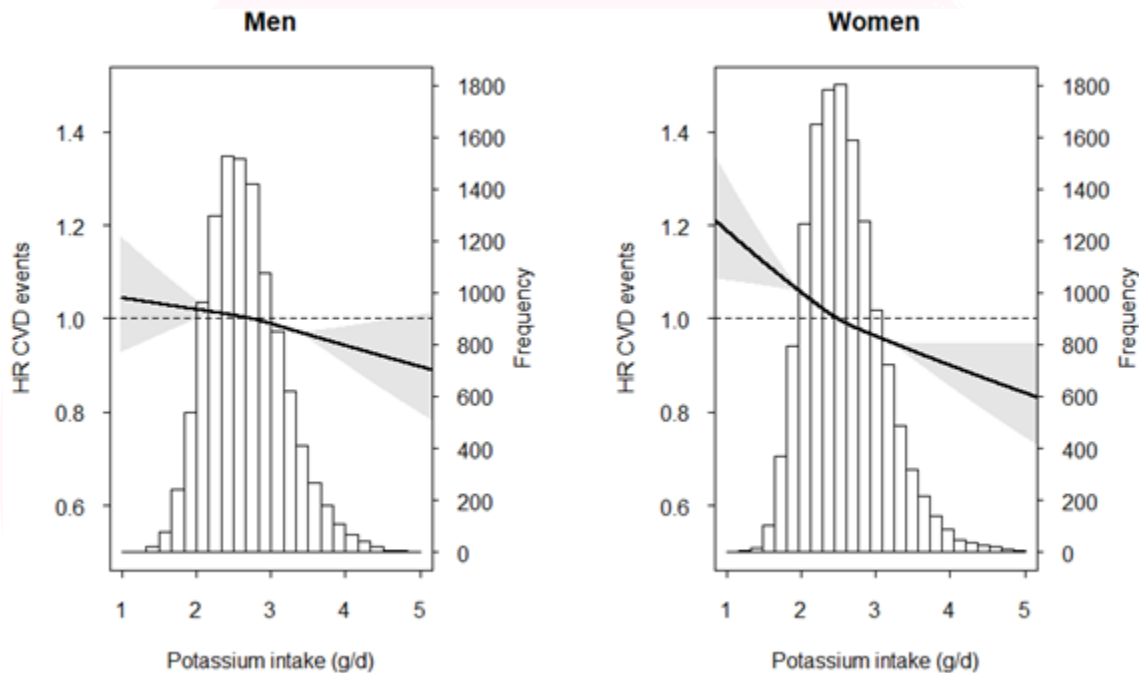
HR 0.93

95% CI 0.87-1.00

Adapted from: [Wouda et al., Eur Heart J, ehac313](#)

© The Author(s) 2022. Published by Oxford University Press on behalf of European Society of Cardiology.

- Interaction by sex was observed for the association between potassium intake (g/day) and CVD events, with risk reduction being significant for women, but not men:
 - Women: HR of 0.92 (95% CI 0.88-0.96)
 - Men: HR of 0.96 (95% CI 0.92-1.01) - *non-significant*
 - **Adjustments** were made for sex, age, BMI, use of lipid lowering drugs, smoking status, alcohol use, **sodium intake (tertiles)**, diabetes mellitus and history of CVD.
 - See charts below.



Association between potassium intake (g/d) and CVD events in men and women
 Available in the supplementary material of: [Wouda et al., Eur Heart J. ehac313](#)

No interaction by sodium intake (highest vs. lowest tertile) for the association between potassium intake (highest vs. lowest tertile) and CVD events was present in both men and women.

Conclusions

1. These findings are suggestive that the association between potassium consumption and both systolic blood pressure and CVD risk is sex specific.
2. An inverse relation between potassium intake and SBP was only present in women within the highest tertile of sodium intake.
3. Women within the highest tertile of potassium intake had a respectively 11% lower risk of incident and/or recurrent CVD events during follow-up of almost 20 years, compared with women within the lowest tertile of potassium intake.
4. In men, the risk of CVD events was 7% lower for those within the highest tertile of potassium intake compared with those within the lowest tertile of potassium intake.
5. Both in men and in women, the association between potassium intake and CVD events was not modified by sodium intake.
6. The reduction in CVD risk with higher potassium is likely in part related to the blood pressure lowering effect, although potassium has other effects in the body that may contribute to the lowering of CVD risk.
7. An important limitation of this study is that only one random spot urine sample was collected for estimation of 24-h excretion of sodium and potassium.
8. High potassium consumption may reflect a better diet quality and/or nutritional status. And although the researchers did adjust for many potential confounding variables, it is impossible to completely exclude residual confounding.

Practical Application

- Having a potassium-rich diet has a beneficial health effect, relative to a potassium-poor diet.
- Specifically, this can have an important impact on blood pressure and hence risk of cardiovascular events and mortality.
- Consuming a healthy dietary pattern with a variety of potassium-containing foods should be recommended.
- However, sodium intake can independently impact blood pressure and CVD risk.
- Therefore, the overall weight of evidence strongly suggests that sodium intake in the diet should be limited to below the limits set by public health agencies.
- While potassium is beneficial and can moderate the effect of sodium, it likely won't abolish the impact, and therefore a high-sodium intake is detrimental to health even in the context of a high potassium intake.
- The BP-lowering impact of increasing potassium intake may be sex-specific.