Salt: a silent killer

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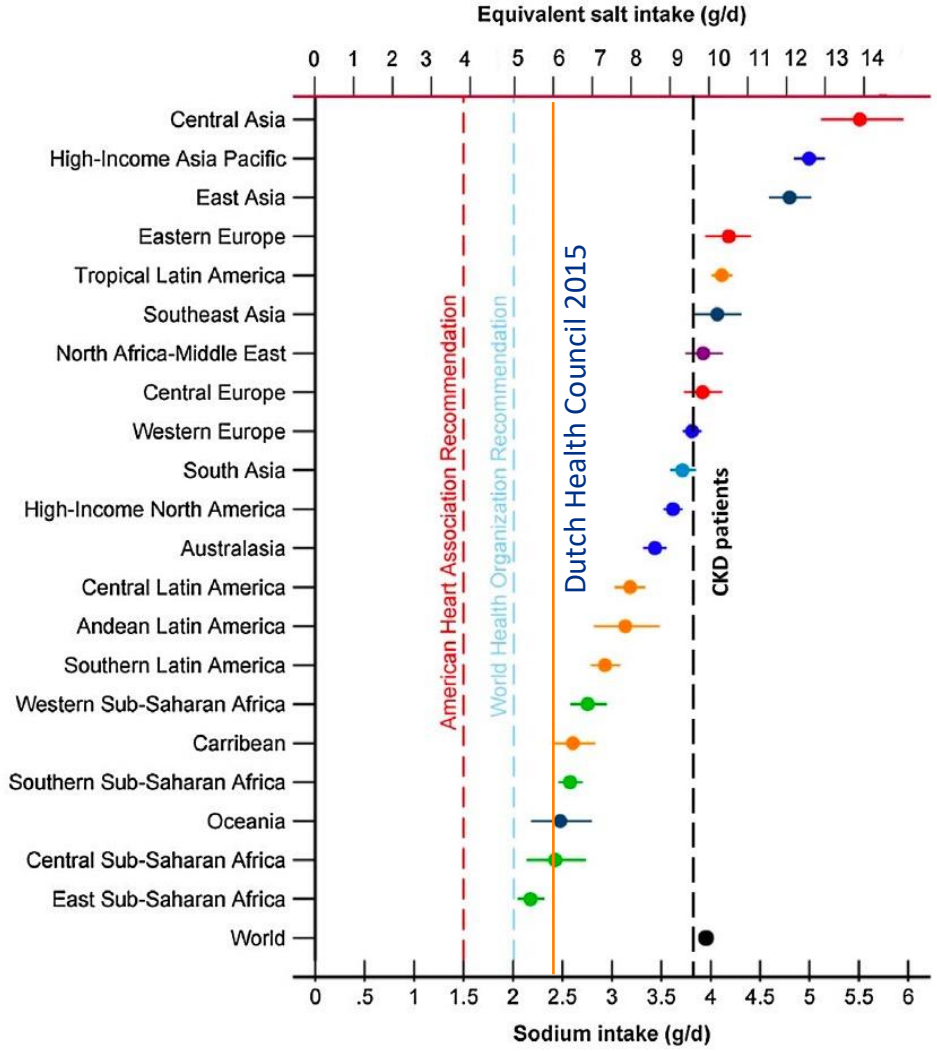
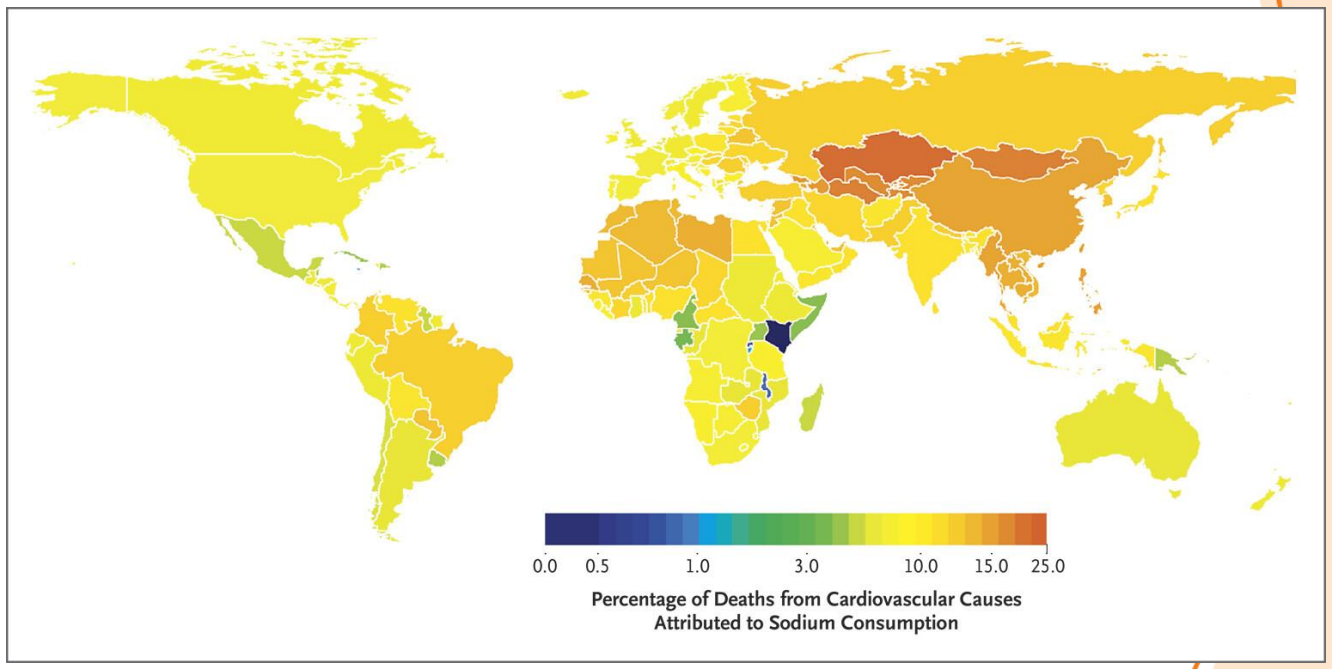
Salt intake: a global challenge

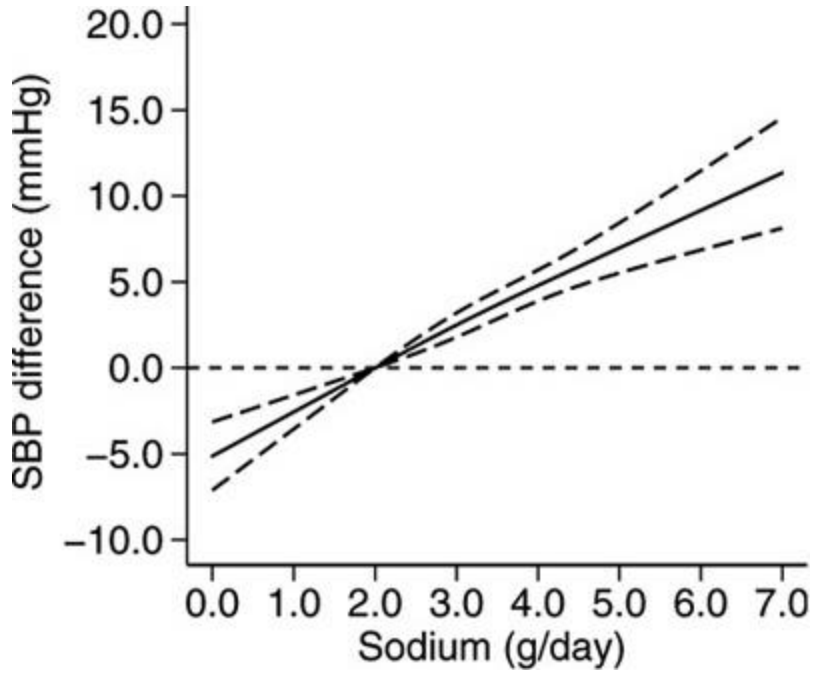




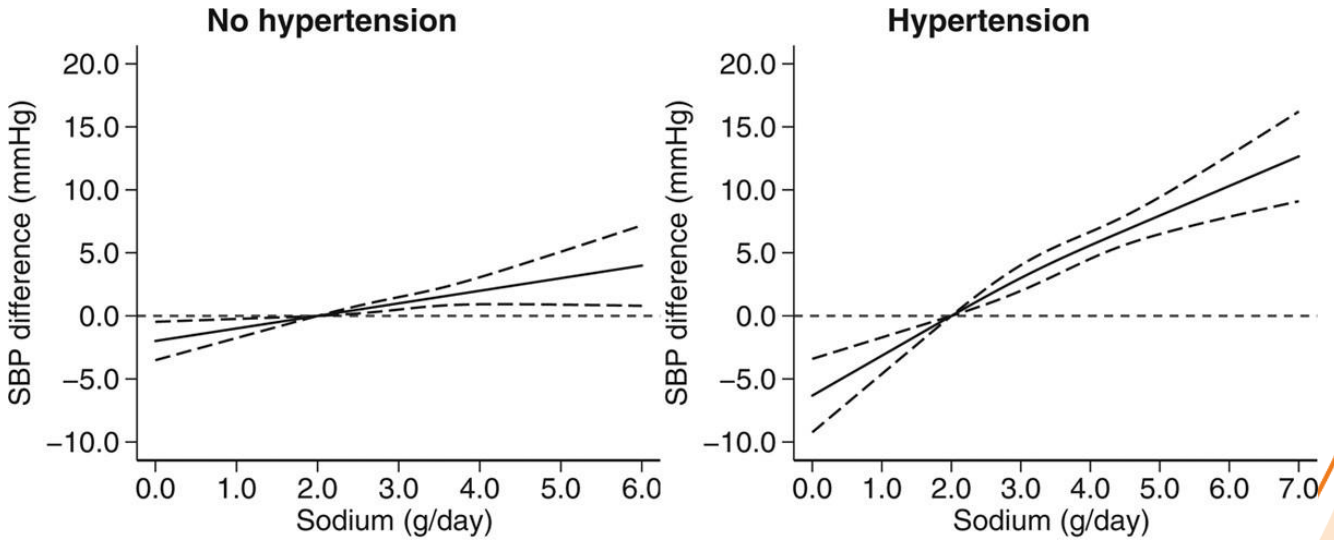
Forget Mediterranean cuisine. Experts say this East African diet could be key to better health

De Borst MH & Navis G. Pharmacol Res 2016;107:344-351; Mozaffarian et al. NEJM 2014;371:624-634

Higher sodium intake leads to higher blood pressure



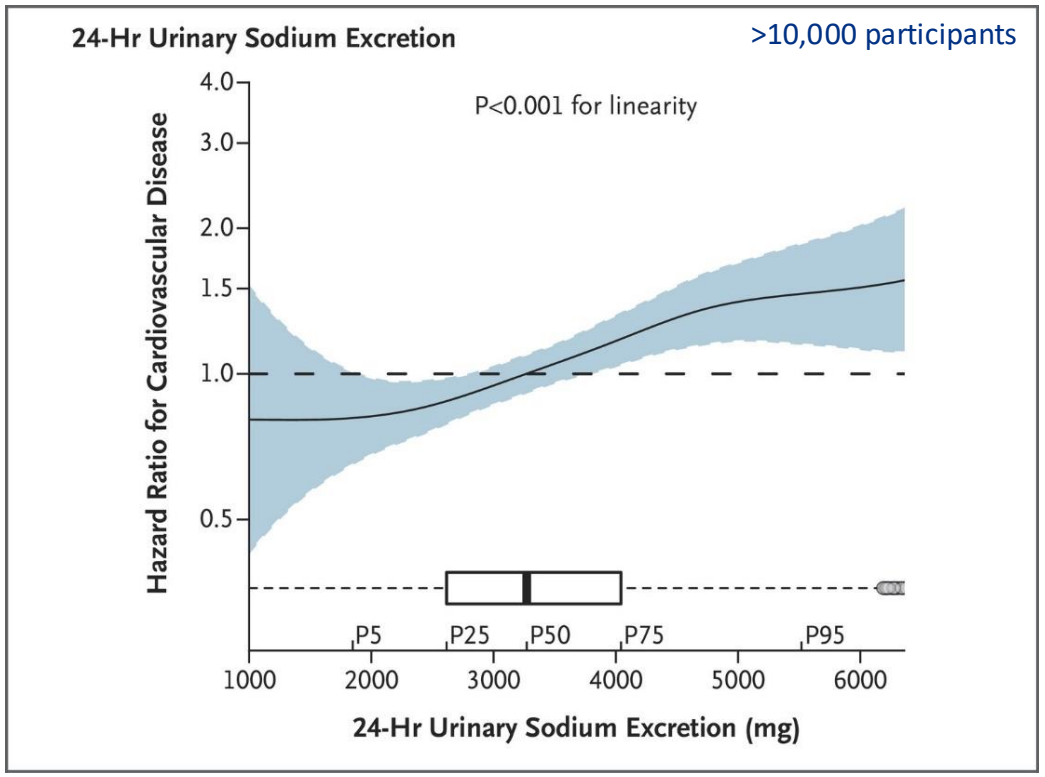
For each 1 g/d more sodium intake (=2.5 g salt): systolic blood pressure 2.42 mmHg higher



Global prevalence of hypertension: 30%

Fillipini T et al. Circulation 2021;143:1542-69

Higher salt intake increases the risk of heart disease and death



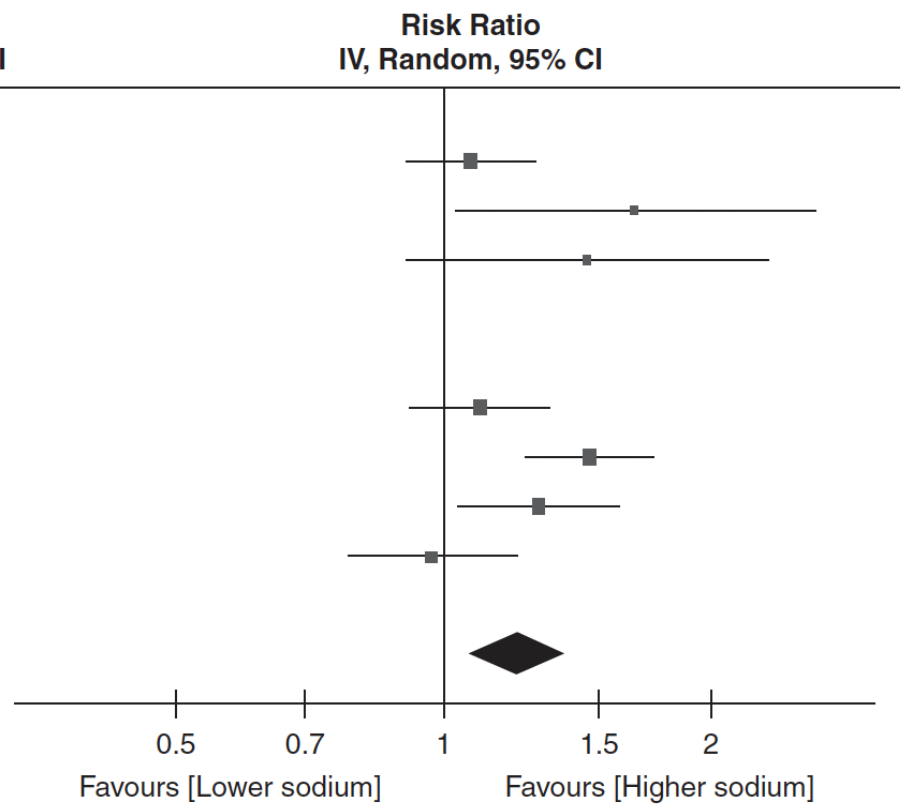
Each daily increment of 1000 mg in sodium excretion was associated with an 18% increase in cardiovascular risk

Ma Y et al. NEJM 2021;386:252-263

Higher salt intake increases the risk of chronic kidney disease

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
Asghari 2017	0.6729	0.2765		Not estimable
Dunkler 2015	0.0705	0.0829	19.0%	1.07 [0.91, 1.26]
Farhadnejad 2016	0.4947	0.2373	6.3%	1.64 [1.03, 2.61]
Kieneker 2016	0.3716	0.2377	6.2%	1.45 [0.91, 2.31]
Mirmiran 2018b	0.4187	0.2086		Not estimable
Rebholz 2016a	-0.0943	0.0987		Not estimable
Rebholz 2016b	0.0935	0.0919	17.8%	1.10 [0.92, 1.31]
Sugiura 2018	0.3771	0.0826	19.0%	1.46 [1.24, 1.71]
Yoon 2018	0.2469	0.1059	16.1%	1.28 [1.04, 1.58]
Yoon 2018	-0.0305	0.1112	15.5%	0.97 [0.78, 1.21]
Total (95% CI)			**100.0%**	**1.21 [1.06, 1.38]**

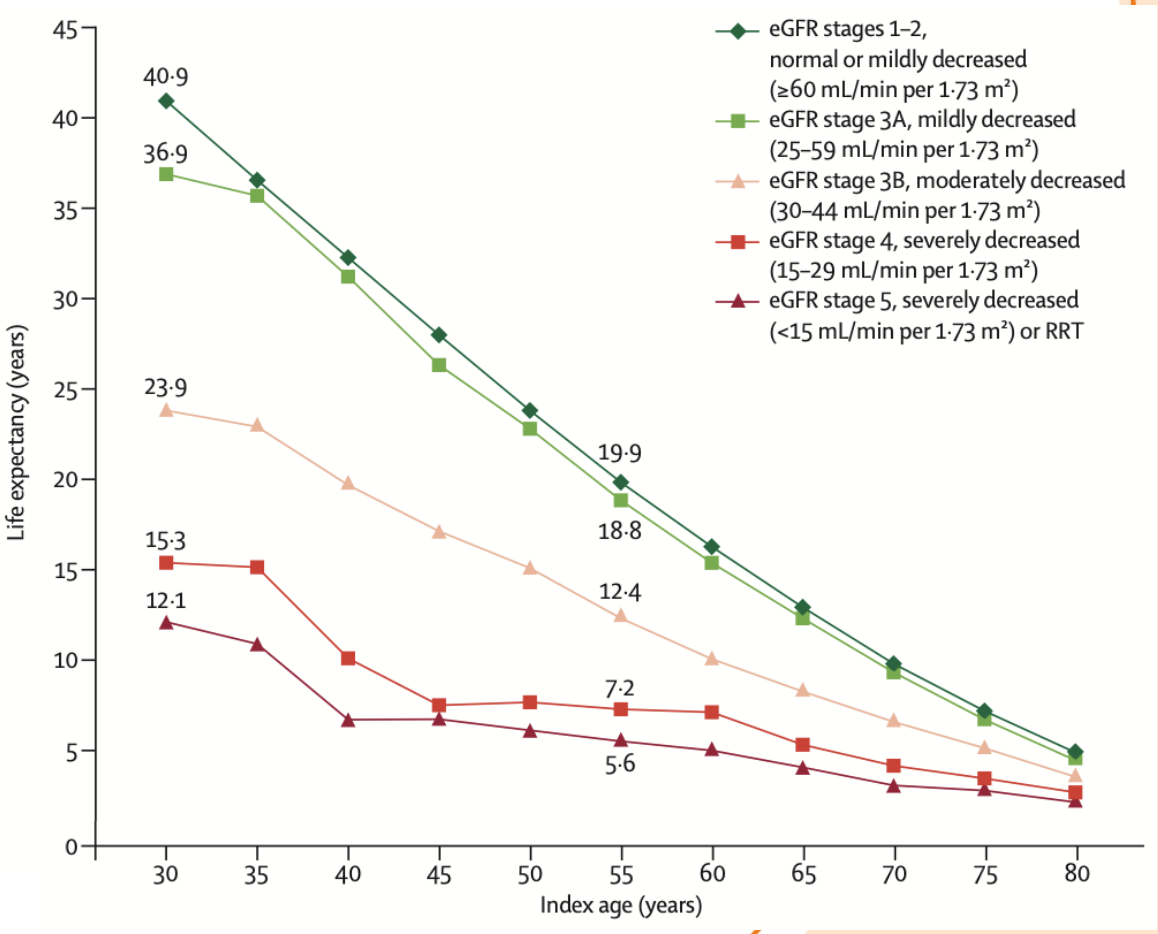
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 14.71$, df = 6 (P=0.02); $I^2 = 59\%$
Test for overall effect: Z = 2.81 (P = 0.005)



Kelly JT et al. J Am Soc Nephrol 2021;32:239-253

Prevalence and impact of chronic kidney disease

- Chronic kidney disease (CKD) affects one in ten individuals, i.e. 1.8 million in NL
- CKD is a major risk factor for cardiovascular disease, with a strong impact on life expectancy
- CKD is expected to be the fifth cause of death globally by 2040



GBD Chronic Kidney Diseaese Collaboration. Lancet 2020;395:709-733; Gansevoort RT et al. Lancet 2013;382:339-352

Impact of reducing salt intake

- Current average salt intake in Western Europe: ±10 g/d

- Reducing salt intake to 5 g/d:
  - BP reduction -5 mmHg
    - Risk of stroke -14%
    - Risk of coronary heart disease -9%
    - Risk of premature cardiovascular death: -7%

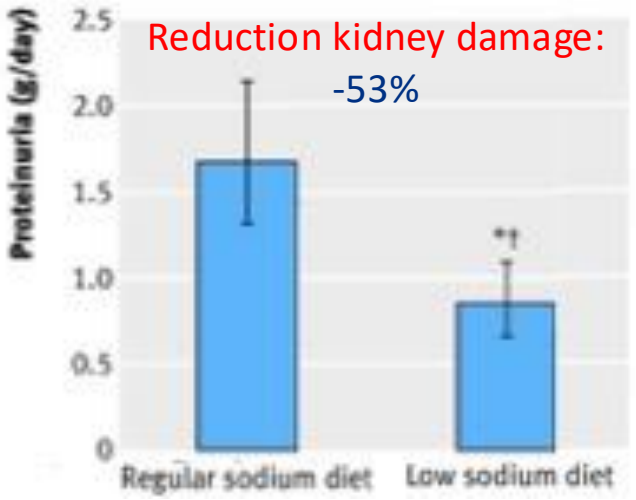
Blood Pressure Lowering Treatment Trialists' Collaboration. Lancet 2003;362:1527-1535; Law MR et al. BMJ 2009;338:b1665; Ettehad et al. Lancet 2016;387:957-967

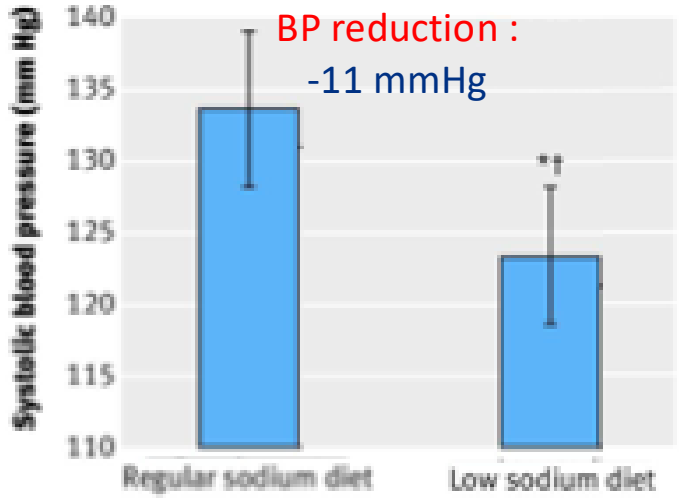
What can be done to reduce salt intake?

- Dietary salt restriction
- Replace sodium salt by alternatives – salt substitutes

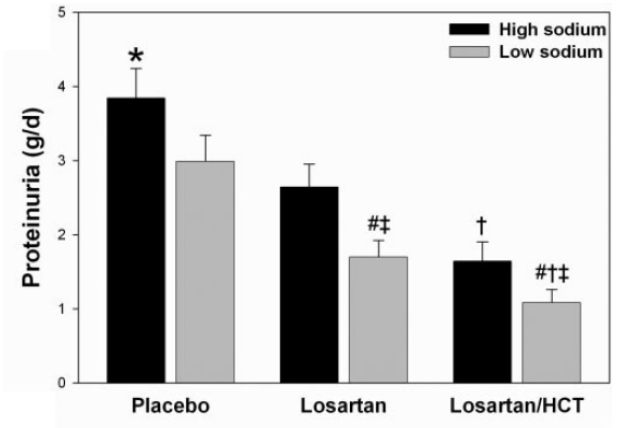
Lowering salt intake reduces kidney damage

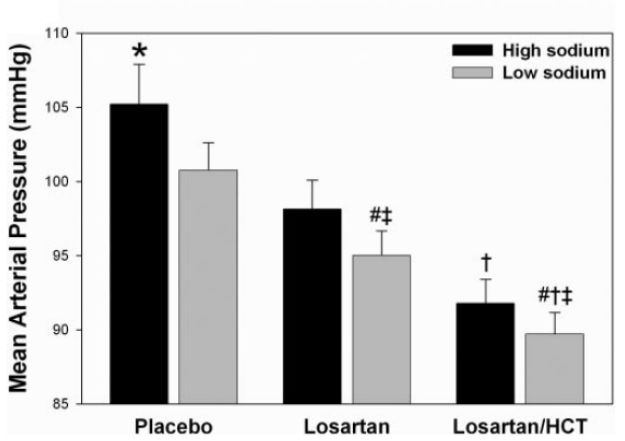
Patients with mild to moderate CKD
Salt intake reduction:
10.6 g/d >> 6.2 g/d





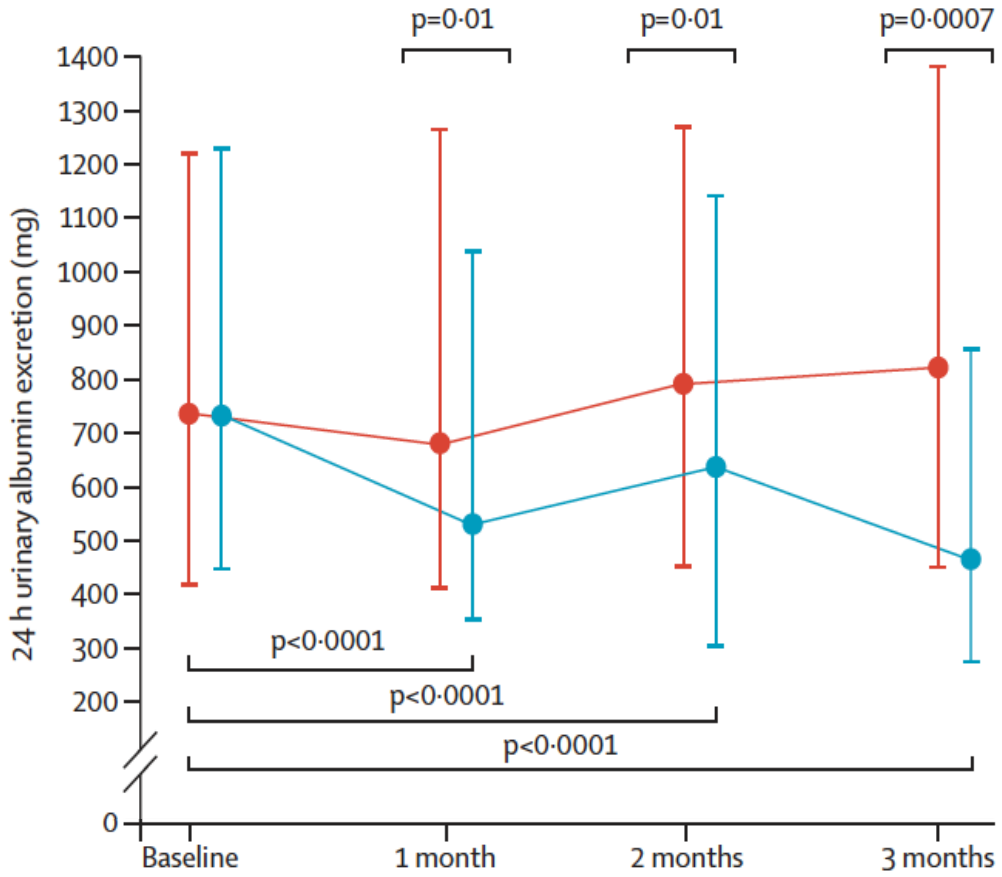
Patients with mild to moderate CKD
Salt intake reduction:
11.6 g/d >> 5.4 g/d





Slagman MCJ et al. BMJ 2011;343:d4366
Vogt L et al. J Am Soc Nephrol 2008;19:999-1007

Even a small reduction in salt intake protects the kidneys



Salt intake 12.2 g/d

Reduction kidney damage:
-37%

Salt intake 9.9 g/d
(-19%)

Parvanova A et al. Lancet DE 2018;6:27-40

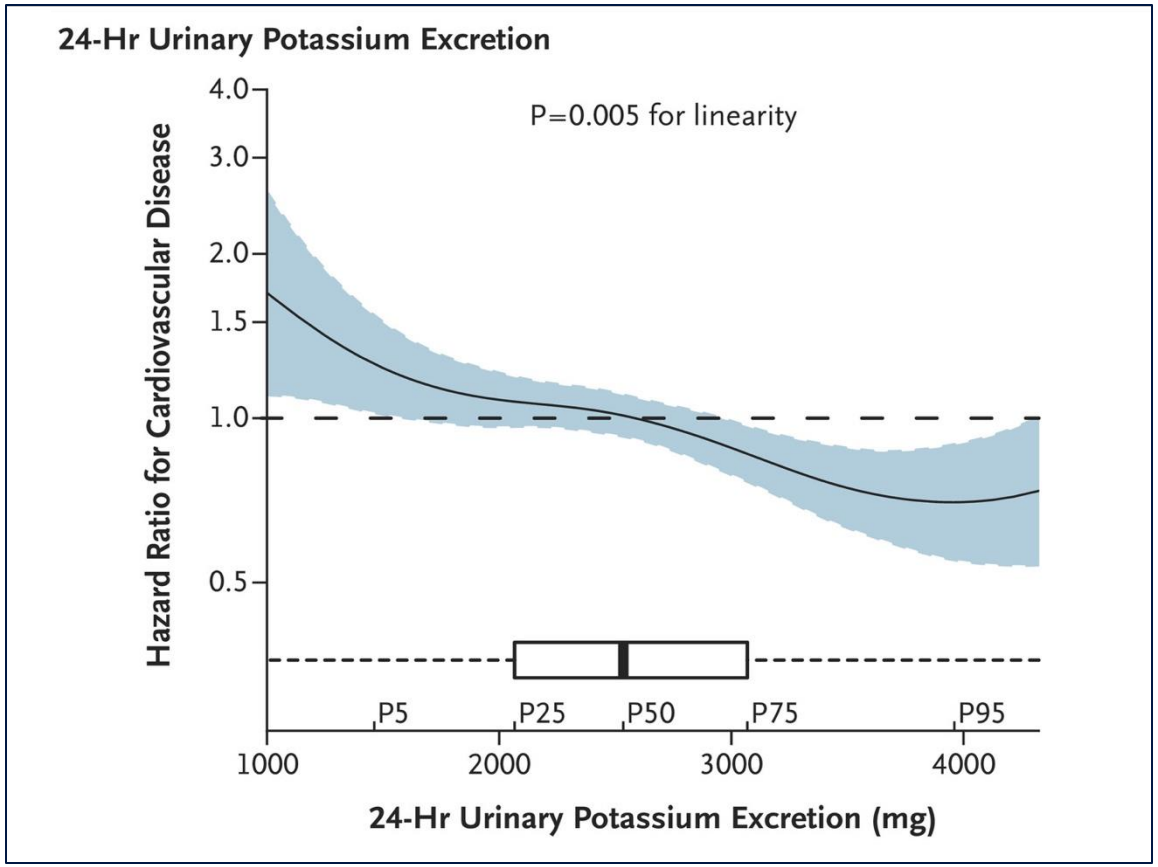
Reducing salt intake: impact on quality of life and costs

Intervention	U.S. Population				
	Cost of Intervention (billions of dollars)	Reduction in Health Care Costs (billions of dollars)†	Gain in QALYs (thousands)	Cost per QALY Gained (dollars)‡	Cost Saved per Dollar Spent on Intervention (dollars)‡
Reduction in dietary salt					
1 g/day					
Low estimate	0.3§	4.1±0.8	75±9	Cost savings	15.4±3.0
High estimate	0.3§	7.0±1.4	120±15	Cost savings	26.1±5.2
3 g/day					
Low estimate	0.3§	12.1±2.4	220±26	Cost savings	45.2±9.1
High estimate	0.3§	20.4±4.1	350±42	Cost savings	76.0±15.4
Hypertension treatment¶	19.5±0.1	14.2±2.7	360±42	15,800±9,900	0.7±0.1

NICE (UK): campaign to reduct salt intake (costs £15 mln) can lead to £1.5 bln saving per year

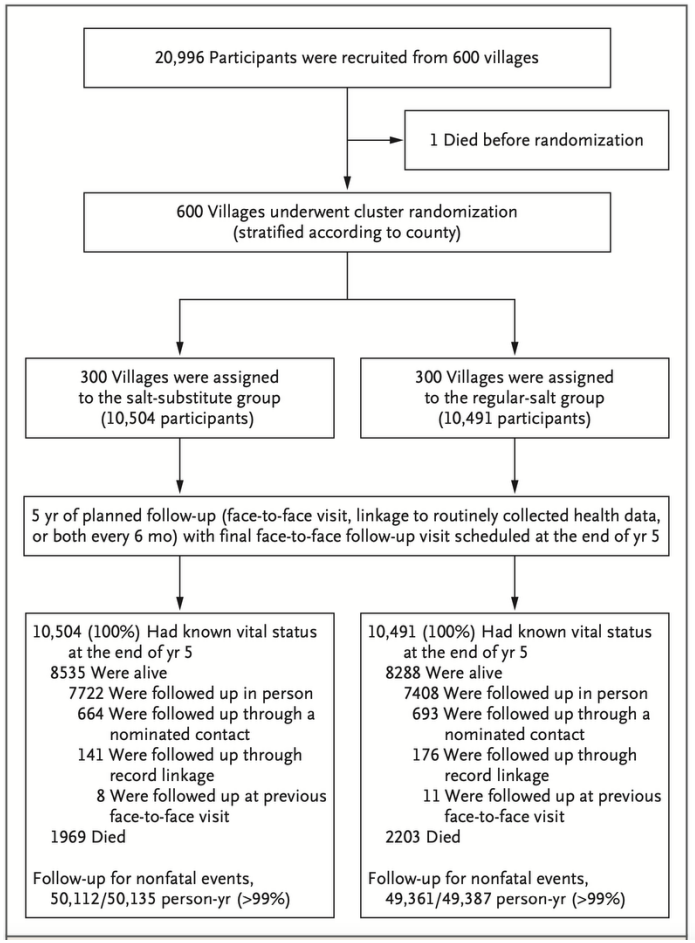
Bibbins-Domingo et al. NEJM 2010;362:590-599
Cardiovascular disease prevention: public health guideline [PH25]. London: National Institute for Health and Care Excellence; 2010 (https://www.nice.org.uk/guidance/ph25)

Low potassium intake is also a cardiovascular risk factor



Ma Y et al. NEJM 2021;386:252-263

Salt substitution (Na ➢ K): Cluster randomized controlled trial



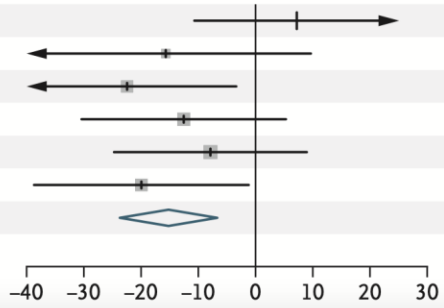
- 20,995 patients with history of stroke or age >60 years and poorly controlled blood pressure
- Primary outcome: stroke
- Secondary outcomes: major CV events or all-cause mortality

Neal B et al. NEJM 2021;385:1067-77

Salt substitution (Na ➢ K): Na^+ and K^+ excretion

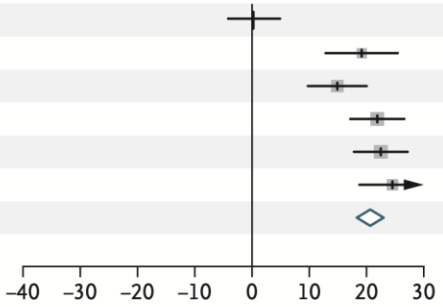
C 24-Hr Urinary Sodium Excretion (mmol)

Time Point	Salt Substitute (*no. of participants*)	Regular Salt (*no. of participants*)	Mean Difference (95% CI)
Baseline	276	268	9.96 (–12.39 to 32.32)
12 Mo	577	445	–15.69 (–41.05 to 9.66)
24 Mo	1,047	939	–22.45 (–41.52 to –3.37)
36 Mo	428	392	–12.55 (–30.41 to 5.31)
48 Mo	444	383	–7.89 (–24.73 to 8.95)
60 Mo	424	358	–19.95 (–38.71 to –1.20)
Fixed-Effects Model			**–15.21 (–23.72 to –6.70)**
Heterogeneity: I^2=0%; P=0.81			



D 24-Hr Urinary Potassium Excretion (mmol)

Time Point	Salt Substitute (*no. of participants*)	Regular Salt (*no. of participants*)	Mean Difference (95% CI)
Baseline	276	268	0.63 (–3.36 to 4.62)
12 Mo	577	445	19.13 (12.82 to 25.45)
24 Mo	1,047	939	14.88 (9.73 to 20.03)
36 Mo	428	392	21.87 (17.15 to 26.60)
48 Mo	444	383	22.48 (17.78 to 27.18)
60 Mo	424	358	24.52 (18.74 to 30.30)
Fixed-Effects Model			**20.64 (18.30 to 22.98)**
Heterogeneity: I^2=47.4%; P=0.11			



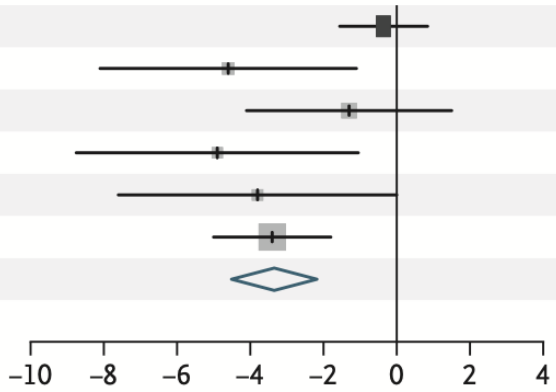
Neal B et al. NEJM 2021;385:1067-77

Salt substitution (Na ➢ K): Effect on blood pressure

A Systolic Blood Pressure (mm Hg)

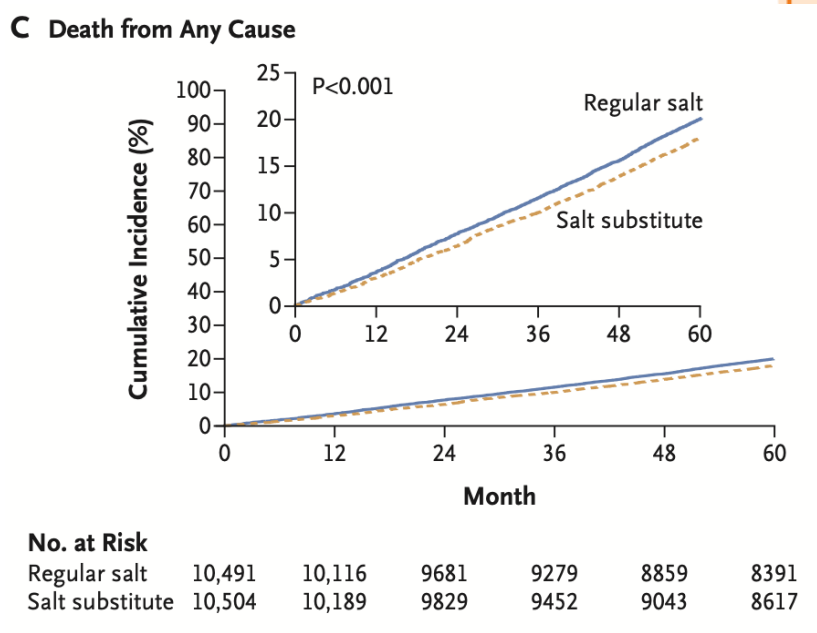
Time Point	Salt Substitute	Regular Salt	Mean Difference (95% CI)
	no. of participants		
Baseline	10,504	10,491	−0.40 (−2.50 to 1.70)
12 Mo	768	658	−4.60 (−8.10 to −1.10)
24 Mo	1,412	1,374	−1.30 (−4.10 to 1.50)
36 Mo	584	584	−4.90 (−8.75 to −1.05)
48 Mo	587	559	−3.80 (−7.60 to 0.00)
60 Mo	7,436	7,081	−3.40 (−5.00 to −1.80)
Fixed-Effects Model			**−3.34 (−4.51 to −2.18)**

Heterogeneity: I^2=0%; P=0.52



Neal B et al. NEJM 2021;385:1067-77

Salt substitution (Na ➢ K): Stroke, MACE, mortality



- Were beneficial effects mostly attributable to lower Na intake or higher K intake?
- How about effects on kidney outcomes?

Neal B et al. NEJM 2021;385:1067-77

Use of lower-sodium salt substitutes

WHO guideline

WHO recommendation

To reduce blood pressure and risk of cardiovascular diseases, WHO has recommended reducing sodium intake to less than 2 g/day (*strong* recommendation).[4] In this context, using less regular table salt[5] is an important part of an overall sodium reduction strategy. If choosing to use table salt, WHO suggests replacing regular table salt with lower-sodium salt substitutes that contain potassium (*conditional* recommendation).[6] This recommendation is intended for adults (not pregnant women or children) in general populations, excluding individuals with kidney impairments or with other circumstances or conditions that might compromise potassium excretion.

Use of lower-sodium salt substitutes: WHO guideline 2025 https://www.who.int/publications/i/item/9789240105591

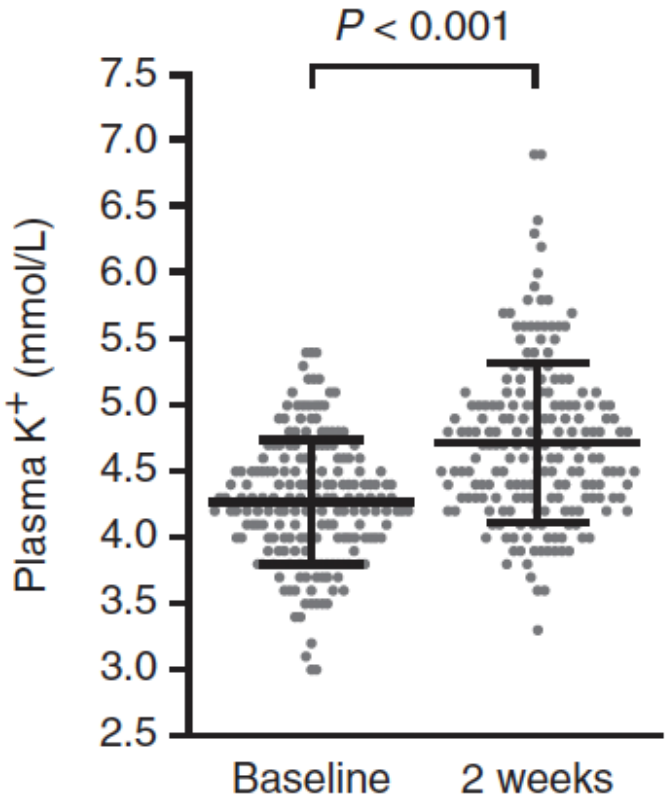
Risk of hyperkalemia in CKD with limited increase in K+ intake is low

CKD stage	eGFR, mL/min/1.73 m^2	Global prevalence, %	Numer of people, millions	Median blood potassium level, mmol/L	Hyperkalemia incidence rate, per 100 person-years
G1	>90	3.2	256	3.9	1.32
G2	60-90	2.8	224	4.0	2.48
G3a	45-59	3.7	296	4.1	2.39
G3b	30-44	1.2	96	4.2	4.31
G4	15-29	0.4	32	4.4	8.80
G5	<15	0.1	8	4.4	9.37

Hoorn EJ, De Borst MH et al. Submitted 2025

Risk of hyperkalemia in CKD with limited increase in K+ intake is low

- 191 patients with moderate to severe CKD (stage 3b-4)
- Intervention: 40 mmol potassium chloride (1.56 g potassium)
- Aim: bring potassium intake to recommended level (instead of low)
- Main findings:
  - Limited effect on plasma K+ level
  - 11% developed hyperkalemia



KALIUMSTUDIE
NIERSTICHTING
K'ONSORTIUM

Gritter M et al. J Am Soc Nephrol 2022;33:1779-1789

Developments in NL since 2006

2007

Federation Dutch Food Industry (FNLI) founded taskforce *Salt in Food* (*Zout in Levensmiddelen*)

- Goal: gradual reduction of salt content in food by 20-30%
- Relevant steps taken in e.g. bread (2.5% > 1.8% salt per dry substance, 2009-2013)

2014

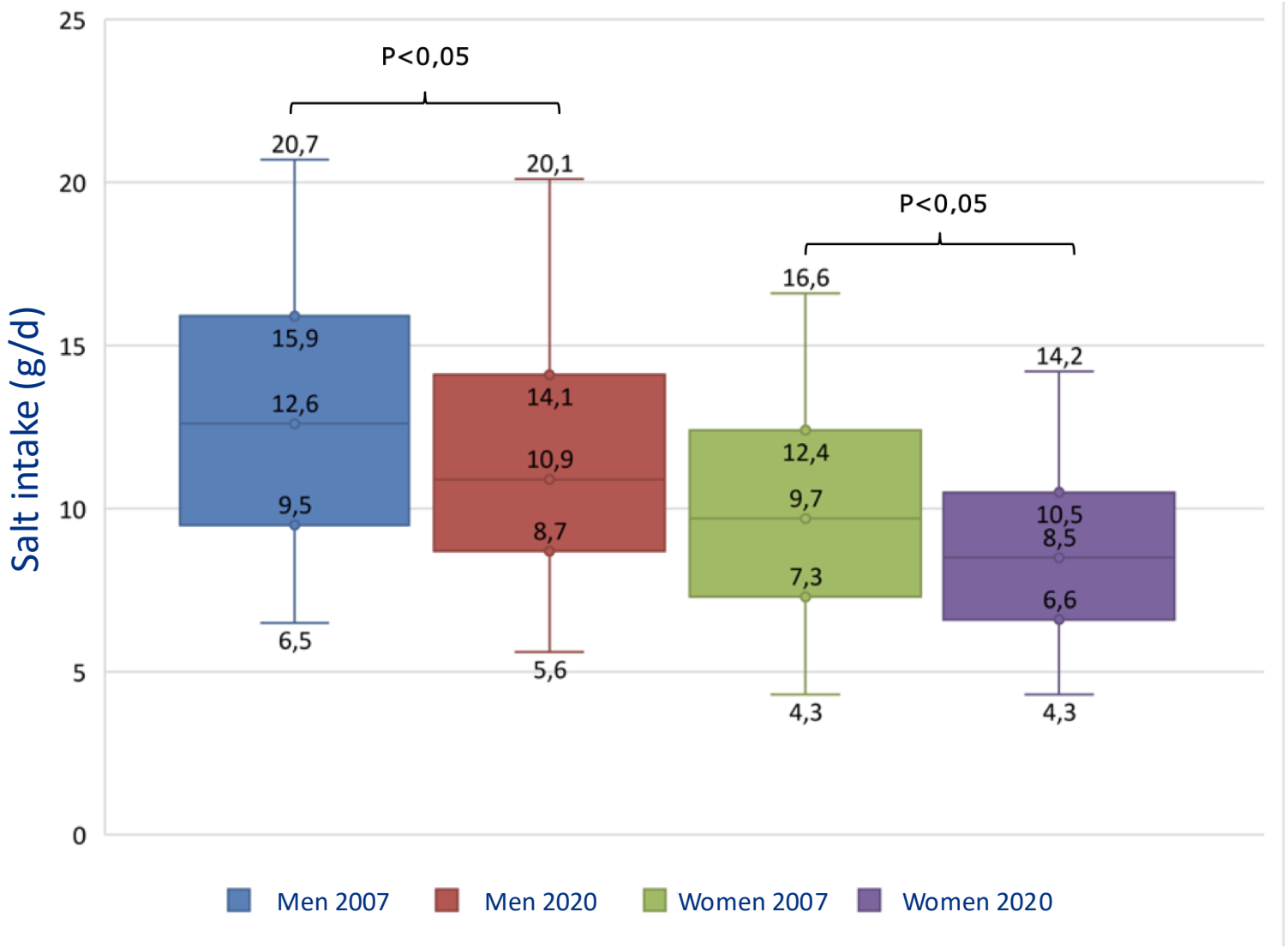
Akkoord Verbetering Productsamenstelling, agreement government and food industry on maximum salt content per product group

2011-2016

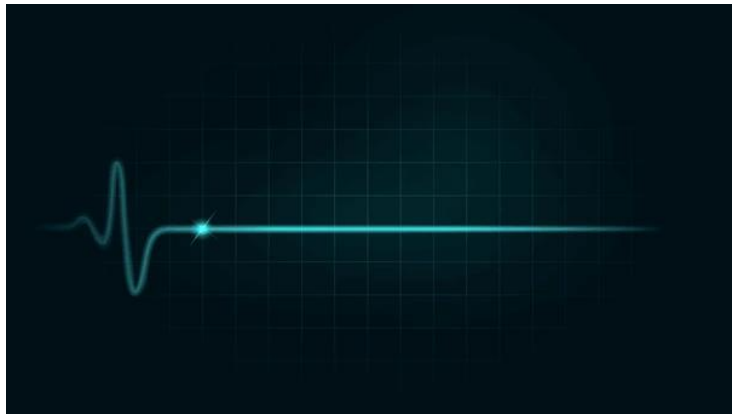
Salt content in bread reduced by 19%

- Several other examples (sauces, canned vegetables, chips etc)
- Analyses until 2020 showed a further decline

Trends in salt intake in NL (2000 - 2020)



Conclusions



- Cardiovascular/kidney disease together are the most common causes of death worldwide (>**one-third** of the population)
- High salt intake is the global standard, but also a major lifestyle-related cause of hypertension and heart/kidney disease
- Each **gram** of salt intake less means a drop in BP by **1 mmHg**, leading to relevant (up to 10%) CV risk reductions

Conclusions

- Reducing diet salt content is challenging but possible, as demonstrated in NL and other countries
- Salt substitution seems a feasible approach
- Collaborative, multidisciplinary efforts are needed to make this happen

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DUTCH KIDNEY FOUNDATION

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