Nefrologia Update 2018

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BREAKING NEWS

26 agosto 2018 | STORIE&VOLTI

ilcaffè
Settimanale di attualità, politica, sport e cultura

Il benessere.

Uno studio mondiale rivaluta quei gustosi granellini bianchi. Ma per Berna e per molti medici è pericoloso superare la dose di 5 grammi al giorno

Le strategie

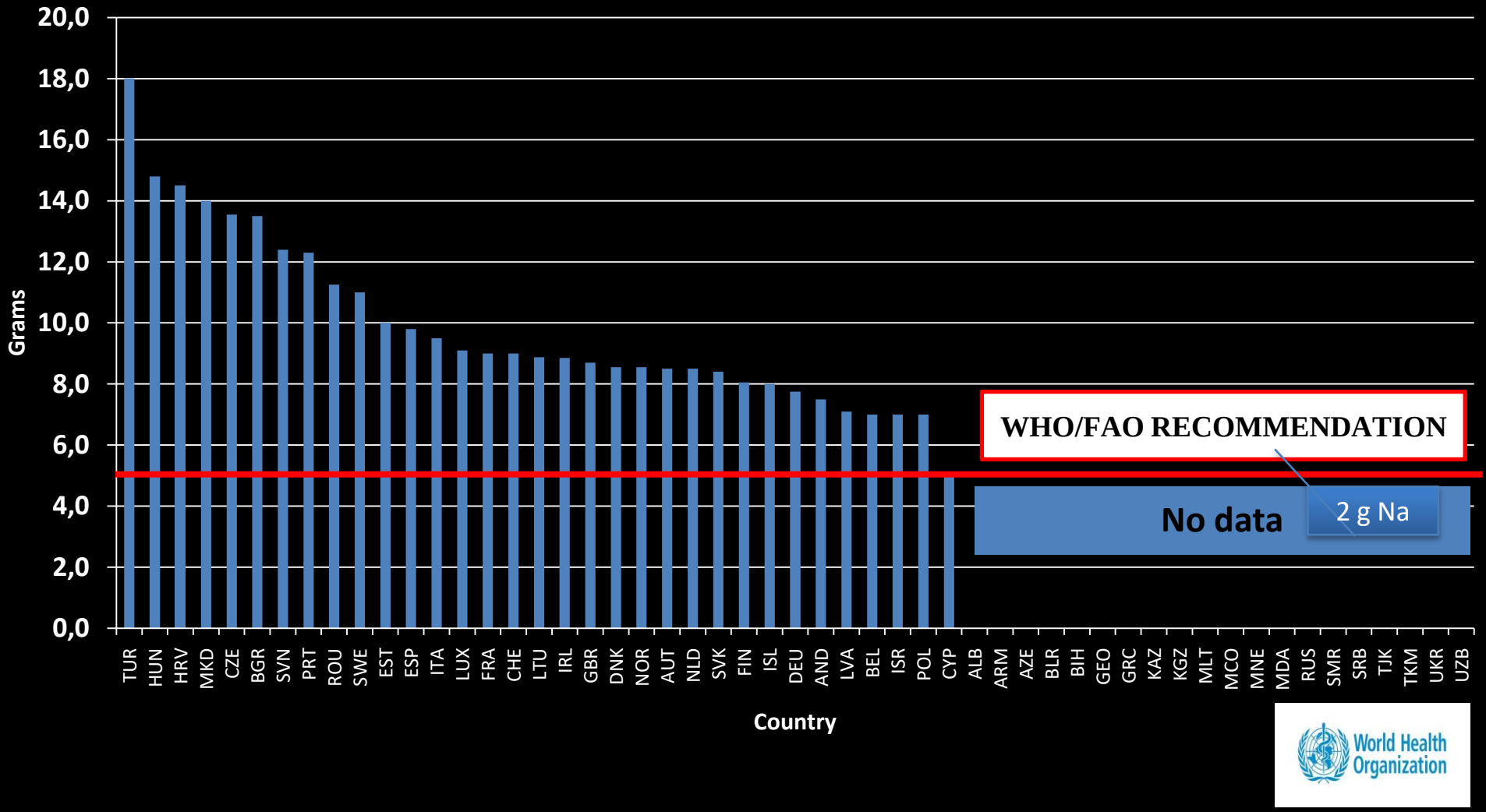
IN SVIZZERA
La Confederazione da tempo ha avviato studi e ricerche per cercare di ridurre la quantità di sale negli alimenti. Alcuni supermercati, da tempo vendono pane con un contenuto ridotto di sale

IN INGHILTERRA
Da tempo il governo inglese ha deciso di diminuire il consumo di sale del 10% in quattro anni intervenendo direttamente su chi produce alimenti. Una misura che non avrebbe influito sulle vendite

NEGLI STATI UNITI
Negli ultimi 18 anni gli Usa hanno ridotto del 12% il sale negli alimenti confezionati, ma non basta. Il 98% delle famiglie continua a comperare alimenti e bevande con un'eccessiva densità di sodio

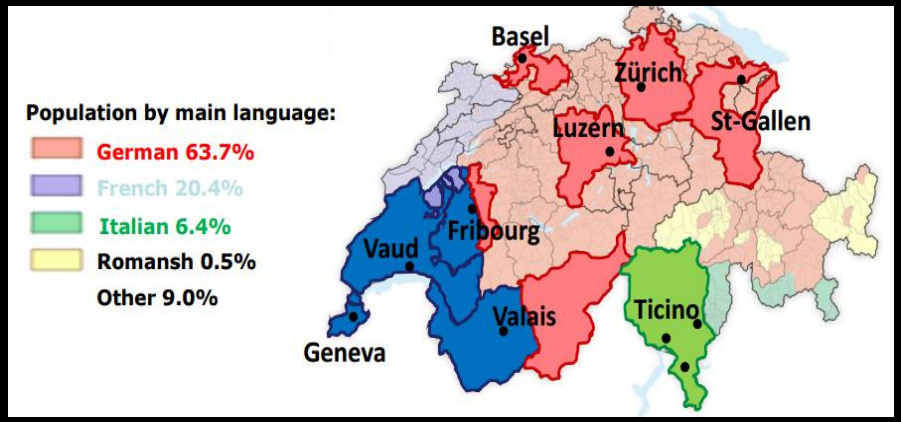
Troppo sale fa male alla salute? Macché, fa vivere più a lungo

Salt intake per person per day for adults in the WHO European Regions from individual country-based surveys, various years



The Swiss Survey on Salt (SSS) 2010 - 2012

1624 subjects (729 men, 777 women) from 3 linguistic regions (11 centers)



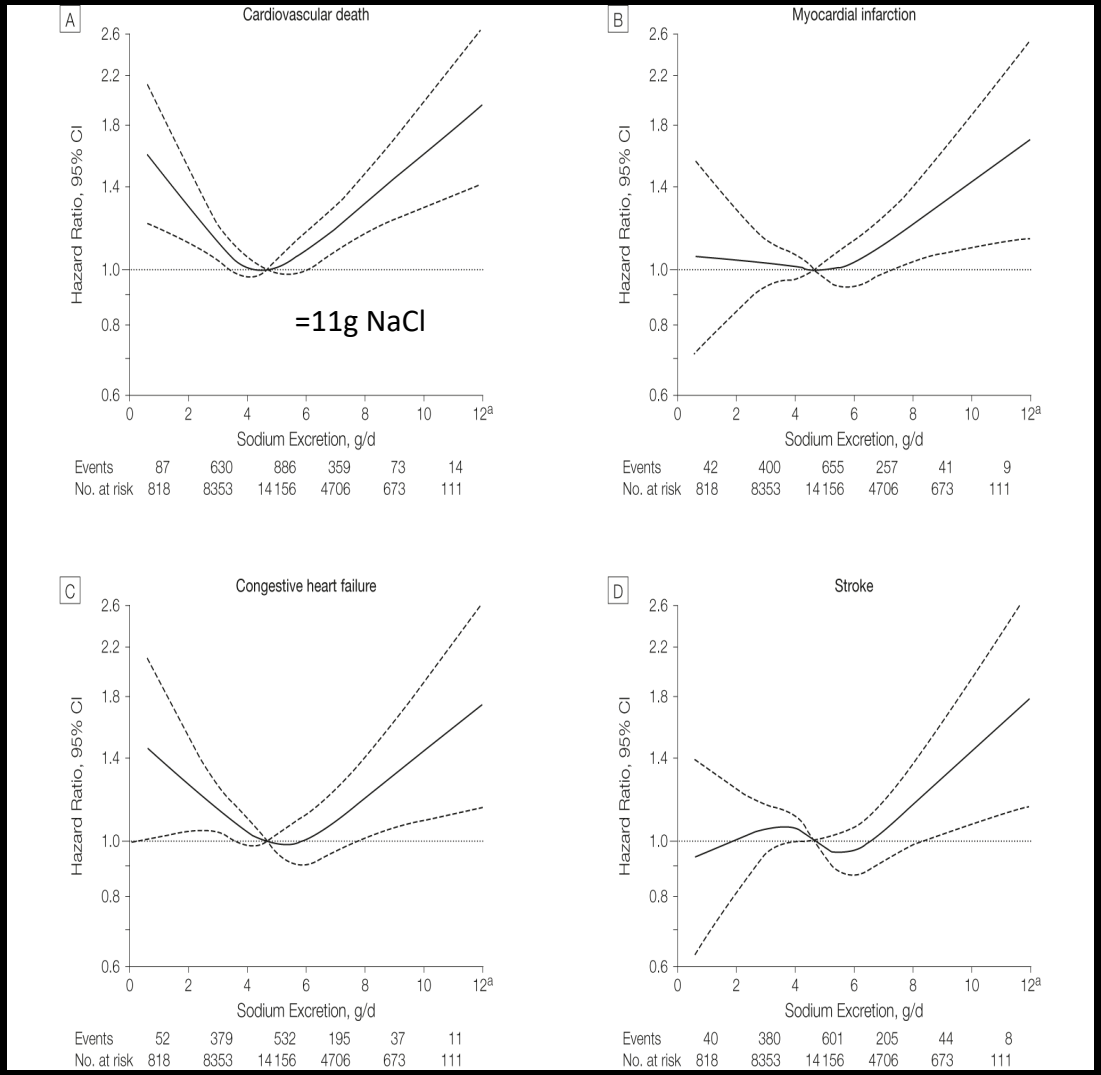
	Mean urinary NaCl excretion (g/24h)										
	Men					Women					
	15-29	30-44	45-59	≥60	Total Men	15-29	30-44	45-59	≥60	Total Women	Total
Linguistic region											
French (n=411)	9.3	10.6	11.3	10.1	**10.3**	6.7	7.9	7.8	6.4	**7.2**	**8.7**
German (n=820)	9.7	11.5	11.4	10.4	**10.7**	8.3	8.3	8.7	7.2	**8.1**	**9.4**
Italian (n=216)	10.7	10.7	11.3	9.5	**10.5**	7.7	8.2	7.0	7.4	**7.6**	**9.0**
Total (n=1447)	9.8	11.1	11.3	10.2	**10.6**	7.8	8.2	8.2	7.0	**7.8**	**9.1**

4.2 g Na

3.1 g Na

Urinary sodium and potassium excretion and risk of CV events

Observational analyses of 2 cohorts (N = 28,880) included in the ONTARGET and TRANSCEND trials



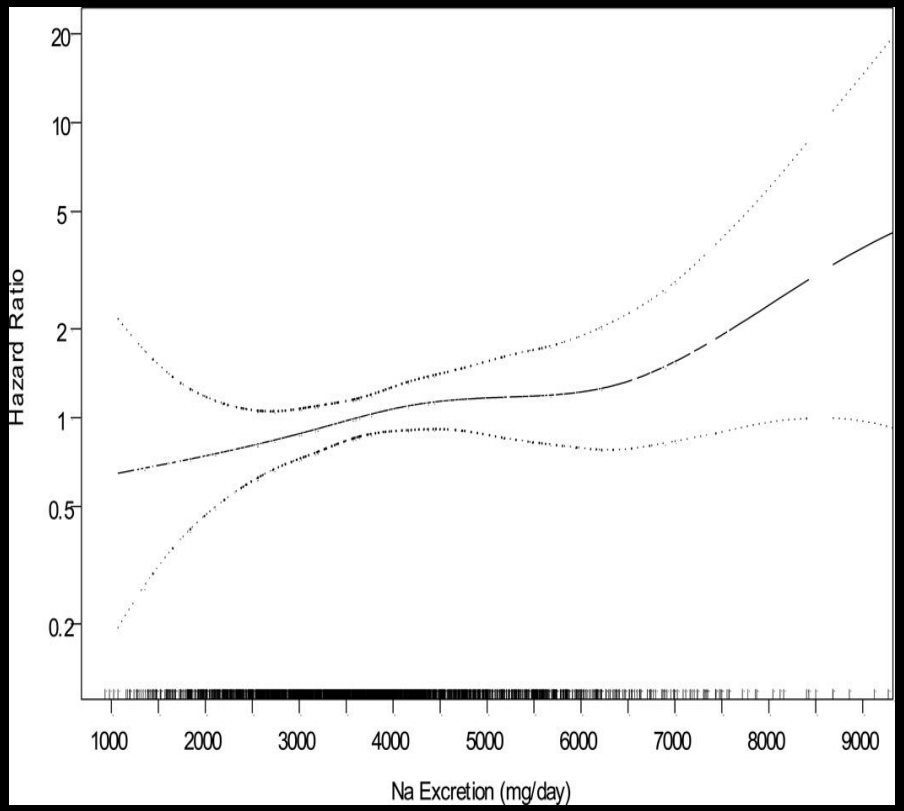
O'Donnell et al. JAMA. 2011 Nov 23;306(20):2229-38

Sodium excretion and risk of developing coronary heart disease

7543 adults 28-75 years free of cardiovascular and kidney disease in 1997/1998 of the Prevention of Renal and Vascular End-stage Disease (PREVEND) study

median follow-up of 10.5 years, 452 CHD events

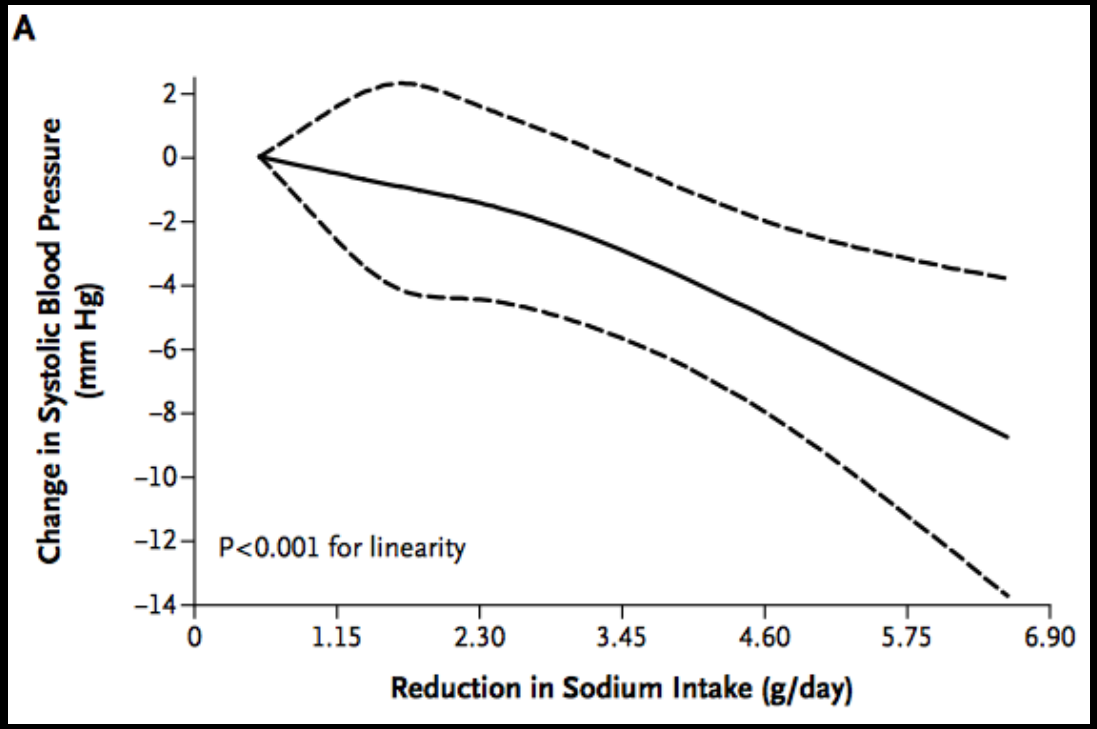
No association between sodium excretion and risk of CHD.
Higher sodium excretion was associated with an increased CHD risk among subjects with increased NT-proBNP concentrations or with hypertension



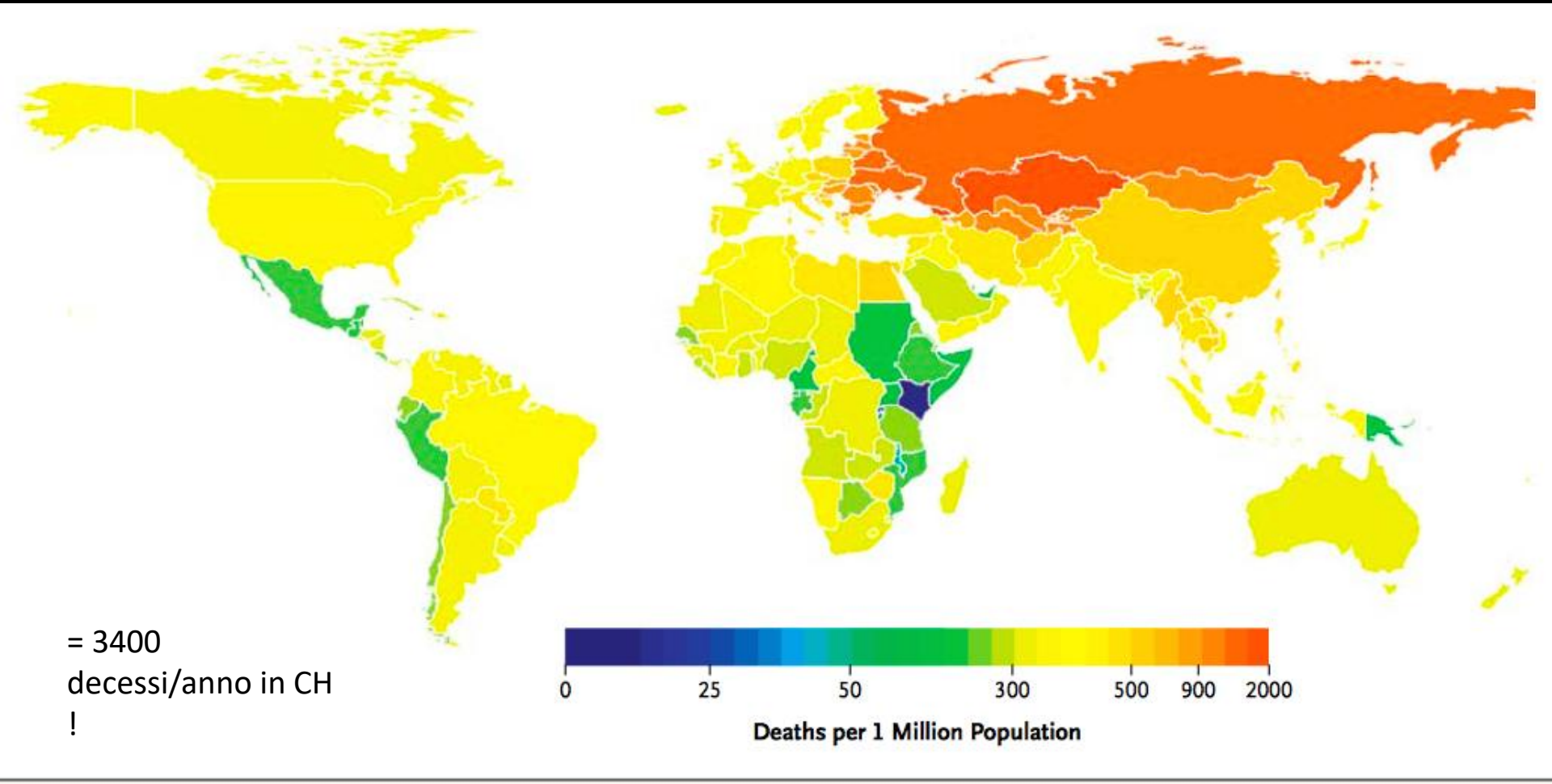
Joosten et al. Circulation. 2014 Mar 11;129(10):1121-8

Global Sodium Consumption and Death from CV Causes

- Data from surveys on sodium intake as determined by urinary excretion and diet from 66 countries
- Effects of sodium on blood pressure, according to age, race, and the presence or absence of hypertension, calculated from data in a meta-analysis of 107 randomized interventions
- The effects of blood pressure on CV mortality, were calculated from a meta-analysis of cohorts

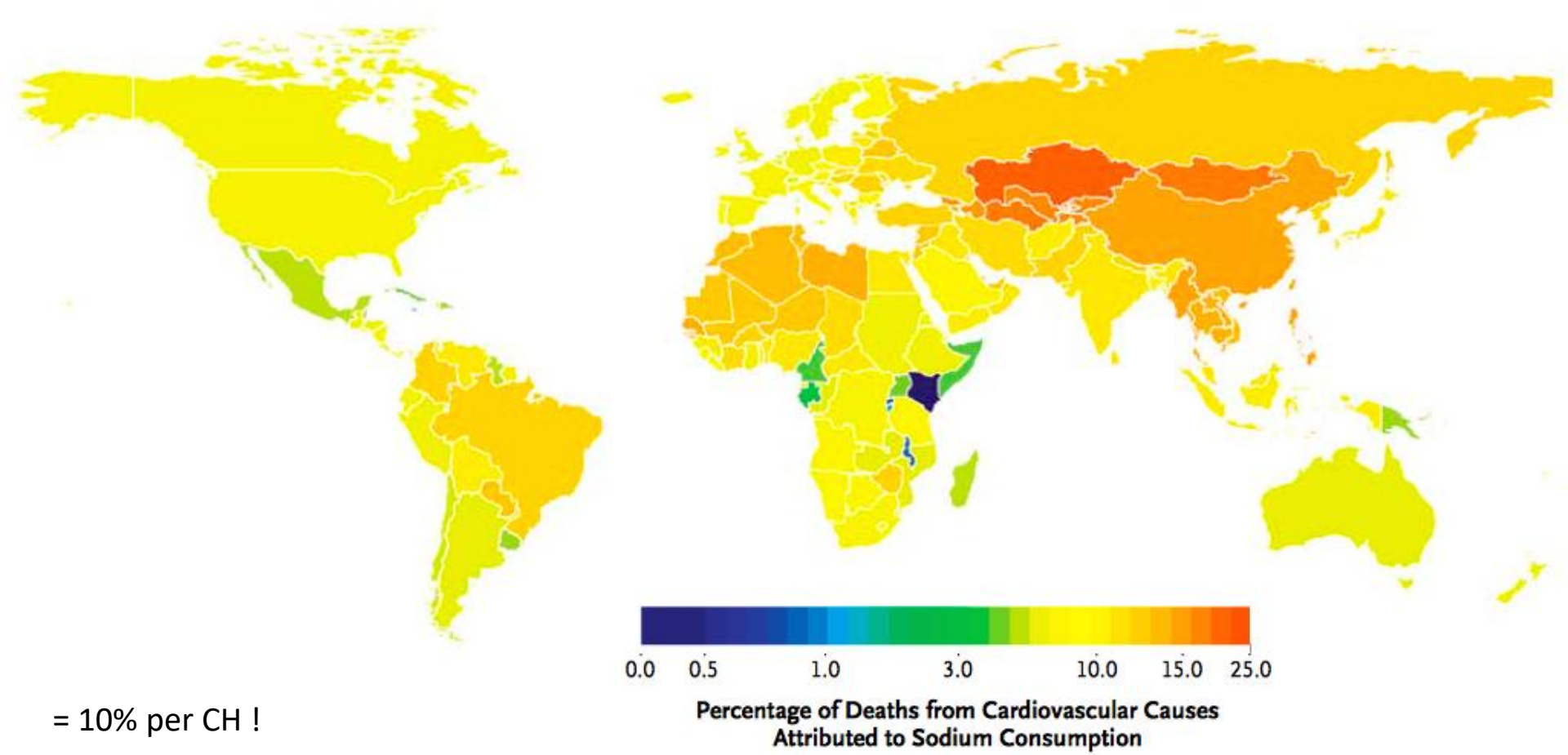


Mozaffarian et al. N Engl J Med 2014;371:624-34



= 3400
decessi/anno in CH
!

Figure 3. Absolute Cardiovascular Mortality Attributed to Sodium Consumption of More than 2.0 g per Day in 2010, According to Nation.
The scale is based on the number of deaths from cardiovascular causes (per 1 million persons) in 2010 that were attributed to sodium consumption of more than 2.0 g per day.



= 10% per CH !

Figure 4. Proportion of Deaths from Cardiovascular Disease Attributed to Sodium Consumption of More than 2.0 g per Day in 2010, According to Nation.

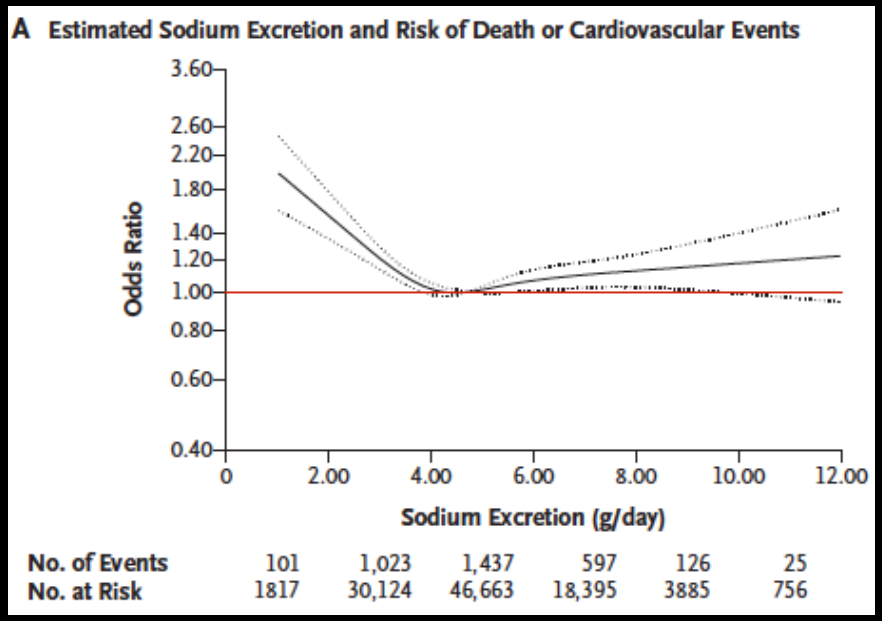
The scale is based on the percentage of all deaths from cardiovascular causes in 2010 that were attributed to sodium consumption of more than 2.0 g per day.

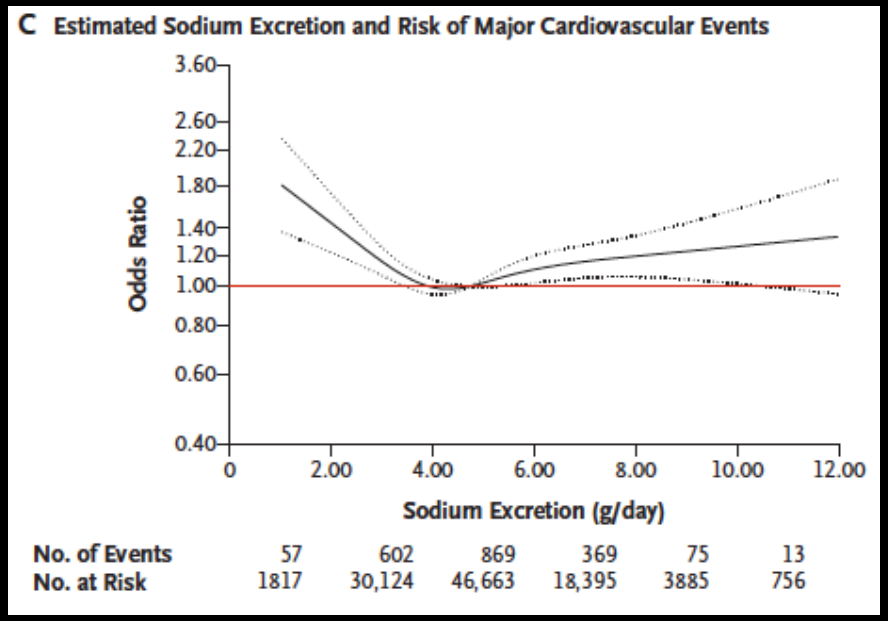
Urinary Sodium and Potassium Excretion, Mortality, and Cardiovascular Events

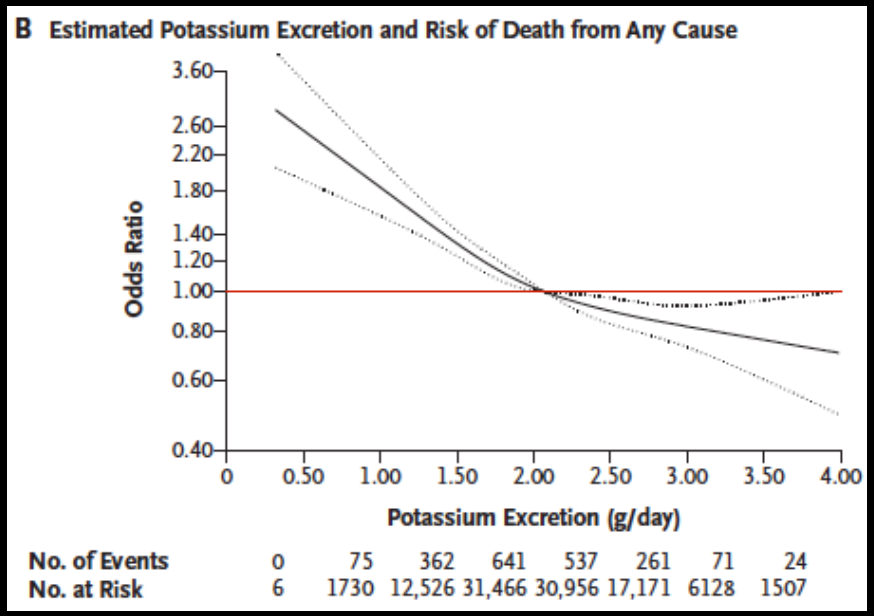
- Prospective Urban Rural Epidemiology cohort study
- 156,424 persons, 35 to 70, residing in 628 urban and rural communities in 17 countries:
  Argentina, Bangladesh, Brazil, Canada, Chile, China, Colombia, India, Iran, Malaysia, P akistan, Poland, South Africa, Sweden, Turkey, United Arab Emirates, and Zimbabwe
- Morning fasting urine from 101,945 persons to estimate 24-hour sodium and potassium excretion
- Composite outcome of death and major CV events.

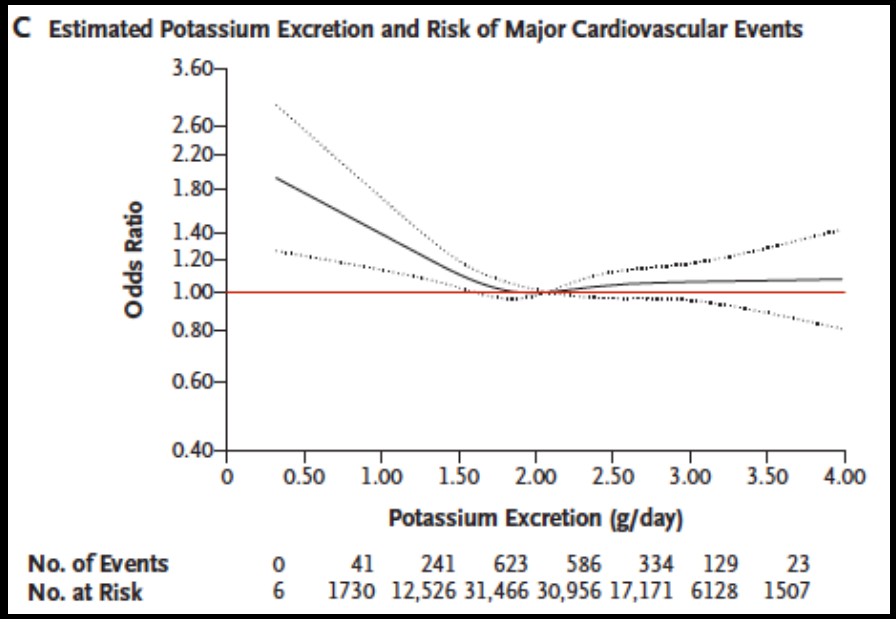
An estimated sodium intake between 3 g (7.5 g NaCl) per day and 6 g (15 g NaCl) per day was associated with a lower risk of death and cardiovascular events

O'Donnell et al. N Engl J Med 371;7 august 14, 2014


A Estimated Sodium Excretion and Risk of Death or Cardiovascular Events
Odds Ratio
3.60
2.60
2.20
1.80
1.40
1.20
1.00
0.80
0.60
0.40
0
2.00
4.00
6.00
8.00
10.00
12.00
Sodium Excretion (g/day)
No. of Events 101 1,023 1,437 597 126 25
No. at Risk 1817 30,124 46,663 18,395 3885 756


C Estimated Sodium Excretion and Risk of Major Cardiovascular Events
Odds Ratio
3.60
2.60
2.20
1.80
1.40
1.20
1.00
0.80
0.60
0.40
0
2.00
4.00
6.00
8.00
10.00
12.00
Sodium Excretion (g/day)
No. of Events 57 602 869 369 75 13
No. at Risk 1817 30,124 46,663 18,395 3885 756

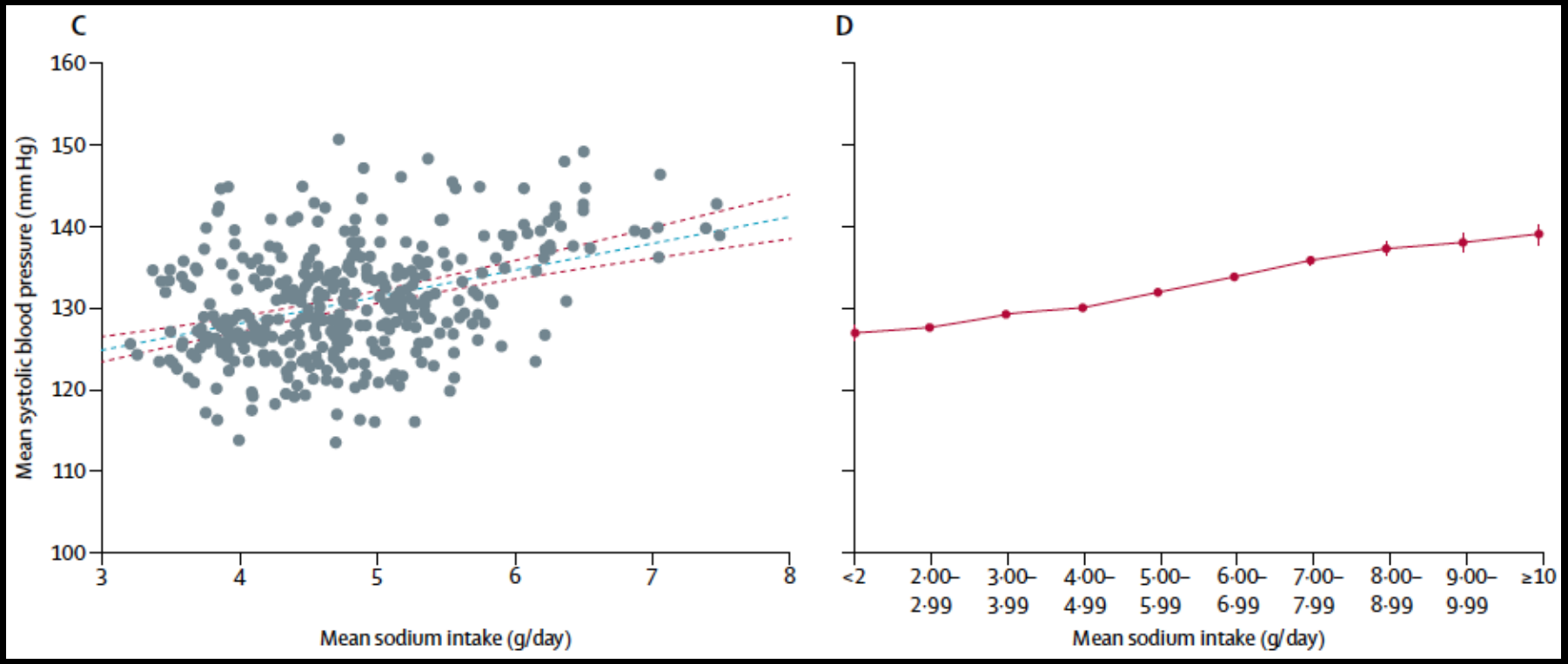

B Estimated Potassium Excretion and Risk of Death from Any Cause
Odds Ratio
3.60
2.60
2.20
1.80
1.40
1.20
1.00
0.80
0.60
0.40
0
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
Potassium Excretion (g/day)
No. of Events 0 75 362 641 537 261 71 24
No. at Risk 6 1730 12,526 31,466 30,956 17,171 6128 1507


C Estimated Potassium Excretion and Risk of Major Cardiovascular Events
Odds Ratio
3.60
2.60
2.20
1.80
1.40
1.20
1.00
0.80
0.60
0.40
0
0.50
1.00
1.50
2.00
2.50
3.00
3.50
4.00
Potassium Excretion (g/day)
No. of Events 0 41 241 623 586 334 129 23
No. at Risk 6 1730 12,526 31,466 30,956 17,171 6128 1507

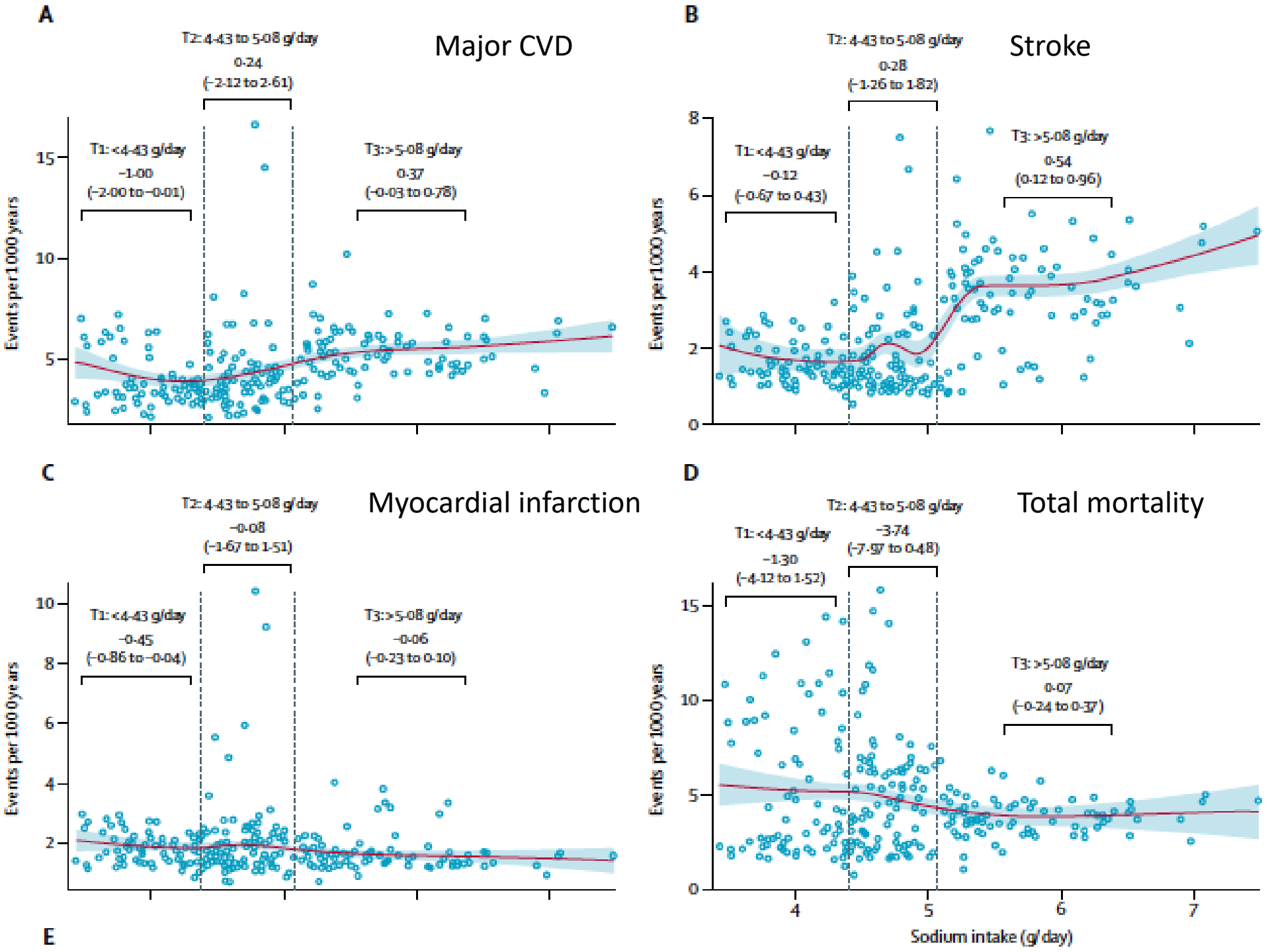
Urinary sodium excretion, blood pressure, cardiovascular disease, and mortality: a community-level prospective epidemiological cohort study

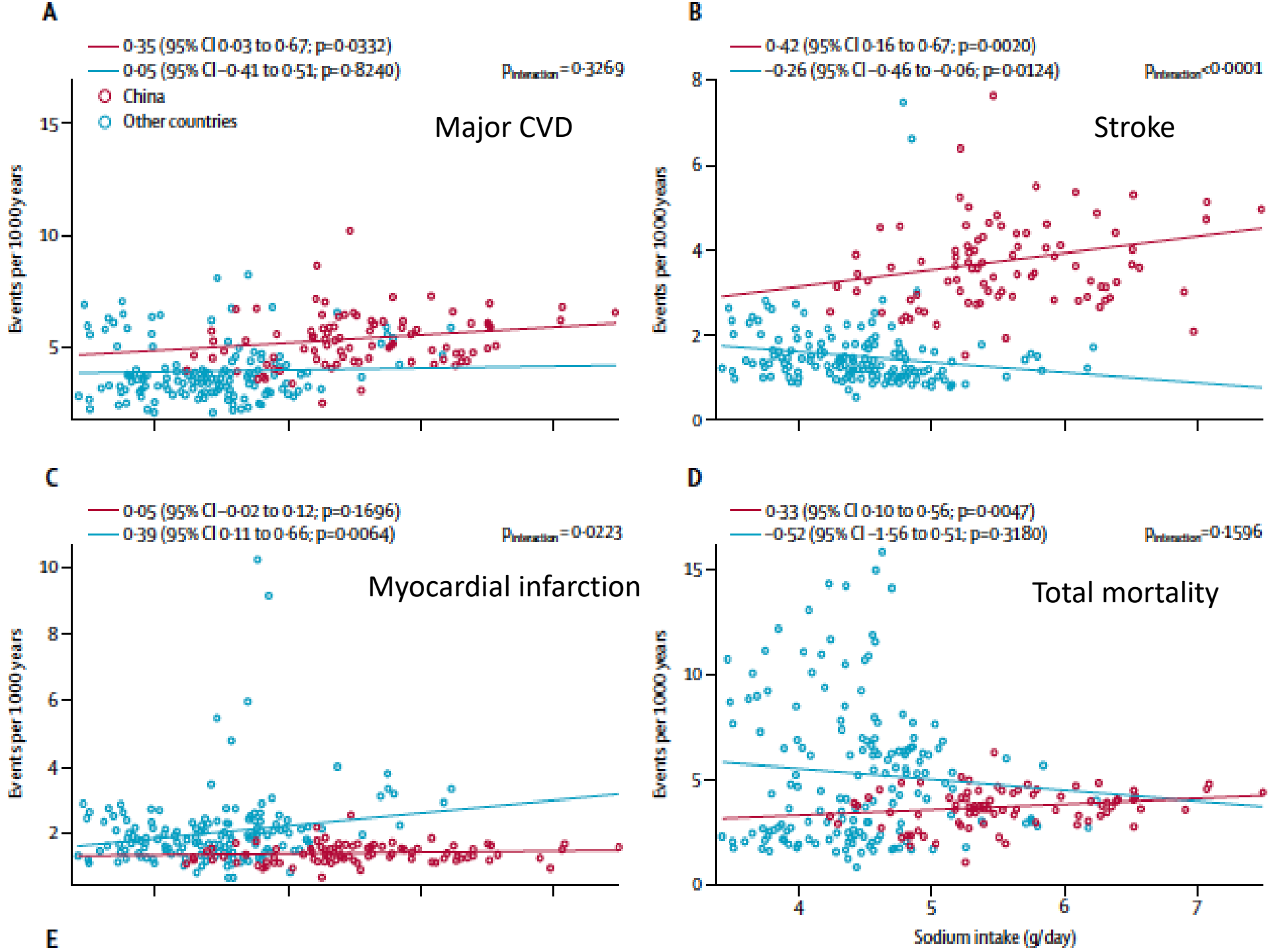
- Prospective Urban and Rural Epidemiology study ongoing in 21 countries.
- Analysis done in 18 countries
- Participants 35–70 years without CV disease
- Morning fasting urine to estimate 24 h Na and K excretion
- The community-level associations between sodium and potassium intake and BP in 369 communities (>50 participants) and CV disease and mortality in 255 communities (>100 participants) was assessed
- 95 767 participants were assessed for BP and 82 544 for CV outcomes with a median follow-up 8.1 years
- 80% of the communities in China had a mean sodium intake greater than 5 g/day (12.5 g NaCl), whereas in other countries 224 (84%) of 266 communities had a mean intake of 3–5 g/day (7.5-12.5 g NaCl).

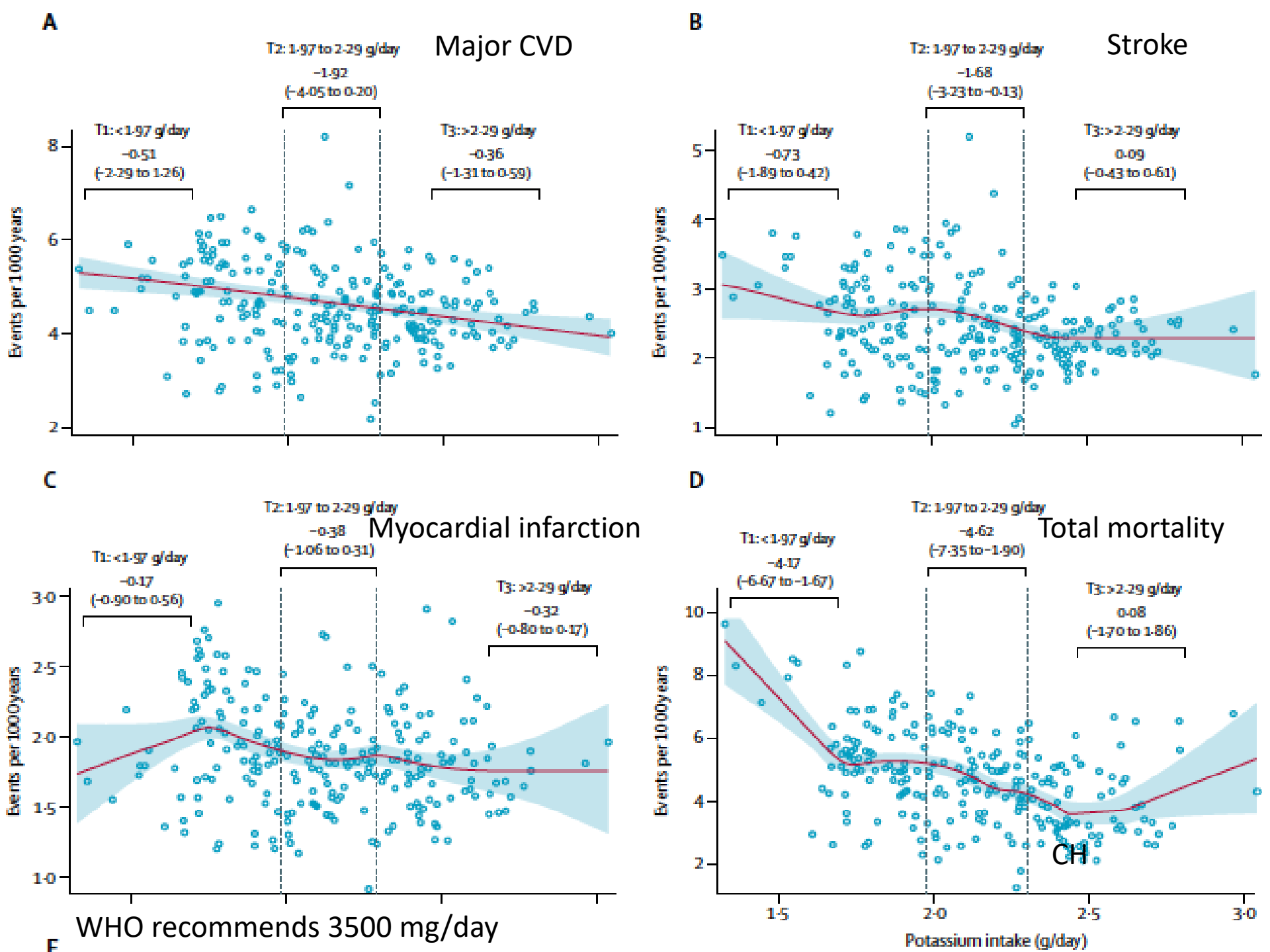
A. Mente et al. Lancet 2018; 392: 496–506



2.9 mmHg systolic BP increase per 1 g increase in sodium intake (positive associations were only seen among the communities in the highest tertile of sodium intake)


A
Major CVD
T2: 4-43 to 5-08 g/day
0·24
(−2·12 to 2·61)
T1: <4-43 g/day
−1·00
(−2·00 to −0·01)
T3: >5-08 g/day
0·37
(−0·03 to 0·78)
Events per 1000 years
B
Stroke
T2: 4-43 to 5-08 g/day
0·28
(−1·26 to 1·82)
T1: <4-43 g/day
−0·12
(−0·67 to 0·43)
T3: >5-08 g/day
0·54
(0·12 to 0·96)
Events per 1000 years
C
Myocardial infarction
T2: 4-43 to 5-08 g/day
−0·08
(−1·67 to 1·51)
T1: <4-43 g/day
−0·45
(−0·86 to −0·04)
T3: >5-08 g/day
−0·06
(−0·23 to 0·10)
Events per 1000 years
D
Total mortality
T2: 4-43 to 5-08 g/day
−3·74
(−7·57 to 0·48)
T1: <4-43 g/day
−1·30
(−4·12 to 1·52)
T3: >5-08 g/day
0·07
(−0·24 to 0·37)
Events per 1000 years
Sodium intake (g/day)
E


A
0·35 (95% CI 0·03 to 0·67; p=0·0332)
0·05 (95% CI −0·41 to 0·51; p=0·8240)
$P_{interaction}$=0·3269
China
Other countries
Major CVD
Events per 1000 years
B
0·42 (95% CI 0·16 to 0·67; p=0·0020)
−0·26 (95% CI −0·46 to −0·06; p=0·0124)
$P_{interaction}$<0·0001
Stroke
Events per 1000 years
C
0·05 (95% CI −0·02 to 0·12; p=0·1696)
0·39 (95% CI 0·11 to 0·66; p=0·0064)
$P_{interaction}$=0·0223
Myocardial infarction
Events per 1000 years
D
0·33 (95% CI 0·10 to 0·56; p=0·0047)
−0·52 (95% CI −1·56 to 0·51; p=0·3180)
$P_{interaction}$=0·1596
Total mortality
Events per 1000 years
Sodium intake (g/day)
E


A
Major CVD
T2: 1·97 to 2·29 g/day
−1·92
(−4·05 to 0·20)
T1: <1·97 g/day
−0·51
(−2·29 to 1·26)
T3: >2·29 g/day
−0·36
(−1·31 to 0·59)
Events per 1000 years
B
Stroke
T2: 1·97 to 2·29 g/day
−1·68
(−3·23 to −0·13)
T1: <1·97 g/day
−0·73
(−1·89 to 0·42)
T3: >2·29 g/day
0·09
(−0·43 to 0·61)
Events per 1000 years
C
Myocardial infarction
T2: 1·97 to 2·29 g/day
−0·38
(−1·06 to 0·31)
T1: <1·97 g/day
−0·17
(−0·90 to 0·56)
T3: >2·29 g/day
−0·32
(−0·80 to 0·17)
Events per 1000 years
D
Total mortality
T2: 1·97 to 2·29 g/day
−4·62
(−7·35 to −1·90)
T1: <1·97 g/day
−4·17
(−6·67 to −1·67)
T3: >2·29 g/day
0·08
(−1·70 to 1·86)
Events per 1000 years
CH
Potassium intake (g/day)
WHO recommends 3500 mg/day

Authors interpretation

- association with CV disease and strokes only in communities with mean intake > 5 g/day.
- A community strategy of sodium reduction in other countries might not be appropriate.

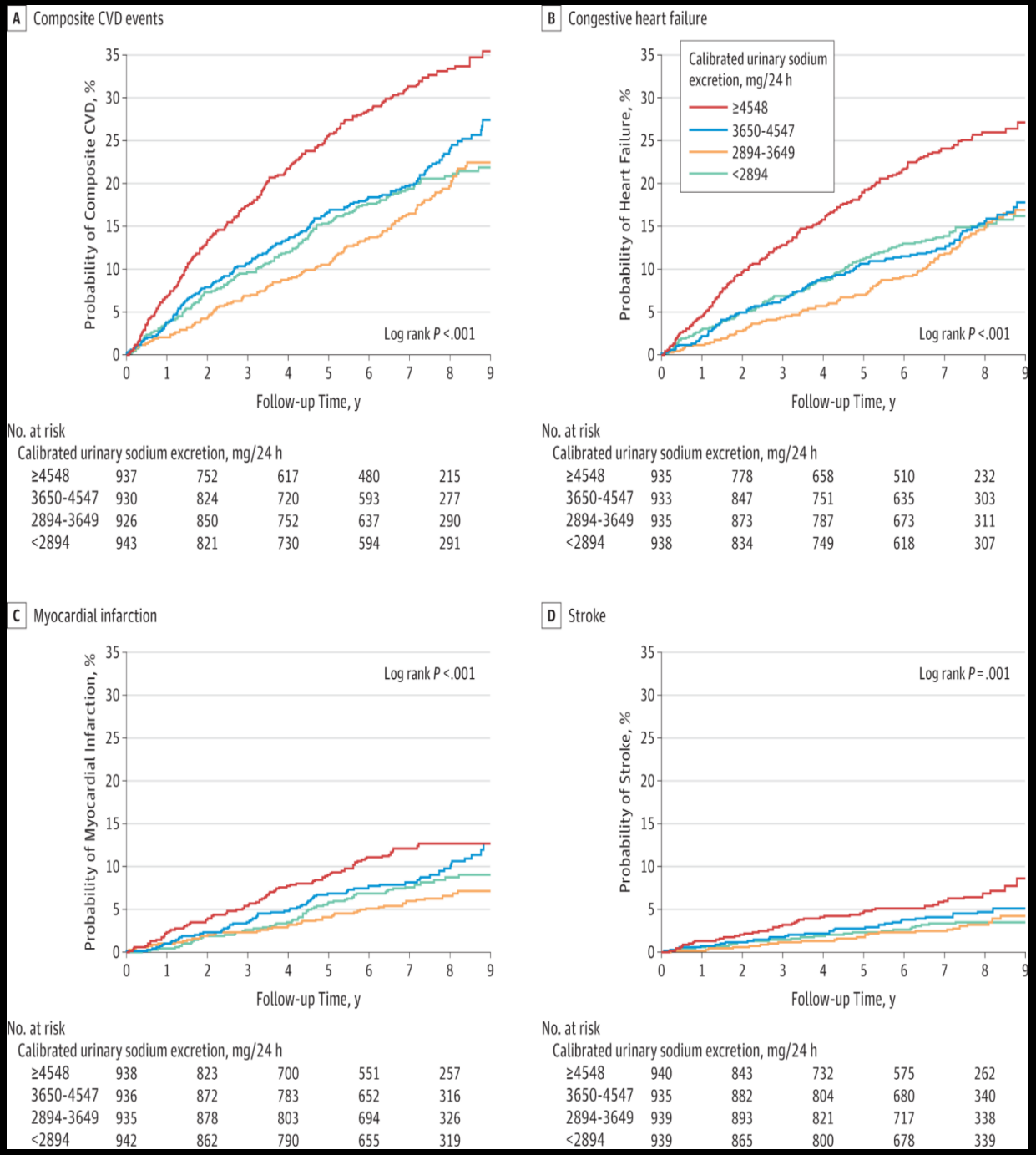
Original Investigation

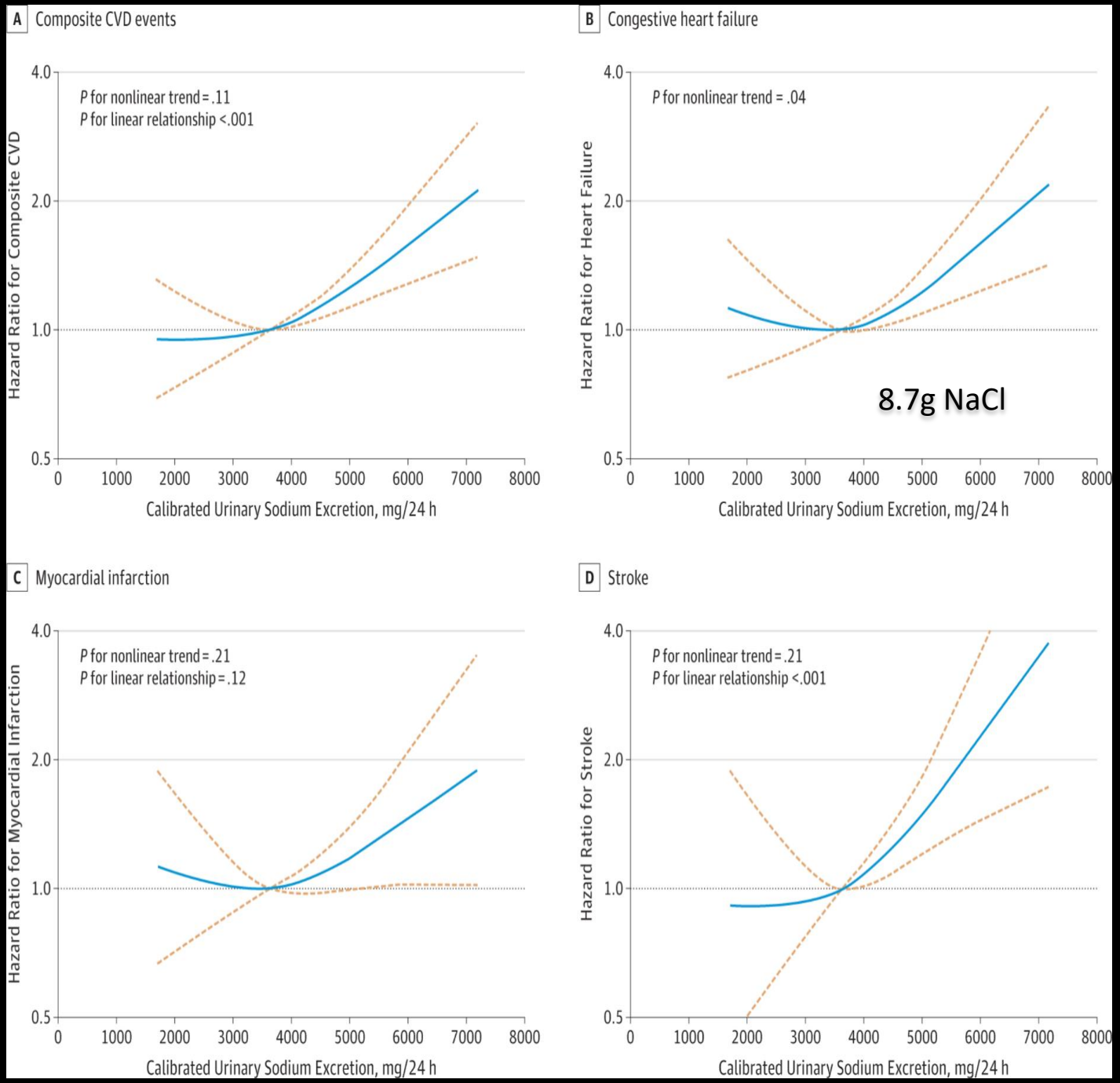
Sodium Excretion and the Risk of Cardiovascular Disease in Patients With Chronic Kidney Disease

Katherine T. Mills, PhD; Jing Chen, MD; Wei Yang, PhD; Lawrence J. Appel, MD; John W. Kusek, PhD; Arnold Alper, MD; Patrice Delafontaine, MD; Martin G. Keane, MD; Emile Mohler, MD; Akinlolu Ojo, MD, PhD; Mahboob Rahman, MD; Ana C. Ricardo, MD; Elsayed Z. Soliman, MD; Susan Steigerwalt, MD; Raymond Townsend, MD; Jiang He, MD, PhD; for the Chronic Renal Insufficiency Cohort (CRIC) Study Investigators

3757 CKD Patients According to Quartile of 24-Hour Urinary Sodium Excretion

Mills et al. JAMA. 2016;315(20): 2200-2210


A Composite CVD events
Probability of Composite CVD, %
Log rank P <.001
Follow-up Time, y
No. at risk
Calibrated urinary sodium excretion, mg/24 h
≥4548 937 752 617 480 215
3650-4547 930 824 720 593 277
2894-3649 926 850 752 637 290
<2894 943 821 730 594 291
B Congestive heart failure
Calibrated urinary sodium excretion, mg/24 h
≥4548
3650-4547
2894-3649
<2894
Probability of Heart Failure, %
Log rank P <.001
Follow-up Time, y
No. at risk
Calibrated urinary sodium excretion, mg/24 h
≥4548 935 778 658 510 232
3650-4547 933 847 751 635 303
2894-3649 935 873 787 673 311
<2894 938 834 749 618 307
C Myocardial infarction
Probability of Myocardial Infarction, %
Log rank P <.001
Follow-up Time, y
No. at risk
Calibrated urinary sodium excretion, mg/24 h
≥4548 938 823 700 551 257
3650-4547 936 872 783 652 316
2894-3649 935 878 803 694 326
<2894 942 862 790 655 319
D Stroke
Probability of Stroke, %
Log rank P = .001
Follow-up Time, y
No. at risk
Calibrated urinary sodium excretion, mg/24 h
≥4548 940 843 732 575 262
3650-4547 935 882 804 680 340
2894-3649 939 893 821 717 338
<2894 939 865 800 678 339


A Composite CVD events
P for nonlinear trend = .11
P for linear relationship <.001
Hazard Ratio for Composite CVD
Calibrated Urinary Sodium Excretion, mg/24 h
B Congestive heart failure
P for nonlinear trend = .04
Hazard Ratio for Heart Failure
Calibrated Urinary Sodium Excretion, mg/24 h
8.7g NaCl
C Myocardial infarction
P for nonlinear trend = .21
P for linear relationship = .12
Hazard Ratio for Myocardial Infarction
Calibrated Urinary Sodium Excretion, mg/24 h
D Stroke
P for nonlinear trend = .21
P for linear relationship <.001
Hazard Ratio for Stroke
Calibrated Urinary Sodium Excretion, mg/24 h

Renoprotective effects of sodium-glucose cotransporter-2 (SGLT2) inhibitors

Table 1 | Summary of primary renal endpoint trials with SGLT2 inhibitors

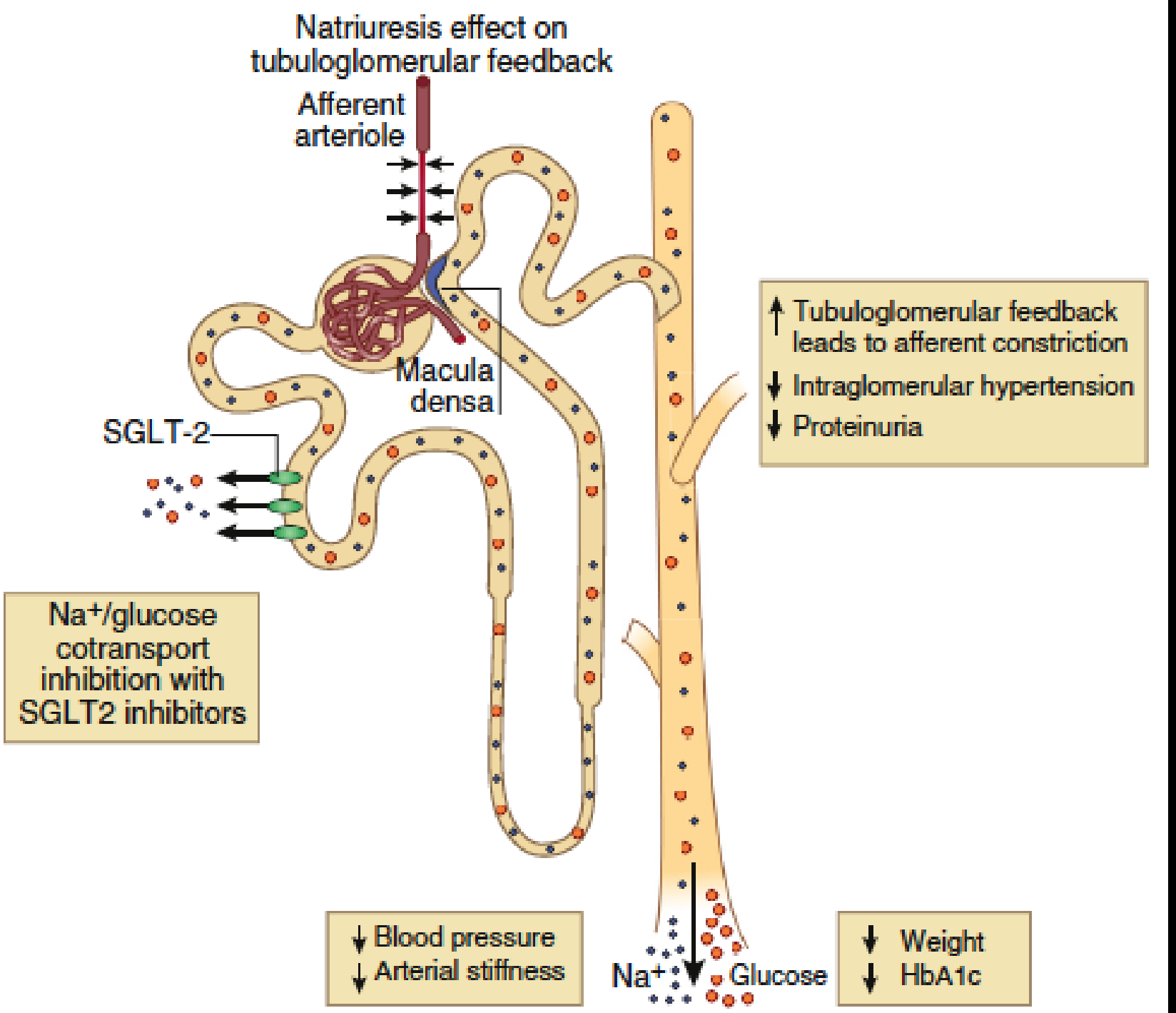
Study characteristics	CREDENCE	DAPA-CKD
Target enrollment	4200	4000
Agent	100 mg canagliflozin or matching placebo	10 mg dapagliflozin or matching placebo
Primary endpoint composite	ESKD, doubling of serum creatinine, renal or cardiovascular death	ESKD, 50% eGFR decline, renal or cardiovascular death
Main renal clinical endpoint	Composite of ESKD, doubling serum creatinine, renal death	Composite of ESKD, 50% eGFR decline, renal death
Population specifics		
Diabetes status	Type 2 diabetes	Type 2 diabetes and nondiabetic kidney disease
eGFR	≥30 to <90 ml/min per 1.73 m^2	≥25 to <75 ml/min per 1.73 m^2
UACR	>300 to ≤5000 mg/g	>200 to ≤5000 mg/g
ACE inhibition or angiotensin receptor blockade use at enrollment	Mandatory	Mandatory unless contraindicated
Cardiovascular disease history inclusion	No requirement	No requirement

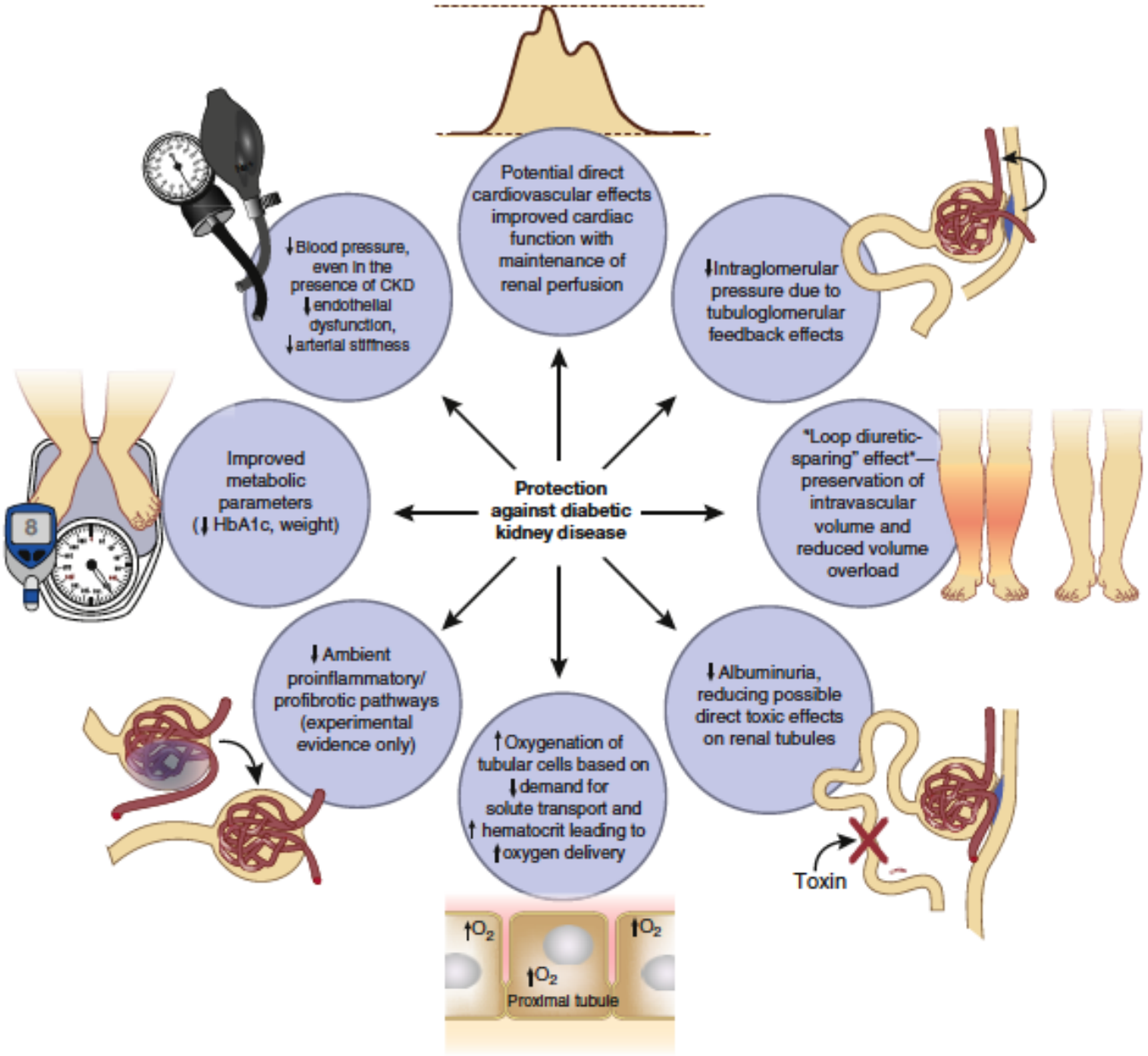
ACE, angiotensin-converting enzyme; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; SGLT2, sodium glucose cotransport-2; UACR, urine albumin-to-creatinine ratio.

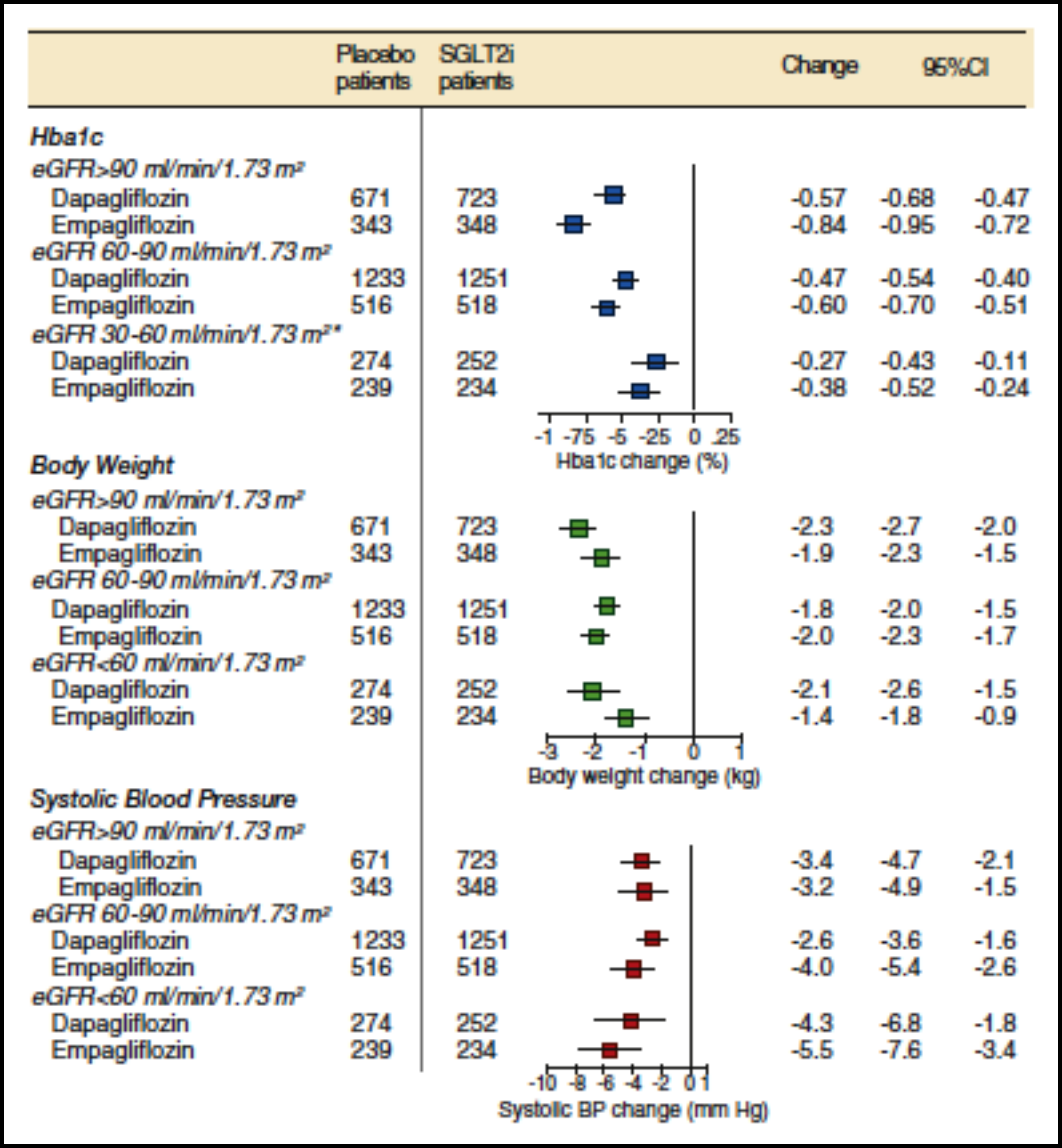
2017-2020; ongoing

07/2018 CREDENCE was halted early for efficacy

Heerspink; Kidney Int. 2018 Jul;94(1):26-39.

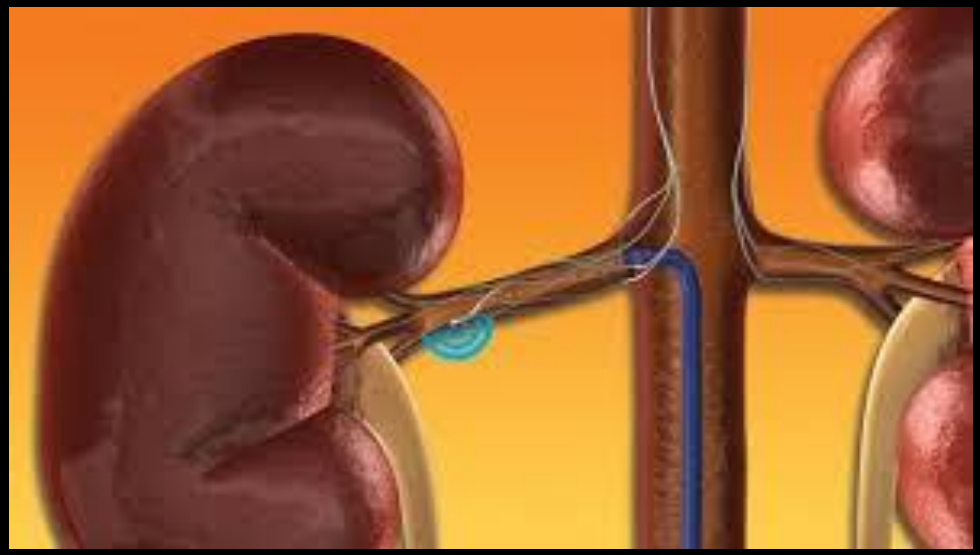

Natriuresis effect on tubuloglomerular feedback
Afferent arteriole
Macula densa
SGLT-2
Tubuloglomerular feedback leads to afferent constriction
Intraglomerular hypertension
Proteinuria
Na+/glucose cotransport inhibition with SGLT2 inhibitors
Blood pressure
Arterial stiffness
Na+
Glucose
Weight
HbA1c


Potential direct cardiovascular effects improved cardiac function with maintenance of renal perfusion
↓Blood pressure, even in the presence of CKD ↓endothelial dysfunction, ↓arterial stiffness
↓Intraglomerular pressure due to tubuloglomerular feedback effects
Improved metabolic parameters (↓HbA1c, weight)
"Loop diuretic-sparing" effect"—preservation of intravascular volume and reduced volume overload
Protection against diabetic kidney disease
↓Ambient proinflammatory/ profibrotic pathways (experimental evidence only)
↑Oxygenation of tubular cells based on ↓demand for solute transport and ↑hematocrit leading to ↑oxygen delivery
↓Albuminuria, reducing possible direct toxic effects on renal tubules
Toxin
↑O2
↑O2
↑O2
Proximal tubule



Glycemic, weight, and systolic blood pressure lowering effects of empagliflozin and dapagliflozin at chronic kidney disease stages 1, 2, and 3.

Renal denervation: one step backwards, three steps forward



Schlaich and al; Nature Reviews Nephrology, 2018 Jul 6

Percutaneous renal denervation in patients with treatment-resistant hypertension: final 3-year report of the Symplicity HTN-1 study

Henry Krum, Markus P Schlaich, Paul A Sobotka, Michael Böhm, Felix Mahfoud, Krishna Rocha-Singh, Richard Katholi, Murray D Esler

-Open-label study, 153 patients, 111 consented to follow-up for 36 months.

-Eligible patients: systolic BP > 160 mm Hg with 3 drugs, including a diuretic, at the optimum doses

-88 patients had complete data at 36 months

-Funding: Ardian LLC/Medtronic Inc.

Lancet 2014; 383: 622–29

Background

- Hypertension <-> Overactivity of the sympathetic nervous system
- Surgical sympathectomy <-> BP reduction
- Bilateral nephrectomy <-> BP reduction
- 14 clinical trials and one randomised trial (2009-2013) <-> BP lowering effect after radiofrequency ablation

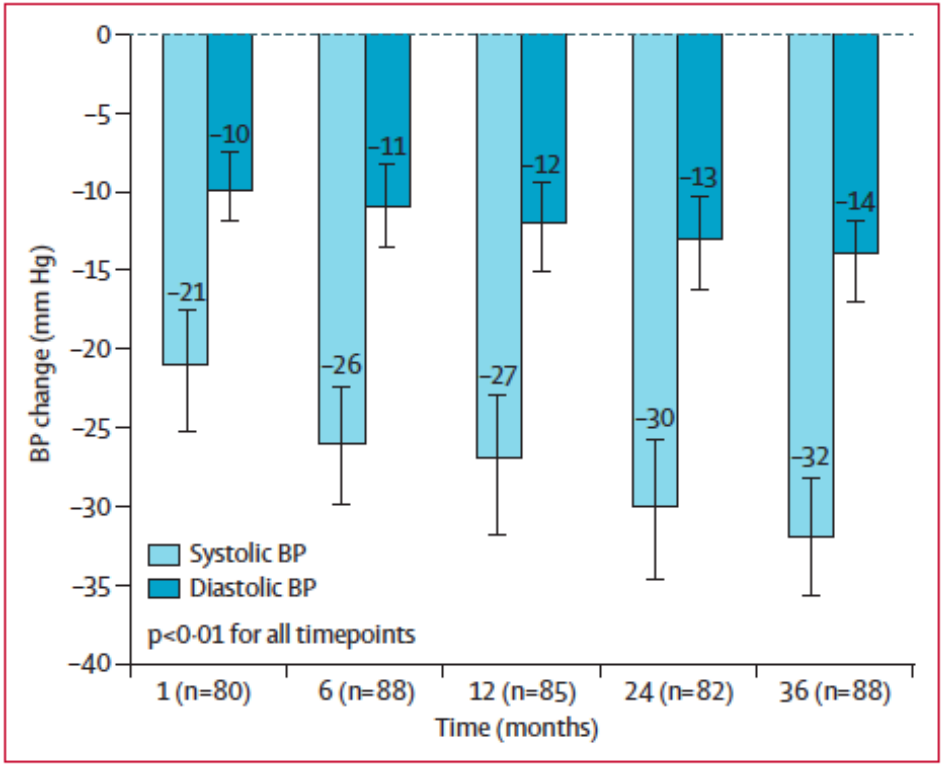


Figure 2: Change from baseline in office blood pressure in patients who completed 36 months of follow-up

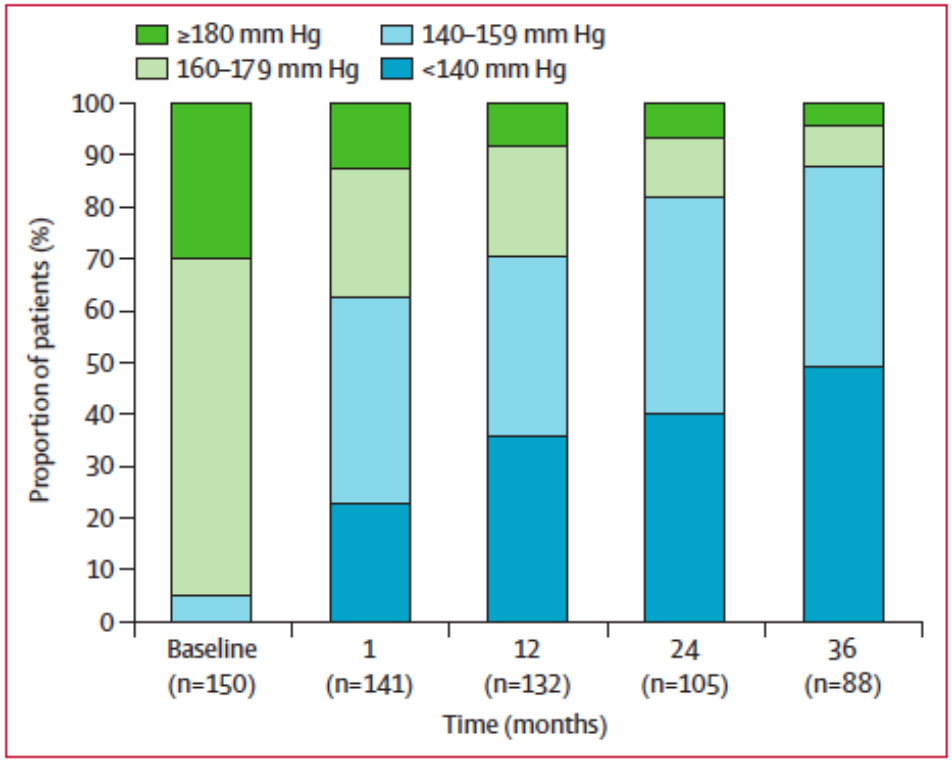
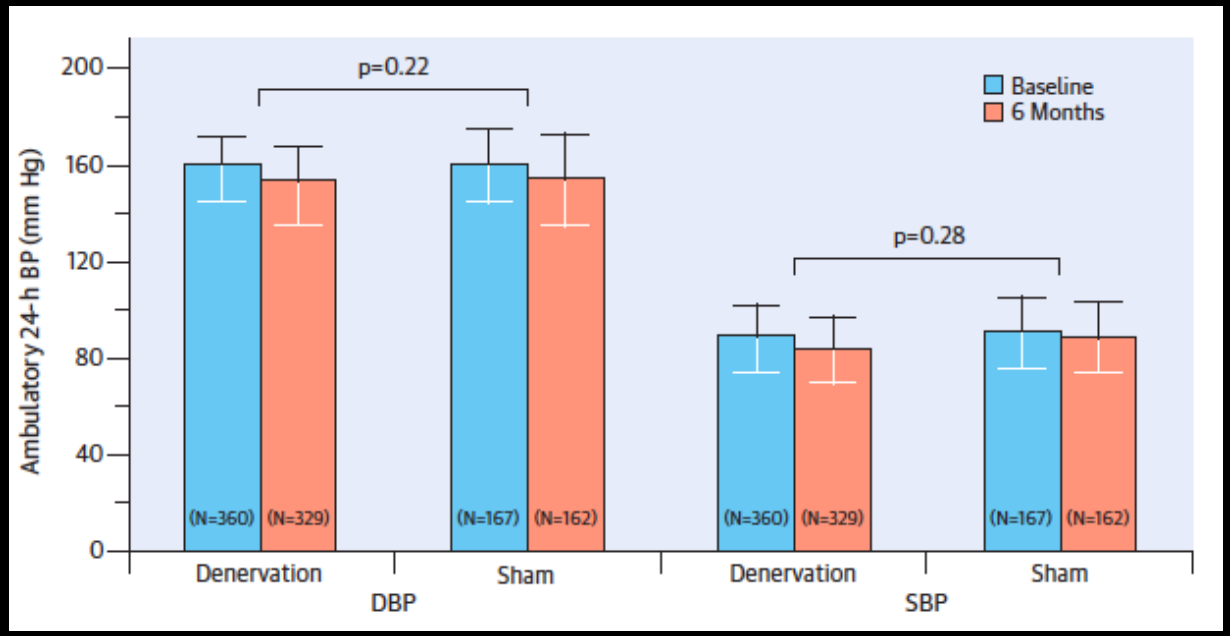


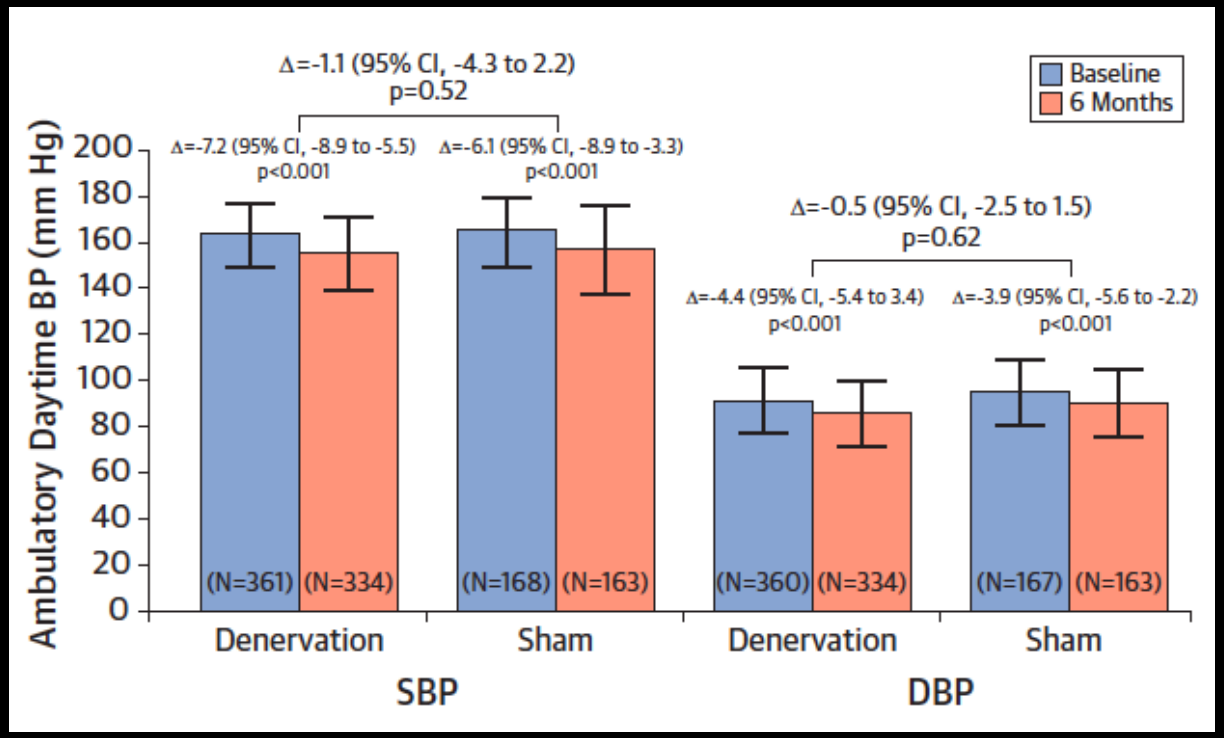
Figure 3: Distribution of changes in systolic blood pressure for all treated patients

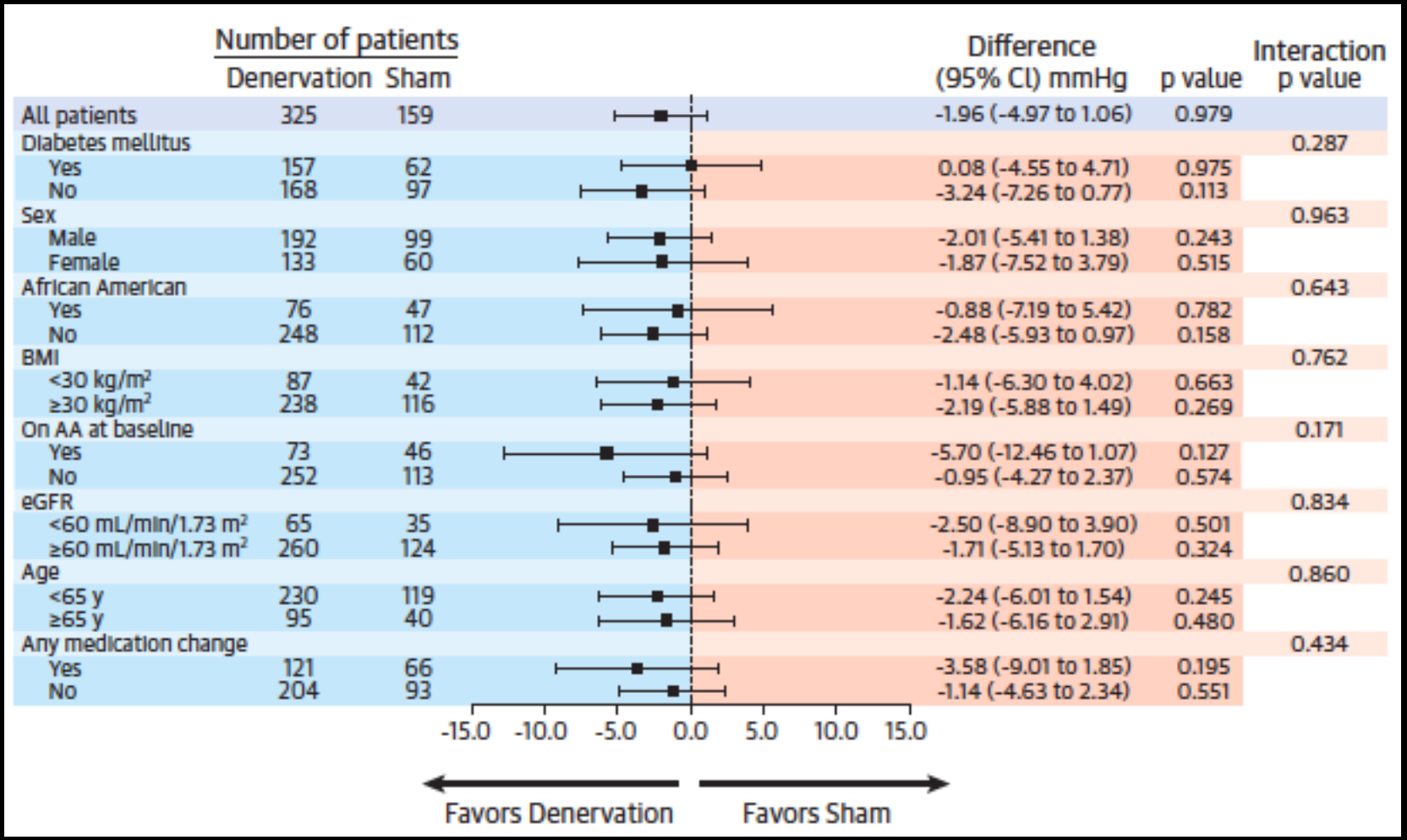
Impact of Renal Denervation on 24-Hour Ambulatory Blood Pressure
Results From SYMPLICITY HTN-3

- Prospective, blinded, randomized, sham-controlled trial
- resistant hypertension randomized 2:1 to renal denervation or sham control
- Patients were on a stable antihypertensive regimen with maximally tolerated doses of at least 3 drugs including a diuretic before randomization.
- The efficacy endpoint was a change in mean 24-h ambulatory systolic blood pressure

JACC VOL. 64, NO. 11, 2014


Ambulatory 24-h BP (mm Hg)
200
160
120
80
40
0
p=0.22
p=0.28
Baseline
6 Months
(N=360)
(N=329)
(N=167)
(N=162)
(N=360)
(N=329)
(N=167)
(N=162)
Denervation
Sham
Denervation
Sham
DBP
SBP


Δ=-1.1 (95% CI, -4.3 to 2.2)
p=0.52
Baseline
6 Months
Ambulatory Daytime BP (mm Hg)
200
180
160
140
120
100
80
60
40
20
0
Δ=-7.2 (95% CI, -8.9 to -5.5)
p<0.001
Δ=-6.1 (95% CI, -8.9 to -3.3)
p<0.001
Δ=-0.5 (95% CI, -2.5 to 1.5)
p=0.62
Δ=-4.4 (95% CI, -5.4 to 3.4)
p<0.001
Δ=-3.9 (95% CI, -5.6 to -2.2)
p<0.001
(N=361)
(N=334)
(N=168)
(N=163)
(N=360)
(N=334)
(N=167)
(N=163)
Denervation
Sham
Denervation
Sham
SBP
DBP


Number of patients
Denervation Sham
Difference (95% CI) mmHg
p value
Interaction p value
All patients 325 159 -1.96 (-4.97 to 1.06) 0.979
Diabetes mellitus 0.287
Yes 157 62 0.08 (-4.55 to 4.71) 0.975
No 168 97 -3.24 (-7.26 to 0.77) 0.113
Sex 0.963
Male 192 99 -2.01 (-5.41 to 1.38) 0.243
Female 133 60 -1.87 (-7.52 to 3.79) 0.515
African American 0.643
Yes 76 47 -0.88 (-7.19 to 5.42) 0.782
No 248 112 -2.48 (-5.93 to 0.97) 0.158
BMI 0.762
<30 kg/m² 87 42 -1.14 (-6.30 to 4.02) 0.663
≥30 kg/m² 238 116 -2.19 (-5.88 to 1.49) 0.269
On AA at baseline 0.171
Yes 73 46 -5.70 (-12.46 to 1.07) 0.127
No 252 113 -0.95 (-4.27 to 2.37) 0.574
eGFR 0.834
<60 mL/min/1.73 m² 65 35 -2.50 (-8.90 to 3.90) 0.501
≥60 mL/min/1.73 m² 260 124 -1.71 (-5.13 to 1.70) 0.324
Age 0.860
<65 y 230 119 -2.24 (-6.01 to 1.54) 0.245
≥65 y 95 40 -1.62 (-6.16 to 2.91) 0.480
Any medication change 0.434
Yes 121 66 -3.58 (-9.01 to 1.85) 0.195
No 204 93 -1.14 (-4.63 to 2.34) 0.551
-15.0 -10.0 -5.0 0.0 5.0 10.0 15.0
Favors Denervation
Favors Sham

Catheter-based renal denervation in patients with uncontrolled hypertension in the absence of antihypertensive medications (SPYRAL HTN-OFF MED): a randomised, sham-controlled, proof-of-concept trial

- multicentre, international, single-blind, randomised, sham-controlled, proof of concept trial
- drug-naive or after antihypertensive medication discontinuation
- office systolic blood pressure > 150 mm Hg and 24-h > 140 mm Hg or greater at second screening
- Renal angiography and randomly assigned to denervation or sham control
- patients, caregivers, and those assessing BP were blinded to randomisation assignments
- 24-h BP at 3 months, was compared between groups
- *Funding: Medtronic.*

Townsend, Lancet 2017; 390: 2160–70

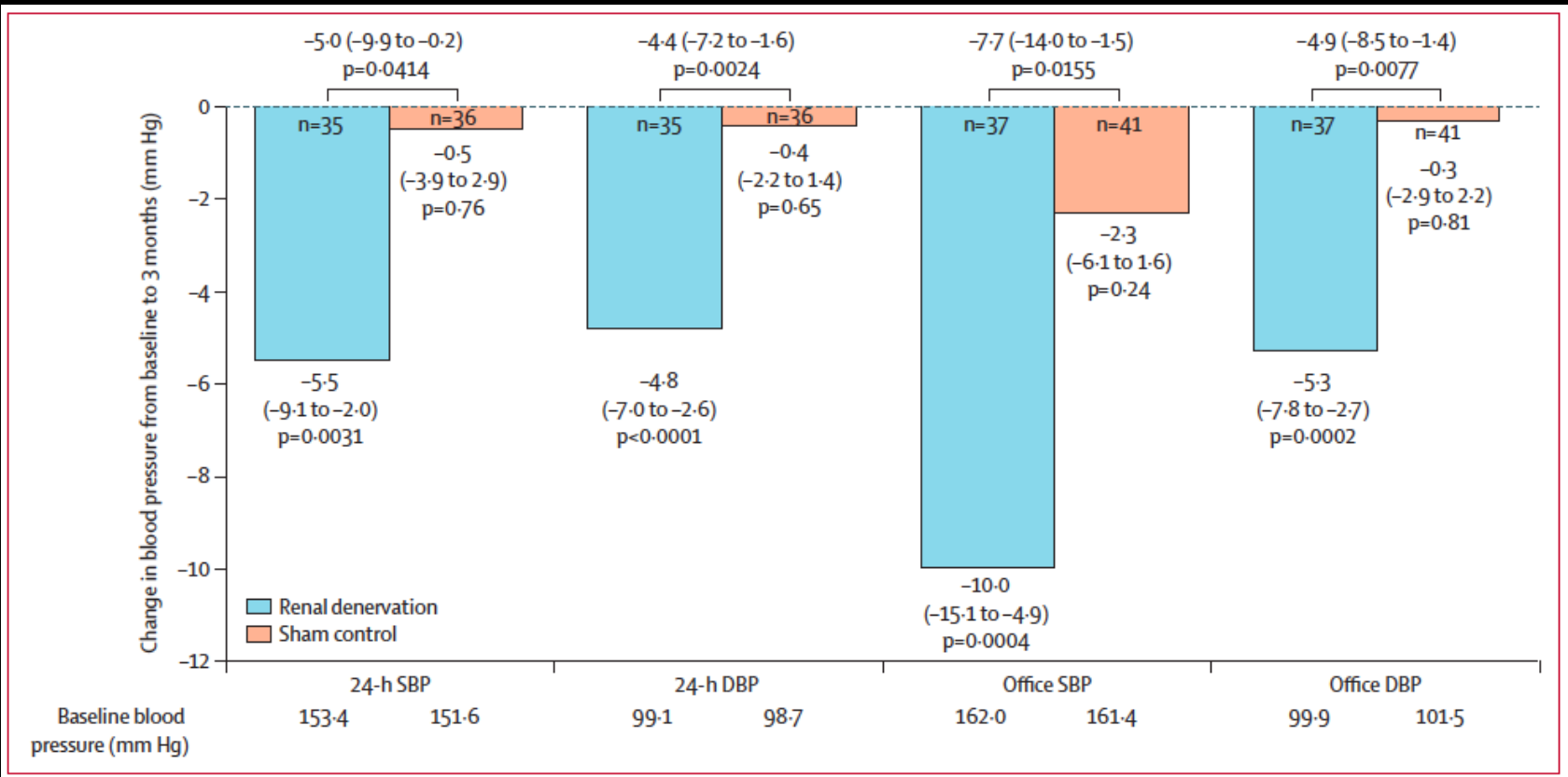


***Figure 3*: Changes at 3 months in office and ambulatory SBP and DBP for renal denervation and sham control groups**

95% CIs and unadjusted p values shown. SBP=systolic blood pressure. DBP=diastolic blood pressure.

Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomised trial

- international, randomised, single-blind, sham-control, proof-of-concept trial
- office systolic blood pressure > 150 mm Hg and 24-h > 140 mm Hg or greater at second screening
- Renal angiography and randomly assigned to denervation or sham control
- Endpoint: BPc hange from baseline based on ambulatory 24h measurements assessed at 6 months

Kandzari, Lancet 2018; 391: 2346–55

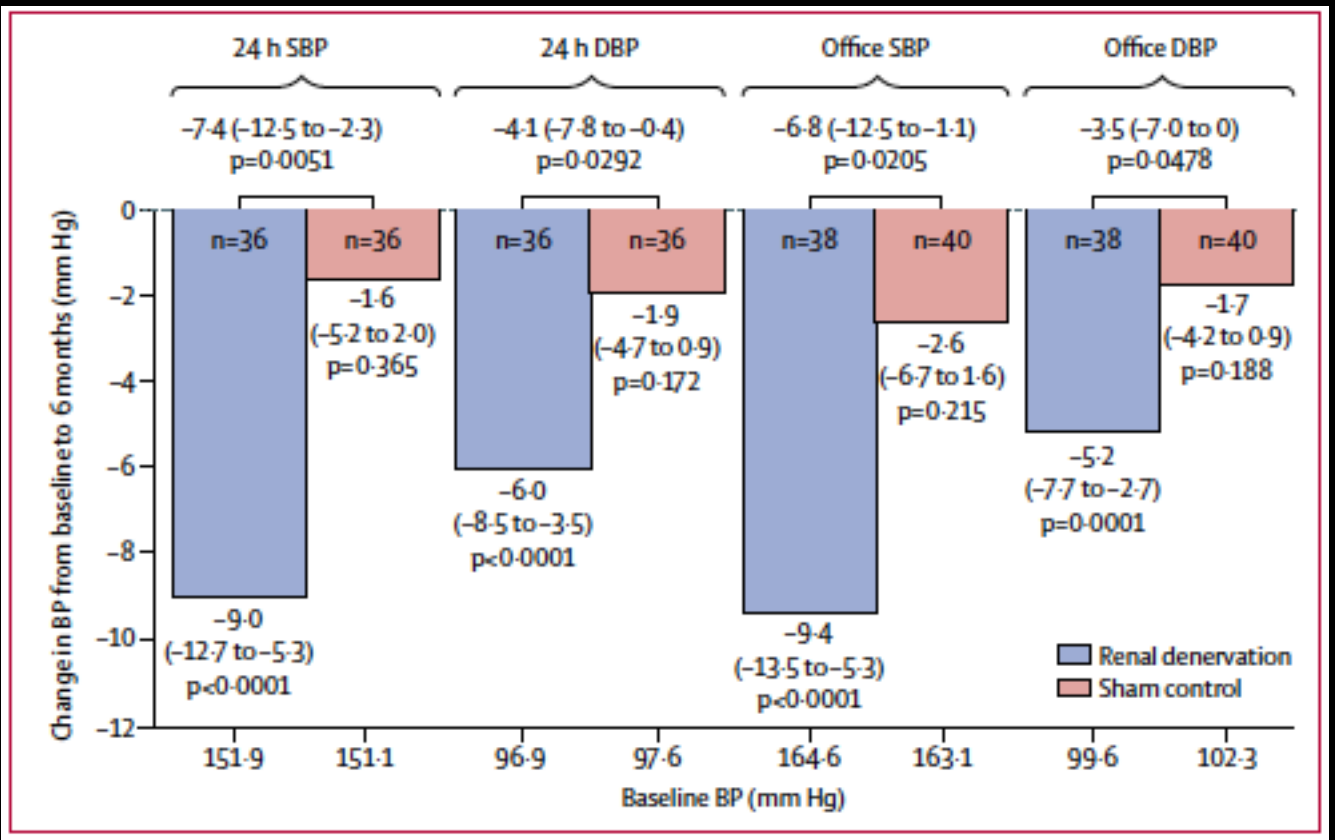


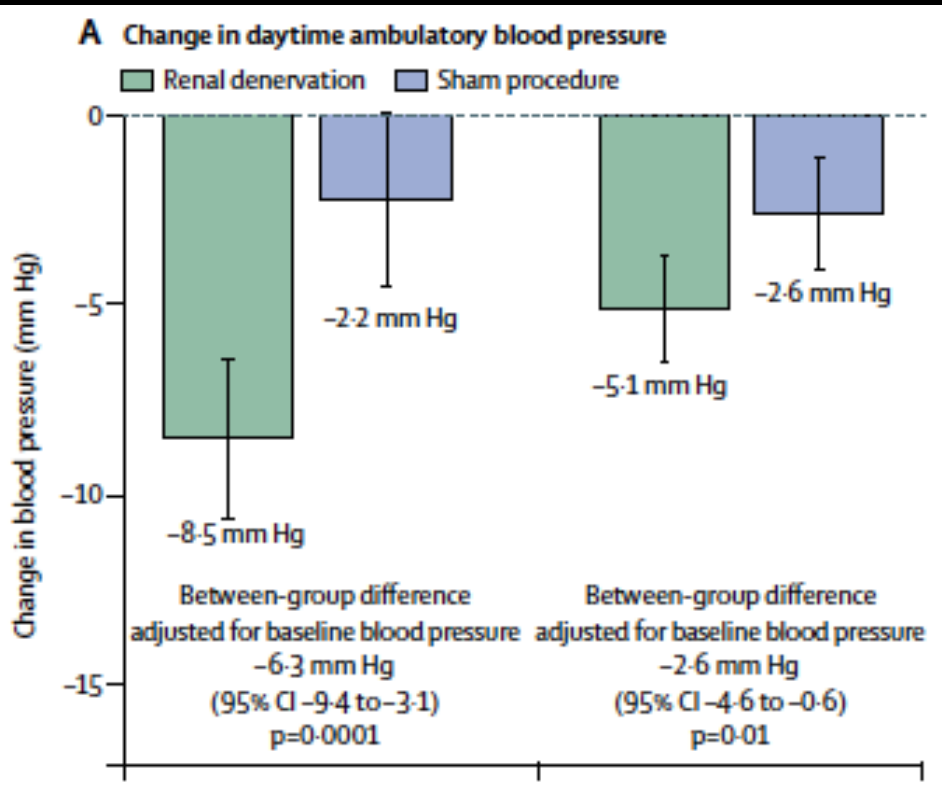
***Figure 2*: Change at 6 months in office and ambulatory systolic blood pressure and diastolic blood pressure for treatment and sham control patients**

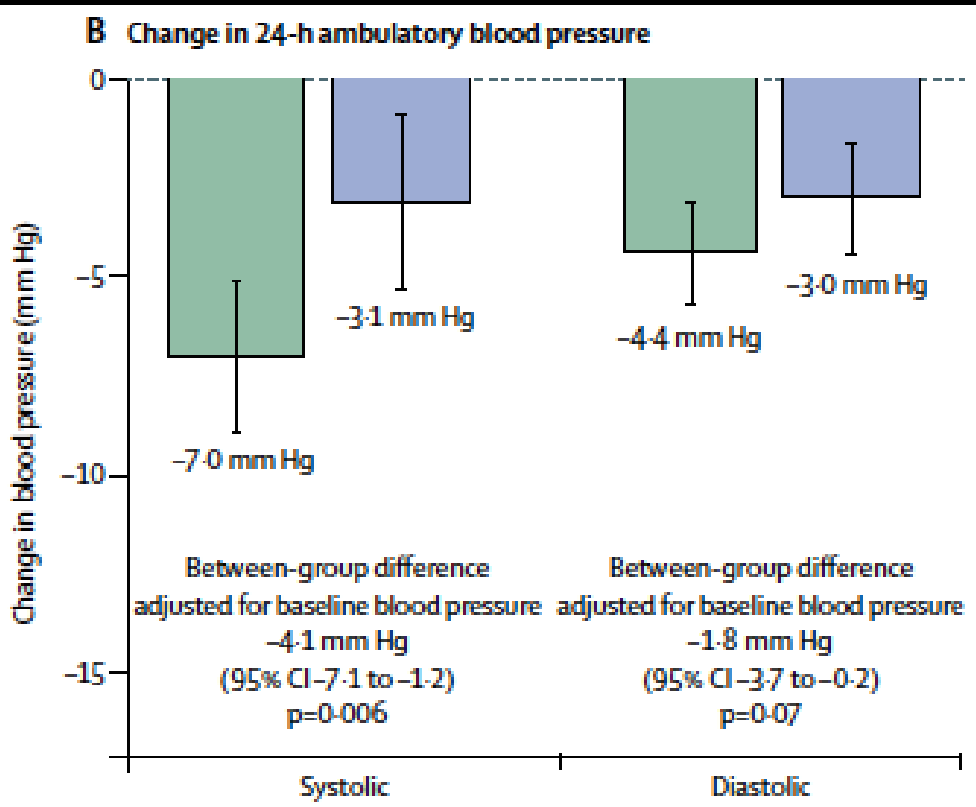
Data are mean (95% CI). SBP=systolic blood pressure. DBP=diastolic blood pressure.

Endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO): a multicentre, international, single-blind, randomised, sham-controlled trial

- multicentre, international, single-blind, randomised, sham-controlled trial
- ambulatory blood pressure greater than or equal to 135/85 mm Hg
- 4-week discontinuation of the antihypertensive medications
- randomised (1:1) to undergo renal denervation or a sham procedure consisting of renal angiography only
- change in daytime ambulatory systolic blood pressure at 2 months
- Patients were to remain off antihypertensive medications throughout the 2 months of follow-up

Azizi, Lancet 2018; 391: 2335–45


A Change in daytime ambulatory blood pressure
Renal denervation
Sham procedure
Change in blood pressure (mm Hg)
0
−5
−10
−15
−8·5 mm Hg
−2·2 mm Hg
−5·1 mm Hg
−2·6 mm Hg
Between-group difference adjusted for baseline blood pressure
−6·3 mm Hg
(95% CI −9·4 to −3·1)
p=0·0001
Between-group difference adjusted for baseline blood pressure
−2·6 mm Hg
(95% CI −4·6 to −0·6)
p=0·01


B Change in 24-h ambulatory blood pressure
Change in blood pressure (mm Hg)
0
−5
−10
−15
−7·0 mm Hg
−3·1 mm Hg
−4·4 mm Hg
−3·0 mm Hg
Between-group difference adjusted for baseline blood pressure
−4·1 mm Hg
(95% CI −7·1 to −1·2)
p=0·006
Between-group difference adjusted for baseline blood pressure
−1·8 mm Hg
(95% CI −3·7 to −0·2)
p=0·07
Systolic
Diastolic

Renal denervation: one step backwards, three steps forward

Study	Patients (*n*)	Follow-up (months)	Change in 24 h SBP (mmHg)	Change in 24 h DBP (mmHg)	Refs
SYMPLICITY HTN-3					
Denervation	364	6	−6.75 ± 15.11	−4.1 ± 9.2	[9]
Control	171		−4.79 ± 17.25	−3.1 ± 10.1	
Difference	NA		−1.96 (95% CI −4.97 to 1.06)	Not provided	
SPYRAL HTN-OFF MED					
Denervation	38	3	−5.5 (95% CI −9.1 to −2.0)	−4.8 (95% CI −7.0 to −2.6)	[1]
Control	42		−0.5 (95% CI −3.9 to 2.9)	−0.4 (95% CI −2.2 to 1.4)	
Difference	NA		−5.0 (95% CI −9.9 to −0.2)	−4.4 (95% CI −7.2 to −1.6)	
SPYRAL HTN-ON MED					
Denervation	38	6	−9.0 (95% CI −12.7 to −5.3)	−6.0 (95% CI −8.5 to −3.5)	[2]
Control	42		−1.6 (95% CI −5.2 to 2.0)	−1.9 (95% CI −4.7 to 0.9)	
Difference	NA		−7.4 (95% CI −12.5 to −2.3)	−4.1 (95% CI −7.8 to −0.4)	
RADIANCE-HTN SOLO					
Denervation	74	2	−7.0 ± 8.6	−4.4 ± 5.8	[3]
Control	72		−3.1 ± 9.7	−3.0 ± 6.1	
Difference	NA		−4.1 (95% CI −7.1 to −1.2)	−1.8 (95% CI −3.7 to −0.2)	

Markus P. Schlaich and George L. Bakris; Nature Reviews Nephrology, 2018 Jul 6

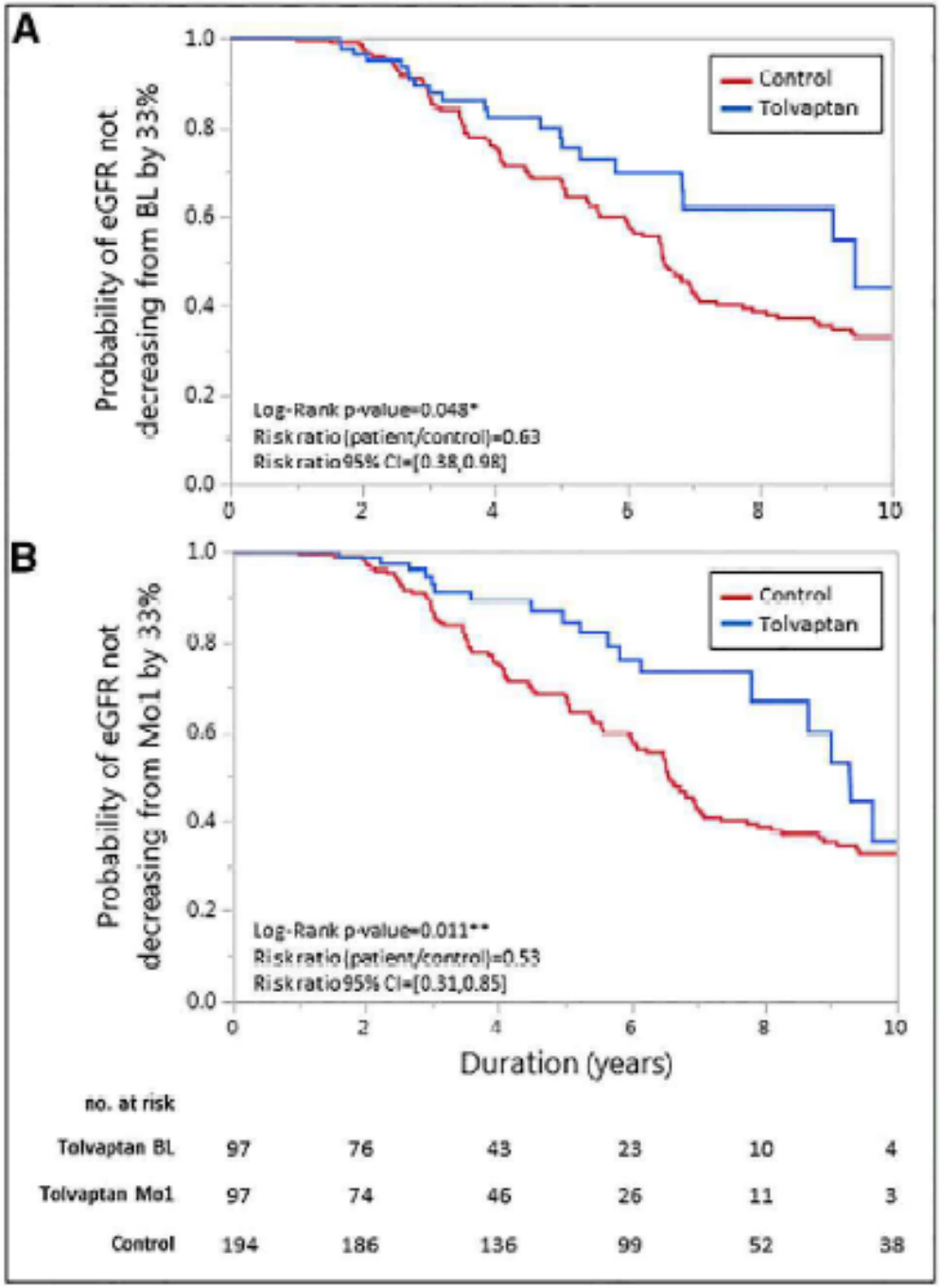
Conclusions

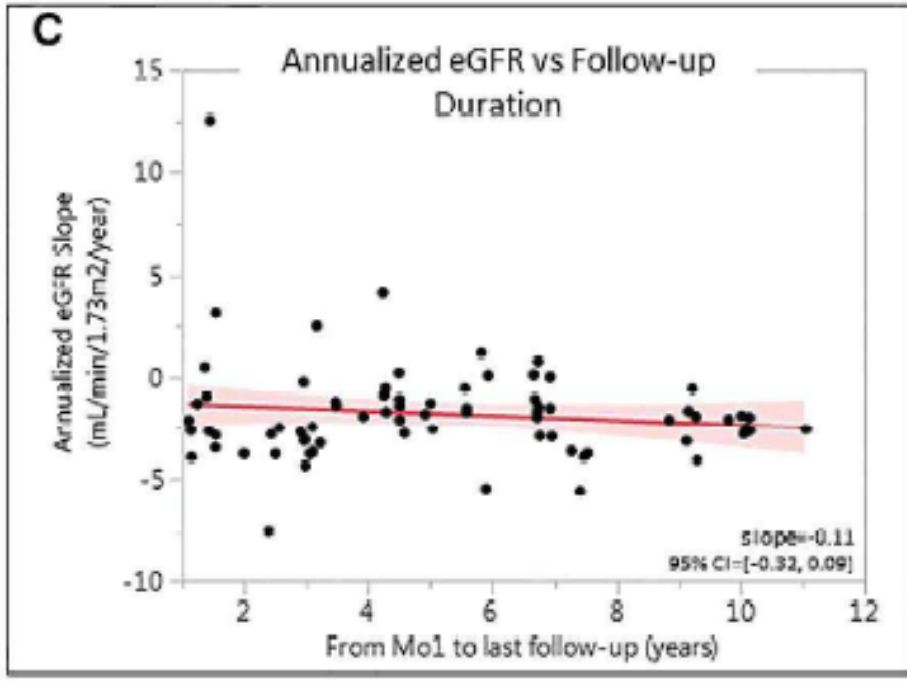
- Larger studies are required to explore the benefits not only to lower BP, but also to improve CV outcomes.
- Importantly, in all trials conducted thus far renal denervation has had a favourable safety profile.
- The saga of renal denervation as a tool to reduce cardiovascular risk factors continues

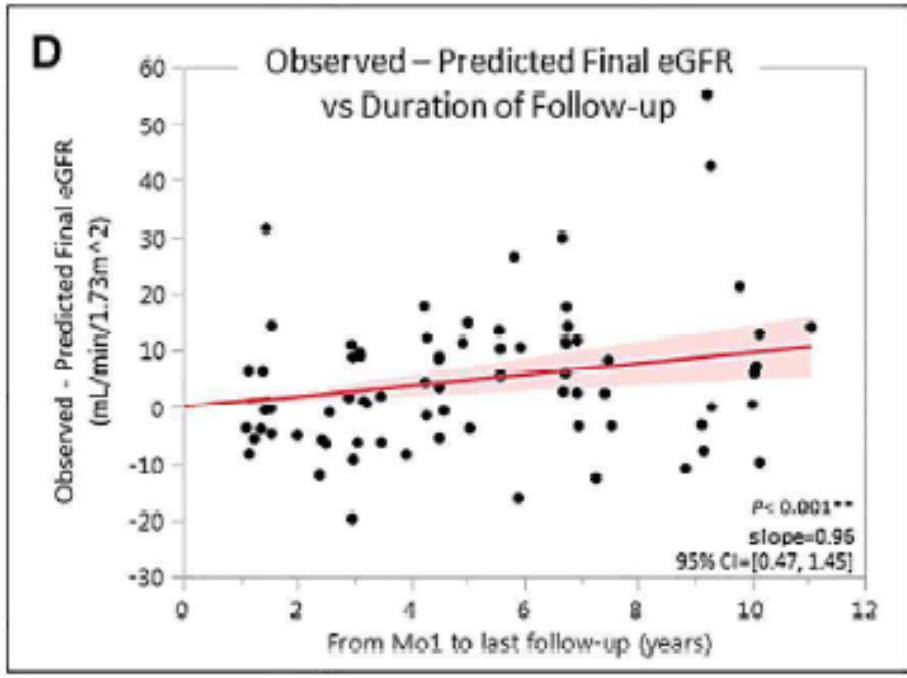
Long-Term Administration of Tolvaptan in Autosomal Dominant Polycystic Kidney Disease

- Patients participating in TEMPO an REPRISE trials at the Mayo Clinic
- 97 patients treated for ≥1 year (mean±SD, 4.6±2.8; range, 1.1-11.2) were analyzed using three approaches: (*1*) comparison of eGFR slopes and outcome (*2*) Stability of eGFR slopes (*3*) comparison of observed and predicted eGFRs
- Patients had lower eGFR slopes (-2.20ml/min per year) compared with controls (mean±SD, -3.50 ml/min per year; $P<0.001$); annualized eGFR slopes of patients treated with tolvaptan did not change during follow-up and differences between observed and predicted eGFRs at last follow-up increased with duration of treatment.

Edwards et al. Clin J Am Soc Nephrol. 2018 Aug 7;13(8):1153-1161


A
Probability of eGFR not decreasing from BL by 33%
Control
Tolvaptan
Log-Rank p-value=0.048*
Risk ratio (patient/control)=0.63
Risk ratio 95% CI=[0.38,0.98]
B
Probability of eGFR not decreasing from Mo1 by 33%
Control
Tolvaptan
Log-Rank p-value=0.011**
Risk ratio (patient/control)=0.53
Risk ratio 95% CI=[0.31,0.85]
Duration (years)
no. at risk
Tolvaptan BL 97 76 43 23 10 4
Tolvaptan Mo1 97 74 46 26 11 3
Control 194 186 136 99 52 38

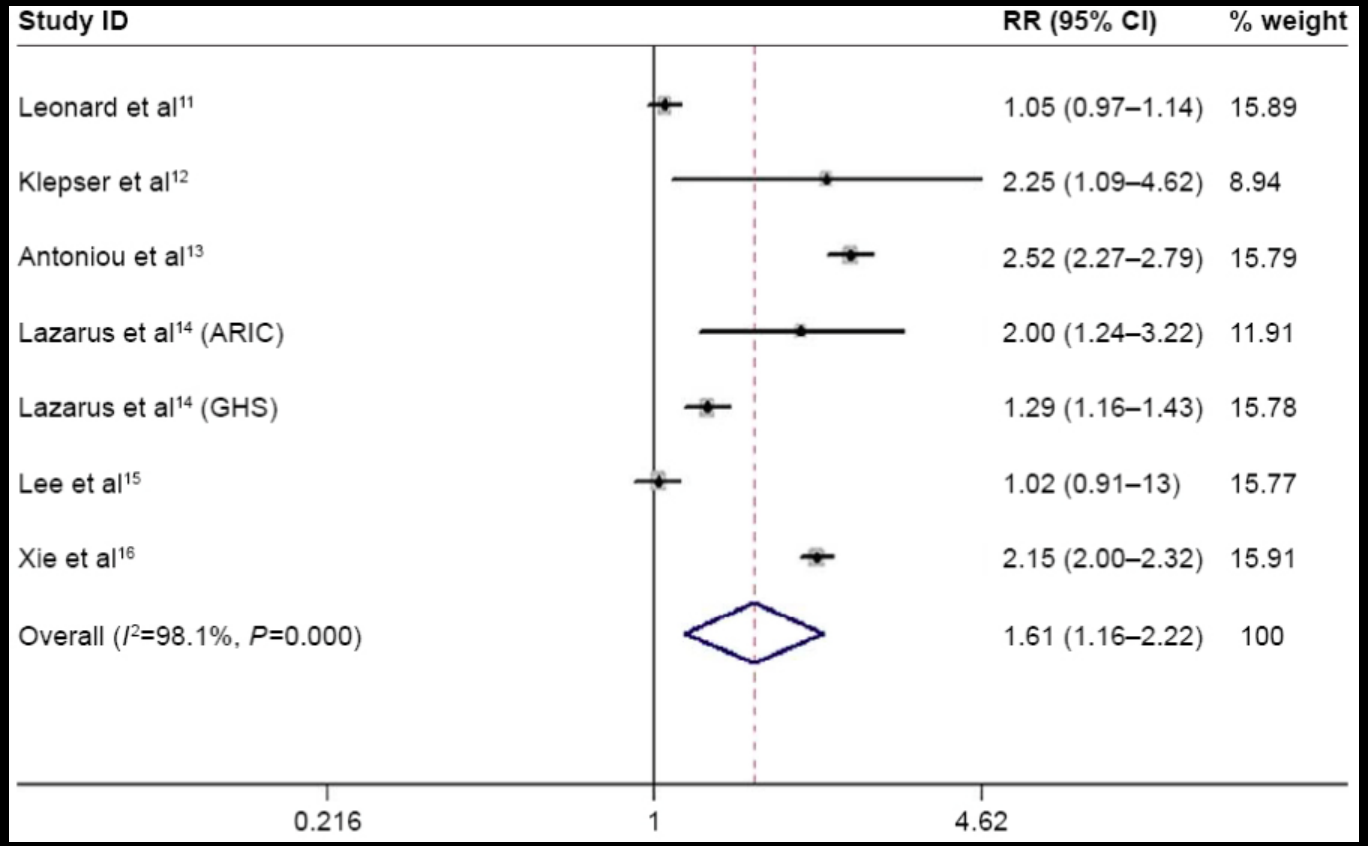

C
Annualized eGFR vs Follow-up Duration
Annualized eGFR Slope (mL/min/1.73m2/year)
slope=-0.11
95% CI=[-0.32, 0.09]
From Mo1 to last follow-up (years)


D
Observed – Predicted Final eGFR vs Duration of Follow-up
Observed - Predicted Final eGFR (mL/min/1.73m^2)
P< 0.001**
slope=0.96
95% CI=[0.47, 1.45]
From Mo1 to last follow-up (years)

Proton-pump inhibitors use, and risk of acute kidney injury: a meta-analysis of observational studies

7 observational studies (f5 cohort and 2case–control) and a total of 513,696 cases of PPI use among 2,404,236 participants were included in the meta-analysis

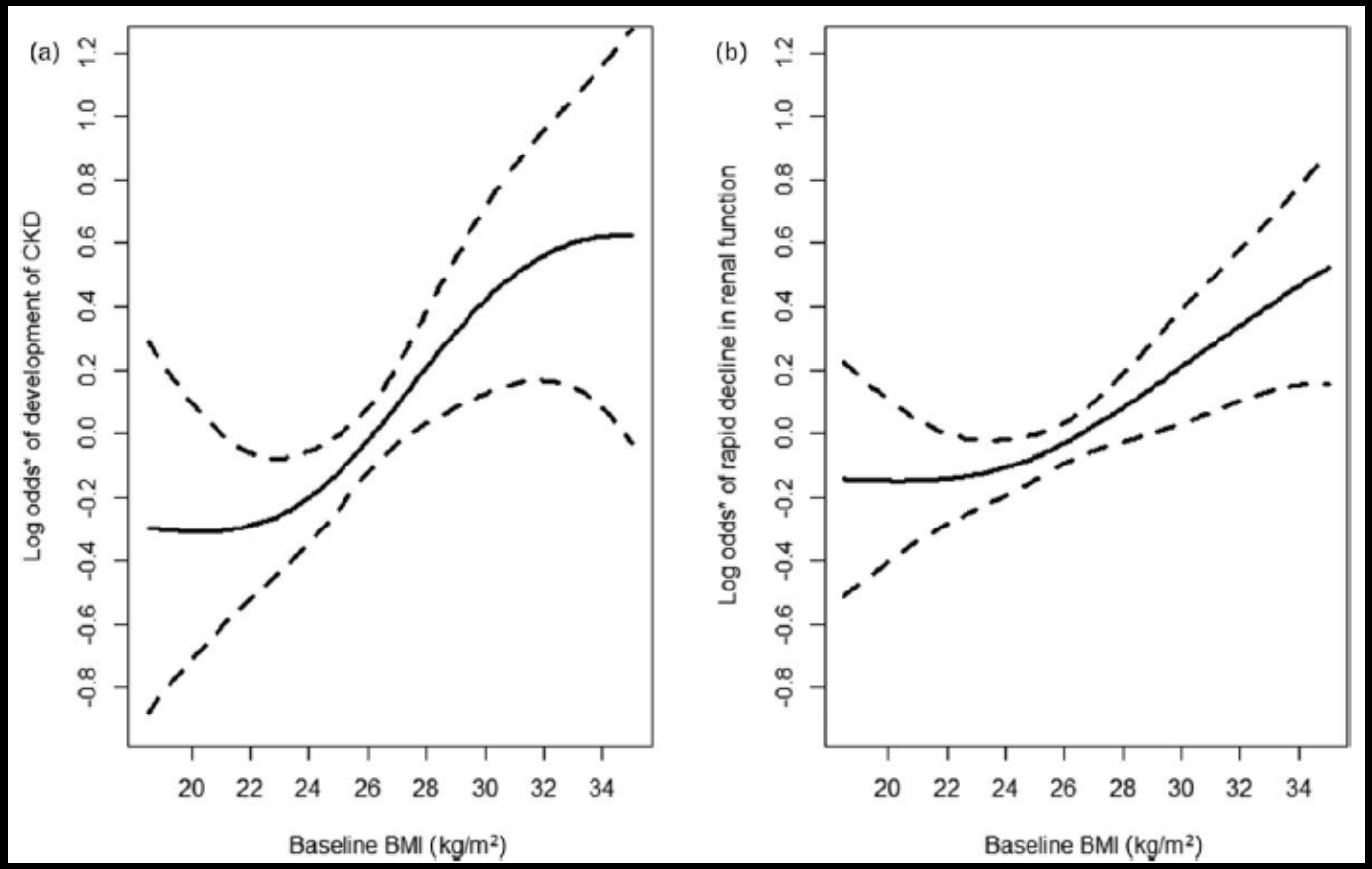
44,973 patients. At admission, comparing internal medicine vs. surgery departments, 44.9 vs. 23.3% of patients were already treated with a PPI. Eur J Intern Med. 2018 Apr;50:52-59



The pooled adjusted RR of AKI in patients with PPIs use was 1.61 (95% CI: 1.16–2.22; I^2=98.1%)

Yang et al. Drug Des Devel Ther. 2017 Apr 24;11:1291-1299

BMI is associatedwith the development of chronic kidney diseases in hypertensive patients with normal renal function

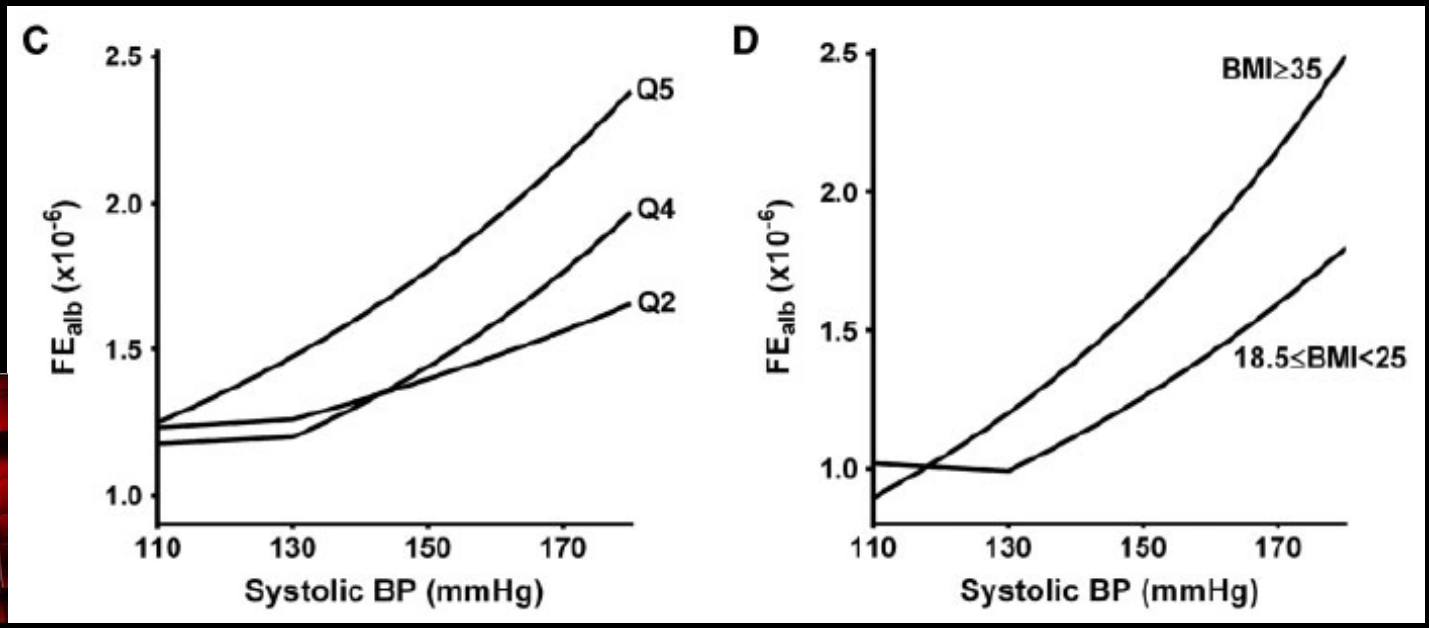


12 672 hypertensive patients with eGFR > 60 ml/min from the renal sub-study of the China Stroke Primary Prevention Trial (CSPPT); median follow-up of 4.4 years,

Xie et al. Journal of Hypertension 2018, 36:000–000

Obesity modulates the association between systolic blood pressure and albuminuria

US National Health and Nutrition Examination Survey 1999–2010 cohorts (N. 23’710). Associations between sBP and albuminuria were examined across strata of waist circumference



Effects of obesity on the threshold from which increasing systolic BP is accompanied by increasing albumin excretion.

Fotheringham et al Nephrol Dial Transplant (2018) 33: 607–613

Take home messages

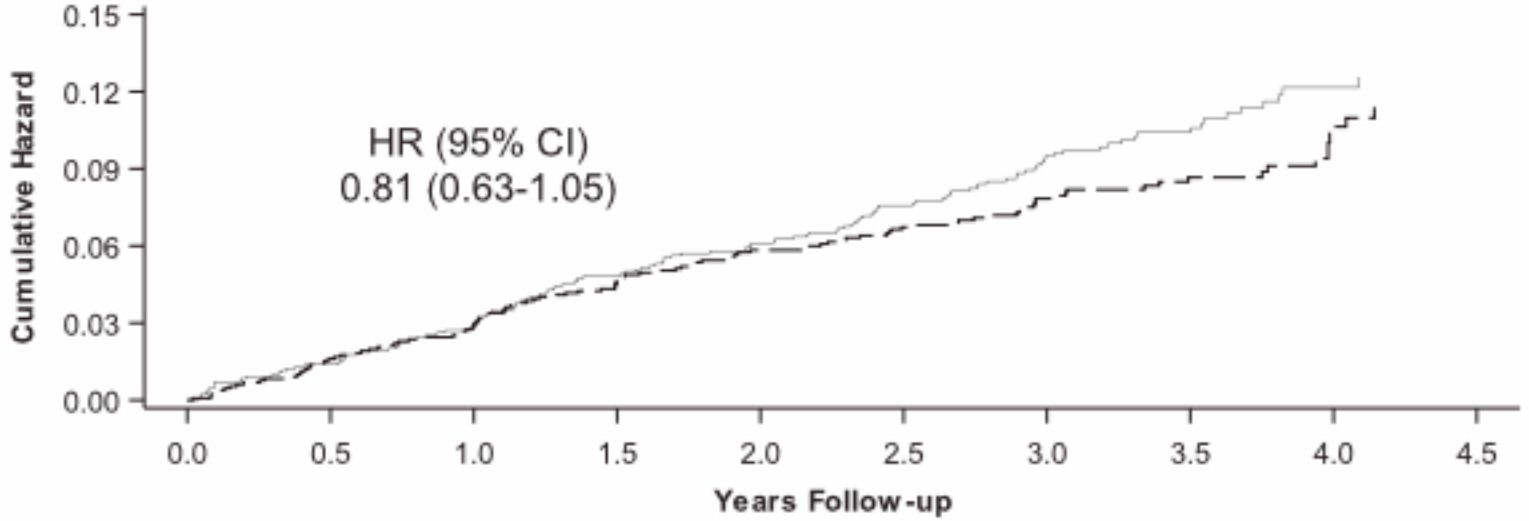
- Less sodium and more potassium
- SGLT2 inhibitors and renal endpoints in CKD
- Renal denervation is not dead
- Tolvaptan can be prescribed in ADPKD
- Less PPI
- Less obesity

Effects of Intensive BP Control in CKD

- Subgroup analyses of outcomes in participants with baseline CKD in the Systolic Blood Pressure Intervention Trial (SPRINT)
- BP target of <120 mm Hg (intensive group; *n*=1330) or <140 mm Hg (standard group; *n*=1316)
- follow-up of 3.3 years
- primary composite CV outcome in 112 intensive group and 131 standard group CKD participants HR 0.81; 95% CI 0.63 to 1.05). The intensive group also had a lower rate of all-cause death (HR 0.72; 95% CI, 0.53 to 0.99)
- the intensive group had a slightly higher rate of change in eGFR (-0.47 versus -0.32 ml/min per year; *P*<0.03)

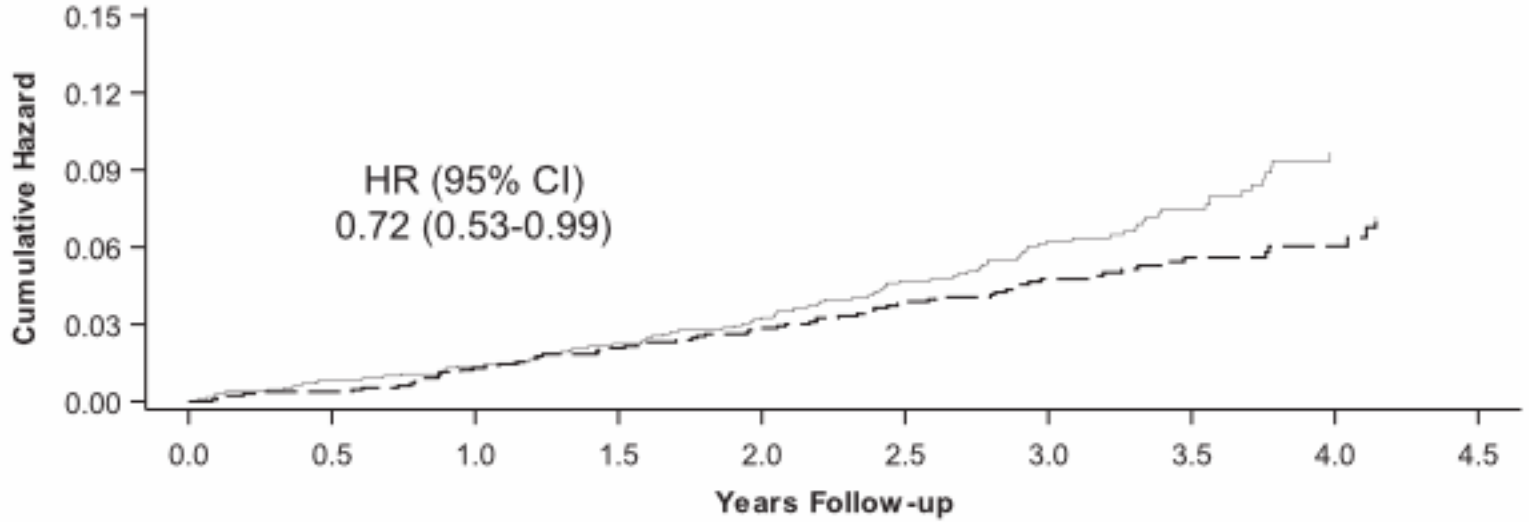
Cheung et al. J Am Soc Nephrol. 2017 Sep;28(9):2812-2823

A

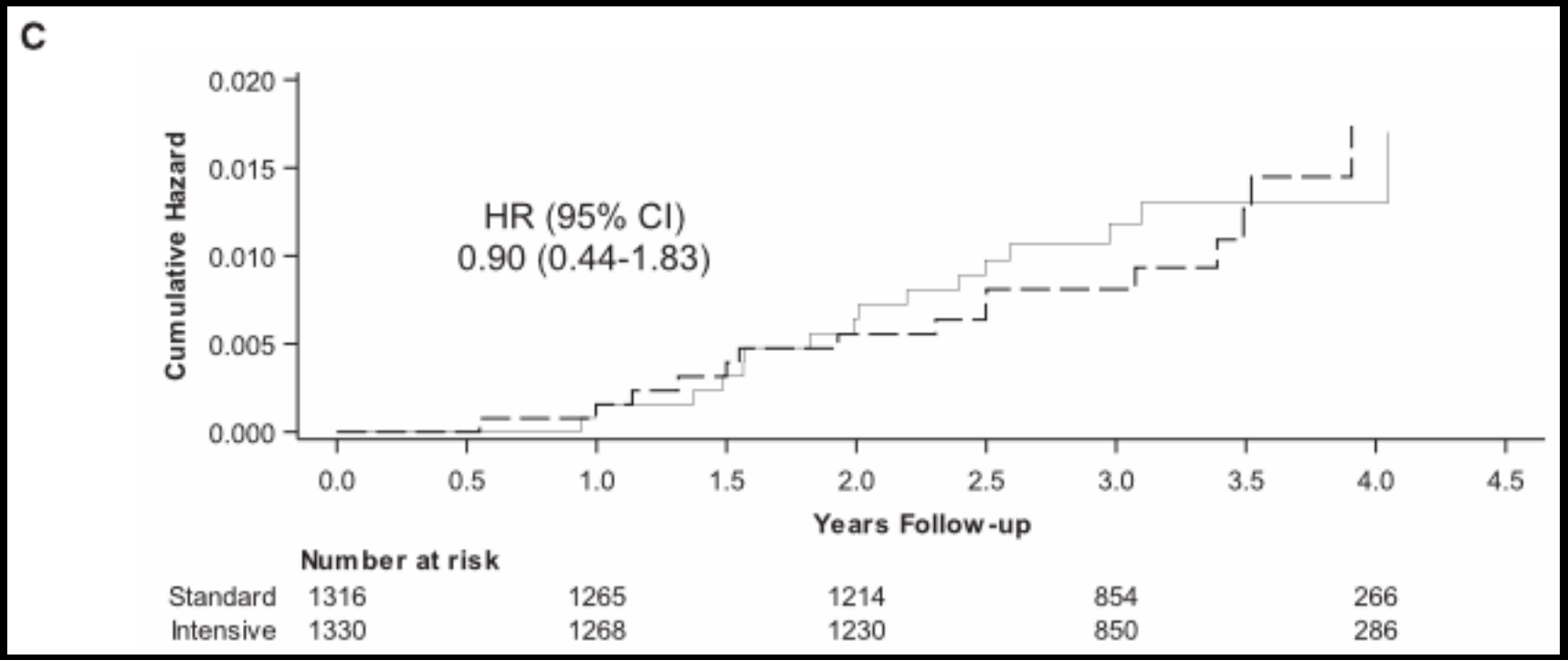


Number at risk					
Standard	1316	1241	1164	801	245
Intensive	1330	1243	1181	808	278

B



Number at risk					
Standard	1316	1277	1227	865	269
Intensive	1330	1279	1244	859	295



Panel A shows the primary CV outcome, defined as the composite of myocardial infarction, acute coronary syndrome, stroke, acute decompensated heart failure, and death from cardiovascular causes. Panel B shows the all-cause death outcome. Panel C shows the main kidney outcome, defined as the composite of a decrease in eGFR of 50% from baseline (confirmed by repeat testing 90 days later) or the development of ESRD. The broken lines depict the intensive group; the solid lines depict the standard group

hypertension management in CKD

A SPRINT to the finish, or just the beginning? Implications of the SPRINT results for nephrologists

Michael V. Rocco[1] and Alfred K. Cheung[2]

- To minimize the risk of AKI, eGFR should be monitored after the addition of an antihypertensive agent or an increase in dose
- The escalation in treatment should be gradual with close attention to adverse events

Kidney International (2016) **89,** 261–263; http://dx.doi.org/10.1016/j.kint.2015.12.024

Managing Hypertension in Patients with CKD: A Marathon, Not a SPRINT

Glenn M. Chertow,* Srinivasan Beddhu,† Julia B. Lewis,‡ Robert D. Toto,§ and Alfred K. Cheung†

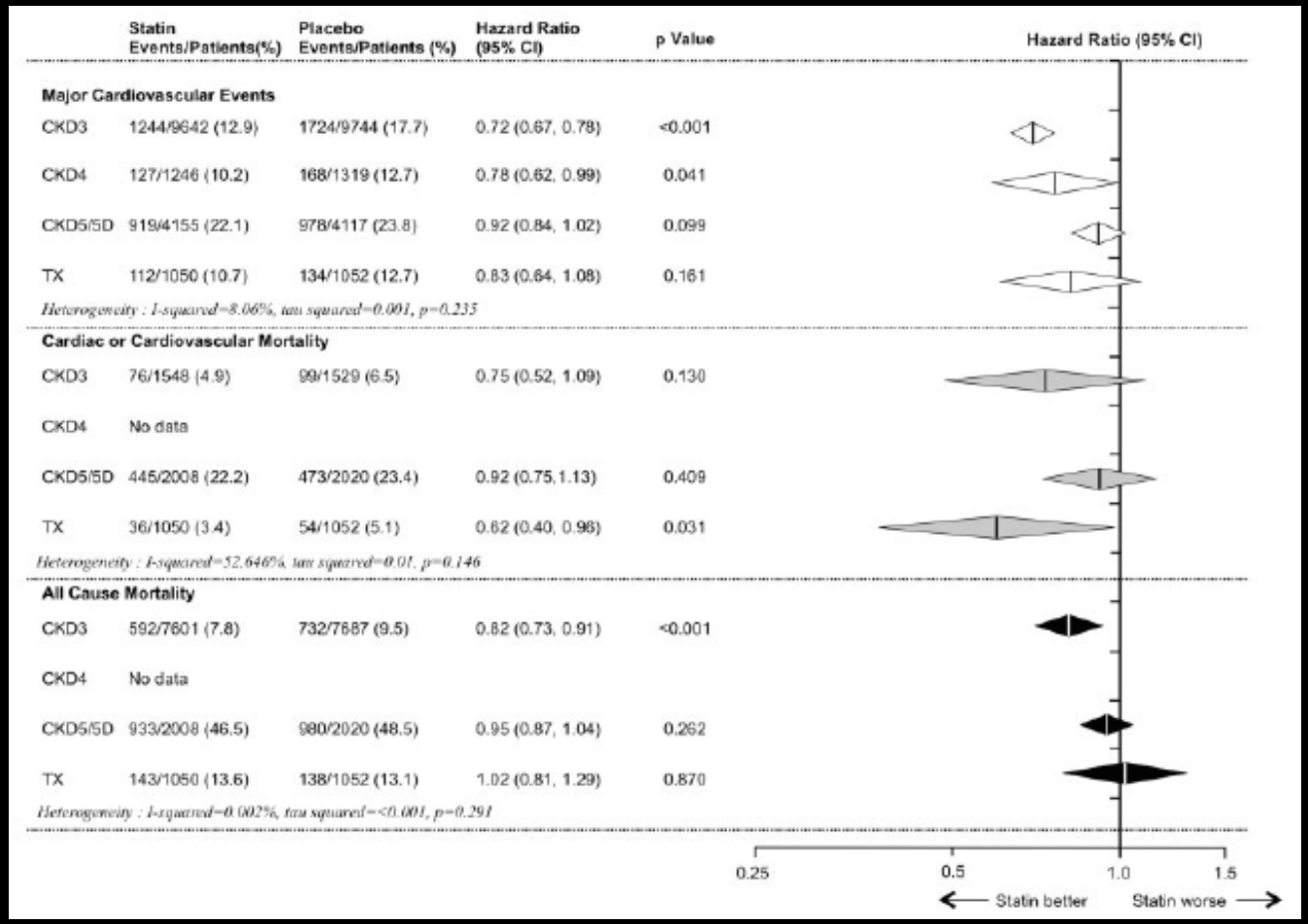
- Determining the optimal BP targets for all patients with CKD will likely take one to two decades of effort: a marathon, not a sprint…

J Am Soc Nephrol 00: ccc–ccc, 2015. doi: 10.1681/ASN.2015101125

Meta-analysis of statins in chronic kidney disease: who benefits?

- randomized trials of statin vs. placebo for CKD3, CKD4, CKD5/5D and transplant patients. Data from the Cholesterol Triallists' Treatment Collaboration and previously published meta-analyses. Outcome measures were major cardiovascular events (MACE), cardiovascular death and all-cause mortality (ACM).

- 13 studies provided 19 386 participants with CKD3, 2565 with CKD4, 7051 with CKD5/5D and 2102 with a functioning renal transplant.



Messow QJM: An International Journal of Medicine, 2017, 493–500

Grazie per l'attenzione