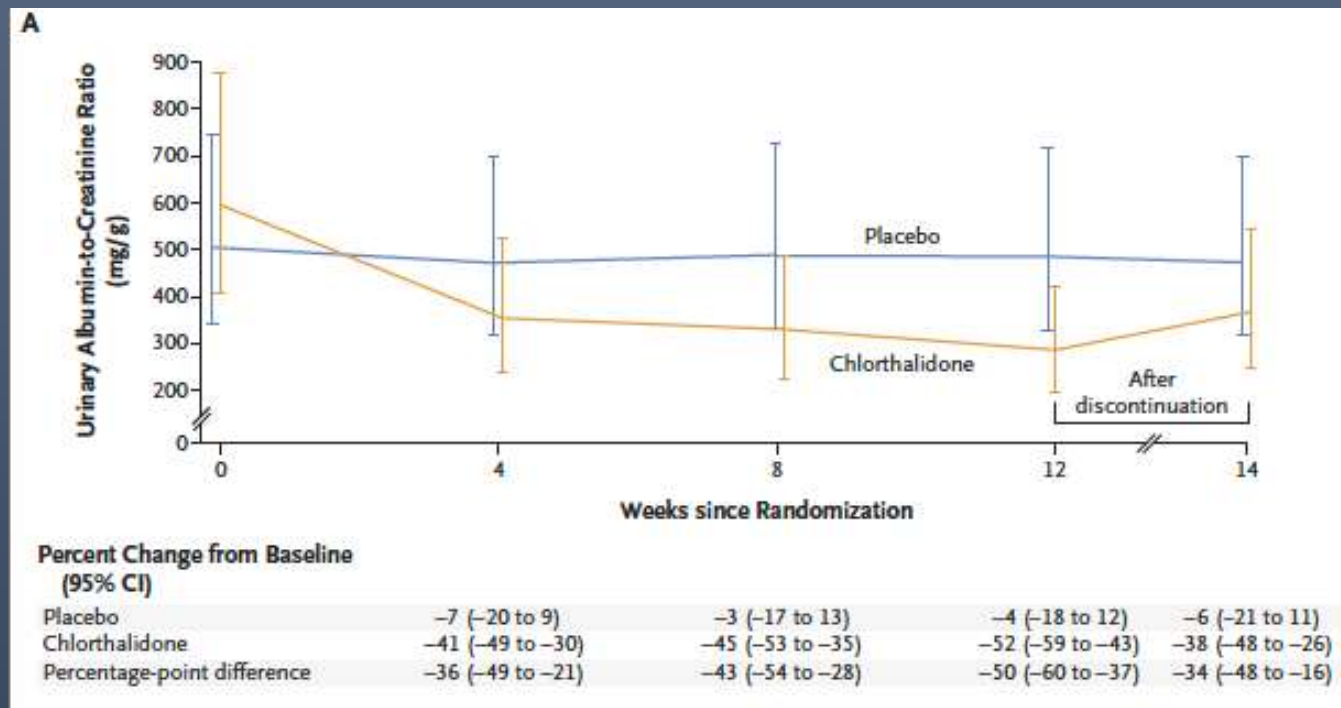


CLICK study: Change in urine ACR



Urine ACR -52% from baseline in chlorthalidone group vs -4% in placebo group at 12 weeks

3-year follow up post trial

Figure S10: Time from treatment completion to the composite outcome event of first of eGFR <10 mL/min/1.73m², kidney replacement, or death.

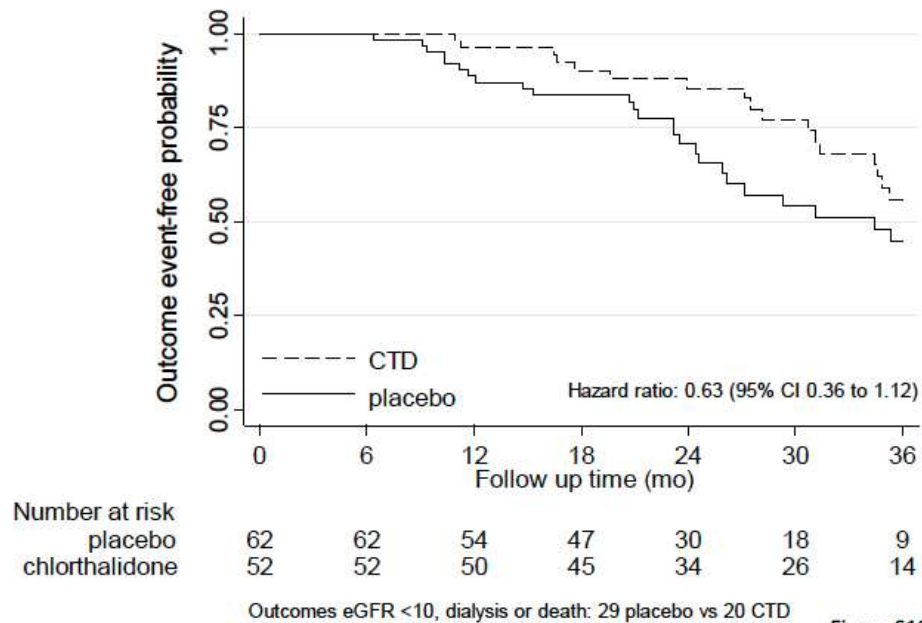


Figure S10

Adverse events

Adverse Events during the Treatment Period		
no. with event/total no. (%)	Chlorthalidone	Placebo
Increase in serum creatinine level (>25% from baseline)	33/74 (45)	10/77 (13)
Hypokalemia	8/81 (10)	0
Hypomagnesemia	19/81 (23)	13/79 (16)
Hyponatremia	9/81 (11)	6/79 (8)
Hyperglycemia	13/81 (16)	4/79 (5)
Hyperuricemia	16/81 (20)	7/79 (9)
Dizziness	20/81 (25)	13/79 (16)

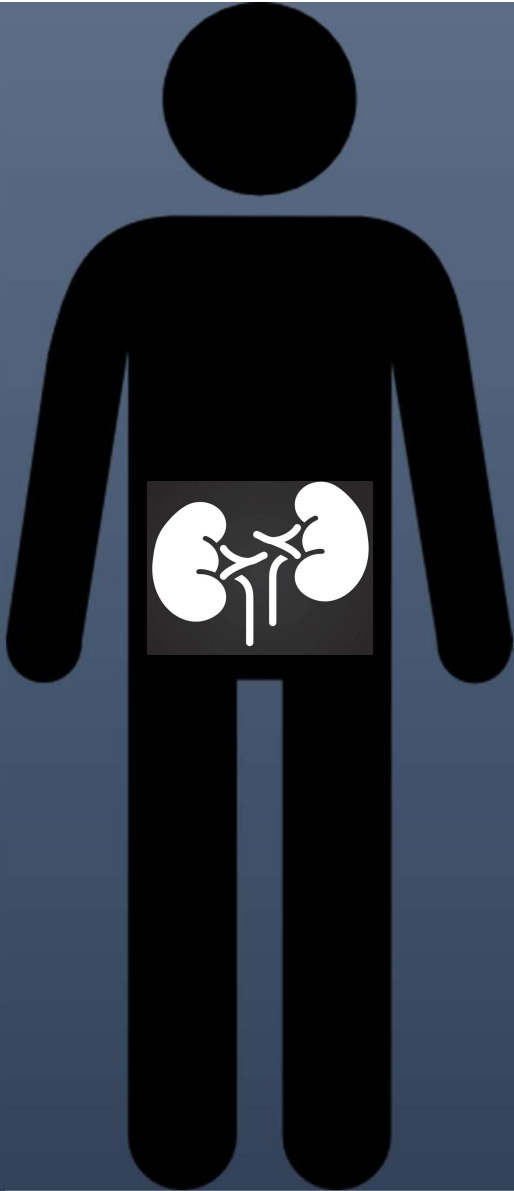
Higher AKI events in Chlorthalidone group:

- 45% compared to 13% in placebo group
- More pronounced in patients on concurrent loop diuretics (59% vs 21% vs 13% placebo).

OR 9.2 and 1.9 respectively

Summary

- Several limitations to the study
- Chlorthalidone is effective in advanced CKD in BP and uACR reduction
- Concurrent use with loop diuretics require further review



Patient with CKD 4 G2 (eGFR 28 ml/min/1.73m²) has poorly controlled hypertension 150/85 mmHg on optimally dosed Candesartan, Amlodipine and furosemide. His BMI is 35. His aldo/renin ratio is elevated.

Next best step in management?

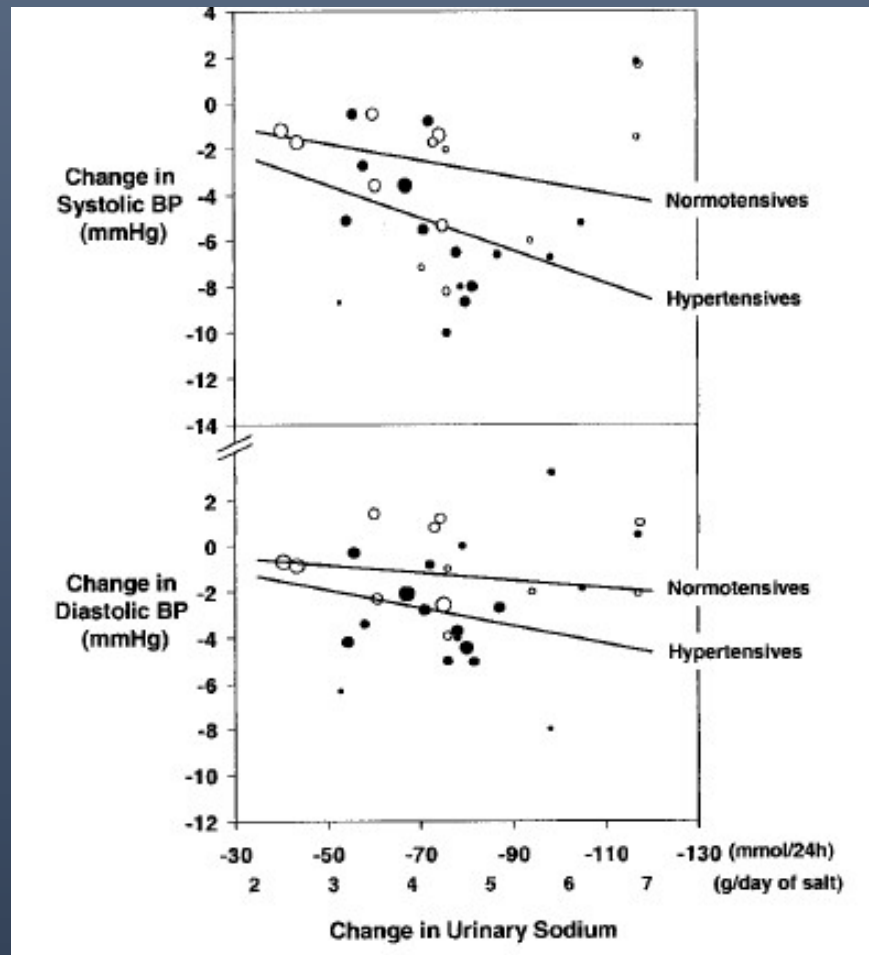
- A. Salt reduction
- B. Add Spironolactone
- C. Add Chlorthalidone
- D. DASH diet



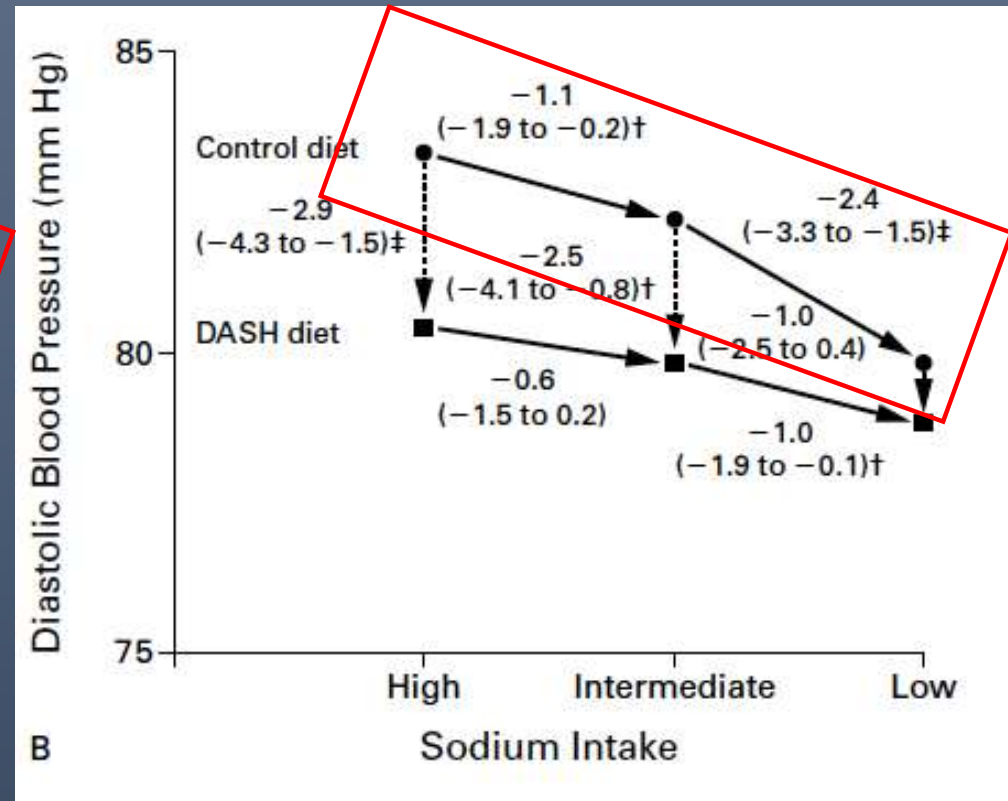
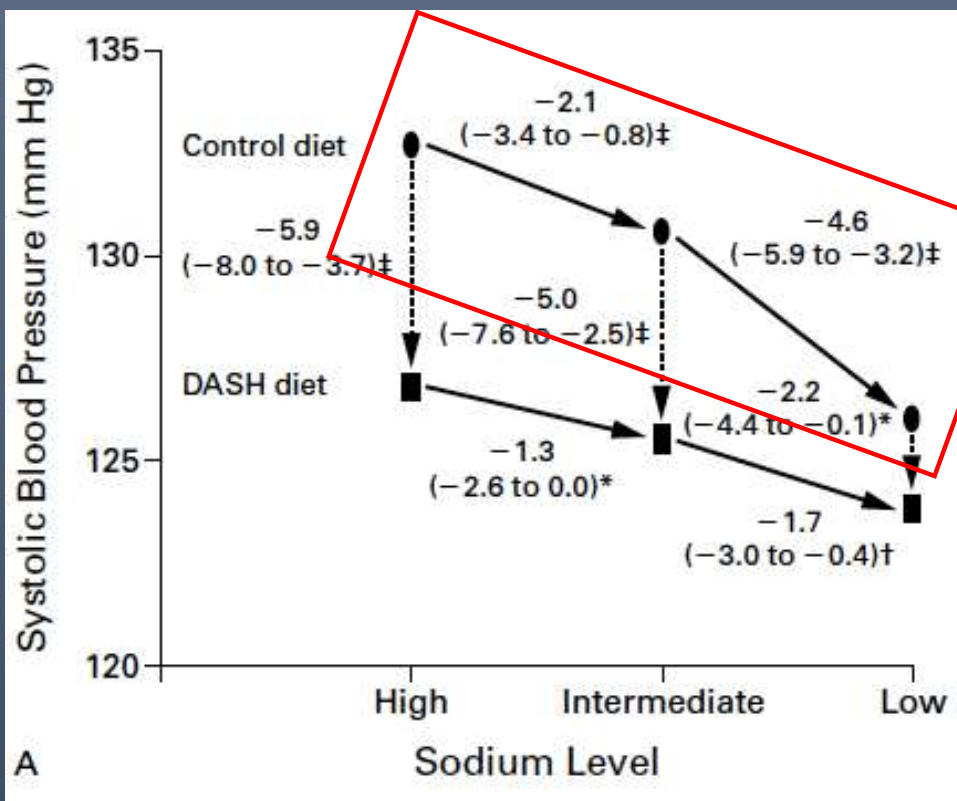
Which statement is true?

- A. Most people with >100 mmol of sodium intake per day are hypertensive
- B. Patients with chronic kidney disease have reduced salt sensitivity
- C. Urinary K to Na ratio has an inverse relationship with BP
- D. Increase in urinary Na to K ratio is associated with increased CV risk

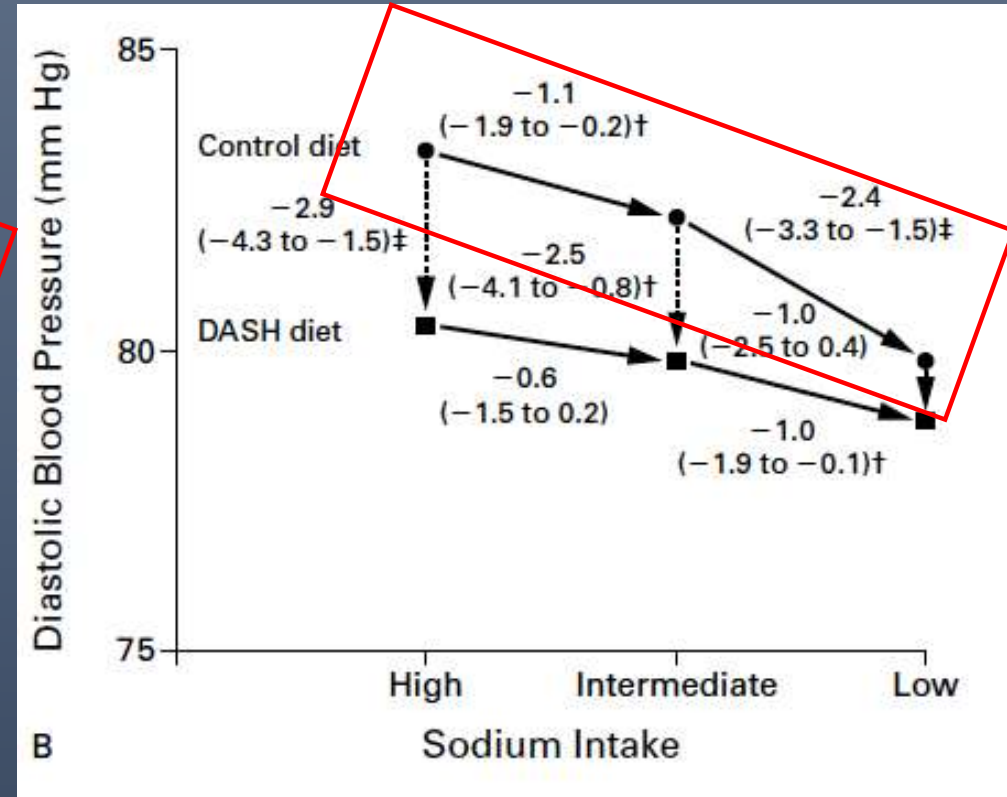
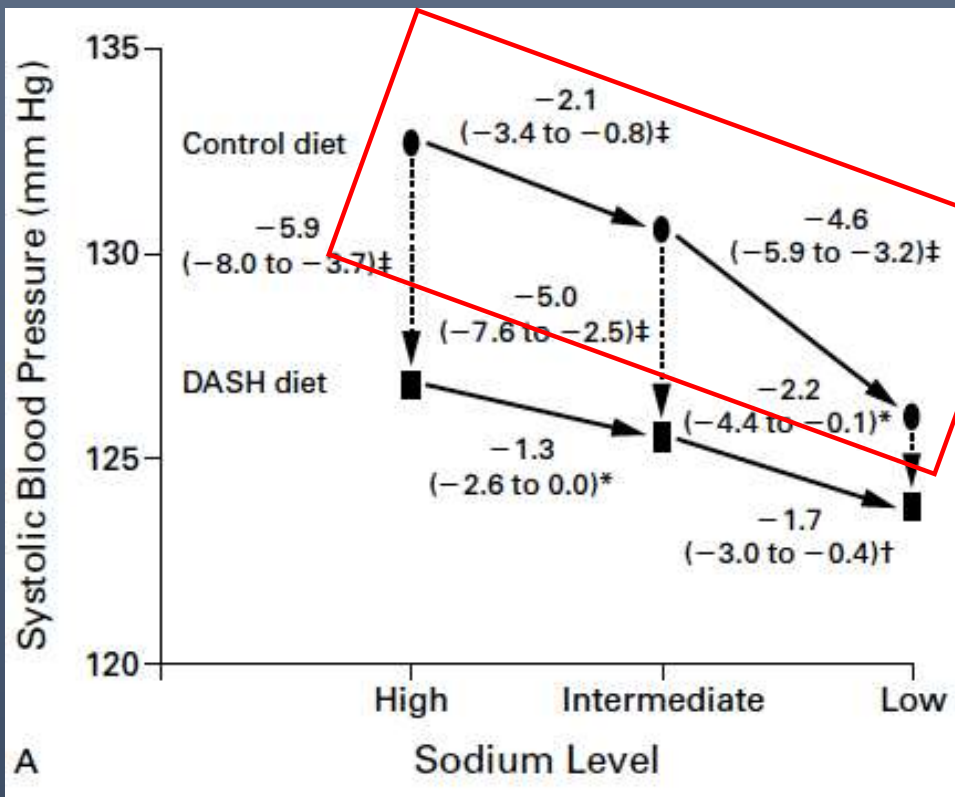
Positive correlation between sodium intake and BP



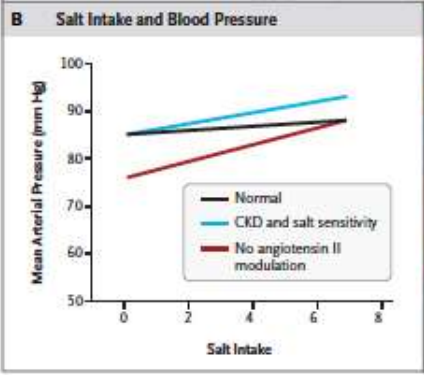
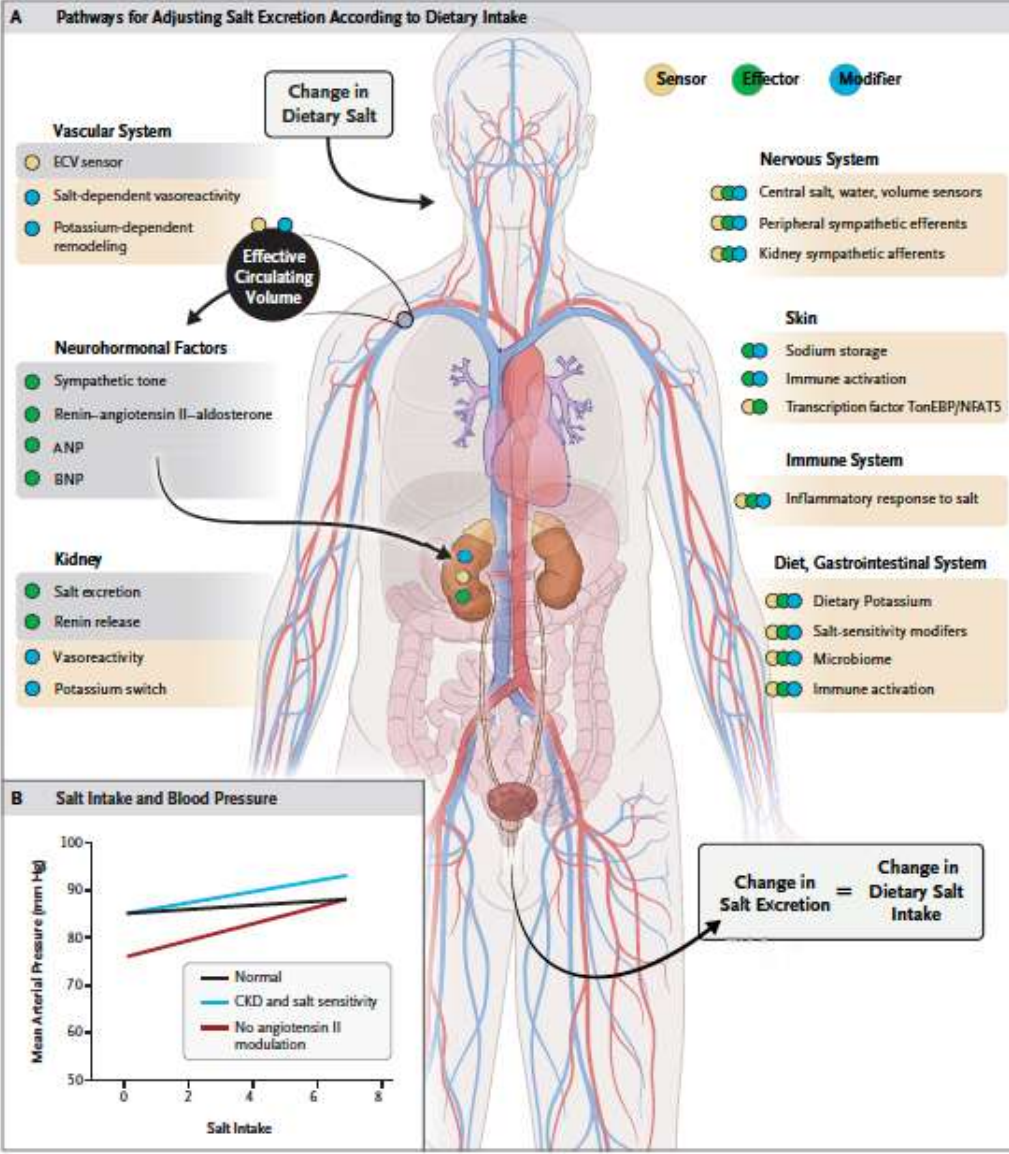
- Dose response reduction in BP and salt intake
- More pronounced in patients with hypertension
- Current WHO guidelines recommend <5 g salt/day (24 hr urine sodium <100 mmol)



- Salt reduction improved both SBP and DBP



- Salt reduction improved both SBP and DBP
- Na: K ratio <1 was associated with SBP and DBP beyond simply salt restriction within the low sodium phase in the DASH diet



Dietary potassium and BP

- Salt sensitivity defined by response of vascular tone to salt loading
- High potassium intake lowers BP and reduces sodium sensitivity:
 - Mediating vasodilation through activation of Na⁺/K⁺ ATPase or changes in endothelial-cell deformability and nitric oxide release.
 - via kinase-signalling pathway in the kidney affecting NaCl reabsorption in the distal nephron
- Reducing sympathetic nerve activity and increasing baroreceptor sensitivity