# Are Diuretics Useful at Reducing Blood Pressure in Chronic Kidney Disease (CKD)?

# Yes!

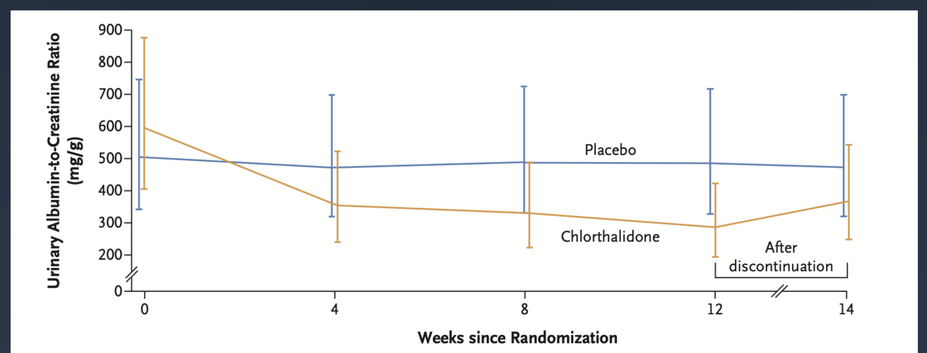
## Background

- The kidneys remove waste, produce hormones, and control blood pressure (BP)
- CKD is a disease spectrum, with stage one being least severe and stage five being the most severe often requiring dialysis
- In CKD, the kidneys gradually stop working and manifest in various systemic issues such as heart disease, nerve damage, weak bones, fluid buildup, and hypertension
- 10% of Americans are affected by CKD and hypertension often accompanies
- Hypertension, a common risk factor for both cardiovascular disease and CKD, is often poorly controlled in patients with advanced CKD (stage 4)
- Additionally, hypertension accelerates the progression of CKD
- Therefore, it should be treated, and diuretics are helpful in doing this

## Diuretics

- Most diuretics decrease blood pressure by reducing the kidney's uptake of sodium
- There are various diuretic classes such as loop diuretics, potassium sparing diuretics, and thiazide diuretics
- The focus for this poster is placed on thiazide and thiazide-like diuretics
- Chlorthalidone, a thiazide-like diuretic, reduces blood pressure, reduces cardiovascular morbidity, such as the incidence of stroke and heart failure, and cardiovascular morbidity
- Since it's discovery in 1957, chlorthalidone has been a mainstay therapy for reducing blood pressure
- Loop diuretics are effective in treating hypervolemia and hypertension in CKD but often cause acute kidney injury (AKI)
- Conversely, thiazide diuretics are less potent and longer acting
- Until recently, there was no firm data that supported the use of thiazides for improving blood pressure in advanced CKD
- Previous guidelines instructed physicians to switch from thiazide diuretics to loop diuretics when estimated glomerular filtration rate (eGFR) fell below 30 mL/min/1.73$^2$
- However, recent evidence suggests that thiazides may have a greater role in controlling blood pressure in patients with an eGFR below 30

| Variable | Chlorthalidone (N=81) | Placebo (N=79) | Treatment Effect (95% CI)† |
|---|---|---|---|
| **Systolic blood pressure** | | | |
| 24-hr blood pressure — mm Hg | | | |
| At randomization | 142.6±8.1 | 140.1±8.1 | |
| Adjusted change at 12 wk (95% CI) | −11.0 (−13.9 to −8.1) | −0.5 (−3.5 to 2.5) | −10.5 (−14.6 to −6.4)‡ |
| Daytime blood pressure — mm Hg | | | |
| At randomization | 145.2±8.8 | 142.7±8.8 | |
| Adjusted change at 12 wk (95% CI) | −11.3 (−14.4 to −8.3) | −0.7 (−3.9 to 2.5) | −10.6 (−15.0 to −6.3) |
| Nighttime blood pressure — mm Hg | | | |
| At randomization | 138.0±10.0 | 135.4±10.2 | |
| Adjusted change at 12 wk (95% CI) | −10.5 (−15.2 to −5.8) | 0.6 (−3.0 to 4.2) | −11.1 (−16.6 to −5.6) |
| **Diastolic blood pressure** | | | |
| 24-hour blood pressure — mm Hg | | | |
| At randomization | 74.6±10.1 | 72.8±9.3 | |
| Adjusted change at 12 wk (95% CI) | −4.9 (−6.6 to −3.2) | −1.0 (−2.8 to 0.7) | −3.9 (−6.3 to −1.5) |
| Daytime blood pressure — mm Hg | | | |
| At randomization | 77±10.6 | 75.1±9.5 | |
| Adjusted change at 12 wk (95% CI) | −5.4 (−7.3 to −3.6) | −1.3 (−3.1 to 0.6) | −4.2 (−6.8 to −1.6) |
| Nighttime blood pressure — mm Hg | | | |
| At randomization | 70.4±10.5 | 68.9±10.2 | |
| Adjusted change at 12 wk (95% CI) | −4.7 (−7.5 to −2.0) | −0.6 (−2.8 to 1.6) | −4.1 (−7.4 to −0.9) |
| **Patients with a nocturnal dip in systolic blood pressure§** | | | |
| At randomization — no./total no. (%) | 14/79 (18) | 18/79 (23) | |
| At 12 wk — no./total no. (%) | 14/65 (22) | 13/72 (18) | 1.0 (0.98 to 1.01) |




| Percent Change from Baseline (95% CI) | | | | |
|---|---|---|---|---|
| Placebo | −7 (−20 to 9) | −3 (−17 to 13) | −4 (−18 to 12) | −6 (−21 to 11) |
| Chlorthalidone | −41 (−49 to −30) | −45 (−53 to −35) | −52 (−59 to −43) | −38 (−48 to −26) |
| Percentage-point difference | −36 (−49 to −21) | −43 (−54 to −28) | −50 (−60 to −37) | −34 (−48 to −16) |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## CLICK Trial

- Chlorthalidone in Chronic Kidney Disease (CLICK) Trial
- Double Blind, randomized, placebo-controlled trial of chlorthalidone in patients with advanced CKD and poorly controlled hypertension
- Hypothesized that chlorthalidone would both decrease systolic blood pressure and albuminuria over 12 weeks
- Eligible patients: stage 4 CKD and blood pressure of >130/80 mmHg
- Nine visits in total with yearly follow-ups for three years post trial completion

## Results

- 160 patients underwent randomization
- At baseline, the mean eGFR was 23.2±4.2 ml/min/1.73m$^2$
- The mean number of antihypertensive medications prescribe was 3.4±1.4
- Use of gold standard blood pressure monitoring – ambulatory blood pressure
- At randomization, mean systolic BP was 142.6±8.1 mmHg in the chlorthalidone group and 140.1±8.1 mmHg in the placebo group and the mean diastolic BP was 74.6±10.1 mmHg and 72.8±9.3 mmHg, respectively
- The adjusted change in SBP from baseline to 12 weeks was -11.0 mmHg in the chlorthalidone group and -0.5 mmHg in the placebo group
- The percent change in urinary albumin-to-creatinine ratio from baseline to 12 weeks was lower in the chlorthalidone group than in the placebo group by 50 percentage points

## Takeaways

- Among patients with advanced CKD and poorly controlled hypertension, chlorthalidone therapy improved blood pressure at 12 weeks as compared with placebo
- This study proved that chlorthalidone, a drug that has been around for 65 years, is beneficial for reducing blood pressure in those with advanced CKD when it previously was contraindicated
- This brings up the importance of taking a second look at older medications for new indications
- New does not always mean better