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AMBIENT HEAT EXPOSURE AND ESTIMATED GLOMERULAR FILTRATION RATE TRAJECTORY: A POST-HOC ANALYSIS OF THE DAPA-CKD TRIAL

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Background and Aims: Higher ambient temperatures have been associated with higher rates of admission for kidney stones and acute kidney injury. Occupational heat stress is also a risk factor for impaired kidney function in several rural resource-poor settings. It is unclear if higher ambient heat exposure is associated with a faster loss of kidney function in patients with established, all-cause, chronic kidney disease (CKD). We therefore undertook a post-hoc analysis of the DAPA-CKD trial linking participant data to publicly available climate measurements.

Method: The DAPA-CKD trial randomized 4304 patients with proteinuric CKD (estimated glomerular filtration rate, eGFR, 25-75 mL/min/1.73 m^2; urine albumin-to-creatinine ratio, ACR, 23-566 mg/mmol) to dapaglifozin or placebo in addition to standard of care. We examined the association between daily study centre-level ambient heat exposure (defined as a mean heat index, HI, >30; European Centre for Medium-Range Weather Forecasts ERA5 reanalysis dataset) and individual-level change in eGFR using both a linear-mixed effects model and a case-time series approach to address potential unmeasured individual- and centre-level confounding.

Results: Climate and eGFR data were available on 3915 (91%) participants across 361 centres in 21 countries. Over a median of 28 months, participants (mean age: 62 years; mean eGFR: 43mL/min/1.73 m^2) were followed-up at centres where there was a median of 1 day (interquartile range: 0 to 64 days) with an HI>30. Each 30-day period of HI>30 over the study period was associated with a change in eGFR of -0.7% (95% CI: -1.0% to -0.3%), equivalent to an additional eGFR loss of between 1.2 and 4.0mL/min/1.73 m^2 per year in a patient with an eGFR of 45mL/min/1.73 m^2 located in a very hot versus temperate environment. Similar estimates were obtained using the case time series approach. This association persisted after adjustment for potential haemoconcentration effects on the day of testing and further analyses provided no evidence that these findings varied with baseline eGFR, albuminuria or randomised treatment arm (Figure 1), or by high- versus middle-income country study centre location.

Conclusion: Higher ambient heat exposure is associated with a more rapid decline in kidney function among patients with CKD. Efforts to mitigate heat exposure should be prospectively tested as part of a comprehensive strategy to slow the progression of kidney disease.

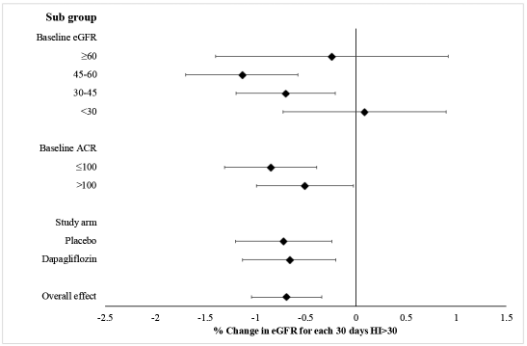

Figure 1: Association between heat index and change in eGFR in subgroups. Linear mixed model of eGFR measures nested within individual-level random effects nested within centre-level random effects. Model adjusted for the following baseline variables: age; sex; ethnicity; smoking status; diagnosis of diabetes; history of cardiovascular disease; BMI; systolic blood pressure; urinary ACR; eGFR; ACE/ARB use; statin use; diuretic use; DAPA-CKD study arm; and time interactions (reflecting associations with eGFR slope) with age; BMI; systolic BP; eGFR; urinary ACR and DAPA- CKD study arm. Average marginal effects estimates presented for subgroups. Error bars show 95% confidence intervals.

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