Are thiazide or thiazide-like diuretics (THZs) associated with a greater risk of Type 2 diabetes mellitus than Angiotensin-converting-enzyme inhibitors (ACEi) in patients initiated on treatment for hypertension?

A LEGEND-HTN study

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INTRODUCTION

- The LEGEND-HTN study (Large-scale Evidence Generation and Evaluation in a Network of Databases) (1) found that THZs were more effective than ACEi in terms of cardiovascular benefits and had improved safety on 19 different endpoints (including cardiovascular-related mortality, dementia and chronic kidney disease) compared to ACEis, with the exception of hypokalemia and hyponatraemia.
- However, ACEis are by far the most prescribed first line antihypertensive treatment world-wide (2).
- One of the barriers to doctors initiating treatment with THZs are that they are seen as a less favourable treatment option than ACEi due to their perceived risk of type 2 diabetes mellitus (T2DM).
- LEGEND-HTN found no difference between ACEis and THZs at the class level for the development of T2DM (HR 0.95; 95% Confidence Interval 0.85, 1.07), however, results for individual products were not presented.

METHODS

In this study we used evidence from LEGEND-HTN (3). See (1) for detailed methods. Analyses were performed at the class level (THZ v ACEi) and by individual product (hydrochlorothiazide v ACEi and chlorthalidone v ACEi). To compare individual THZ products to the ACEi class, hierarchical meta-analysis (4) on the log-scale was used to account for repeated HR estimates ACEi products and over databases.

RESULTS

- 768,174 patients initiated on THZ, 1,882,630 patients initiated on ACEi monotherapies
- No association with new onset T2DM risk with hydrochlorothiazide compared to ACEIs (meta-analysis HR = 0.89, 95% CI (0.74 - 1.07))
- Chlorthalidone associated with increased risk of new onset T2DM compared to ACEis (meta-analysis HR = 1.19, 95% CI (1.05 - 1.34)).

Thiazide medicines for hypertension are not **consistently** associated with diabetes onset.

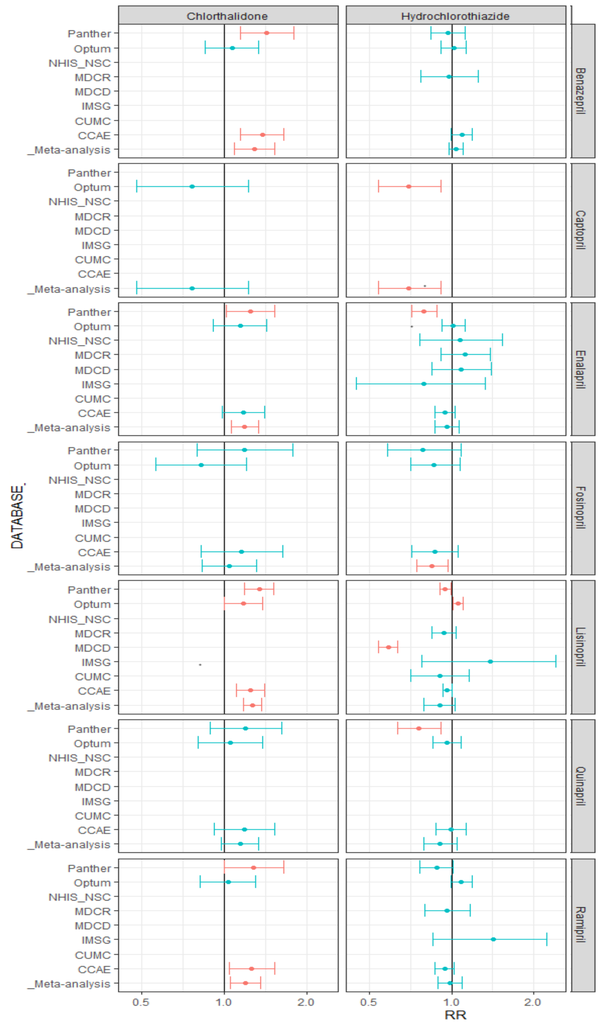
LEGEND_HTN Suchard et al.

Treatment Pathways Hripcsak et al.

LEGEND Basic Viewer

Hierarchial meta-analysis Pastor et al.

LEGEND_HTN Hripcsak et al.



	Calibrated HR (95% CI)
TZD v ACEi	0.95 (0.85, 1.07)
Chlorthalidone v ACEi	1.19 (1.05, 1.34)
Hydrochlorothiazide v ACEi	0.89 (0.74, 1.07)

CONCLUSION

- Clinicians may consider hydrochlorothiazide as first line treatment for hypertension particularly as previous LEGEND-HTN results have also found no evidence to support current recommendations to prefer chlorthalidone over hydrochlorothiazide (5).
- This paper demonstrates the ongoing utility of the LEGEND-HTN results to help inform and support clinical treatment decisions in hypertension.

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