

DSEN ABSTRACT

A Systematic Review with Network Meta-Analyses and Economic Evaluation Comparing Therapies for Hypertension in Non-Diabetic Patients

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What is the issue?

- Hypertension has been cited as the most common attributable risk factor for death worldwide, and an independent predictor of stroke mortality and ischemic heart disease mortality.
- Past reviews have studied drug efficacy in several populations with comorbidities. An identified population of interest was those without diabetes.

What was the aim of the study?

- How does monotherapy with a thiazide diuretic compare to monotherapy with other pharmacotherapeutic agents [i.e. ACE inhibitors, calcium channel blockers (CCBs), beta blockers (BBs), angiotensin receptor blockers (ARBs), etc.] in patients without diabetes with hypertension?
- How do combination treatments involving a thiazide diuretic (TZD) compare to combination treatments not involving a thiazide diuretic in patients without diabetes with moderate/severe hypertension or cardiovascular risk?
- What is the relative cost-effectiveness of monotherapies and combination therapies used to manage non-diabetic patients with hypertension?

How was the study conducted?

- We leveraged existing systematic reviews to identify randomized trials reporting on eight outcomes: overall mortality, cardiovascular mortality, stroke, myocardial infarction, incident cancers, incident diabetes, sexual dysfunction, and depression.
- Studies in patients with hypertension were included if they studied relevant antihypertensive treatments, if relevant outcomes were reported, and if data on the population of interest was available. Network meta-analyses of RCTs were used to explore the relative frequencies of each of the above outcomes. All screening and data collection were performed independently by two reviewers.

What did the study find?

- A total of 88 RCTs (>200,000 patients) were included. Study populations were variable in terms of severity of hypertension and co-medications. Trial publication dates ranged from 1960-2011. Studies involving ACE inhibitors (ACE-I), angiotensin receptor blockers (ARB), beta blockers (BB), calcium channel blockers (CCB), thiazide diuretics (TZD), combinations thereof, and no treatment were included.

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A Network Meta-Analysis of Cardiovascular Risk Associated with Stalevo (levodopa/carbidopa/entacapone)

Research Question 1: Comparison of thiazide diuretics with other interventions

- Regarding all-cause mortality, comparisons of TZD monotherapy with other monotherapies were inconclusive based on conventional statistical significance at an alpha value of 5%, though comparison against BB suggested a potentially important benefit with TZD; only one significant difference (favoring CCB over BB) amongst comparisons between different active monotherapies was identified. There was also a potentially important benefit with CCB compared to BB for cardiovascular mortality, however most comparisons for this outcome were inconclusive, including all comparisons related to TZD. Regarding stroke, TZD were more effective than BB, but were comparable with other monotherapies. TZD were potentially more effective than CCB, ARB and BB for reducing myocardial infarctions, however these comparisons were associated with high uncertainty; no evidence of a potential benefit compared to ACE-I was noted.
- Secondary measures of intervention effectiveness generated from network meta-analysis (i.e. treatment rankings) suggested TZD was the preferred monotherapy for stroke and MI incidence reduction, but TZD also were associated with the worst rank regarding incident diabetes. The analyses provide some clinical evidence of potential differences between therapeutic classes in non-diabetic hypertensive patients, which were not fully explained by clinical and methodologic heterogeneity in the included trials.

Research Question 2: Comparison of TZD-based combination therapy interventions with other combination therapy interventions

- We classified combination regimens according to the groups of TZD+other active agents, TZD+BB, and BB+other active agents. Few studies involved combination therapy. We also did not have evidence in our treatment networks on some combination regimens relevant to clinical practice.
- Analyses for mortality outcomes, stroke and MI all demonstrated strong and statistically significant benefits of TZD+other active agents compared to most other monotherapies and combination therapies. Given challenges in the evidence base (i.e. few head-to-head studies, limited sample size), the size of these benefits should be interpreted cautiously.
- Past guidance has suggested that therapy with BB+TZD is effective, however few data were eligible. BB+TZD has demonstrated clinical benefits previously, however some clinical guidelines note this regimen may be associated with concerns regarding incident diabetes while other combinations are also effective.

Research Question 3: Comparing the Cost-Effectiveness of Competing Monotherapy and Combination Therapy Interventions

- The economic analysis found little to choose from between each of the drug treatments in terms of effectiveness with results primarily driven by drug costs. Treatment with BB in combination with TZD is the most cost effective treatment option for all men and women aged less than 75. For women aged 75 and over, ARB in combination with TZD is the most cost effective treatment option.

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