

BACKGROUND & OBJECTIVES

- Treatment-resistant hypertension (TRH) is associated with significant cardiovascular morbidity and mortality and its prevalence is increasing
- In 2008, the American Heart Association (AHA) published a scientific statement with recommendations for pharmacologic management of TRH, including appropriate use of diuretics and the addition of aldosterone antagonists
- However, little is currently known regarding trends in antihypertensive drug use for patients with TRH in the U.S. since 2008
- We aimed to characterize antihypertensive use among patients with TRH from July 2008 through December 2014 (most recent data available)

METHODS

Data Source

- Marketscan commercial claims data (nationally-representative for patients in employer-based insurance programs) from 2008 through 2014

Study Population

- We included adults, aged 18 to 64 years, with ≥ 1 ICD-9 diagnosis of HTN (401.X), and ≥ 6 months of continuous enrollment prior to having a TRH episode
- TRH episodes were defined as overlapping fills of ≥ 4 antihypertensives from multiple classes, lasting ≥ 60 days, and with ≥ 2 antihypertensive fills of each agent; BP was not considered in the definition since the Marketscan database contains no vitals
- Patients with heart failure diagnosis (ICD-9 428.X) were excluded

Analysis

- Antihypertensive use was assessed during each "episode" of TRH, such that a single patient could have ≥ 1 distinct episode(s) of TRH
- Episodes of TRH treatment were used as the denominator to evaluate proportion of antihypertensive use and antihypertensive use was assessed by quarter to assess time trends

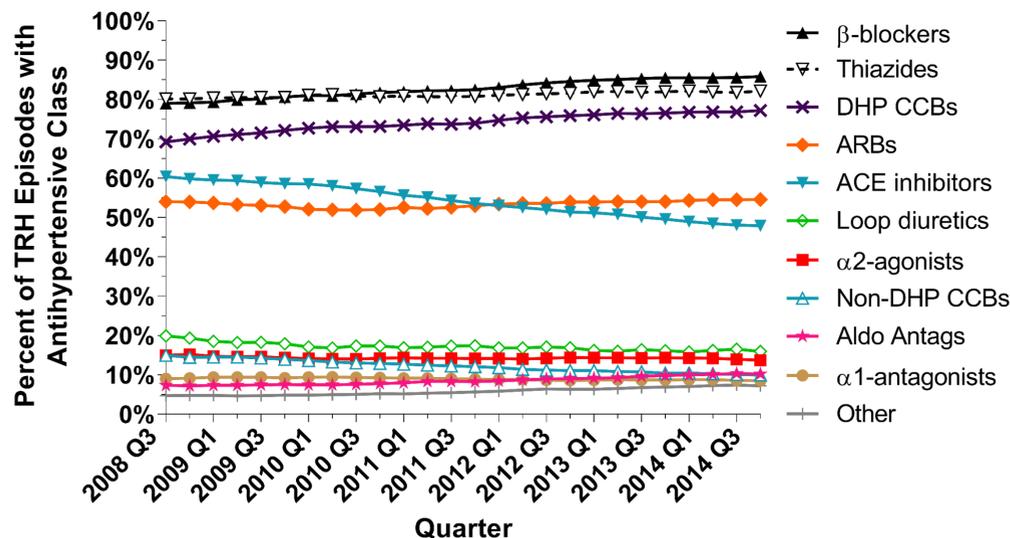
RESULTS

- We identified 411,652 TRH episodes from 261,854 patients; patient baseline characteristics are summarized in **Table 1**
- The mean number of antihypertensive drugs per TRH episode was 4.21
- Notable trends in antihypertensive use from 2008 to 2014 included:
 - ACE inhibitor use decreased steadily from 60.9% of episodes in Q3 2008 to 47.9% of episodes in Q4 2014 (**Figure 1**)
 - DHP CCB use increased from 69% to 77% of TRH episodes, whereas non-DHP CCB use decreased modestly (15% to 10%)
 - β -blockers use increased from 79% in 2008 to 86% in 2014
 - Renin inhibitor use peaked in 2011 at 7.8%, then decreased to 1.3% by Q4 2014
 - Combined ACE inhibitor + ARB use decreased from 17.7% (Q3 2008) to 6.3% (Q4 2014)

Table 1. Baseline demographic characteristics.

Characteristic	N (%) or mean (SD)
No. of patients	261,854
No. of treatment episodes	411,652
Follow-up time, days	220.74 (195.53)
Age, years	55.89 (7.12)
Male	248,962 (60.47%)
Comorbidities	
DM	151,592 (36.82%)
CKD	27,798 (6.75%)
MI or other ischemic HD	50,930 (12.37%)
Hemorrhagic stroke	1,539 (0.37%)
Ischemic stroke/TIA	16,157 (3.95%)
PAD/PVD	9,944 (2.42%)

Figure 1. Trends in antihypertensive class use by quarter, 2008 through 2014.



- Thiazide diuretic use was largely unchanged from 2008 (80.1%) to Q4 2014 (82.1%): HCTZ remains by far the most prevalent thiazide diuretic, whereas chlorthalidone use increased only from 3.8% (2008) to 6.4% (2014) (**Figure 2**)
- Use of K^+ -sparing diuretics increased modestly from 2008 to 2014, almost exclusively due to a small increase in spironolactone use (**Figure 3**)

Figure 2. Thiazide diuretic use by individual drugs from 2008 to 2014.

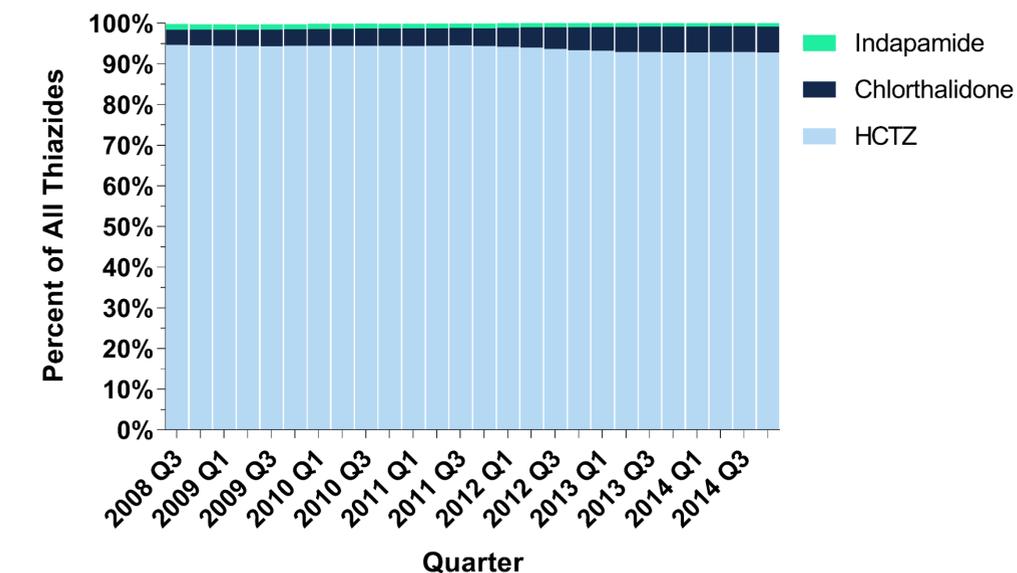
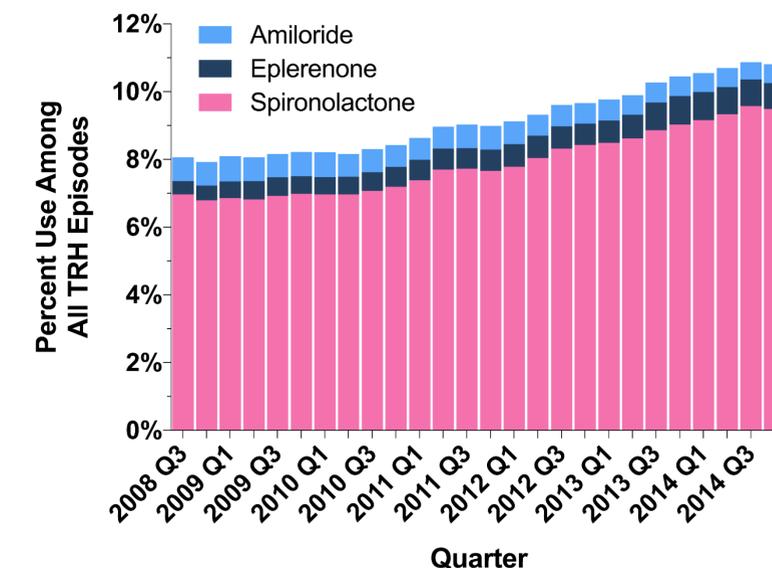


Figure 3. Aldosterone antagonist and amiloride use by drug from 2008 through 2014.



LIMITATIONS

- Marketscan commercial claims data do not contain blood pressure data, thus patients with TRH defined by uncontrolled BP on 3 antihypertensives were misclassified as having non-resistant HTN
- We were not able to ascertain whether optimal doses of antihypertensives were being utilized

CONCLUSIONS

- The infrequent use of recommended therapies, spironolactone and chlorthalidone, persisted from 2008 through 2014
- Interestingly, an unanticipated decrease in the use of ACE inhibitors was also observed from 2008 through 2014
- Our results reinforce and extend previous data documenting the underutilization of effective medications for resistant hypertension
- These results suggest greater efforts are needed to increase use of recommended antihypertensive treatments among patients with TRH, especially given recently published evidence demonstrating their efficacy