Characterization of US Adult Users of Antihypertensive Medications

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CONFLICT OF INTEREST

BACKGROUND

- More than 59 million Americans (28% of the US adult population) are estimated to have hypertension (Fields LE et al., 2004).
- The ultimate public health goal of antihypertensive (AHT) therapy is the reduction of cardiovascular and renal morbidity/mortality (The JNC 7 Report, 2003).
- Patients with hypertension and associated comorbidities require certain antihypertensive drugs. Multiple AHT drug classes are also indicated to treat other cardiovascular and non-cardiovascular conditions; among the most frequent is heart failure, with or without hypertension.

OBJECTIVE

To characterize the population of adult users of AHT medications in the US, focusing particularly on those patients with heart failure.
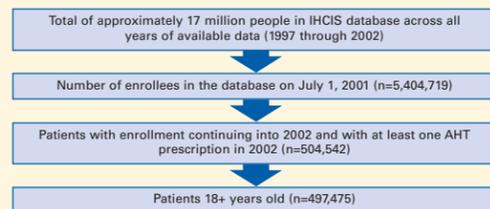
METHODS

Data Source: Integrated Healthcare Information Services (IHCIS), which collects and maintains HIPAA-compliant information on patients in health plans across eight geographic census regions. IHCIS' database contained demographic, eligibility, outpatient, inpatient, and pharmaceutical data for over 17 million patients from 30 health plans.

Study Period: January 1 through December 31, 2002

Study Population: The following figure shows the process used to select the study cohort from the IHCIS database.
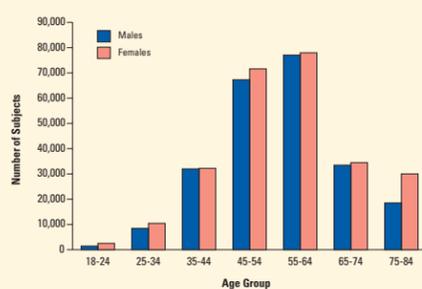
Selection of Study Cohort from IHCIS Database

Total of approximately 17 million people in IHCIS database across all years of available data (1997 through 2002)

Number of enrollees in the database on July 1, 2001 (n=5,404,719)

Patients with enrollment continuing into 2002 and with at least one AHT prescription in 2002 (n=504,542)

Patients 18+ years old (n=497,475)

Identification of Treatment Episodes and Treatment Patterns

- AHT categories:
  1. Spironolactone
  2. Triamterene, amiloride
  3. Thiazide diuretics
  4. Loop diuretics
  5. Other diuretics
  6. Beta-blockers (BBs)
  7. Calcium channel blockers (CCBs)
  8. Angiotensin-converting enzyme inhibitors (ACEIs)
  9. Angiotensin II receptor antagonists (ARA-IIs)
  10. Other antihypertensive drugs
- Treatment episodes were defined as continuous periods of time during which a patient is taking one AHT (monotherapy) or a combination of AHTs (combination therapy). Episodes are regimen-specific.
- Treatment episodes were constructed, starting 6 months prior to January 2002, for each patient in order to describe AHT use over time.

Examples of AHT Treatment Patterns

Patient A:
Switch from **ACEI** monotherapy to **spironolactone** monotherapy.

Patient B:
ACEI monotherapy, followed by **ACEI + spironolactone** combination therapy, followed by **spironolactone** monotherapy

Patient C:
ACEI + loop diuretic combination therapy, followed by **spironolactone + loop diuretic** combination therapy, followed by **spironolactone** monotherapy

- Patients may change their treatment regimens over time, by switching to a different AHT, initiating treatment with one or more different AHTs in conjunction with their existing treatment, or terminating the use of one or more AHTs while continuing treatment with at least one AHT. Therefore, patients may have multiple treatment episodes.
- For each subject, the first treatment episode for each regimen during the study period was considered the index treatment episode for that regimen. The first treatment episode of any regimen during the study period for each subject was considered to be the overall index treatment episode for that subject.

- Concomitant use of other selected medications (excluding AHTs) was defined as the use of a given drug within 60 days of the index date for a treatment episode.

Identification of Medical Conditions

We identified all conditions that may be considered indications by searching for specific diagnoses that occurred within 6 months before or after the index date for a treatment episode. A hierarchical search was performed to identify patients with the following clinical indications[a]:
1. Heart failure only
2. Heart failure with acute myocardial infarction (AMI) (with or without hypertension)
3. Heart failure with hypertension
4. Heart failure with ischemic heart disease (IHD) (other than AMI, without hypertension)
5. Heart failure with any other listed indication
6. Hypertension only
7. Hypertension with AMI (without heart failure)
8. Hypertension with IHD (other than AMI, without heart failure)
9. Hypertension with any other listed indication
10. AMI (without heart failure or hypertension)
11. Other listed indications only (including IHD)

Analysis: All analyses were conducted using SAS 8.2 (SAS Institute, Cary, NC USA).

[a] ICD-9-CM diagnosis codes: heart failure (428), AMI[b] (410 or 411.0), hypertension (401-405), IHD[b] (411-414, excluding 411.0), other indications (242, thyrotoxicosis[b]), 255.1 (hyperaldosteronism), 346 (migraine[b]), 276.6 (fluid overload), 276.8 (hypopotassemia), 427 (cardiac dysrhythmia[b]), 571 (chronic liver disease and cirrhosis), 581 (nephrotic syndrome), 584-587 (renal failure[b]), 588.8 (other specified disorders resulting from impaired renal function, including hypokalemic nephropathy and secondary hyperparathyroidism, of renal origin), 782.3 (edema)

[b] AMI, IHD, thyrotoxicosis, migraine, cardiac dysrhythmia and renal failure are not considered to be indications for spironolactone use and were not counted as such for that AHT.

RESULTS

The age and gender distribution of the study sample is presented below. The small number of patients over 65 years of age is typical of US health claims data, representing a shift from private medical coverage to Medicare programs.
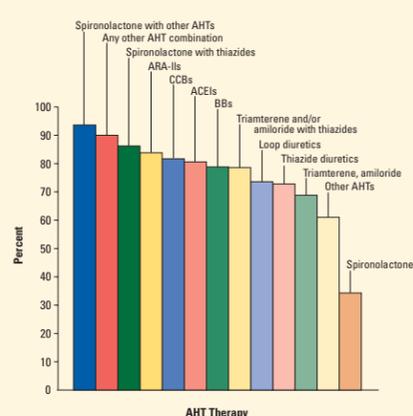
Age and Gender Distribution of Study Sample

For the 497,475 subjects in the study sample, 729,496 index treatment episodes (ITxs) were identified during the study period (mean=1.5 ITxs per patient).

Indications for AHT Use

- Over 75% of monotherapy ITxs for BBs, CCBs, ACEIs and ARA-IIs were associated with an indication.
- Over 75% of all the combination therapies considered were associated with an indication.
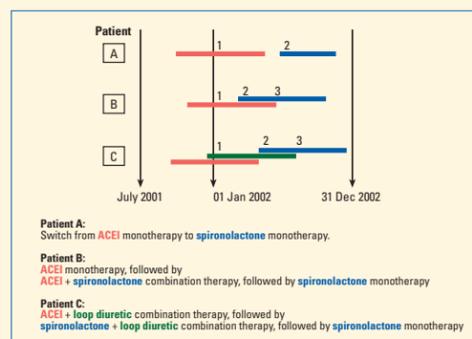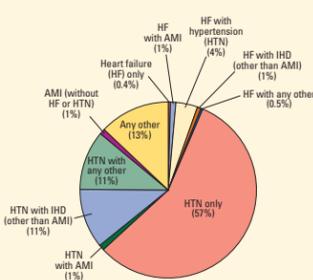
Percentage of Index Treatment Episodes with Identified Indication(s)

Concomitant Use of Other AHTs

Based on the first ITxs for each drug class, diuretics were associated with the highest proportion (over 70%) of concomitant use of other AHTs, followed by ARA-IIs (68%), CCBs (64%), spironolactone (62%), ACEIs (56%) and BBs (50%).

Percentage of Index Treatment Episodes for Each AHT Drug Class that Include Concomitant Use of One or More Other AHTs

Of AHT drugs, loop diuretics (26.2%), BBs (21.4%), and ACEIs (21.4%) were most frequently prescribed concomitantly with spironolactone at the spironolactone ITx.

Of those monotherapy ITxs for which one of our indications could be found, most were associated with an indication of hypertension only. However, over 25% of indications for spironolactone or loop diuretics were associated with an indication for heart failure.

The combination treatments had a similar pattern, with the exception of the combination of spironolactone with "other" AHTs (i.e., other than thiazides), which was more frequently associated with a heart failure diagnosis (with or without other indication diagnoses). AMI without hypertension or heart failure was very uncommon (<2%) (data not shown).

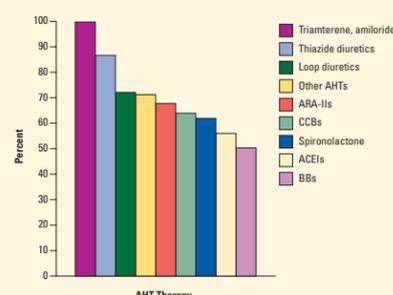### Distribution of Indications at Index Treatment Episodes for AHT Monotherapy

Across all AHT regimens, most ITxs associated with a heart failure indication were also linked with an indication for hypertension. Among monotherapy AHT regimens, monotherapy with BBs was the regimen most frequently associated with a heart failure indication in combination with an AMI indication (22%) (data not shown).

Concomitant Use of Drugs Associated with Hyperkalemia

Seventeen percent of spironolactone ITxs (as monotherapy or combination therapy with other AHTs) were concomitant with potassium supplements. Among first spironolactone ITxs, 21% included concomitant use of ACEIs and 37% included concomitant use of other drugs that could potentially increase the risk of hyperkalemia.[c]

Percent of Index Treatment Episodes for Each AHT Drug Class that Include Concomitant Use of Medications Associated with Hyperkalemia
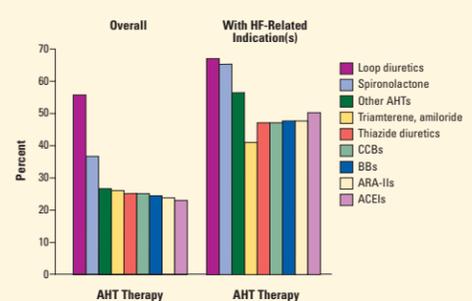
[c] Potassium supplements, penicillin G potassium, digitalis glycosides, NSAIDs, heparin, trimethoprim-sulfamethoxazole, cyclosporine, tacrolimus

CONCLUSION

Patterns of use of AHT medications differ by treatment indications and concomitant cardiovascular and non-cardiovascular conditions. Therapy-specific patient populations should be carefully characterized before initiating epidemiological studies of outcomes associated with AHTs.

REFERENCES

Fields LE, Burt VL, Cutler JA, et al. The Burden of Adult Hypertension in the United States 1999 to 2000. A Rising Tide. *Hypertension* 2004; 44: 398–404.

Chovanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The JNC 7 Report. *JAMA* 2003; 289: 2560–72.