Anti-Hypertensive Medication Combinations in the United States

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Background: Examining the anti-hypertensive regimens of individuals with different comorbidities may offer insights into how we can improve hypertension management.

Methods: The Medical Expenditure Panel Survey (2013–2015) was used to describe the most common single-, two-, three-, and four-drug hypertension regimens among hypertensive adults in four different comorbidity groups: 1. Hypertension only; 2. Hypertension and diabetes; 3. Hypertension and cardiovascular disease (coronary heart disease or stroke history); and 4. Hypertension, diabetes, and cardiovascular disease.

Results: 15,901 adults with hypertension taking anti-hypertensive medications were included in the study. 58.6% (95% CI: 57.3–59.8) took multiple anti-hypertensive medications, but the proportion of adults taking multiple anti-hypertensives varied by comorbidity group. Regimens including an ACE-inhibitor/ARB were the most prevalent regimens among individuals taking ≥2 anti-hypertensive medications. The most common two-drug regimen for both the hypertension-only and hypertension-diabetes groups was an ACE-inhibitor/ARB with thiazide. The most prevalent regimen for the two cardiovascular disease groups was an ACE-inhibitor/ARB with beta-blocker.

Conclusions: Most individuals with hypertension use between 2–5 medications and the medications comprising these regimens vary by comorbidity. The ACCOMPLISH trial suggested that certain combinations may lead to superior cardiovascular outcomes. Research comparing the efficacy of different hypertension medication combinations among individuals with different comorbidities could lead to better patient hypertension-related outcomes. (J Am Board Fam Med 2020;33:143–146.)

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Most adults taking antihypertensives in the United States take multiple agents.1 In addition, the Eighth Joint National Committee recommends providers initiate 2-drug regimens for patients newly diagnosed with stage 2 hypertension.2 Studies of hypertension drug regimens in the United States have investigated 2-drug regimens for adults1 and Medicare recipients4 but haven’t compared multi-drug regimens for individuals with different comorbidities. Analyzing...
Table 1. Proportion of Adult 2013 to 2017 Medical Expenditure Panel Survey Respondents Taking Each Medication Regimen by Comorbidity Group

| Comorbidity Group | HTN Only | HTN-DM | HTN-CVD | HTN-DM-CVD |
|-------------------|----------|--------|---------|------------|
| Number of individuals | 8016 | 3480 | 2533 | 1872 |
| Proportion of sample | 52.8 (51.5, 54.2) | 19.0 (18.0, 20.1) | 17.2 (16.1, 18.3) | 10.9 (10.2, 11.7) |
| Number of HTN medications | | | | |
| 1 | 48.9 (47.0, 50.8) | 37.8 (34.9, 40.7) | 33.9 (31.3, 36.6) | 27.3 (20.8, 26.8) |
| 2 | 35.7 (33.9, 37.5) | 33.9 (31.3, 36.5) | 37.2 (34.4, 40.1) | 37.2 (33.8, 40.7) |
| 3 | 12.7 (11.7, 13.8) | 20.8 (18.5, 23.3) | 20.1 (17.7, 22.6) | 26.2 (23.1, 29.5) |
| 4 | 2.3 (1.9, 2.8) | 6.2 (5.0, 7.7) | 7.3 (5.9, 9.1) | 10.3 (8.5, 12.6) |
| ≥5 | 0.4 (0.2, 0.6) | 1.4 (0.9, 2.1) | 1.5 (1.0, 2.4) | 2.6 (1.9, 3.7) |

1 Medication

| Medication | HTN Only | HTN-DM | HTN-CVD | HTN-DM-CVD |
|------------|----------|--------|---------|------------|
| ACE/ARB | 25.2 (23.8, 26.8) | 28.3 (25.6, 31.1) | 12.6 (10.8, 14.6) | 13.2 (10.8, 16.0) |
| Thiazide | 6.2 (5.4, 7.1) | 2.4 (1.8, 3.4) | 2.4 (1.6, 3.6) | 0.9 (0.4, 2.0) |
| Beta-blocker | 9.2 (8.2, 10.3) | 3.0 (2.3, 4.0) | 13.1 (11.2, 15.2) | 5.2 (4.1, 6.5) |
| CCB | 7.0 (6.3, 7.8) | 3.2 (2.4, 4.3) | 4.7 (3.7, 5.9) | 2.6 (1.7, 4.1) |
| Clonidine/hydralazine/loop/spironolactone | 1.3 (1.0 to 1.7) | 0.9 (0.5, 1.5) | 1.1 (0.7, 1.7) | 1.8 (1.2, 2.9) |

2 Medications

| Medication | HTN Only | HTN-DM | HTN-CVD | HTN-DM-CVD |
|------------|----------|--------|---------|------------|
| ACE/ARB & CCB | 6.0 (5.2, 6.9) | 6.6 (5.4, 8.0) | 4.8 (3.6, 6.3) | 3.9 (2.8, 5.3) |
| ACE/ARB & Beta-Blocker | 4.5 (3.9, 5.2) | 6.6 (5.3, 8.2) | 12.4 (10.6, 14.5) | 15.9 (13.5, 18.8) |
| ACE/ARB & Thiazide | 15.5 (14.0, 17.1) | 12.9 (11.1, 14.9) | 5.7 (4.3, 7.4) | 6.3 (4.5, 8.5) |
| ACE/ARB & Clonidine/Hydralazine/Loop/Spiroolactone | 0.8 (0.6, 1.2) | 2.3 (1.5, 3.5) | 1.7 (1.1, 2.7) | 2.7 (1.8, 3.9) |
| CCB & Thiazide | 1.6 (1.2, 2.0) | 0.7 (0.4, 1.2) | 1.0 (0.5, 1.7) | 0.3 (0.1, 0.7) |
| CCB & beta-blocker | 1.8 (1.4, 2.3) | 1.0 (0.7, 1.5) | 4.0 (3.0, 5.3) | 2.1 (1.3, 3.1) |
| CCB & Clonidine/hydralazine/loop/spironolactone | 0.4 (0.3, 0.7) | 0.4 (0.2, 0.7) | 0.7 (0.4, 1.3) | 1.3 (0.7, 2.5) |
| Thiazide & Beta-blocker | 4.4 (3.6, 5.2) | 2.3 (1.7, 3.1) | 3.5 (2.6, 4.6) | 1.7 (1.0, 2.8) |
| Thiazide & clonidine/hydralazine/loop/spironolactone | 0.2 (0.1, 0.4) | 0.1 (0.0, 0.3) | 0.3 (0.2, 0.7) | 0.1 (0.0, 0.5) |
| Beta-blocker & clonidine/hydralazine/loop/spironolactone | 0.6 (0.4, 0.9) | 0.8 (0.5, 1.4) | 3.1 (2.2, 4.2) | 2.8 (1.9, 4.2) |
| Clonidine/hydralazine/loop/spironolactone combination | 0.0 (0.0, 0.1) | 0.1 (0.0, 0.6) | 0.0 (0.0, 0.2) | 0.1 (0.0, 0.3) |

3 Medications

| Medication | HTN Only | HTN-DM | HTN-CVD | HTN-DM-CVD |
|------------|----------|--------|---------|------------|
| ACE/ARB & CCB & beta-blocker | 1.8 (1.4, 2.3) | 2.8 (2.1, 3.9) | 3.9 (3.0, 5.2) | 5.5 (4.1, 7.4) |
| ACE/ARB & CCB & thiazide | 4.2 (3.6, 5.0) | 6.7 (5.3, 8.5) | 2.0 (1.3, 3.0) | 3.1 (2.1, 4.4) |
| ACE/ARB & beta-blocker & thiazide | 3.6 (3.0, 4.2) | 6.0 (4.6, 7.6) | 6.4 (5.1, 8.0) | 7.3 (5.7, 9.3) |
| ACE/ARB & clonidine/hydralazine/diuretic/spiro & 1 other | 1.6 (1.3, 2.0) | 3.3 (2.6, 4.3) | 4.9 (3.9, 6.3) | 7.6 (5.9, 9.6) |
| CCB & beta-blocker & thiazide | 0.8 (0.6, 1.2) | 0.9 (0.4, 2.0) | 1.0 (0.6, 1.8) | 0.6 (0.3, 1.1) |
| Remaining 3 medication combinations without ACE/ARB | 0.6 (0.4, 0.9) | 0.9 (0.5, 1.7) | 1.7 (1.1, 2.7) | 2.2 (1.4, 3.4) |

4 or More Medications

| Medication | HTN Only | HTN-DM | HTN-CVD | HTN-DM-CVD |
|------------|----------|--------|---------|------------|
| ACE/ARB included combinations | 2.5 (2.1, 3.1) | 7.1 (5.7, 8.8) | 8.1 (6.6, 9.9) | 11.9 (9.8, 14.3) |
| 4 or more medication classes without ACE/ARB | 0.2 (0.1, 0.3) | 0.5 (0.3, 0.9) | 0.8 (0.4, 1.4) | 1.1 (0.5, 2.2) |

ACE, angiotensin converting-enzyme; ARB, angiotensin II receptor blocker; CCB, calcium channel blocker; CVD, cardiovascular disease; DM, diabetes mellitus; HTN, hypertension.

There were 15,901 hypertensive adults without heart failure taking hypertension medication in the Medical Expenditure Panel Survey from 2013 through 2015. We divided our sample into four different comorbidity groups based on hypertension, diabetes, and cardiovascular disease (coronary heart disease or stroke) diagnoses. We then calculated the proportion of adults taking different single-drug and multi-drug hypertension medications regimens in each comorbidity group. Numbers in parentheses represent upper and lower limits of 95% CIs.
multi-drug regimens for individuals by comorbid- 

bidity is worthwhile because certain drugs and 
drug combinations may offer differential benefits 
by comorbidity.

Methods

Using data from the 2013 through 2015 Medical 
Expenditure Panel Survey (MEPS), we describe 
the most common single-, 2-, 3-, and 4-drug 
hypertension regimens among hypertensive ad-
utls with 1) hypertension only (HTN-only); 2) 
hypertension and diabetes (HTN-DM); 3) hy-
pertension and cardiovascular disease (ie, coro-
nary heart disease or history of stroke) (HTN-
CVD); and 4) hypertension, diabetes, and CVD 
(HTN-DM-CVD) (Table 1).

MEPS is a nationally representative survey of 
the noninstitutionalized US civilian population. 
Every year, MEPS collects sociodemographic, self-
reported medical conditions, and medication infor-
mation from 2 overlapping panels of respondents, 
following each panel for 2 years. Self-reported 
chronic prescriptions from MEPS have been vali-
dated using claims data.3

Our sample included hypertensive adults with-
out heart failure who took any antihypertensives 
during the year. We categorized antihypertension 
medications into 5 classes: 1) angiotensin con-
verting-enzyme inhibitors (ACEI) or angiotensin II re-
ceptor blockers (ARB); 2) thiazide diuretics; 3) cal-
cium-channel blockers (CCB); 4) β-blockers; and 
5) other agents (loop diuretics, spironolactone, clo-
nidine, hydralazine). Individuals with ≥3 prescrip-
tions or ≥90 tablets/capsules during each year were 
considered medication users.

We used STATA (version 13, StataCorp LLC, 
College Station, TX) and applied complex sur-
vey weights to all analyses. The OhioHealth 
Institutional Review Board ruled this study 
exempt.

Results

Of the 76,792 adults included in the survey, 15,901 
adults, or a survey adjusted 22.6% (95% CI, 21.9 to 
23.3), had hypertension and took antihyperten-
sive(s). Seventy percent (95% CI, 68.4 to 70.9) took 
an ACEI/ARB, 39.2% (95% CI, 37.9 to 40.5) took 
a β-blocker, 36.1% (95% CI, 34.7 to 37.5) took a 
thiazide, and 28.7% (95% CI, 27.6 to 29.9) took a 
CCB. Most (58.6% [95% CI, 57.3 to 59.8]) of our 
sample took multiple antihypertensives, but this 
varied by comorbidity group. The HTN-only 
group had the smallest proportion taking multiple 
antihypertensives; followed by the HTN-DM, 
HTN-CVD, and HTN-DM-CVD groups. Regi-
mens including an ACEI/ARB were the most prev-
alent regimens among individuals taking ≥2 anti-
hypertensives. The most common 2-drug regimen 
for both the HTN-only and HTN-DM groups was 
an ACEI/ARB with thiazide. The most prevalent 
regimen for the 2 CVD (HTN-CVD and HTN-
DM-CVD) groups was an ACEI/ARB with 
β-blocker. Among individuals with CVD, 61.2% 
(95% CI, 58.7 to 63.4) took a β-blocker.

Discussion

Most individuals in our sample took multi-drug 
regimens, a finding compatible with previous 
studies.1,4 Notably, the ACEI/ARB-CCB combi-
nation was used less often than the ACEI/ARB-
thiazide combination. One large randomized 
control trial applicable to the United States pop-
ulation, ACCOMPLISH, tested these combina-
tions among individuals at high-risk of cardiovas-
cular events and showed an ACEI-CCB may 
prevent more cardiovascular events than ACE-
thiazide. However, ACCOMPLISH was stopped 
early for benefit and has not been replicated or 
adopted into guidelines.

Our study has several limitations. Self-reported 
medications may not accurately represent 
important conditions used to select antihyperten-
sives (eg, chronic renal failure). The lack of exact 
medication-usage dates may overestimate the num-
ber of medications taken at 1 time.

Most individuals with hypertension use between 
2 and 5 medications, which vary by comorbidity, 
but nearly all randomized clinical trials examine 
outcomes for single agents. A better understanding 
of the outcomes associated with different antihy-
pertensive combinations among individuals with 
different comorbidities could improve hyperten-
sion management.

To see this article online, please go to: http://jabfm.org/content/ 
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