

Hypertension

JOURNAL OF THE AMERICAN HEART ASSOCIATION



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Hypertension 2005;46;273-279; originally published online Jun 27, 2005;

DOI: 10.1161/01.HYP.0000172753.96583.e1

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

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Effects of Noncardiovascular Comorbidities on Antihypertensive Use in Elderly Hypertensives

Philip S. Wang, Jerry Avorn, M. Alan Brookhart, Helen Mogun, Sebastian Schneeweiss, Michael A. Fischer, Robert J. Glynn

Abstract—Although the benefits of antihypertensive drugs have been clearly established, they remain underused by vulnerable older populations. We examined whether the presence of noncardiovascular comorbidity deters use of antihypertensives in elderly with hypertension. We conducted a retrospective cohort study among 51 517 patients ≥ 65 years of age in the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE) Program during 1999 and 2000. All were hypertensive and had diagnoses and used treatments during 1999 to qualify for entry into 1 of the following 5 mutually exclusive cohorts: asthma/chronic obstructive pulmonary disease (COPD), depression, gastrointestinal (GI) disorders, osteoarthritis, or none of the 4 comorbidities. Proportions using antihypertensives in 2000 were assessed. Logistic regression analysis was used to identify the independent effects on antihypertensive use of the 4 comorbidities of interest, sociodemographic characteristics, other cardiovascular and noncardiovascular comorbidity, and health care utilization variables. After adjustments in multivariable analyses, antihypertensive use was consistently lower in patients with asthma/COPD (odds ratio [OR], 0.43; 95% confidence interval [CI], 0.40 to 0.47), depression (OR, 0.50; 95% CI, 0.45 to 0.55), GI disorders (OR, 0.59; 95% CI, 0.54 to 0.64), and osteoarthritis (OR, 0.63; 95% CI, 0.59 to 0.67) relative to those without these conditions. Reduced antihypertensive use was also associated with older age, female gender, white race, more severe other comorbidities, absence of some cardiovascular indications, hospitalizations, nursing home care, physician visits, and use of fewer other medications. Highly prevalent, noncardiovascular conditions appear to deter use of antihypertensives in elderly with hypertension. (*Hypertension*. 2005;46:273-279.)

Key Words: antihypertensive agents ■ morbidity ■ elderly

Hypertension afflicts ≈ 65 million Americans, including the majority of elderly,¹ and imposes enormous burdens through associated myocardial infarctions, heart failure, stroke, and kidney disease.² Although the benefits of antihypertensive medications are clearly established,^{3,4} only 60% of hypertensive patients are currently treated, and only 34% are adequately controlled.⁵ Identifying reasons for this underutilization is a critical first step in developing interventions to improve use of this highly effective therapy.

Multiple chronic conditions are present in $>60\%$ of older persons.⁶⁻⁹ Studies have begun recently to shed light on the impact that comorbid illness can exert on use of treatments such as antihypertensive medications. One investigation found that having multiple conditions substantially increases the risk of avoidable hospitalizations and preventable complications during hospitalizations, leading the authors to hypothesize that comorbidity decreases the use of preventive therapies.¹⁰ Some studies have indeed found reduced use of cardiovascular treatments such as aspirin and thrombolysis when comorbidity is present.¹¹

Results concerning the impact of comorbidity on specifically antihypertensive use in the elderly are limited and

mixed. Most previous research has focused exclusively on the impact of comorbid cardiovascular conditions.^{12,13} Not surprisingly, comorbid coronary artery disease, congestive heart failure, cerebrovascular disease, diabetes, and hyperlipidemia are associated with increased antihypertensive use as a result of compelling evidence of benefits when such indications are present.¹⁴⁻¹⁷

On the other hand, research examining the impact of noncardiovascular comorbidities on antihypertensive use has been lacking. One study reported reduced antihypertensive use when physical or cognitive impairment was present, although it is not clear whether and what comorbid conditions may have been responsible.¹⁸ Reasons for such findings are uncertain, but some investigators have proposed that primary conditions are neglected by patients and providers when unrelated chronic medical illnesses are copresent.¹⁹

The current study had 3 aims. First, we sought to investigate whether comorbidities, unrelated to indications for antihypertensive therapy or sequelae of hypertension, decrease antihypertensive use. We purposefully chose 4 unrelated conditions that are symptomatic: asthma/chronic ob-

Received January 18, 2005; first decision February 8, 2005; revision accepted May 4, 2005.

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Hypertension is available at <http://www.hypertensionaha.org>

DOI: 10.1161/01.HYP.0000172753.96583.e1

structive pulmonary disease (COPD), depression, gastrointestinal (GI) disorders such as dyspepsia and ulcerative disease, and osteoarthritis. Our a priori hypothesis was that symptomatic comorbidities especially reduce antihypertensive use because the asymptomatic nature of hypertension may spuriously make it seem less pressing to treat.²⁰ Our second aim was to determine whether there are differences across the 4 conditions in terms of their impacts on antihypertensive use. Some investigators have suggested that mood disorders and chronic airway diseases may be particularly associated with underutilization of health care despite their high levels of disability.²¹ Finally, without information on blood pressures, we could not be certain that lower rates of antihypertensive use in patients with comorbidities truly represented underuse. Therefore, our third aim was to examine whether comorbidities deter antihypertensive use in subgroups with clear cardiovascular indications.

Methods

Data Sources

Pennsylvania Pharmaceutical Assistance Contract for the Elderly Program

The Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PACE) program is the largest state prescription benefits program for the elderly in the United States. Information was available from January 1, 1999, to December 31, 2000, and included demographic characteristics and data for all filled prescriptions (including medication, quantity dispensed, and days supply). The PACE program has no deductibles and no maximum annual benefit. There is a modest copayment of \$6 for each prescription. The income ceiling for PACE eligibility is \$14 000 if single and \$17 200 for a couple, resulting in a recipient population that is inclusive of indigent as well as nonindigent elderly. These benefits and eligibility requirements for enrollment result in essentially no out-of-pocket (ie, out-of-system) medication.

Pennsylvania Medicare

Medicare data used in the present study included Medicare part A data on hospitalizations and nursing home stays, and Medicare part B data on outpatient professional services and procedures. These data were available for all Pennsylvania residents >65 years of age enrolled in the PACE program during January 1, 1999, to December 31, 2000.

We first identified all Medicare beneficiaries ≥ 65 years of age who were also enrolled in the PACE program (because the latter program, but not Medicare, provides comprehensive data on all prescription drug use). Data on all filled prescriptions, procedures, physician encounters, hospitalizations, and long-term care were assembled into a relational database using Sybase software. All traceable person-specific identifiers from both programs were transformed into anonymous, coded study numbers to protect the privacy of subjects. This study was approved by the institutional review board of the Brigham and Women's Hospital.

Study Population

The study population consisted of all individuals ≥ 65 years of age who had ≥ 1 International Classification of Diseases, 9th revision (ICD-9) diagnoses of hypertension in their administrative records and fulfilled the following criteria from January 1, 1999, to December 31, 1999, for entry into 1 of 5 mutually exclusive cohorts.

Asthma/COPD

The asthma/COPD cohort received ≥ 1 ICD-9 diagnosis of asthma or COPD, filled ≥ 1 prescription for an inhaled corticosteroid or an inhaled β -agonist, and had no diagnoses or treatments for depression, GI disorders, or osteoarthritis during the calendar year.

Depression

Those in the depression cohort received an ICD-9 diagnosis of depression, filled ≥ 1 prescription for an antidepressant drug, and had no diagnoses or treatments for asthma/COPD, GI disorders, or osteoarthritis during the calendar year.

GI Disorders

The GI disorders cohort received an ICD-9 diagnosis for dyspepsia or GI ulcerative disease, filled ≥ 1 prescription for a proton pump inhibitor or histamine-2 blocker, and had no diagnoses or treatments for asthma/COPD, depression, or osteoarthritis during the calendar year.

Osteoarthritis

Those in the osteoarthritis cohort received an ICD-9 diagnosis of osteoarthritis, filled ≥ 1 prescription for a nonsteroidal anti-inflammatory drug, including selective cyclooxygenase-2 inhibitors, and had no diagnoses or treatments for asthma/COPD, depression, or GI disorders during the calendar year.

No Evidence of the 4 Comorbidities

Finally, those with no evidence of the 4 comorbidities had no diagnoses or treatments for asthma/COPD, depression, GI disorders, or osteoarthritis as defined above during calendar year 1999.

To ensure uniform periods of eligibility during calendar years 1999 and 2000, during which covariates and the study outcome could be assessed, all subjects were required to have used ≥ 1 health care service and filled ≥ 1 prescription in each of the following 4 time periods: the first 6 months of 1999, the second 6 months of 1999; the first 6 months of 2000; and the second 6 months of 2000.

Definition of Antihypertensive Drug Use During the Follow-Up Year

We began by identifying all prescriptions filled by subjects during calendar year 2000. We then defined antihypertensive medication use during 2000 as filling ≥ 1 prescription for α -blockers, $\alpha\beta$ -blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, β -blockers, calcium antagonists, or diuretics typically used to treat hypertension in ambulatory settings.

Other Covariates

We defined the following variables during calendar year 1999.

Sociodemographic Characteristics

Program enrollment information was used to determine each subject's age, gender, and race.

Cardiovascular Conditions

We scanned all ICD-9 diagnostic information and use of all treatments and services to assess the presence in 1999 of the following cardiovascular conditions potentially related to use of antihypertensive medications: coronary artery disease, cerebrovascular disease, congestive heart failure, and diabetes.

Other Clinical Comorbidity

We scanned all ICD-9 diagnostic information from subjects' inpatient and outpatient encounters in 1999 to calculate a modified Charlson score, a commonly used measure of the extent of comorbid illness.^{22,23} Charlson scores were calculated such that none of the diagnoses of primary interest (ie, asthma/COPD, depression, GI disorders, or osteoarthritis) or cardiovascular conditions described above contributed points to subjects' scores.

Health Care Utilization

The extent of specific forms of health care utilization was assessed during calendar year 1999, including the number of medications used (excluding medications used to define the 4 comorbidity cohorts of interest), days hospitalized, days spent in a nursing home, and physician visits.

TABLE 1. Characteristics of the Study Population in 1999 (n=51 517)

Variable	Comorbidity Cohort				
	Asthma/COPD	Depression	GI Disorders	Osteoarthritis	None of the 4
n	5753	3284	4851	13 577	24 052
Age					
65–74 (%)	32.5	26.1	25.5	23.5	28.2
75–84 (%)	51.1	49.9	52.1	53.6	49.4
>85 (%)	16.4	24.0	22.4	22.9	22.4
Gender					
Female (%)	74.7	88.5	84.0	90.3	82.1
Male (%)	25.3	11.5	16.0	9.7	17.9
Race					
White (%)	93.8	95.5	94.5	93.1	93.9
Nonwhite (%)	6.2	4.5	5.5	6.9	6.1
Cardiovascular conditions (%)					
Coronary artery disease	23.9	22.4	27.0	16.9	13.7
Cerebrovascular disease	19.8	29.6	24.2	17.3	15.0
Congestive heart failure	52.4	42.2	42.9	38.8	28.6
Diabetes	29.6	32.3	32.6	31.3	32.4
Charlson comorbidity score (mean)	0.7	0.8	0.8	0.6	0.4
Use of health care in 1999					
No. of medications (mean)	12.3	10.9	10.9	10.1	5.8
Hospital days (mean)	5.4	7.7	6.2	3.3	1.0
Nursing home days (mean)	1.6	4.5	2.1	1.7	0.4
Physician visits (mean)	10.4	9.4	11.2	10.3	6.7
Antihypertensive use in 2000 (%)	76.2	76.4	79.4	80.0	83.5

Analyses

Initially, we identified the distributions of sociodemographic, clinical, and health care utilization characteristics among the 5 study cohorts during calendar year 1999. We then calculated the frequency of use of antihypertensive drugs in the 5 cohorts of interest during calendar year 2000. To examine the independent effects of the 4 comorbidities of primary interest (sociodemographic characteristics, cardiovascular conditions, other comorbidity, and health care utilization variables on antihypertensive use), we constructed multiple logistic regression models²⁴ of antihypertensive drug use during calendar year 2000. Variables representing the 4 comorbidities of primary interest were included. Models also contained age, gender, race, individual cardiovascular conditions, Charlson comorbidity score, total number of medications, days hospitalized, days in nursing homes, and physician visits in 1999. To directly compare the effects of the individual comorbid conditions on antihypertensive use in 2000, we constructed additional multivariable models in which subjects with none of the 4 comorbidities were excluded and those with osteoarthritis served as the referent. We also conducted analyses restricted to just patients with coronary artery disease, cerebrovascular disease, peripheral vascular disease, or diabetes mellitus to study whether comorbidities have deterring effects on antihypertensive use in patients with clear indications. The statistical significance of relationships was assessed with 95% confidence intervals (CIs).

Results

Table 1 presents the distributions of demographic, clinical, and health care utilization characteristics among the 5 study cohorts. Approximately half of subjects in all cohorts were 75 to 84. Mean ages in the cohorts with asthma/COPD, depression, GI disorders, osteoarthritis, and none of the 4 comor-

bidities were 78.3, 79.6, 79.6, 79.8, and 79.9, respectively. Women made up the large majority, more so in the cohorts with osteoarthritis and depression cohorts and less so in cohorts with asthma/COPD, GI disorders, and none of the 4 comorbidities. The majority of cohorts were of white race.

Proportions with coronary artery disease ranged from a high of 27.0% in those with GI disorders to a low of 13.7% among those with none of the 4 comorbidities. The presence of cerebrovascular disease ranged from 29.6% of those with depression to 15.0% of those with none of the 4 comorbidities. Congestive heart failure prevalence ranged from 52.4% of those with asthma/COPD to 28.6% of those with none of the 4 comorbidities. Diabetes was most prevalent in those with GI disorders (32.6%) and least prevalent in those with asthma/COPD (29.6%). Subjects without any of the 4 comorbidities had lower Charlson comorbidity scores than other cohorts. Those without the 4 comorbidities also had less utilization of health care in 1999 than other cohorts, including their total number of medications, days hospitalized, days in a nursing home, and physician visits. On the other hand, a greater proportion of the cohort without the 4 comorbidities used antihypertensives in 2000, relative to the cohorts with 1 of the comorbidities of interest.

Results from a multivariable logistic regression model of the independent effects of patient sociodemographic, clinical, and health care utilization characteristics assessed in 1999, on antihypertensive use in 2000, are shown in Table 2. Younger

TABLE 2. Independent Predictors of Using Antihypertensive Medications in 2000

Variable	Adjusted OR* (95% CI*) of Using Antihypertensives	
Age		
65–74		
75–84	0.99	(0.94–1.05)
>85	0.92	(0.86–0.99)
Gender		
Female	1.09	(1.03–1.16)
Male		
Race		
White	—	
Nonwhite	1.15	(1.04–1.26)
Comorbid conditions†		
Asthma/COPD	0.43	(0.40–0.47)
Depression	0.50	(0.45–0.55)
GI disorders	0.59	(0.54–0.64)
Osteoarthritis	0.63	(0.59–0.67)
Cardiovascular conditions		
Coronary artery disease	1.31	(1.23–1.40)
Cerebrovascular disease	1.03	(0.97–1.10)
Congestive heart failure	1.05	(0.99–1.11)
Diabetes	1.16	(1.10–1.22)
Charlson comorbidity score‡	0.98	(0.96–0.99)
Health care use in 1999§		
Total No. of medications	2.15	(2.01–2.30)
Hospital days	0.90	(0.87–0.93)
Nursing home days	0.94	(0.92–0.97)
Physician visits	0.82	(0.79–0.85)

*From a multivariable logistic regression model incorporating all variables shown; †referent is not having any of the 4 conditions; ‡ORs shown are per 1 unit increase in Charlson scores; §ORs shown are per 10 unit increases in the variable shown.

subjects, females, and nonwhites were significantly more likely to receive antihypertensive treatments. The presence of any of the 4 comorbid conditions of interest significantly reduced the likelihood of antihypertensive use. The presence of coronary artery disease or diabetes were associated with increased use of antihypertensives. Higher Charlson comorbidity scores (ie, indicating greater severity of other comorbid illness) were associated with diminished use of antihypertensives. Antihypertensive use in 2000 was associated with more use of medications in 1999, but less use of inpatient services, nursing home care, and physician visits.

In a model restricted to patients with clearer indications for antihypertensive therapy (ie, coronary artery disease, cerebrovascular disease, peripheral vascular disease, diabetes mellitus), the 4 comorbid conditions were still significantly associated with reduced antihypertensive use of generally the same magnitude (the adjusted odds ratios [and 95% CIs] for arthritis, asthma/COPD, depression, and GI disorders were 0.66 [0.61 to 0.71], 0.44 [0.40 to 0.49], 0.51 [0.45 to 0.57], and 0.60 [0.54 to 0.67], respectively) as in our main analyses.

TABLE 3. Comparison of the Effects of Individual Comorbidities on Antihypertensive Use in 2000

Comorbid Condition	Adjusted OR* (95% CI*) of Using Antihypertensives	
Asthma/COPD	0.70	(0.65–0.76)
Depression	0.79	(0.72–0.87)
GI Disorders	0.93	(0.86–1.01)
Osteoarthritis	1.00	—

*From a multivariable logistic regression model adjusted for age, gender, race, cardiovascular conditions (coronary artery disease, cerebrovascular disease, congestive heart failure, and diabetes), Charlson comorbidity score, and health care use in 1999 (No. of medications, hospital days, nursing home days, and physician visits).

Results from a multivariable logistic regression model directly comparing the effects of the 4 individual comorbid conditions on antihypertensive use in 2000 are shown in Table 3. Subjects with asthma/COPD or depression but not GI disorders were significantly less likely to use antihypertensives relative to those with osteoarthritis.

Discussion

We found that chronic conditions unrelated to indications for antihypertensive therapy or the sequelae of hypertension appear to have deterring effects on antihypertensive use. Elderly hypertensive patients with these unrelated comorbidities were generally half as likely to receive this already underused class of treatments.⁵ These results are problematic in light of the very clear evidence of the benefits of antihypertensive therapy for primary and secondary prevention at multiple end organs.^{3,4}

Significant reductions in antihypertensive use were seen consistently across the 4 comorbidities examined, suggesting that other conditions not studied here are also likely to reduce antihypertensive use. This possibility that unrelated comorbidity in general diminishes antihypertensive use is further supported by the significant reduction in antihypertensive use with higher Charlson comorbidity scores. Comorbid conditions are present in as many as 60% of older populations.^{6–9} This high frequency makes any general deterring effect of comorbidities on use of beneficial treatments an important public health issue to address.

Although all 4 conditions were associated with diminished antihypertensive use, the retarding effects of asthma/COPD and depression were significantly larger than for osteoarthritis or GI disorders. This confirms some previous findings that identified mood disorders and chronic airway diseases as being especially associated with underuse of health care in general²¹ and treatments for cardiovascular conditions in particular.^{19,25–28}

Potential mechanisms underlying these findings should be considered. One possibility is that biological or physiological bases explain these findings (eg, lower blood pressures have been observed in some²⁹ but not other³⁰ studies of depressed patients). However, this is unlikely to explain the equally strong deterring effects of comorbidity on antihypertensive use we observed in subgroups with more clear cardiovascular indications. Furthermore, the limited evidence that does exist suggests the comorbidities examined here or their treatments

may actually increase risks for negative cardiovascular outcomes and cardiovascular disability.^{31–38}

Factors related to patients, providers, and health care systems may more readily explain these results. Patients with a greater number of conditions have less time and resources to attend to each.²⁰ Symptomatic comorbidities may also become a higher priority for patients and providers than asymptomatic but no less serious conditions such as hypertension.^{39,40} It is important to keep in mind that PACE recipients do not pay much for their medications; other elderly may face much larger financial barriers, leading to even less antihypertensive use, especially among those constrained by multiple comorbidities. Widespread poor adherence and premature discontinuation may also cut utilization short among elderly patients who initiate antihypertensives.^{41,42}

Important changes have occurred in primary care in which most hypertension is treated, including an increase in competing demands on physicians.^{43,44} Physicians may perceive there will be interactions, real or otherwise, between antihypertensives and medications used to treat comorbidities.⁵ Features of health care systems may also be important, including the extent to which there is coordination among providers caring for patients with multiple conditions.¹⁰ Although not present in PACE, restrictions on the number of prescriptions and formularies may deter antihypertensive use in other health care systems, especially among elderly with comorbidities.^{45–47}

This study confirmed some previous findings regarding correlates of antihypertensive use. The reduced use seen previously among the oldest old may be attributable to their more limited abilities to pay for and access care, real or perceived frailty, and even outright “ageism.”^{18,48} Greater use by nonwhites could reflect the higher prevalence and severity of hypertension or possibly the success of recent programs to increase hypertension awareness and treatment in these populations.^{49,50} The diminished antihypertensive use observed among males may be attributable to their greater reluctance to receive such therapies but is paradoxical in light of their potentially greater needs.¹⁸

As expected, we observed that some cardiovascular indications for antihypertensive therapy (ie, coronary artery disease and diabetes) were associated with increased use, although probably short of what should be expected in such high-risk populations.^{12–15} Greater antihypertensive use has been observed among those receiving more medications generally,¹⁸ whereas nursing homes have been identified previously as settings with low-intensity use of several medication classes.^{51,52} Hospitalizations and ambulatory visits may be markers of more severe comorbidity and have been associated with diminished antihypertensive use previously.¹⁴

These results should be interpreted with the following 4 sets of potential limitations in mind. First, although most evidence⁵ suggests that antihypertensives are underused in the elderly, we were unable to assess blood pressures in the study population. For this reason, we cannot say with certainty that the lower proportions of antihypertensive use observed among patients with comorbidities represent underuse; alternatively, the higher proportions observed among those without comorbidities could represent overuse. Our

requirements for ≥ 1 diagnosis of hypertension in 1999 may have minimized the latter possibility. Furthermore, the equally strong deterring effects of comorbidities in subgroups with clear indications provides additional evidence that the lower rates of antihypertensive use in our main analyses do represent underuse. Second, although we believe our adjustments corrected any imbalances in the distribution of indications for antihypertensives across our cohorts, the possibility of residual or unmeasured confounding should be considered. Third, medications that we presumed were being prescribed for hypertension may actually have been given to patients exclusively for other cardiovascular indications. Requiring ≥ 1 hypertension diagnosis in patients’ administrative records may have decreased this possibility; however, if patients with other cardiovascular indications were not intentionally prescribed and using their medications to also treat specifically hypertension, we may be underestimating the degree to which antihypertensive drugs are poorly used. Finally, the applicability of these results to other older populations is enhanced by the facts that Pennsylvania is second only to Florida in terms of the proportion of its citizens >65 years of age, PACE is the largest state medication benefit program for elderly in the United States, and PACE includes a wide range of socioeconomic strata because of its generous eligibility requirements.⁵³ Nonetheless, the use of antihypertensives may be substantially different in other states and health care systems.

Despite these potential limitations, our findings suggest that the negative impact of comorbidity on antihypertensive use may be an important intervention target. Assuming 60% of elderly are afflicted by multiple comorbid conditions^{6–9} that reduce antihypertensive use by as much as the 50% observed in this study, successful interventions on these deterring effects have the potential to improve antihypertensive underuse in the elderly by approximately one third.⁵⁴ One effective strategy may be to emphasize antihypertensive use by patients with comorbidities in widely disseminated guidelines.⁵ Whether growing direct-to-consumer advertising can increase awareness in this regard could be investigated.⁵⁵ Greater use of community awareness, blood pressure screening, and disease management programs to increase antihypertensive initiation in patients with comorbidities may be needed.⁵⁶ Even after antihypertensives are initiated, interventions to enhance adherence should be explored, especially in light of evidence of their utility in other cardiovascular conditions.^{57,58} Expanding drug coverage may be needed to ease financial barriers faced by patients with multiple conditions.^{46,47} Drug utilization review programs could alert physicians to instances of suboptimal antihypertensive use⁴⁵ and performance standards⁵⁹ or “report cards” (eg, National Committee for Quality Assurance standards⁶⁰) could help monitor the impact of interventions on antihypertensive use in patients with comorbidities. A combination of all of these may be needed if the quality of hypertension care and the clinical outcomes of vulnerable elderly with comorbidities are to be improved.⁶¹

Perspectives

Antihypertensive drugs remain underused in vulnerable older populations, making it imperative to identify potentially

modifiable determinants. In this study, we found that highly prevalent noncardiovascular comorbidities (osteoarthritis, asthma/COPD, depression, and GI disorders) were all significantly related to diminished use of antihypertensives by elderly with hypertension. Clearly, more research is necessary to elucidate the reasons for these findings, including the extent to which biologic, patient, provider, economic, and health care system factors may play a role. However, if confirmed, these results suggest that there could be substantial public health benefits from intervening on the deterring effects that unrelated comorbidities appear to have on antihypertensive medication use. We speculate on what future initiatives might be necessary to successfully address the negative impacts noncardiovascular comorbidities may have on the use of this highly beneficial preventive therapy.

Acknowledgments

This research was supported by National Institute on Aging grant R01-AG18833 (R.J.G.), National Institute of Mental Health grants R01-MH69772 and K01-MH01651 (P.S.W.), and National Institute on Aging grant R03-AG18395 (J.A.).

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