Antihypertensive Adherence Trajectories Among Older Adults in the First Year After Initiation of Therapy

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BACKGROUND

Adherence to antihypertensives is suboptimal, but previous methods of quantifying adherence fail to account for varying patterns of use over time. We sought to improve classification of antihypertensive adherence using group-based trajectory models, and to determine whether individual factors predict adherence trajectories.

METHODS

We identified older adults initiating antihypertensive therapy during 2008–2011 using a 20% sample of Medicare (federal health insurance available to US residents over the age of 65) beneficiaries enrolled in parts A (inpatient services), B (outpatient services), and D (prescription medication). We developed monthly adherence indicators using prescription fill dates and days supply data in the 12 months following initiation. Adherence was defined as having at least 80% of days covered. Logistic models were used to identify trajectory groups. Bayesian information criterion and trajectory group size were used to select the optimal trajectory model. We compared the distribution of covariates across trajectory groups using multivariable logistic regression.

RESULTS

During 2008–2011, 282,520 Medicare beneficiaries initiated antihypertensive therapy (mean age 75 years, 60% women, 84% White). Six trajectories were identified ranging from perfect adherence (12-month adherence of 0.97, 40% of beneficiaries) to immediate stopping (12-month adherence of 0.10, 18% of beneficiaries). The strongest predictors of nonadherence were initiation with a single antihypertensive class (adjusted odds ratio = 2.08 (95% confidence interval: 2.00–2.13)), Hispanic (2.93 (2.75–3.11)) or Black race/ethnicity (2.04 (1.95–2.13)), and no prior history of hypertension (2.04 (2.00–2.08)) (Area under the receiving operating characteristic curve: 0.53).

CONCLUSIONS

There is substantial variation in antihypertensive adherence among older adults. Certain patient characteristics are likely determinants of antihypertensive adherence trajectories.

Keywords: antihypertensive adherence; blood pressure; epidemiology; hypertension; older adults.

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An estimated 65% of older adults have elevated blood pressure (hypertension) or take antihypertensive medications.[1] The prevalence of hypertension increases with age due to changes in metabolic and vascular functioning.[2,3] Hypertension increases the risk for cardiovascular diseases, kidney disease, and death.[2,4] Antihypertensive medications reduce the risk of cardiovascular disease among hypertensive patients,[5–7] yet few older adults are adherent to these medications.[8] A meta-analysis reported antihypertensive adherence of 49% after 1 year.[9] Failure to remain adherent can lead to increased risk of cardiovascular disease, hospitalizations, and mortality.[5,10–12] Older adults are at greater risk of nonadherence due to polypharmacy and increased comorbidities.[2] Female gender, low income, presence of comorbidities, mental health disorders, and cognitive impairment are associated with nonadherence.[2,9,13,14]

Commonly used adherence measures, such as proportion days covered (PDC) and the medication possession ratio, quantify the number of days covered with medications over a defined period of time,[8,13] but miss the time-varying nature of medication adherence.[8,15] Good control of this variability in medication adherence may be critical in studies of factors that strongly depend on age. Group-based trajectory models (GBTM) can quantify these time-varying patterns,[16–18] accounting for dynamic patterns of medication use without assumptions about trajectory shape.[15,19] In a study of adults initiating statins, GBTMs distinguished between adherent and nonadherent users better than time-static adherence measures.[15]

Despite these advantages, no prior study has used GBTMs to model antihypertensive adherence trajectories among older adults initiating therapy. Our objectives were to (i) use GBTMs to identify antihypertensive adherence trajectories in the first year following initiation, (ii) compare adherence trajectories to traditional adherence measures, and (iii) examine whether patient characteristics predict adherence trajectories.

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METHODS

Data

We used a 20% nationwide, random sample of fee-for-service Medicare beneficiaries who were enrolled at least 1 month in Medicare parts A (inpatient care), B (outpatient care), and D (prescription drug) coverage between 2007 and 2011. Medicare is the federally provided health insurance available to all US residents ≥65 years old and fee-for-service is the part of Medicare where individual insurance claims are sent directly to the Centers for Medicare and Medicaid Services (CMS). Data were obtained under an agreement between CMS and the University of North Carolina at Chapel Hill (UNC). The study protocol was approved by the UNC's Institutional Review Board (#15–1704).

Cohort

The cohort included Medicare beneficiaries initiating antihypertensive therapy during 2008–2011 who were continuously enrolled in Medicare Parts A, B, and D for at least 12 months prior to initiation (index date). New use was defined as no prior prescription in the last 12 months of angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, or thiazide diuretics (Supplementary Table 1A).

We limited the cohort to first time new users of antihypertensives. To ensure 1 full year of Medicare enrollment prior to initiation, beneficiaries were >66 years old. Beneficiaries with nursing home stays or metastatic cancer claims in the last 12 months were excluded since these factors could affect medication adherence. To capture patterns of antihypertensive use, only beneficiaries enrolled in Medicare for ≥1 year following initiation were included (Figure 1).

Antihypertensive adherence

Patterns of antihypertensive use were defined using date of dispensing and days supply data. Starting on the index date, we counted the number of days each month a beneficiary was covered by an antihypertensive drug class recommended for hypertension treatment in older adults (angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, or thiazide diuretics).[2] If a new prescription was filled prior to the end of the last day's supply, the day of the new prescription began the day after the prior prescription would have ended.

After counting days covered each month, binary indicator variables specified whether coverage by an antihypertensive occurred for ≥24 of 30 days (80%). The 80% threshold has high sensitivity (92%) and specificity (89%) for distinguishing adherent from nonadherent antihypertensive patients[20] and is associated with improved cardiovascular health.[12] We calculated 2 common adherence measures: proportion months covered (PMC) and PDC. PMC was the number of months a beneficiary had ≥80% days covered divided by 12 (total follow-up months). PDC was the number of days covered with an antihypertensive medication divided by 360 (total follow-up days).

Predictors of adherence trajectories

Potential predictors of antihypertensive adherence trajectories were selected based on literature[2,9,13,21,22] and defined based on claims during the 12 months prior to initiation. Demographics (age, gender, and race/ethnicity) were identified using the Medicare Denominator File. We categorized antihypertensive medication initiated on the index date as combination therapy (more than one class of antihypertensive) or monotherapy. Concurrent medication use was the number of distinct drugs prescribed in the 14 days prior to the index date. We identified whether beneficiaries were in the Medicare coverage gap during the baseline period. Medicare covers most drug-related expenses until a beneficiary reaches a threshold amount each year, at which time Medicare no longer covers these expenses unless the costs exceed another threshold amount.[23] We identified whether beneficiaries were eligible for the Medicare low-income subsidy (LIS) program (proxy for sociodemographic status), which offers medication at a reduced cost for beneficiaries that are eligible due to income, family size, and household resources. Finally, we identified whether beneficiaries had prescriptions for loop diuretics, antiarrhythmics, antidepressants, antiepileptics, anxiolytics, benzodiazepines, opioids, and hypnotics.

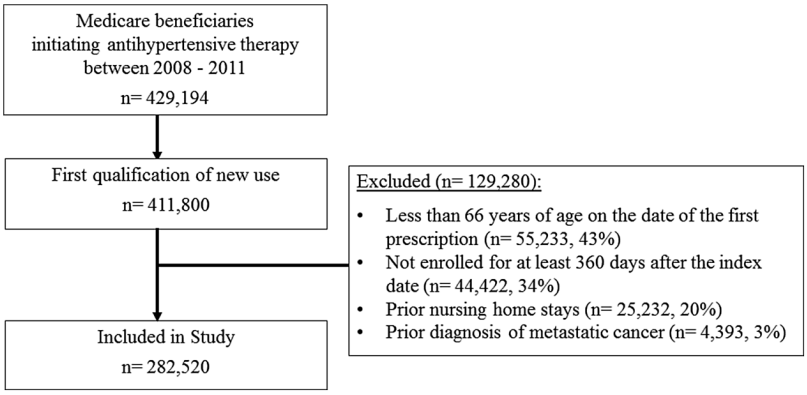

Figure 1. Eligibility flow chart for the study cohort.

Chronic health predictors included: diabetes, chronic kidney disease, Parkinson's disease, Alzheimer's disease, chronic obstructive pulmonary disease, congestive heart failure, arrhythmia, osteoarthritis, rheumatoid arthritis, stroke, myocardial infarction, hypertension, obesity, and fractures (Supplementary Table 2A).

We used the frailty index score (FIS) as a proxy measure of frailty.[24] FIS was developed using Medicare data to predict limitations in activities of daily living based on factors associated with frailty including: demographics, chronic health conditions, geriatric syndromes, medical equipment use, and health screenings. We examined variables positively (ambulance transfer, wheelchair/walker use, home oxygen use, hospital bed, difficulty walking, and vertigo) and inversely (cancer screenings) associated with limitations in activities of daily living.[24] Finally, we assessed examined hospital admissions, long-term hospital stays, and short-term hospital stays in the year prior to the index date.

ANALYSIS

Trajectory models

We used GBTMs to group beneficiaries by patterns of antihypertensive use. GBTMs are a type of mixed models originally developed to model changes in behavior.[19,25] We chose to use GBTMs over other modeling techniques because GBTMs do not require prior assumptions about trajectory shapes.[19]

GBTMs were estimated using logistic regression models. Dependent variables were the monthly binary indicators of antihypertensive use, and the independent variables were months since initiation. GBTMs were not adjusted for baseline covariates. Time was modeled using linear and cubic terms. We started with a 2-group model and subsequently added up to 7 groups. The maximum of 7 groups was imposed to avoid small group sizes. We used Bayesian information criterion, group size, and the average posterior probability to identify the optimal number of groups. Bayesian information criterion is a measure of model fit with lower scores signifying better fit. The average posterior probability signifies how well beneficiaries fit within the trajectory group they are assigned (typical threshold for defining good fit is 0.7).[19]

We examined spaghetti plots (stacked individual line plots of the number of days covered with antihypertensives each month) for a random sample of 500 beneficiaries to verify that the average trends of use aligned with the trajectories identified with the best-fitting GBTM (results not shown). As a sensitivity analysis, we repeated the GBTM analyses removing beneficiaries who were in the Medicare insurance gap during the follow-up period to verify that the GBTM results were not driven by these individuals. Trajectories were defined using "Proc Traj".[26]

Comparison of adherence measures

We compared the GBTM results to traditional static adherence measures, PDC and PMC, using the monthly binary indicators as the gold standard. We separated months into adherent vs. nonadherent and assigned adherence measures to each month. GBTM values varied across months, but PDC and PMC did not. Area under the receiving operating characteristic curves compared adherence measures ability to discriminate between adherent vs. nonadherent months, with a value of one indicating perfect discrimination.[27–29]

Predictors of adherence

We evaluated predictors of adherence by first examining the distribution of covariates across trajectory groups. Next, we used multivariable logistic models to examine associations between baseline covariates and trajectory groups. Adjusting for all baseline covariates, we calculated odds ratios (ORs) and 95% confidence intervals (95% CIs). The outcome of interest was being in a specific trajectory group vs. the most adherent group. Strength of the ORs were determined by examining the distance from the null value (OR = 1) and by examining their precision (width of the 95% CIs). Area under the receiving operating characteristic curve statistics quantified the ability of the predictors to discriminate between trajectory groups.

Since previous medication persistence is predictive of future use,[30,31] we examined whether prior persistence with statins (medications frequently prescribed to older adults) improved prediction of antihypertensive trajectories in a subgroup of beneficiaries who had any statin filled ≥180 days prior to the index date. Statin persistence was defined as ≥180 days continuously covered by a statin, allowing for a 30-day grace period between prescription fills.

Lastly, we conducted *post-hoc* subgroup analyses stratified by Medicare race/ethnicity (White, Black, and Hispanic) to see if the GBTMs and adjusted multivariable models differed according across racial/ethnic groups.

RESULTS

During 2008–2011, 282,520 Medicare beneficiaries initiated antihypertensive therapy. On average beneficiaries were 75 years old, 60% were women, and 84% were White. Most beneficiaries initiated therapy with 1 antihypertensive class (86%) and the mean days supplied on the index date was 32.

Antihypertensive adherence trajectories

After fitting GBTMs with different groupings, the 6-group trajectory model was the best fit (Figure 2, Supplementary Table 3A). Beneficiaries were grouped as adherent (40%, mean adherence: 0.97); early drop-off then rebound to almost full adherence (10%, mean adherence: 0.73); partial drop-off (10%, mean adherence: 0.35); gradual drop-off (14%, mean adherence: 0.63); rapid drop-off (8%, mean adherence: 0.27); and immediate drop-off (18%, mean adherence: 0.10) (Table 1). When we removed beneficiaries in the insurance gap period during follow-up (n = 43,595, 15%), the 6-group model remained the best-fitting model and the trajectories were similar to those from the full cohort (Supplementary Figure 1A).

Comparison of GBTMs to traditional adherence measures

The 6-group trajectory model discriminated better between adherent and nonadherent months than PDC and PMC (Area

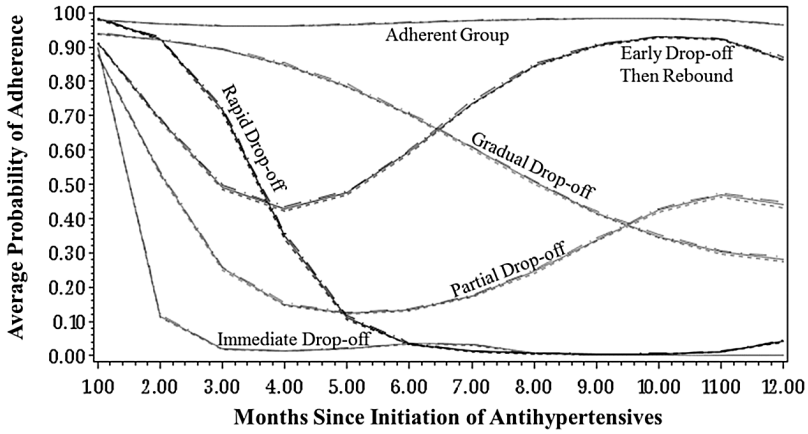

Figure 2. Antihypertensive adherence trajectories in the 12 months following initiation of therapy.

Table 1. Antihypertensive adherence trajectories in the 12 months following initiation according to adherence measures

	Group size		Average probability of adherence[a]		Proportion days covered (PDC)		Proportion months covered (PMC)		Average posterior probability[b]	
Trajectory group	*N*	%	Mean	Std	Mean	Std	Mean	Std	Mean	Std
Immediate drop-off	50,797	18.0	0.095	0.257	0.136	0.092	0.099	0.050	0.887	0.174
Rapid drop-off	22,404	7.9	0.267	0.385	0.318	0.093	0.281	0.064	0.856	0.177
Gradual drop-off	39,953	14.1	0.629	0.258	0.708	0.137	0.636	0.135	0.855	0.170
Partial drop-off	29,429	10.4	0.346	0.226	0.465	0.147	0.352	0.118	0.865	0.161
Early drop-off then rebound	28,304	10.0	0.733	0.196	0.789	0.100	0.720	0.100	0.818	0.151
Adherent	111,633	39.5	0.973	0.016	0.979	0.031	0.975	0.043	0.956	0.086
Comparison of adherence measures ability to distinguish between adherent and nonadherent months										
Adherence measure			AUC[c]				95% Confidence interval (CI)			
PDC			0.914				0.914, 0.914			
PMC			0.918				0.918, 0.919			
Six-group trajectory model			0.954				0.954, 0.955			

Overall model BIC for 6-group trajectory model: -1300277. BIC is used as a measure of model fit. Lower BIC values signify better model fit. Logistic regression models were used to identify trajectory groups. The dependent variables were the monthly binary indicators of antihypertensive use and months since start of antihypertensive therapy were the independent variables. Time was modeled using cubic terms. Abbreviations: BIC, Bayesian information criterion.

[a]Average probability of being at least 80% adherent over 12 months of follow-up.

[b]Indicates how well beneficiaries fit in their assigned group. 0.70 is typically used as a threshold to signify good model fit.

[c]Area under the curve (AUC) statistics are used to quantify the ability of the measures to discriminate between adherent and nonadherent months. Values of 1 symbolize perfect discrimination.

under the receiving operating characteristic curve 95%, 91%, and 92%, respectively; Table 1). In results stratified a ccording to trajectory group, the trajectory model outperformed PDC and PMC for all groups except the adherent group (Area under the receiving operating characteristic curve 66%, 87%, and 89%, respectively; Supplementary Table 4A).

Predictors of adherence trajectories

Individual factors that varied between trajectory groups were race/ethnicity, initiation with combination therapy, days supply on the index date, opioid use, history of chronic obstructive pulmonary disease or cardiovascular disease (e.g., arrhythmia, hypertension, or myocardial infarction), vertigo, prior cancer screenings, and hospital utilization (Table 2). In the adjusted, multivariable analysis, factors most predictive of being nonadherent were: initiation with monotherapy vs. more than one class of antihypertensive drug (adjusted [aOR]: 2.08, 95% CI: 2.00–2.13), non-White race/ethnicity (Black vs. White aOR: 2.04, 95% CI: 1.95–2.13, Hispanic vs. White aOR: 2.93, 95% CI: 2.75–3.11), and having no prior history of hypertension (aOR: 2.04, 95% CI: 2.00–2.08) or myocardial infarction (aOR: 2.00, 95% CI: 1.85–2.17) (OR > 1.0 indicates nonadherence). Other factors

Table 2. Distribution of baseline characteristics according to adherence trajectory among Medicare beneficiaries initiating antihypertensives

	Trajectory group, %					
	Immediate drop-off	Rapid drop-off	Gradual drop-off	Partial drop-off	Early drop-off then rebound	Adherent
Covariates	***n* = 50,797**	***n* = 22,404**	***n* = 39,953**	***n* = 29,429**	***n* = 28,304**	***n* = 111,633**
Female gender	59.9	57.3	58.9	59.8	61.1	60.8
Mean age (std)	75.3 (7.1)	75.0 (7.0)	75.0 (7.0)	75.1 (7.0)	75.2 (7.1)	75.0 (7.1)
Race/ethnicity						
White	80.8	82.2	83.6	77.9	83.4	88.6
African American	8.4	6.8	6.9	10.4	7.6	5.2
Hispanic	4.8	4.7	3.6	5.0	3.5	1.9
Other[a]	6.0	6.4	5.9	6.7	5.6	4.3
Initiated with combination therapy	8.7	12.1	13.6	11.8	13.5	17.7
Average days supply on index date (std)	27.3 (9.0)	40.6 (25.9)	35.1 (21.9)	29.6 (15.1)	30.6 (17.5)	32.6 (19.7)
Medication use 14 days prior to index date						
1–2 Meds	55.0	56.0	55.6	57.0	55.3	53.5
3–4 Meds	30.1	29.3	28.9	29.1	29.1	29.1
5 or More meds	15.0	14.7	15.5	13.9	15.6	17.3
Insurance gap during baseline	16.0	15.7	16.4	14.5	16.5	16.7
Eligible for low-income subsidy	5.6	5.3	5.6	6.1	5.7	5.6
Loop diuretic	9.5	9.6	10.4	9.4	10.7	11.1
Antiarrhythmic	5.2	4.5	4.5	4.7	4.8	4.6
Antidepressant[b]	17.4	17.1	17.7	16.5	17.8	16.8
Antiepileptic	10.5	10.1	9.6	9.2	10.2	9.1
Anxiolytic	4.9	4.4	4.2	4.4	4.1	3.7
Benzodiazepine	1.5	1.3	1.2	1.2	1.2	1.2
Opioid	37.1	33.2	33.0	34.2	34.0	30.2
Hypnotic	8.5	8.0	7.3	7.5	7.7	6.7
Diabetes	24.8	28.3	27.6	28.3	28.6	25.5
Chronic kidney disease	11.9	11.8	12.0	11.8	12.4	11.5
Parkinson's disease	2.0	1.7	1.7	1.5	1.7	1.5
Alzheimer's disease	3.3	2.8	3.3	2.7	3.3	3.5
COPD	19.5	17.3	17.5	17.3	17.7	16.4
Congestive heart failure	10.1	9.8	10.7	9.9	10.6	11.5
Arrhythmia	20.9	20.5	20.9	18.3	20.4	23.4
Osteoarthritis	18.7	18.0	17.4	18.5	18.2	16.1
Rheumatoid arthritis	3.8	3.5	3.5	3.8	3.5	3.1
Stroke	16.1	15.9	16.1	15.2	16.8	16.6
Myocardial infarction	1.8	2.0	2.4	1.5	2.1	3.8
Hypertension	66.4	73.2	77.8	74.6	79.1	79.6
Obesity	4.6	4.8	5.0	4.8	5.3	5.0
Fracture history	9.8	8.2	8.4	8.8	8.7	7.9
Average frailty predictor index (std)[c]	0.11 (0.1)	0.10 (0.1)	0.10 (0.1)	0.10 (0.1)	0.11 (0.1)	0.10 (0.1)
Home oxygen use	5.1	4.5	4.2	4.3	4.4	4.1
Walker or wheelchair use	4.5	4.0	3.9	4.2	4.2	3.8

Table 2. *Continued*

Covariates	Trajectory group, %					
	Immediate drop-off	Rapid drop-off	Gradual drop-off	Partial drop-off	Early drop-off then rebound	Adherent
	n = 50,797	*n* = 22,404	*n* = 39,953	*n* = 29,429	*n* = 28,304	*n* = 111,633
Hospital bed	1.2	0.8	1.0	1.0	1.0	0.9
Difficulty walking	11.4	10.6	10.5	10.4	11.0	10.3
Vertigo	15.9	14.6	13.7	14.5	14.0	12.7
Ambulance transport	14.8	11.8	12.6	11.7	12.9	13.7
Cancer screenings	34.6	35.5	37.3	34.8	37.7	39.5
Hospital admissions	25.2	21.2	21.5	19.6	21.7	23.8
Long stay admissions	2.1	1.5	1.6	1.5	1.8	1.8
Short-term hospital stays	24.3	20.6	20.8	18.8	20.8	23.0

Abbreviations: COPD, chronic obstructive pulmonary disease; Index date, start of antihypertensive therapy; std, standard deviation.
[a]Other includes Asian, North American Native, and other race/ethnicities.
[b]Antidepressants include selective serotonin reuptake inhibitors, tricyclics, monoamine oxidase inhibitors, serotonin, and norepinephrine inhibitors.
[c]Higher scores denote a higher probability of being frail.

strongly predictive of nonadherence were having a high probability of being frail, Parkinson's disease, opioid use, no prior history of being in the Medicare insurance gap, vertigo, chronic obstructive pulmonary disease, and no prior history of having hospital admissions during baseline (Table 3).

In the *post-hoc* stratified analysis, we found similar adherence trajectories across racial/ethnic groups, but the distribution of beneficiaries w ithin t rajectory groups v aried (Supplementary Figure 2A, Table 6A). The proportion in the adherent group was higher for White than Black and Hispanic beneficiaries (45% vs. 32% and 26%, respectively). In multivariable models stratified by race/ethnicity, overall the same covariates were predictive of being adherent across race/ethnic groups (Supplementary Table 7A and 8A). However, in contrast to White beneficiaries, female gender and history of being in the low-income subsidy were strongly associated with being adherent among Black and Hispanic beneficiaries.

Prior statin persistence and adherence trajectories

Statins were dispensed ≥180 days prior to the start of antihypertensive use for 25% of beneficiaries (*n* = 69,668). Of those, 68% (*n* = 47,668) were persistent for ≥180 days. Prior statin persistence was predictive of being more adherent (Table 4). After adjustment, prior statin persistence was strongly associated with not being in the partial drop-off group vs. adherent (aOR: 0.40, 95% CI 0.38–0.42).

DISCUSSION

Overall, GBTMs are effective for identifying patterns of antihypertensive adherence among older adults initiating therapy. We identified 6 adherence trajectories ranging from fully adherent to beneficiaries who never returned after their first prescription. Nearly half of beneficiaries remained adherent in the year following initiation. Compared to traditional adherence measures, GBTMs were better at distinguishing fluctuating adherence patterns. Individual factors predictive of adherence included initiation with combination therapy, White race, and history of cardiovascular disease.

To our knowledge, no previous study has used GBTMs to identify antihypertensive adherence trajectories among Medicare beneficiaries initiating therapy. The 6 trajectories identified are similar to previous studies that used GBTMs to model medication adherence to other drugs.[15,16,31,32] Similar to other studies,[15,32] GBTMs were better than PMC and PDC at distinguishing between adherent and nonadherent patients, especially for beneficiaries with fluctuating adherence. Physician visits, health screenings, and hospitalizations can influence patients stopping and reinitiating with statins,[33] and these factors should be confirmed for other chronic medications. Future research could use GBTMs to identify time-dependent factors influencing fluctuations in medication behavior.

Similar to past studies,[21,22] beneficiaries with cardiovascular diseases and those who initiated therapy with more than one class of antihypertensive were more likely to be adherent. These older adults may be more aware of the importance of being adherent due to more severe hypertension and a history of cardiovascular disease. However, a large proportion of beneficiaries with a history of cardiovascular disease were not adherent. For instance, 21% of beneficiaries in the immediate drop-off group had arrhythmia and 10% had congestive heart failure. Our results suggest clinicians should encourage older adults with cardiovascular disease to remain adherent to antihypertensives.

Our results that prior statin persistence predicted antihypertensive adherence confirm that past medication behavior predicts future medication adherence.[30,31] Bushnell *et al.* found that prior persistence to chronic medication was associated with improved antidepressant persistence among

Table 3. Strongest predictors of antihypertensive nonadherence among Medicare beneficiaries initiating antihypertensive therapy

	Multivariable odds ratios (ORs) and 95% confidence intervals (CIs)					
	Immediate drop-off	Rapid drop-off	Gradual drop-off	Partial drop-off	Early drop-off then rebound	Adherent
Initiation with monotherapy[a]	2.08 (2.00, 2.13)	1.49 (1.43, 1.56)	1.33 (1.28, 1.37)	1.54 (1.47, 1.59)	1.32 (1.27, 1.37)	1
Race/ethnicity						
White race	Ref	Ref	Ref	Ref	Ref	1
Black race	2.04 (1.95, 2.13)	1.69 (1.59, 1.79)	1.51 (1.44, 1.59)	2.42 (2.30, 2.54)	1.59 (1.51, 1.68)	1
Hispanic race	2.93 (2.75, 3.11)	2.77 (2.56, 2.99)	2.02 (1.88, 2.16)	2.85 (2.66, 3.06)	1.88 (1.74, 2.03)	1
Other race[b]	1.66 (1.58, 1.74)	1.61 (1.51, 1.72)	1.48 (1.40, 1.56)	1.81 (1.71, 1.91)	1.44 (1.35, 1.53)	1
No history of hypertension	2.04 (2.00, 2.08)	1.49 (1.45, 1.56)	1.15 (1.12, 1.19)	1.41 (1.37, 1.45)	1.08 (1.04, 1.11)	1
No history of myocardial infarction	2.00 (1.85, 2.17)	1.52 (1.35,1.67)	1.28 (1.19, 1.39)	1.92 (1.72, 2.13)	1.49 (1.35, 1.64)	1
Frailty predictor index	1.32 (1.16, 1.47)	1.20 (1.03, 1.43)	1.11 (0.98, 1.27)	1.59 (1.37, 1.85)	1.32 (1.15, 1.52)	1
Parkinson's disease	1.37 (1.26, 1.49)	1.27 (1.13, 1.44)	1.18 (1.07, 1.30)	1.18 (1.05, 1.32)	1.20 (1.08, 1.34)	1
No history of arrhythmia	1.30 (1.25, 1.33)	1.15 (1.10, 1.19)	1.14 (1.10, 1.16)	1.32 (1.27, 1.35)	1.18 (1.14, 1.22)	1
Opioid use	1.33 (1.30, 1.36)	1.18 (1.14, 1.22)	1.16 (1.13, 1.19)	1.25 (1.22, 1.29)	1.18 (1.15, 1.22)	1
No history of being in the insurance gap	1.25 (1.22, 1.30)	1.14 (1.09, 1.19)	1.09 (1.04, 1.12)	1.27 (1.22, 1.32)	1.12 (1.08, 1.16)	1
Vertigo	1.26 (1.22, 1.30)	1.21 (1.15. 1.26)	1.10 (1.06, 1.14)	1.17 (1.13, 1.22)	1.08 (1.04, 1.13)	1
COPD	1.24 (1.20, 1.28)	1.15 (1.10, 1.20)	1.15 (1.11, 1.19)	1.17 (1.13, 1.22)	1.14 (1.09, 1.18)	1
No history of hospital admissions	1.23 (1.05, 1.43)	1.43 (1.12, 1.82)	1.22 (1.02, 1.47)	1.19 (0.96, 1.47)	1.19 (0.98, 1.45)	1

Odds ratios and 95% CIs are adjusted for all baseline covariates. ORs >1 are predictive of nonadherence. AUC-statistic for fully adjusted model: 0.525. Only the strongest predictors of nonadherence are shown, see Table 5A in Supplementary for full listing of baseline covariates. Prevalence of baseline characteristics were assessed in the 12 months prior to initiation. Abbreviation: AUC, Area under the receiving operating characteristic curves; COPD, chronic obstructive pulmonary disease.

[a]Initiated with more than one class of antihypertensive drug vs. more than one class of antihypertensive drug. We did not distinguish between single and combination therapy medications.

[b]Other includes Asian, North American Native, and other race/ethnicities.

Table 4. Influence of prior statin persistence on antihypertensive adherence trajectories following initiation of antihypertensive therapy

	Trajectory group (*n*, %)											
Statin persist subcohort (*n* = 69,668)	Immediate drop-off		Rapid drop-off		Gradual drop-off		Partial drop-off		Early drop-off then rebound		Adherent	
Persistent ≥ 180 days (*n* = 47,668)	6,727	14.1	3,295	6.9	6,517	13.7	3,781	7.9	4,759	10.0	22,589	47.4
Not persistent at least 180 days (*n* = 22,000)	4,215	19.2	2,003	9.1	3,501	15.9	2,973	13.5	2,454	11.2	6,854	31.2
Baseline prediction model + prior statin persistence												
Multivariable odds ratio (95% CI)[a]	0.48 (0.46, 0.51)		0.49 (0.46, 0.53)		0.56 (0.54, 0.59)		0.40 (0.38, 0.42)		0.60 (0.57, 0.64)		Referent	

AUC-statistic adjusted for all baseline covariates and prior statin persistence: 0.531. Abbreviation: AUC, Area under the receiving operating characteristic curves; CI, confidence interval; OR, odds ratio.

[a]Odds ratio comparing prior statin persistence and the odds of belonging to the adherent group. Adjusted for all baseline covariates. ORs <1 are predictive of being more adherent. Sixty-eight observations were removed due to missing beneficiary race/ethnicity.

adults.[30] Similarly, Franklin *et al.* found that initial statin adherence improved the prediction of future statin adherence trajectories.[31] Prior persistence to other chronic medications may help clinicians identify patients who are more or less likely to remain adherent to antihypertensives therapy.

In our *post-hoc* analysis, we found similar adherence trajectories across racial/ethnic groups; however, the distribution of beneficiaries within these trajectories varied. These differences are likely explained by intrinsic variations in barriers to adherence across racial/ethnic groups. For instance,

history of cardiovascular disease was predictive of being adherent across race/ethnic groups. However, the strength of these associations was strongest among White beneficiaries. Despite having the highest prevalence of stroke, hypertension, and congestive heart failure, Black beneficiaries had fewer adherent beneficiaries. O ther f actors, b esides p rior health experiences, may be stronger predictors of adherence among Black beneficiaries. Previous studies found social support, health literacy, and access to a primary care to be strong predictors of adherence among Black hypertensive adults.[34,35] Cost was cited a stronger barrier to adherence than medication-related side effects and perceived need for the medication among Black and Hispanic older adults.[36] However, these barriers cannot be examined in Medicare claims data. Given that hypertension prevalence is highest among Non-Hispanic Blacks,[1] more research is needed to identify differences in barriers to antihypertensive adherence across various race/ethnicity subpopulations. Expanding access to the Medicare low-income subsidy may be one mechanism to improve adherence among racial minority groups.

This study has limitations. An antihypertensive prescription dispensed does not guarantee that the beneficiary is taking the medication as prescribed. However, since a copayment is required for most dispensed prescriptions, it is reasonable to assume that patients actually take their antihypertensives after t he fi rst re fill. Ant ihypertensive medications obtained outside of Part D (e.g., medication purchased out-of-pocket, through private insurance, or samples provided by physicians) were not captured. Fortunately, most antihypertensives are generic and sample use is less likely.[37,38] Additionally, multiple- vs. single-pill combination therapy were not distinguished. Adherence tends to decrease with increasing treatment complexity[14]; therefore, beneficiaries initiating with single-pill combination therapy may have been more likely to remain adherent compared to beneficiaries i nitiating c ombination t herapy with multiple pills.

Our results may be subject to residual confounding related to uncontrolled frailty measures and time-varying factors affecting medication adherence. Physician visits, frailty, and medication-related adverse events are time-varying factors that likely affect antihypertensive adherence. For instance, a history of fractures was weakly associated with being nonadherent, potentially because individuals with prior fractures stop use of antihypertensive medication due to unwanted side effects. A dramatic decline in blood pressure (e.g., hypotension or hypoperfusion) with initiation of antihypertensives may increase the risk of falls and subsequent fractures, and older adults may discontinue use of these new medications.[39] Further research is needed to examine the impact of time-varying covariates, including those affected by prior treatment, on antihypertensive adherence trajectories.

Lastly, results of traditional adherence measures vs. GBTMs should be interpreted with caution. We included PDC and PMC to highlight that these static adherence measures fall short of separating adherence from persistence. Further research using external indicators, such as mortality outcomes or cardiovascular events, could validate the use of GBTMs over traditional adherence measures.

Our finding that nearly half of Medicare beneficiaries were adherent to their antihypertensive medication in the year following initiation is encouraging. GBTMs are an effective tool for visualizing and capturing patterns of antihypertensive use among older adult populations. Future studies can use GBTMs to identify factors related to a return to adherence after an initial decline and to assess the link of adherence trajectories with improved clinical outcomes. Interventions for improving antihypertensive medication adherence may need to be tailored for subpopulations of patients with hypertension. These results may guide researchers and clinicians in identifying older adult populations for interventions to increase adherence.

SUPPLEMENTARY MATERIAL

Supplementary data are available at *American Journal of Hypertension* online.

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