



Original Investigation | Public Health

Association of Baseline Adherence to Antihypertensive Medications With Adherence After Shelter-in-Place Guidance for COVID-19 Among US Adults

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Abstract

IMPORTANCE Adherence to selected antihypertensive medications (proportion of days covered [PDC]) declined after guidance to shelter in place for COVID-19.

OBJECTIVES To determine whether PDC for all antihypertensive medications collectively fell from the 6 months before sheltering guidance (September 15, 2019, to March 14, 2020 [baseline]) compared with the first (March 15 to June 14, 2020) and second (June 15 to September 14, 2020) 3 months of sheltering and to assess the usefulness of baseline PDC for identifying individuals at risk for declining PDC during sheltering.

DESIGN, SETTING, AND PARTICIPANTS This retrospective cohort study included a random sample of US adults obtained from EagleForce Health, a division of EagleForce Associates Inc. Approximately one-half of the adults were aged 40 to 64 years and one-half were aged 65 to 90 years, with prescription drug coverage, hypertension, and at least 1 antihypertensive medication prescription filled at a retail pharmacy during baseline.

MAIN OUTCOMES AND MEASURES Prescription claims were used to assess (1) PDC at baseline and changes in PDC during the first and second 3 months of sheltering and (2) the association of good (PDC \geq 80), fair (PDC 50-79), and poor (PDC < 50) baseline adherence with adherence during sheltering.

RESULTS A total of 27 318 adults met inclusion criteria (mean [SD] age, 65.0 [11.7] years; 50.7% women). Mean PDC declined from baseline (65.6 [95% CI, 65.2-65.9]) during the first (63.4 [95% CI, 63.0-63.8]) and second (58.9 [95% CI, 58.5-59.3]) 3 months after sheltering in all adults combined ($P < .001$ for both comparisons) and both age groups separately. Good, fair, and poor baseline adherence was observed in 40.0%, 27.8%, and 32.2% of adults, respectively. During the last 3 months of sheltering, PDC declined more from baseline in those with good compared with fair baseline adherence (-13.1 [95% CI, -13.6 to -12.6] vs -8.3 [95% CI, -13.6 to -12.6]; $P < .001$), whereas mean (SD) PDC increased in those with poor baseline adherence (mean PDC, 31.6 [95% CI, 31.3-31.9] vs 34.4 [95% CI, 33.8-35.0]; $P < .001$). However, poor adherence during sheltering occurred in 1034 adults (9.5%) with good baseline adherence, 2395 (31.6%) with fair baseline adherence, and 6409 (72.9%) with poor baseline adherence.

CONCLUSIONS AND RELEVANCE These findings suggest that individuals with poor baseline adherence are candidates for adherence-promoting interventions irrespective of sheltering guidance. Interventions to prevent poor adherence during sheltering may be more useful for individuals with fair vs good baseline adherence.

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Key Points

Question Does baseline antihypertensive medication adherence identify individuals who are at risk for poor adherence during sheltering in place for COVID-19?

Findings This cohort study assessed antihypertensive medication adherence as the proportion of days covered (PDC) from filled prescriptions claims for 6 months before and after COVID-19 sheltering guidance in a random sample of 27 318 US adults. Poor adherence (PDC < 50) during sheltering occurred in 73% with poor baseline adherence, 32% with fair baseline adherence (PDC 50-79), and 10% with good baseline adherence (PDC \geq 80).

Meaning These findings suggest that adherence-promoting interventions may be useful irrespective of sheltering for poor baseline adherence and during sheltering for fair baseline adherence.

+ Supplemental content

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Introduction

Given the rapidly growing impact of COVID-19 during the first quarter of 2020,¹ the Centers for Disease Control and Prevention (CDC) advised against gatherings of more than 50 people on March 15, 2020.² By April 2020, many states issued shelter-in-place orders.³ The impact of COVID-19 on health care delivery was rapid and profound. During 2018 and 2019, 93% of outpatient visits were office based, where most hypertension is managed.⁴ During April through June 2020, outpatient visits declined 21% from the second quarters of 2018 and 2019, reflecting a 50% fall in office-based visits and a 35% increase in telemedicine visits. Blood pressure assessment decreased by 50%, occurring on only 10% of telemedicine visits.⁴

Effective hypertension management provides the greatest opportunity for preventing cardiovascular events.⁵ Access to and adherence with antihypertensive medications is a key to controlling hypertension.⁶ Concerns were raised that access to medications would be limited given closure of some pharmacies, shelter-in-place orders, and social distancing recommendations.⁷ After an initial surge in mid-March 2020, weekly fill rates for the 2 most often obtained antihypertensive medications in the US,^{8,9} lisinopril and amlodipine, fell roughly 14% and 8%, respectively, in mid-April.

The 6-percentage point decline in hypertension control during 2020 from levels in 2018 and 2019¹⁰ was clinically significant, yet many adults with hypertension apparently took sufficient medication to maintain control. If the subset with a significant decline in antihypertensive medication adherence during prolonged social isolation could be reliably identified, then resources could be targeted at that group. Several theoretical and atheoretical analyses^{11,12} assessed the association of various combinations of socioeconomic and demographic factors and medical morbidities with adherence. These models provided statistical associations with adherence but poor discrimination of individual adherence. Prior adherence to medications for chronic conditions is almost always a better method of assessment than multivariable models without prior adherence and improves minimally with inclusion of other variables.^{11,12}

To our knowledge, prior prescription refill data have not been used to characterize adherence during COVID-19. Our study was designed to test the hypothesis that the proportion of days covered (PDC) from pharmacy claims^{13,14} in the 6 months prior to sheltering guidance for COVID-19 would be useful in identifying individuals for adherence-promoting interventions during sheltering. Because older age rapidly emerged as a major risk factor for severe COVID-19 illness,¹⁴ we decided a priori to assess adherence (using PDC) in adults aged 40 to 64 years and 65 years or older.

Methods

This retrospective, cross-sectional study used Strengthening the Reporting of Observation Studies in Epidemiology (STROBE) guidelines. A limited data set was obtained from EagleForce Health, a division of EagleForce Associates Inc, under a data use agreement, and analyses were conducted with a waiver of authorization from the American Medical Association Institutional Review Board.

The study used a retrospective cohort design to assess adherence to antihypertensive medication regimens using prescription claims during 2 COVID-19 time periods. The baseline period was defined as the 6 months prior to advisement to limit gatherings by the CDC, that is, from September 15, 2019, through March 14, 2020. The second period was defined as the 6 months after the CDC's advisement, from March 15 through September 15, 2020, referred to as the sheltering period. The sheltering period was divided into two 3-month periods to assess time effects.

The cohort included a random sample of 30 000 adults constructed from an age-stratified random sample of 178 468 adults aged 40 to 65 years and 207 779 adults 65 years or older with hypertension in the EagleForce Health national database of verified claims for filled prescriptions and other health care services for adults with prescription drug coverage during the 1-year study time frame (eFigure 1 in Supplement 1). Hypertension was defined by *International Statistical Classification*

of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code I10 on paid prescription or other health claims.

Fifteen thousand adults were randomly selected in each age strata from community-dwelling adults having at least 1 filled prescription for an antihypertensive medication during the baseline period. Exclusion criteria consisted of having a diagnosis of cancer, substance abuse, or psychiatric conditions other than depression at baseline; institutional residency; and being younger than 40 years. The final analysis cohort of 27 318 was derived from the sample of 30 000 after omitting 2136 adults without any antihypertensive medications in the baseline period and 546 without a diagnostic code for essential hypertension. Demographic characteristics included age, sex, geographical location, and type of prescription insurance. Race and ethnicity data were not collected.

Comorbid chronic conditions were determined from ICD-10-CM codes recorded on or after December 31, 2018, and categorized by Elixhauser criteria; 60.6% of ICD-10-CM codes were from paid prescription claims and 39.4% from other paid medical claims.¹⁵ Additional categorization provided prevalence estimates for myocardial infarction, cerebrovascular disease, dementia, coronary atherosclerosis, heart disease, lipid metabolism disorders, and osteoarthritis.^{16,17} Results are reported for chronic conditions affecting 5% or more of the analysis cohort.

The main outcome measures included the PDC (adherence proxy) during the baseline period and after sheltering guidance and the association between baseline PDC and changes in PDC during sheltering guidance for antihypertensive medications. We calculated PDC as the number of days covered by the prescription divided by the number of days in the time period $\times 100$.^{11,12} A PDC of at least 80 is a commonly cited threshold for good adherence.^{12,18} Fair and poor adherence were arbitrarily defined as PDCs of 50 to 79 and less than 50, respectively.

Statistical Analysis

Descriptive analysis included means (SDs) or frequency (percent) for categorical data. We calculated PDC for each antihypertensive medication and per patient using the patient mean and maximum. Mean patient-level PDC was the main outcome variable. Univariate comparisons of PDC between time periods were examined with paired *t* tests. Bivariate analyses were used to examine PDC differences by time period, age, sex, US region, and comorbid chronic conditions affecting at least 5% of cohort members. *P* values were adjusted for multiple comparison tests to control familywise error rates, using Tukey-Kramer tests for continuous variables and Bonferroni tests for categorical data. A sensitivity analysis was conducted based on categorical assessment of PDC at baseline and changes in PDC categories after sheltering.

Odds ratios of declining PDC from baseline to sheltering were computed using logistic regression models and reported with Wald 95% CIs. Multivariable regression models for the entire cohort and separately for each age cohort included baseline PDC, age, sex, geographical region, payer, and several chronic conditions as independent variables. For patients with more than 1 usual payment source, payer status was determined by the most frequent type. Missing values were not imputed. All statistical analyses were performed using SAS/STAT, version 9.4 (SAS Institute Inc). Two-sided *P* < .05 indicated statistical significance.

Results

Baseline characteristics are shown in the first data column of **Table 1** for the total cohort of 27 318 participants. The mean (SD) age was 65.0 (11.7) years; 50.7% were women and 49.3% were men. The Southeast region contributed the highest percentage of the cohort and the Rocky Mountains region the least. Prescription drug coverage was predominantly Medicare Part D and commercial. In addition to hypertension, 39.3% of the cohort had lipid disorders and 26.3% had type 1 or 2 diabetes.

The cohort was segregated based on baseline PDC as good, fair, and poor adherence (Table 1). Poor baseline adherence was associated with younger age, male sex, and Medicaid insurance.

Coronary heart disease and cardiac arrhythmias occurred more often in those with fair or poor than good baseline adherence.

The characteristics of adults aged 40 to 64 years are contrasted with those aged 65 to 90 years (**Table 2**). The older cohort included a higher proportion of women and higher proportions living in the Midwest and Northeast and fewer in the Southeast than the younger group. The older group also had a higher percentage with the various comorbid conditions described than the younger group, except depression.

Data for patient mean PDC, the primary outcome, are summarized in **Figure 1** and eTable 1 in [Supplement 1](#). In all 27 318 adults, patient mean PDC declined from 65.6 (95% CI, 65.2-65.9) at baseline to 63.4 (95% CI, 63.0-63.8) during the first 3 months and 58.9 (95% CI, 58.5-59.3) during the second 3 months of sheltering. Poor adherence during sheltering occurred in 1034 (9.5%) with good baseline adherence, 2395 (31.6%) with fair baseline adherence, and 6409 (72.9%) with poor

Table 1. Characteristics of Adults With Filled Prescriptions for Antihypertensive Medications at Baseline and Missed Prescriptions During Sheltering

Characteristic	Adherence group at baseline ^a				P value ^b		
	All	Good	Fair	Poor	Good vs fair	Good vs poor	Fair vs poor
Total	27 318 (100)	10 934 (40.0)	7589 (27.8)	8795 (32.2)	NA	NA	NA
Age, mean (SD), y	65.0 (11.7)	65.9 (11.3)	65.4 (11.8)	63.5 (12.1)	.01	<.001	<.001
Sex ^c							
Men	13 458 (49.3)	5532 (50.6)	3732 (49.2)	4194 (47.7)	.17	<.001	.17
Women	13 855 (50.7)	5400 (49.4)	3856 (50.8)	4599 (52.3)			
Geographical region ^d							
Pacific Northwest	3361 (12.4)	1301 (11.9)	951 (12.6)	1109 (12.7)	>.99	>.99	>.99
Rocky Mountains	676 (2.5)	266 (2.4)	191 (2.5)	219 (2.5)	>.99	>.99	>.99
Midwest	5976 (22.0)	2742 (25.2)	1509 (20.0)	1725 (19.7)	<.001	<.001	1.0
Southwest	3343 (12.3)	1232 (11.3)	1021 (13.5)	1090 (12.5)	.001	.25	.83
Southeast	8626 (31.7)	3131 (28.7)	2476 (32.7)	3019 (34.5)	<.001	<.001	.33
Northeast	5231 (19.2)	2223 (20.4)	1415 (18.7)	1593 (18.2)	.08	.002	>.99
No. of filled prescriptions	2 164 790	902 286	678 264	584 240	NA	NA	NA
Payer type, No. (%) of prescriptions							
Commercial	847 516 (39.2)	357 563 (39.6)	257 861 (38.0)	232 092 (39.7)	<.001	1.0	<.001
Internal prescription plan	47 982 (2.2)	18 347 (2.0)	14 212 (2.1)	15 423 (2.6)	.12	<.001	<.001
Managed care Medicaid	95 393 (4.4)	35 901 (4.0)	32 303 (4.8)	27 189 (4.7)	<.001	<.001	.07
Medicaid	117 245 (5.4)	44 266 (4.9)	33 064 (4.9)	39 915 (6.8)	>.99	<.001	<.001
Medicare Part D	1 029 959 (47.6)	435 277 (48.2)	333 241 (49.1)	261 441 (44.7)	<.001	<.001	<.001
All others	26 695 (1.2)	10 932 (1.2)	7583 (1.1)	8180 (1.4)	<.001	<.001	<.001
Chronic condition							
Hypertension	27 318 (100)	10 934 (100)	7589 (100)	8795 (100)	NA	NA	NA
Lipid disorders	10 733 (39.3)	4747 (43.4)	3004 (39.6)	2982 (33.9)	<.001	<.001	<.001
Diabetes	7188 (26.3)	2835 (25.9)	2190 (28.9)	2163 (24.6)	<.001	.77	<.001
Pulmonary disease	3426 (12.5)	1171 (10.7)	1020 (13.4)	1235 (14.0)	<.001	<.001	>.99
Hypothyroidism	2686 (9.8)	1200 (11.0)	731 (9.6)	755 (8.6)	.08	<.001	.48
Osteoarthritis	2282 (8.4)	868 (7.9)	702 (9.3)	712 (8.1)	.04	>.99	.21
Depression	2263 (8.3)	850 (7.8)	653 (8.6)	653 (8.6)	>.99	.65	>.99
Coronary heart disease	1965 (7.2)	656 (6.0)	651 (8.6)	658 (7.4)	<.001	.001	.24
Cardiac arrhythmias	1407 (5.2)	457 (4.2)	480 (6.3)	470 (5.3)	<.001	.003	.18

Abbreviation: NA, not applicable.

^c Data were missing for 5 individuals.

^a Unless otherwise indicated, data are expressed as No. (%) of participants. Percentages have been rounded and may not total 100. Good adherence indicates proportion of days covered (PDC) of 80 or more; fair adherence, PDC of 50 to 79; and poor adherence, PDC of less than 50.

^d Data were missing for 105 individuals.

^b Calculated for differences between patients with filled prescriptions for antihypertensives across all time periods vs patients without filled prescriptions for antihypertensives during one or both sheltering periods.

baseline adherence; among those with good baseline adherence, 8226 (75.2%) sustained good adherence and only 1034 (9.5%) declined to poor adherence. Among adults with good and fair baseline adherence, PDC fell progressively from baseline through the first and second 3 months after sheltering (-13.1 [95% CI, -13.6 to -12.6] and -8.3 [95% CI, -13.6 to -12.6], respectively; $P < .001$). In contrast, among those with poor baseline adherence, adherence was higher during the first and second 3 months of sheltering than at baseline (mean PDC, 31.6 [95% CI, 31.3 - 31.9] vs 34.4 [95% CI, 33.8 - 35.0 ; $P < .001$). The association of baseline PDC category with changes in PDC during sheltering were similar in both age groups (eTable 1 in Supplement 1).

The multivariate associations between independent variables and a decline in PDC during sheltering are shown in Figure 2 and eFigure 2 and eTable 2 in Supplement 1. Among individuals in both age cohorts, associations were observed between baseline PDC and the decline in PDC during sheltering. For each 1% increase in baseline PDC, the probability of declining PDC during sheltering increased more than 2-fold for both age groups combined and separately. While only 40.0% of individuals had baseline PDC of at least 80, a commonly cited threshold for good adherence, they were nearly 17 times more likely to maintain PDC of at least 80 during sheltering than those who had PDC of less than 80 during baseline (odds ratio [OR], 16.9 [95% CI, 15.9 - 17.9]).

The association of age with change in PDC during sheltering diverged in the 2 age groups (eTable 2 in Supplement 1). Among those 65 years or older, each additional 10 years was associated

Table 2. Characteristics of Adults Included in the Analysis, Stratified by Age

Characteristic	Age group ^a		P value ^b
	40-64 y (n = 13 525)	65-90 y (n = 13 793)	
Age, mean (SD), y	55.2 (6.54)	74.5 (6.82)	<.001
Sex ^c			
Men	7476 (55.3)	5982 (43.4)	<.001
Women	6046 (44.7)	7809 (56.6)	
Geographical region ^d			
Pacific Northwest	1571 (11.7)	1790 (13.0)	<.001
Rocky Mountains	350 (2.6)	326 (2.4)	
Midwest	2723 (20.2)	3253 (23.7)	
Southwest	1632 (12.1)	1711 (12.4)	
Southeast	4779 (35.5)	3847 (28.0)	
Northeast	2415 (17.9)	2816 (20.5)	
No. of prescriptions filled	1 039 367	1 125 423	
Payer type, No. (%) of prescriptions ^e			
Commercial	636 523 (61.2)	211 993 (18.8)	<.001
Internal prescription plan	26 045 (2.5)	21 937 (1.9)	
Managed care Medicaid	79 039 (7.6)	16 354 (1.5)	
Medicaid	90 419 (8.7)	26 826 (2.4)	
Medicare Part D	199 132 (19.2)	830 827 (73.8)	
Chronic conditions			
Hypertension	13 525 (100)	13 793 (100)	NA
Lipid disorders	4864 (36.0)	5869 (42.6)	<.001
Type 1 or 2 diabetes	3352 (24.8)	3836 (27.8)	<.001
Pulmonary disease	1515 (11.2)	1911 (13.9)	<.001
Hypothyroidism	957 (7.1)	1729 (12.5)	<.001
Osteoarthritis	873 (6.5)	1409 (10.2)	<.001
Depression	1165 (8.6)	1098 (8.0)	.05
Coronary heart disease	606 (4.5)	1359 (9.9)	<.001
Cardiac arrhythmias	319 (2.4)	1088 (7.9)	<.001

Abbreviation: NA, not applicable.

^a Unless otherwise indicated, data are expressed as No. (%) of participants. Percentages have been rounded and may not total 100.

^b Calculated for 27 318 individuals with the exception of missing data on sex and geographical region.

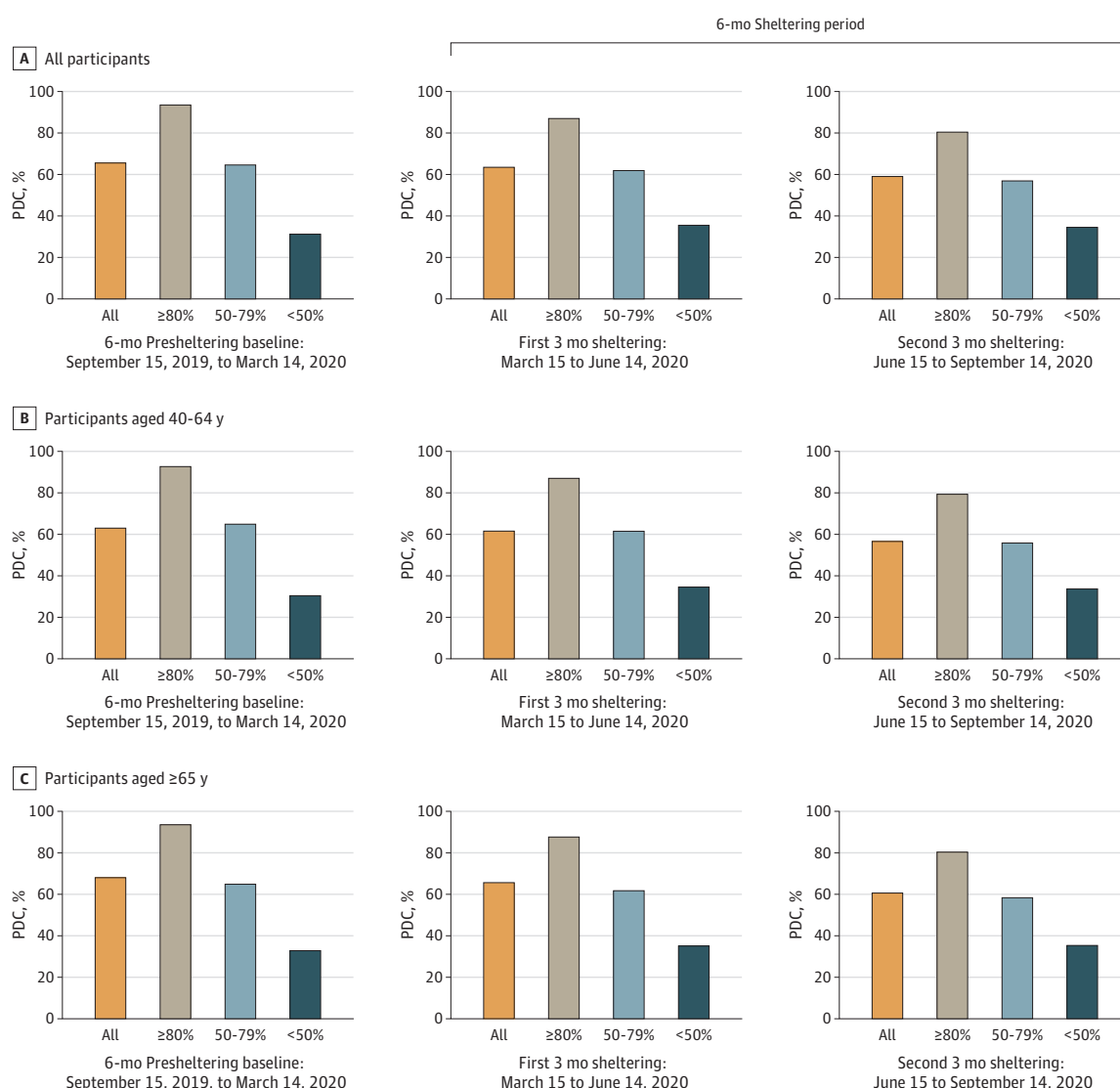
^c Data were missing for 5 individuals.

^d Data were missing for 105 individuals.

^e Payers representing less than 1% of sample not shown (eg, cash payment, 0.02%).

with a 10% increase in likelihood of declining adherence during sheltering. Among those aged 40 to 64 years, each 10-year age increment was associated with a 6% (OR, 0.9% [95% CI, 0.9%-1.0%]) lower risk of declining PDC during sheltering. Residents of the Southwest were 37% (OR, 1.4% [95% CI, 1.3%-1.5%]) more likely to have falling adherence during sheltering than those in the Midwest, with adverse effects somewhat greater in the younger than older age cohorts. Younger and older individuals with Medicaid and commercial insurance were more likely to have a decline in PDC during sheltering than those with Medicare Part D. Adults with lipid disorders and coronary heart disease were 10% (OR, 0.9% [95% CI, 0.8%-0.9%]) less likely to have declining PDC during sheltering than those without these conditions. Younger individuals with depression were 13% (OR, 1.1% [95% CI, 1.0%-1.3%]) more likely and older persons with pulmonary diseases and cardiac arrhythmias were 12% (OR, 1.1% [95% CI, 1.0%-1.2%]) to 18% (OR, 1.2% [95% CI, 1.0%-1.3%]) more likely to have declining PDC during sheltering.

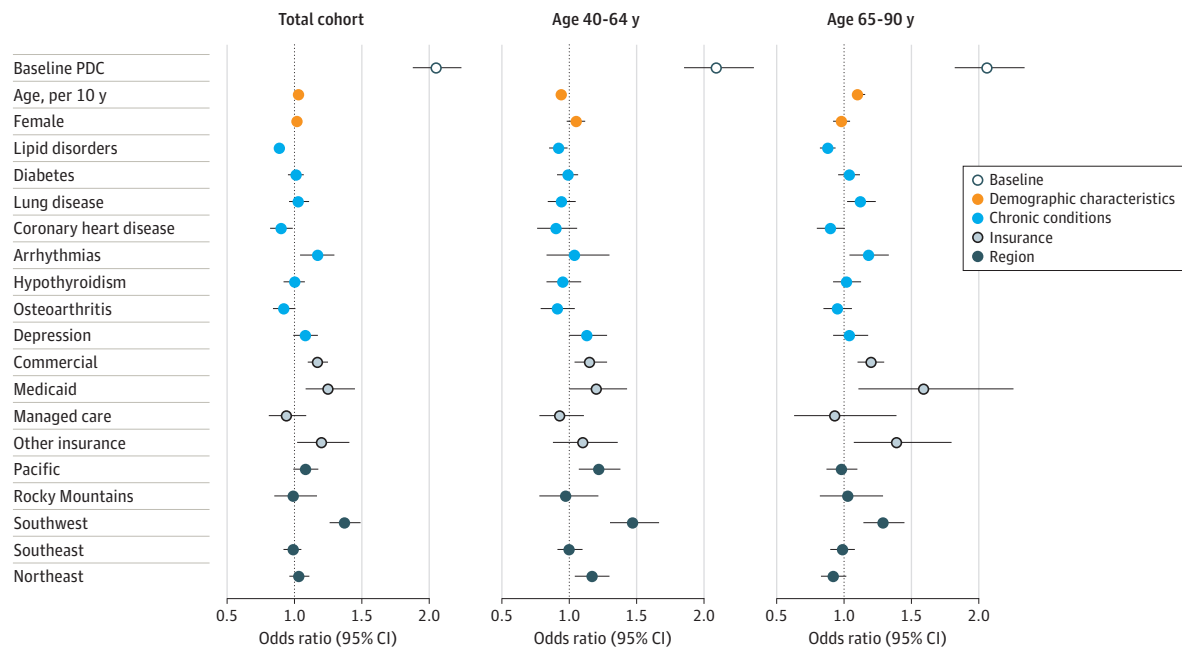
Figure 1. Proportion of Days Covered (PDC) at Baseline and the First and Second 3 Months After Sheltering Guidance



PDC, a proxy for adherence, is shown during the 6-month preshertering baseline and the first 3 months (shelter 1-3) and second 3 months (shelter 4-6) after sheltering guidance with good (PDC ≥ 80), fair (PDC 50-79), and poor (PDC < 50) baseline adherence for all adults and by age group.

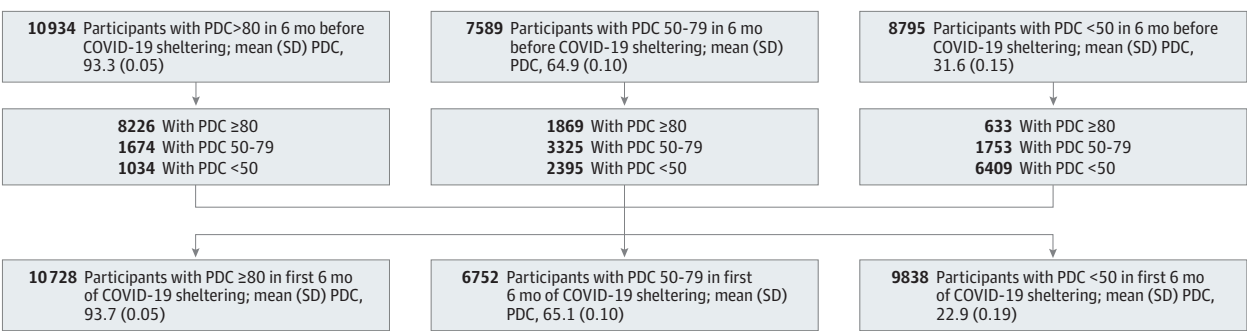
At baseline, 40.0% of adults had good adherence and 39.3% had good adherence during sheltering. Among these, an absolute total of 30.1% originated from the group with good baseline adherence; 6.8%, from the group with fair baseline adherence; and 2.3%, from the group with poor baseline adherence (**Figure 3**). Fair adherence occurred in 27.8% at baseline and 24.7% during sheltering. A plurality (12.2%) of those with fair adherence after guidance had fair baseline adherence, with an absolute total of 6.1% and 6.4% originating from those with good and poor baseline adherence, respectively. Poor adherence occurred in 32.2% of adults at baseline and rose to 36.0% with sheltering. Most adults with poor adherence during sheltering originated from the group with poor baseline adherence (23.5%), with 8.8% and 3.8% originating from those with fair and good baseline adherence, respectively.

Figure 2. Variables Associated With Declining Adherence During Sheltering Guidance During COVID-19 by Age Group



Multivariable adjusted odds ratios and 95% CIs are shown. Odds ratios (ORs) and 95% CIs that do not overlap the line of identity are statistically significant. An OR of greater than 1.0 indicates a greater likelihood of a fall in adherence during guidance to shelter, whereas ORs of less than 1.0 indicate a greater likelihood of an increase in adherence during guidance to shelter. Reference groups include men, individuals with absence of chronic conditions, individuals with Medicare Part D insurance, and individuals from the Midwest region of the US.

Figure 3. Association of Baseline Proportion of Days Covered (PDC) With PDC During Sheltering for COVID-19



Includes all 27 318 patients. During sheltering, poor PDC increased, while good and fair PDC decreased. More than 70% of individuals with poor baseline adherence remained in the poor adherence category with sheltering. More than 30% of those with fair baseline adherence and less than 10% of those with good baseline adherence declined to poor adherence with sheltering.

Discussion

This cohort study had 2 principal findings. First, adherence to antihypertensive medications fell progressively from the 6-month baseline period prior to sheltering for COVID-19 to the first and second 3-month periods after sheltering guidance. Second, baseline adherence was associated with adherence during the stress of sheltering for COVID-19.

In a previous report,⁶ pharmacy claims for commonly prescribed antihypertensive medications declined 15.3% for lisinopril and 9.2% for amlodipine, whereas those for losartan rose 1.7% in April 2020 (after sheltering guidance) compared with the same time frame in 2019. Our report suggests that the PDC for all antihypertensive medications combined declined a relative 3.4% during the initial 3 months and 10.2% during the second 3 months of sheltering.

Hypertension control during 2020 declined roughly 6 percentage points from the 2018-2019 period.⁹ This observation suggests that most patients with controlled hypertension prior to the COVID pandemic sustained adherence to antihypertensive medication during sheltering, whereas a smaller subset had a larger decline in adherence that adversely impacted control. In fact, based on PDC, the overall decline in antihypertensive medication adherence was approximately 2 days during the first 3 months of sheltering and an additional 4 days during the second 3 months. Moreover, the decline in PDC during sheltering was similar in adults aged 40 to 64 and 65 to 90 years (eTable 1 in Supplement 1). The decline is clinically important but relatively modest, which suggests a subset may have been disproportionately affected.

If the subset with declining adherence during sheltering could be prospectively identified, then adherence-promoting support could be directed toward sustaining adherence in that group. Each 1% lower baseline PDC was associated with a 2-fold increase in the probability of rising adherence during sheltering, which is consistent with the phenomenon of regression to the mean. Several sociodemographic and medical variables differed between the groups with good, fair, and poor baseline adherence (Table 1). Moreover, several of these variables were associated with changes in adherence during prolonged social isolation. However, the association with adherence during sheltering was much less than the association with baseline adherence. Our findings are consistent with other reports^{11,12} that variables other than PDC contribute minimally to PDC in discriminating future adherence of individual patients. Our study extends previous reports by documenting that baseline PDC is associated with adherence during sheltering.

Despite substantial evidence for regression to the mean during the first 6 months of sheltering for COVID-19, there was an association between categories of PDC at baseline and during sheltering. Poor adherence during sheltering was observed in 72.9% with poor baseline adherence, 31.6% with fair baseline adherence, and 9.5% with good baseline adherence. Baseline PDC emerges as a potentially more practical tool than complex, multivariable equations^{11,12} for entities such as health care systems and pharmacies to identify clients at risk for declining adherence during prolonged social isolation. However, specific guidance is required for meaningful application.

Adults with poor baseline adherence emerge as good candidates for adherence-promoting interventions, irrespective of sheltering guidance. Among adults with good baseline adherence, 75.2% sustained good adherence and only 9.5% declined to poor or very poor adherence during prolonged social isolation. While fair adherence is not optimal, for patients with good baseline adherence who split tablets or take short drug holidays to stretch medications during sheltering,^{19,20} significant antihypertensive effect is retained; antihypertensive efficacy declines approximately 2 mm Hg of systolic blood pressure for each medication halved.¹⁹ However, among adults with fair baseline adherence, 31.6% declined to poor adherence during sheltering. This group may represent good candidates for interventions to prevent poor adherence and potentially improve adherence during sheltering.

Given recognition early in the COVID-19 pandemic that older age was a major risk factor for severe and fatal disease, we decided a priori to analyze age groups separately. In fact, the association between increasing age and adherence during sheltering was different in the 2 age groups. Among adults aged 40 to 64 years, PDC during sheltering rose 6% for each 10-year increment in age.

Conversely, among adults 65 years or older, PDC during sheltering fell 10% for each 10-year increase in age (Figure 2 and eTable 2 in [Supplement 1](#)). Early evidence that COVID-19 was more severe in older adults¹⁴ appeared to adversely impact their prescription fill rates from outpatient pharmacies.

Similarly, in both age groups, lipid disorders were associated with increasing adherence during sheltering, whereas commercial and Medicaid insurance and Southwest US residence were associated with declining adherence. Depression and residence in the Pacific and Northeast regions were associated with declining adherence during sheltering in adults aged 40 to 64 years, whereas pulmonary disease and cardiac arrhythmias were associated with declining adherence in adults 65 years or older. However, the association of demographic characteristics, prescription drug coverage, and comorbid medical conditions was modest relative to the association with baseline PDC category.

The association of baseline PDC in our study to adherence proxies in previous reports using pharmacy claims data is relevant to the issue of clinical application and generalizability. Mean patient PDC in our study was 65.6 (95% CI, 65.2-65.9). In contrast, baseline PDC based on prescriptions was 61.2 (95% CI, 60.9-61.5) (eTable 1 in [Supplement 1](#)), which suggests that PDC was lower in patients with more antihypertensive medication prescriptions. Another report using pharmacy fill data from 6 studies between 1998 and 2016 with more than 850 000 patients¹⁰ estimated persistence for all antihypertensive medications among US adults with hypertension at 57%. The definition of persistence was not uniform across the 6 studies and not directly comparable to PDC. However, the persistence of 57% is similar to the PDC of 61.2 in our study. Moreover, the higher estimate of baseline adherence in our study vs that of previous reports partially reflects our exclusion of individuals who did not fill antihypertensive medication prescriptions during the baseline period.

Strengths and Limitations

A strength of this study is that we estimated PDC, the measure of adherence, from a random sample of 27 318 adults with hypertension from a large database with verified claims for filled prescriptions and other health services in the US. Additionally, evidence that blood pressure rose,²¹ hypertension control fell,¹⁰ and disparities in control grew during 2021²² is consistent with findings from our study that adherence to antihypertensive medications fell for some adults.

This study has some limitations. Prescription medications paid entirely by patients at retail pharmacies, which can occur with discounted formularies or prescription drug cards,^{23,24} were not reliably captured. This concern is partially mitigated by the fact that all adults in this analysis had prescription drug coverage. However, exclusion of individuals without prescription drug coverage could be viewed as a limitation. Prescriptions mailed from a retail pharmacy to the patient are captured, whereas prescriptions sent by a pharmacy benefits manager are not reliably captured. Thus, a subset of patients with poor adherence during sheltering may have obtained antihypertensive medications through pathways not captured in our database.

Individuals with low baseline adherence or declining adherence during sheltering may have originated disproportionately from members of racial and ethnic minority groups with historically adverse social determinants of health.²¹ While important, inclusion of race and ethnicity and social determinants in previous research generally has not led to large improvements in the discrimination of individual adherence.^{11,12} Prescription claims were assessed in a national sample and did not focus on areas most affected by COVID during the first 6 months of sheltering. The claims databases analyzed did not include blood pressure, which precludes direct assessment of adherence and hypertension control.

Conclusions

The findings of this cohort study suggest that adherence to antihypertensive medications declined during sheltering for COVID-19. Baseline categories of good, fair, and poor baseline adherence were associated with these same adherence categories during sheltering. Poor baseline adherence could identify individuals for adherence-promoting interventions irrespective of sheltering guidance. Among individuals with fair baseline adherence, 31.6% declined to poor and very poor adherence

with sheltering in contrast to 9.5% of those with good baseline adherence. Adults with hypertension and fair baseline adherence may be good candidates for preventing poor baseline adherence during the stress of sheltering.

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SUPPLEMENT 1.

eTable 1. Adherence for Antihypertensive Prescriptions During the 6 Months Before and the First and Second 3-Month Periods After Guidance to Shelter in Place

eTable 2. Variables Associated With the Fall in PDC During the First 6 Months of Guidance to Shelter-in-Place for COVID-19 by Age Cohort

eFigure 1. Flow Diagram of Patient Inclusion and Exclusion for the Analysis of the Antihypertensive Medication Adherence

eFigure 2. Variables Associated With Declining Adherence During Sheltering Guidance During COVID-19 by Age Group

SUPPLEMENT 2.

Data Sharing Statement