

ORIGINAL RESEARCH ARTICLE

Cost-Related Medication Nonadherence in Adults With Atherosclerotic Cardiovascular Disease in the United States, 2013 to 2017

BACKGROUND: Medication nonadherence is associated with worse outcomes in patients with atherosclerotic cardiovascular disease (ASCVD), a group who requires long-term therapy for secondary prevention. It is important to understand to what extent drug costs, which are potentially actionable factors, contribute to medication nonadherence.

METHODS: In a nationally representative survey of US adults in the National Health Interview Survey (2013–2017), we identified individuals ≥ 18 years with a reported history of ASCVD. Participants were considered to have experienced cost-related nonadherence (CRN) if in the preceding 12 months they reported skipping doses to save money, taking less medication to save money, or delaying filling a prescription to save money. We used survey analysis to obtain national estimates.

RESULTS: Of the 14 279 surveyed individuals with ASCVD, a weighted 12.6% (or 2.2 million [95% CI, 2.1–2.4]) experienced CRN, including 8.6% or 1.5 million missing doses, 8.8% or 1.6 million taking lower than prescribed doses, and 10.5% or 1.9 million intentionally delaying a medication fill to save costs. Age < 65 years, female sex, low family income, lack of health insurance, and high comorbidity burden were independently associated with CRN, with > 1 in 5 reporting CRN in these subgroups. Survey respondents with CRN compared with those without CRN had 10.8-fold higher odds of requesting low-cost medications and 8.9-fold higher odds of using alternative, nonprescription, therapies.

CONCLUSIONS: One in 8 patients with ASCVD reports nonadherence to medications because of cost. The removal of financial barriers to accessing medications, particularly among vulnerable patient groups, may help improve adherence to essential therapy to reduce ASCVD morbidity and mortality.

Rohan Khera, MD*
Javier Valero-Elizondo,
MD, MPH*
Sandeep R. Das, MD, MPH
Salim S. Virani, MD, PhD
Bita A. Kash, PhD, MBA
James A. de Lemos, MD
Harlan M. Krumholz, MD,
SM
Khurram Nasir, MD, MPH,
MSc

*Drs Khera and Valero-Elizondo contributed equally.

Key Words: atherosclerosis
■ cardiovascular disease ■ costs and cost analysis ■ medication adherence

Sources of Funding, see page 2074

© 2019 American Heart Association, Inc.

<https://www.ahajournals.org/journal/circ>

Clinical Perspective

What Is New?

- One in 8 patients with atherosclerotic cardiovascular disease report nonadherence to medications because of cost, representing nearly 1.5 million estimated patients missing doses, 1.6 million taking lower than prescribed doses, and 1.9 million intentionally delaying a medication fill to save costs in the United States.
- Patients <65 years of age have 3-fold higher rates of medication noncompliance because of cost, with significantly higher rates in women, patients from low-income families, and those without health insurance.

What Are the Clinical Implications?

- Drug costs represent a significant barrier to medication adherence for patients with atherosclerotic cardiovascular disease.
- Removal of financial barriers to accessing medications, particularly among vulnerable patient groups, may help improve adherence to essential therapy to reduce atherosclerotic cardiovascular disease morbidity and mortality.

The care of patients with atherosclerotic cardiovascular disease (ASCVD), the leading cause of death and disability in the United States, relies on medications that lower the risk of adverse outcomes.^{1,2} However, as many as half of Americans who are prescribed such medications do not take them routinely,³ at a cost to their health^{4,5} and subsequent costs to the health system.^{6,7} The strategy of promoting awareness among patients to improve adherence can be applied only to those with access to medications.⁸ Given the rising cost of medications,⁹ financial considerations may still represent additional challenges for individuals with ASCVD, who often require long-term treatment and may be limited in their ability to access required medications because of their cost. As new, more expensive, medications continue to emerge in the future, affordability will likely worsen.

Although medication nonadherence is complex and multifactorial, nonadherence because of cost represents a specific avenue in which financial investment may translate to direct improvements in access to medications and patient outcomes.¹⁰ Despite emerging attention to these challenges, little empirical evidence addresses the magnitude of cost-related medication nonadherence (CRN) among US adults with ASCVD. An assessment of factors driving nonadherence because of costs may help identify patient subgroups on whom interventions aimed at mitigating these effects can be specifically focused. A better understanding of CRN is

particularly salient in the United States, where a large proportion of the population have healthcare expenses beyond their means¹¹ and are therefore at risk for deferring medications to save costs.

To further evaluate the challenges posed by affordability on medication therapy for US patients with ASCVD, we used nationally representative data to assess the proportion of patients with ASCVD who deferred medication refills or reduced or skipped doses that they attributed to the cost of the medications. We were particularly interested in understanding patterns in CRN in patients with ASCVD <65 years of age, who do not have insurance protections despite long-term healthcare needs for ASCVD, compared with those ≥65 years of age, who receive protection from healthcare costs as a result of access to Medicare.

METHODS

Data Source

We used the NHIS (National Health Interview Survey) for the most recent 5-year period from 2013 to 2017.¹² The NHIS is a nationwide survey of noninstitutionalized individuals in the United States that is conducted and compiled annually by the US National Center of Health Statistics of the Centers for Disease Control and Prevention. The data in the NHIS are collected as part of a multistage probability sampling of households to draw a sample of nearly 35 000 households made up of 87 500 individuals.¹² Through questionnaires delivered by trained interviewers, the NHIS collects data on demographic characteristics of each included family and information on health conditions and access to and use of health services from ≥1 randomly selected member adult from each family. The Sample Adult files of the NHIS, which were used for the present analyses, include the results of this in-depth questionnaire administered to a randomly selected adult per household. Because NHIS data are deidentified and publicly available, this study was exempt from review by the Yale University Institutional Review Board. The data are publicly available from the National Center for Health Statistics. The authors are willing to share the detailed methods and materials required to reproduce these results.

Study Population and Outcomes

We selected all adults (≥18 years of age) with a self-reported history of ASCVD, which was defined as ever having been told by a doctor or other health professional that they had any of the following: coronary heart disease, angina or angina pectoris, heart attack or myocardial infarction, or stroke.

We studied our outcome of CRN using a set of 3 questions assessed in the NHIS survey: (1) "During the past 12 months, have you skipped medication doses to save money?" (2) "During the past 12 months, have you taken less medication to save money?" and (3) "During the past 12 months, have you delayed filling a prescription to save money?" In addition, we assessed whether patients had pursued cost-reducing strategies for prescription medications using these questions: (1) "During the past 12 months, have you asked your doctor for a lower-cost medication to save money?" (2) During the

past 12 months, have you bought prescription drugs from another country to save money?" and (3) During the past 12 months, have you used alternative therapies to save money?" Of the 15 758 individuals with ASCVD, 14 279 (90.6%) completed the individual components for CRN (Figure 1 in the online-only Data Supplement).

Study Variables

In the NHIS, we collected patient demographics (age, sex, race/ethnicity [white, black, Hispanic, and others], family income [in reference to the federal poverty limit from the Census Bureau, classified as middle/high income, ie, $\geq 200\%$ of the federal poverty limit, and low income, ie, $< 200\%$ of the federal poverty limit]),¹³ educational attainment stratified by receipt of college education, insurance status (private, public, uninsured), and geographic region. In addition, to account for differences in clinical characteristics in our assessments, we included the following self-reported comorbidities: obesity, diabetes mellitus, hypertension, hyperlipidemia, tobacco use disorder (based on their history of smoking), cancer, arthritis, and kidney and liver disease.^{12,14} Furthermore, given its association with cardiovascular health and healthcare spending, we also assessed engagement in self-reported physical exercise.¹⁵

Statistical Analyses

We used survey-specific descriptive statistics to obtain weighted national estimates for the proportion of individuals with ASCVD who reported 1 or more of the measures of CRN: attempted to save money by missing doses of medication, taking lower than the prescribed dose, or delaying prescription refills. The overall results represent the average rate of CRN for a year between 2013 and 2017. The study represents a combination of serial cross-sectional data collected annually between 2013 and 2017. The combination of multiple years of data has been suggested by the National Center for Health Statistics, the federal agency responsible for conducting the NHIS, as a strategy to obtain more precise weighted estimates for the national rates. The sampled individuals vary across the years. The patient-level weights are therefore adjusted to incorporate the number of years included in the analysis to report only an average estimate for a calendar year during this period. To evaluate how reported CRN has changed over time, we evaluated temporal trends in these measures of CRN.

We next described differences in characteristics between individuals reporting CRN to all others with ASCVD using the Rao-Scott χ^2 test for categorical variables and survey-specific linear regression to compare continuous variables. Given the differences in access to healthcare insurance coverage across those 65 years of age, we stratified these descriptive analyses by subgroups of patients based on whether they were < 65 or ≥ 65 years of age.

Next, in a multivariate logistic regression model, we examined demographic (age, sex, race), socioeconomic (family income, insurance status, education), and health-related factors were associated with CRN. To ensure that the health-related factors were meaningful, we included the total number of comorbid health conditions and a composite cardiovascular risk factor profile as predictors in the model. Cardiovascular risk factor profile was defined as optimal, average, or poor according to the presence of 0 to 1, 2 to 3, or ≥ 4 cardiovascular risk

factors: hypertension, diabetes mellitus, hypercholesterolemia, lack of physical exercise (defined as not participating in moderate to vigorous physical activity for ≥ 30 minutes ≥ 5 times per week), smoking, and obesity (body mass index ≥ 30 kg/m²).^{16–19} As recommended in analyses using the NHIS, variance of weighted estimates was obtained with the use of tools available from the integrated public-use microdata series, which contains year-specific stratification, clustering, and weighting variables.²⁰ Furthermore, for our primary analyses that aggregated multiple years of data, subject-level weights were pooled together and divided by the number of studied years to report the national weighted estimate for an average year during the study period.¹² In the assessment of calendar-year trends, annual subject-level weights were used to obtain national estimates.

Next, we described rates of cost-reducing behaviors reported by patients, including seeking low-cost alternatives and use of alternative therapies to reduce costs of treatment. After accounting for differences in characteristics of subjects, we reported odds of cost-reducing behaviors in patients who reported CRN compared with all others with ASCVD.

The level of significance was set at a $P=0.05$, and all analyses were performed with survey-specific tools in Stata 16 (StataCorp, College Station, TX).

RESULTS

National Estimates and Temporal Trends

Of the 14 279 individuals with ASCVD captured in NHIS during 2013 through 2017, 1774 individuals reported CRN. This corresponds to 12.6% of US adults with ASCVD, representing an estimated 2.2 million (95% CI, 2.1–2.4 million) patients per year who reported CRN during 2013 to 2017 (Figure 1 in the online-only Data Supplement). Overall, an estimated 1.5 million (1.4–1.6 million) individuals or 8.6% of those with ASCVD missed doses of medicine to save money, 1.6 million (1.5–1.7 million) or 8.8% took less than prescribed dose of medications to save money, and 1.9 million (1.7–2 million) or 10.5% delayed filling prescriptions to save money. Overall, average rates of CRN decreased during this period (P for trend < 0.001), with a decrease from 15.3% in 2013 to 10.9% in 2016, with a nonsignificant change to a numerically higher average rate of 11.9% in 2017 (Figure 1 and Figure II in the online-only Data Supplement).

Characteristics Associated With CRN

The characteristics of those reporting CRN and the 3 components of CRN are reported in Tables 1 and 2. Overall, the prevalence of CRN was significantly higher among patients with ASCVD who were younger, had low income, were uninsured, or had a worse cardiovascular health profile (Table 1). Patients with ASCVD < 65 years of age compared with those ≥ 65 years of age were 3-fold more likely to report saving money by taking fewer medication doses (15.2% versus 4.8%),

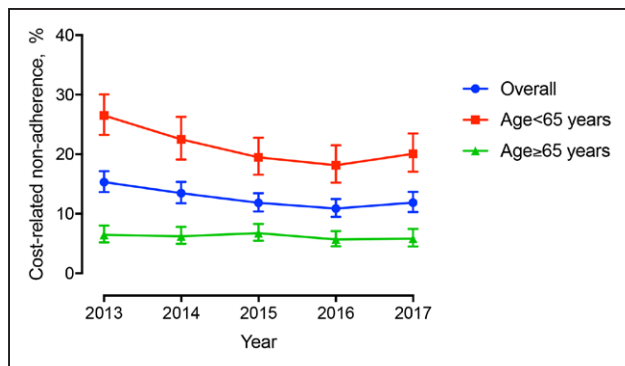


Figure 1. Calendar-year trends in cost-related medication nonadherence.

taking less medications than prescribed (15.5% versus 5.1%), and delaying medication refills (18.3% versus 4.7%; Figure 2). Overall, nearly 1 in 5 patients <65 years of age reported CRN compared with 6.2% in those ≥65 years of age. Certain patient groups <65 years of age were particularly vulnerable to CRN, with 1 in 4 women, 1 in 3 patients from low-income families, and more than half of all patients without health insurance reporting CRN (Table 2 and Table I in the online-only Data Supplement).

In an assessment that accounted for these differences in demographics, comorbidities, family income, and insurance status, younger age groups (18–39 and 40–64 years) were associated with 3.15 (95% CI, 2.01–4.93) and 2.26 (95% CI, 1.87–2.73) times higher odds of CRN compared with those ≥65 years of age, respectively. Similarly, odds of CRN were higher in women compared with men (odds ratio [OR], 1.26 [95% CI, 1.06–1.48]), in patients from low-income families compared with middle/high-income families (OR, 1.61 [95% CI, 1.35–1.92]), in uninsured compared with those with public insurance (OR, 4.20 [95% CI 2.93–6.02]), and in those with a high comorbidity count (OR, 2.11 [95% CI 1.66–2.68]; Figure 3). Similar factors were associated with CRN among both elderly (≥65 years of age) and nonelderly (18–64 years of age) patients with ASCVD (Table II in the online-only Data Supplement). No differences were observed in CRN by race/ethnicity or educational status after multivariate adjustment.

Cost-Reducing Behaviors

Among individuals with ASCVD, 4.6 million (4.4–4.7 million) individuals or 25.7% reported asking doctors for lower-cost medication, and 0.78 million (0.6–0.8 million) or 4.0% reported using alternative therapies. Those with CRN were more likely to report asking doctors for lower-cost medications (73.2% in those with CRN versus 18.8% in those without CRNs) and using alternative therapies (17.1% in CRN versus 1.8% in patients without CRN; Figure 4 and Table III in the online-only Data Supplement). In multivariate analyses

that accounted for differences in patient demographics, clinical characteristics, and socioeconomic status, those with CRN had 10.8-fold higher odds of asking doctors for lower-cost medications (95% CI, 9.0–13.0) and 8.9-fold higher odds of using alternative therapies (95% CI, 6.6–12.1).

DISCUSSION

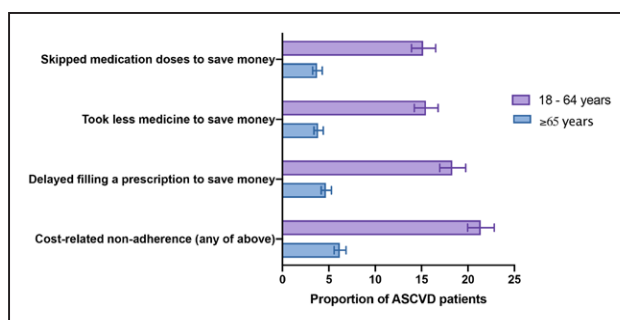
In nationally representative data, we found that 1 in 8 individuals with ASCVD, representing nearly 2.2 million US adults, is nonadherent to medications because of medication costs, with a substantial proportion reporting to skipping doses, taking less than the prescribed dose, and delaying prescription refills. In addition to specific questioning for nonadherence because of cost, these patients frequently report asking physicians for low-cost medication options and alternative therapies and therefore may represent additional cues to pursue an assessment for nonadherence because of cost as a part of clinical encounters.

In our contemporary assessment, individuals <65 years of age, women, and low-income and uninsured individuals are particularly vulnerable, which is concerning given the worse outcomes observed in several of these patient groups.^{21,22} Our assessment builds on prior work that identified women more frequently reporting CRN than men,^{23,24} highlighting the unexplored targets for narrowing the gap in outcomes for women and men with cardiovascular disease. Furthermore, individuals with comorbid health conditions who are most likely to benefit from secondary prevention medications also experience challenges with adherence with therapy, putting them at risk for future adverse health outcomes.⁷ Therefore, CRN remains a major hazard for patient health and likely significantly attenuates the benefits of effective guideline-directed therapies in clinical practice.

The high rates of CRN among those <65 years of age have implications for health policy. Health insurance with Medicare for nearly all individuals ≥65 years of age likely contributed to lower rates of nonadherence because of costs. Although individuals <65 years of age are more likely to be actively employed and to have fewer medical comorbidities^{25,26} and therefore may be financially in a better position to afford medications costs,²⁷ they are still 3-fold more likely to be nonadherent to medical therapies because of cost, arguing for the potential role for expanding the insurance protections offered to the Medicare population to those <65 years of age. Although the cost considerations of wider health insurance coverage for such high-risk individuals are complex, our study highlights an urgent need for health policy interventions to alleviate the financial toxicity from cost of medications.

Table 1. Characteristics Among Adults With Atherosclerotic Cardiovascular Disease Based on Whether They Reported Cost-Related Nonadherence

Variable	No Cost-Related Nonadherence, Weighted % (95% CI)	Cost-Related Nonadherence, Weighted % (95% CI)	P Value
Sample, n	12 505	1774	
Weighted sample, n (weighted %)	15 499 443 (87.4)	2 243 536 (12.6)	
Age category, y			<0.001
18–39	3.8 (3.2–4.4)	9.4 (7.1–11.7)	
40–64	34.5 (33.3–35.7)	62.5 (59.6–65.5)	
≥65	61.7 (60.5–62.9)	28.1 (25.4–30.8)	
Female	42.7 (41.5–43.8)	52.6 (49.5–55.7)	<0.001
Race/ethnicity			<0.001
Non-Hispanic white	76.5 (75.3–77.7)	69.5 (66.5–72.5)	
Non-Hispanic black	11.3 (10.4–12.2)	17.2 (15.1–19.4)	
Non-Hispanic Asian	3.1 (2.6–3.5)	2.1 (1.2–3.1)	
Hispanic	9.1 (8.3–10.0)	11.1 (8.6–13.6)	
Low family income	37.3 (36.0–38.6)	60.6 (57.5–63.6)	<0.001
Less than high school education	49.1 (47.9–50.3)	53.0 (49.7–56.3)	0.03
Insurance status			<0.001
Public	78.4 (77.3–79.4)	61.0 (57.8, 64.3)	
Private	19.4 (18.3–20.4)	21.9 (19.2, 24.6)	
Uninsured	2.3 (1.9–2.6)	17.1 (14.5, 19.7)	
Region			<0.001
Northeast	18.3 (17.1–19.5)	11.6 (9.6–13.5)	
Midwest	25.2 (23.8–26.6)	24.8 (21.9–27.7)	
South	38.2 (36.7–39.7)	49.1 (45.9–52.3)	
West	18.3 (17.1–19.5)	14.6 (12.3–16.8)	
Smoking status			<0.001
Never smoker	42.4 (41.3–43.5)	35.5 (32.7–38.3)	
Former smoker	41.9 (40.7–43.1)	31.4 (28.5–34.3)	
Current smoker	15.7 (14.8–16.6)	33.1 (30.1–36.2)	
Comorbidities			
Obesity	38.5 (37.3–39.8)	50.3 (47.2–53.5)	<0.001
Diabetes mellitus	31.6 (30.5–32.8)	38.1 (35.0–41.2)	<0.001
Hypertension	74.9 (73.8–76.0)	78.9 (76.4–81.3)	0.006
Hypercholesterolemia	65.9 (64.8–67.0)	66.1 (63.1–69.0)	0.91
Cancer	23.2 (22.2–24.1)	21.2 (18.6–23.8)	0.19
Arthritis	53.4 (52.2–54.5)	60.9 (57.5–64.2)	<0.001
Kidney disease	9.2 (8.6–9.8)	13.8 (11.6–16.1)	<0.001
Liver disease	2.7 (2.3–3.1)	5.5 (4.0–7.0)	<0.001
Insufficient physical activity	68.4 (67.2–69.5)	74.3 (71.5–77.0)	<0.001
Cardiovascular risk factor profile			<0.001
Optimal	13.8 (13.0–14.7)	9.2 (7.4–11.1)	
Average	52.2 (51.0–53.4)	40.6 (37.3–44.0)	
Poor	34.0 (32.8–35.1)	50.1 (46.8–53.5)	
Comorbidities, n			<0.001
0	25.2 (24.2–26.2)	16.8 (14.1–19.6)	
1	34.1 (33.0–35.2)	27.8 (25.0–30.6)	
≥2	40.7 (39.5–41.8)	55.4 (52.2–58.6)	

**Figure 2.** Rates of cost-related medication nonadherence and its components by age groups.

ASCVD indicates atherosclerotic cardiovascular disease.

It is notable that there were no significant differences in CRN by race/ethnicity. Therefore, although certain patient groups such as black patients frequently report lower rates of medication nonadherence and have worse cardiovascular outcomes,^{28–31} these differences do not appear to be mediated by nonadherence with medication secondary to cost, especially after accounting for differences in income and access to insurance. Similarly, education, likely a marker for health literacy, was also not independently associated with CRN. These observations highlight that targeting low-income groups and increasing access to insurance may be common avenues to target across major groups of patients rather than to design race- or literacy-specific interventions.

The high rates of CRN merit placing a wider focus on generic substitution of medications^{32–34} wherever possible but also tackling the cumulative financial burden of healthcare services for patients with chronic diseases to ensure that financial considerations do not impede their treatment. Another observation from our study is that average rates of CRN were numerically higher in 2017 after a modest decrease between 2013 and 2016. This does not represent a statistically significant inflection. However, this may be an important trend to monitor, especially given an emergence of novel therapies in the management of cardiovascular disease and the rising costs of medications.^{35,36} Furthermore, healthcare policy has continued to evolve during this period, particularly with respect to access to health insurance,^{37,38} making it critical to ensure that those with ASCVD can continue to access required medications. This observation would require further assessment as more years of data become available.

Our study has a few limitations that merit consideration. The study is based on questions posed to subjects and did not collect the number of medications prescribed or specific medications and dosages prescribed. However, the questionnaire used in the NHIS is a validated instrument delivered by trained interviewers that specifically addresses CRN, which cannot be captured without direct questions. The high rates of concordance between reporting CRN and requesting low-cost medications and pursuing alternative treatments also support the validity of the survey instrument. Moreover,

Table 2. Rates of Cost-Related Nonadherence and Its Components Across Subgroups of Patients With Atherosclerotic Cardiovascular Disease Among Those <65 and ≥65 Years of Age

	Age <65 y				Age ≥65 y			
	(1) Skipped Medication Doses to Save Money	(2) Took Less Medicine to Save Money	(3) Delayed Filling a Prescription to Save Money	1, 2, and/or 3=CRN	(1) Skipped Medication Doses to Save Money	(2) Took Less Medicine to Save Money	(3) Delayed Filling a Prescription to Save Money	1, 2, and/or 3=CRN
Sample, n	830	871	1009	1178	370	399	456	596
Weighted sample, n (weighted %)	1 146 514 (15.2)	1 168 300 (15.5)	1 384 350 (18.3)	1 613 089 (21.4)	380 890 (3.7)	393 918 (3.9)	478 316 (4.7)	630 447 (6.2)
Sex								
Male	12.7 (11.0–14.4)	13.1 (11.4–14.8)	15.2 (13.3–17.0)	18.3 (16.4–20.2)	2.9 (2.2–3.5)	2.9 (2.2–3.5)	3.7 (3.0–4.4)	4.9 (4.1–5.7)
Female	18.5 (16.5–20.4)	18.6 (16.6–20.5)	22.5 (20.4–24.5)	25.4 (23.3–27.6)	4.8 (4.0–5.6)	5.1 (4.3–5.9)	5.9 (5.0–6.9)	7.8 (6.8–8.9)
Race/ethnicity								
Non-Hispanic white	15.2 (13.6–16.7)	15.4 (13.9–16.9)	18.2 (16.5–19.9)	21.4 (19.6–23.1)	3.4 (2.8–4.0)	3.5 (2.9–4.0)	4.2 (3.6–4.8)	5.6 (4.8–6.3)
Non-Hispanic black	18.0 (14.8–21.3)	17.9 (14.5–21.3)	20.4 (17.0–23.8)	24.0 (20.4–27.6)	6.3 (4.6–7.9)	6.4 (4.6–8.1)	8.3 (6.4–10.2)	10.2 (8.0–12.3)
Non-Hispanic Asian	10.0 (2.4–17.6)	10.5 (3.0–18.0)	12.5 (4.3–20.6)	13.0 (4.8–21.2)	3.2 (0.3–6.2)	3.6 (0.9–6.2)	4.1 (1.7–6.4)	6.6 (3.0–10.3)
Hispanic	13.5 (9.6–17.4)	14.4 (10.7–18.2)	17.9 (13.4–22.4)	20.5 (15.8–25.2)	4.8 (2.7–7.0)	5.2 (3.3–7.1)	6.2 (3.8–8.7)	8.1 (5.5–10.7)
Family income								
Middle/high income	10.9 (9.4–12.5)	10.8 (9.3–12.3)	12.7 (11.0–14.4)	15.2 (13.4–17.0)	2.7 (2.1–3.3)	3.0 (2.3–3.6)	3.2 (2.5–3.8)	4.4 (3.6–5.2)
Low income	20.8 (18.6–23.0)	21.8 (19.6–24.1)	25.9 (23.6–28.3)	29.7 (27.3–32.1)	6.2 (5.2–7.3)	6.1 (5.2–7.1)	7.9 (6.7–9.2)	9.9 (8.6–11.3)
Education								
Some college or higher	13.7 (12.1–15.4)	13.7 (12.1–15.3)	16.5 (14.8–18.1)	19.0 (17.2–20.8)	3.8 (3.0–4.6)	3.9 (3.1–4.6)	4.7 (3.8–5.6)	6.1 (5.1–7.1)
High school/GED or below	16.6 (14.6–18.7)	17.3 (15.2–19.3)	20.3 (18.0–22.5)	23.8 (21.5–26.0)	3.7 (3.1–4.3)	3.8 (3.1–4.4)	4.7 (3.9–5.4)	6.2 (5.4–7.1)
Insurance status								
Public	14.2 (12.4–15.9)	15.1 (13.4–16.7)	18.2 (16.3–20.1)	21.3 (19.4–23.3)	3.7 (3.2–4.2)	3.8 (3.3–4.3)	4.7 (4.1–5.2)	6.2 (5.5–6.8)
Private	10.2 (8.5–11.8)	10.1 (8.5–11.8)	12.6 (10.7–14.5)	14.7 (12.8–16.6)	3.6 (–0.4 to 7.5)	3.0 (0.0–6.9)	3.9 (–0.1 to 8.0)	4.5 (0.3, 8.6)
Uninsured	43.9 (37.7–50.1)	42.8 (36.5–49.0)	46.3 (40.1–52.4)	53.3 (47.4–59.3)	23.1 (5.7–40.5)	20.5 (3.8–37.2)	14.3 (–0.0 to 28.6)	25.2 (7.4–43.0)
Financial hardship from medical bills								
No	6.4 (5.1–7.7)	6.5 (5.2–7.9)	7.1 (5.6–8.5)	9.5 (8.0–10.9)	1.9 (1.5–2.2)	1.8 (1.5–2.2)	2.3 (1.8–2.7)	3.3 (2.8–3.9)
Yes	25.2 (22.9–27.4)	25.6 (23.3–27.9)	31.1 (28.7–33.5)	34.9 (32.4–37.4)	11.1 (9.2–13.0)	11.9 (10.0–13.9)	14.3 (12.1–16.4)	17.3 (15.0–19.7)
Region								
Northeast	10.9 (7.9–14.0)	10.3 (7.5–13.2)	12.3 (9.4–15.2)	14.8 (11.5–18.2)	2.7 (1.8–3.5)	2.7 (2.0–3.5)	3.5 (2.5–4.5)	4.4 (3.3–5.5)

(Continued)

Table 2. Continued

	Age <65 y				Age ≥65 y			
	(1) Skipped Medication Doses to Save Money	(2) Took Less Medicine to Save Money	(3) Delayed Filling a Prescription to Save Money	1, 2, and/or 3=CRN	(1) Skipped Medication Doses to Save Money	(2) Took Less Medicine to Save Money	(3) Delayed Filling a Prescription to Save Money	1, 2, and/or 3=CRN
Midwest	14.5	14.8	18.2	20.9	4.0	4.1	4.7	6.4
	(11.7–17.3)	(12.0–17.7)	(15.2–21.3)	(17.8–24.0)	(3.0–5.1)	(3.0–5.2)	(3.6–5.8)	(5.0–7.7)
South	18.6	18.4	21.8	25.5	4.4	4.3	5.8	7.4
	(16.5–20.7)	(16.4–20.4)	(19.6–24.0)	(23.3–27.8)	(3.4–5.3)	(3.4–5.2)	(4.7–6.8)	(6.3–8.6)
West	11.5	13.7	15.3	17.7	3.2	3.7	3.7	5.3
	(8.9–14.1)	(11.0–16.5)	(12.4–18.3)	(14.7–20.7)	(2.1–4.2)	(2.6–4.9)	(2.7–4.8)	(3.9–6.6)
Smoking status								
Never smoker	13.1	12.6	15.8	18.3	2.9	3.3	4.2	5.3
	(11.2–14.9)	(10.9–14.3)	(13.9–17.7)	(16.2–20.3)	(2.3–3.5)	(2.7–3.9)	(3.5–4.9)	(4.5–6.1)
Former smoker	11.7	12.1	14.8	18.0	3.7	3.8	4.5	5.9
	(9.6–13.8)	(10.1–14.1)	(12.5–17.0)	(15.5–20.5)	(3.0–4.5)	(3.0–4.5)	(3.6–5.3)	(4.9–6.9)
Current smoker	21.8	23.0	25.6	29.3	7.1	6.5	7.7	10.8
	(18.7–24.9)	(20.0–26.0)	(22.3–28.9)	(26.1–32.6)	(5.0–9.2)	(4.6–8.4)	(5.6–9.8)	(8.3–13.4)
Comorbidities								
Obesity	16.0	16.2	19.8	23.0	4.8	5.2	6.5	8.2
	(14.1–17.9)	(14.4–18.0)	(17.8–21.7)	(20.9–25.0)	(3.8–5.8)	(4.2–6.1)	(5.3–7.6)	(6.9–9.5)
Diabetes mellitus	17.1	17.2	21.6	24.8	4.8	5.0	6.2	8.0
	(14.7–19.6)	(14.8–19.5)	(19.0–24.2)	(22.1–27.6)	(3.8–5.8)	(4.0–6.0)	(5.1–7.3)	(6.7–9.2)
Hypertension	16.4	16.6	19.5	23.0	4.3	4.4	5.1	6.7
	(14.7–18.1)	(15.0–18.3)	(17.8–21.2)	(21.2–24.8)	(3.6–4.9)	(3.8–5.0)	(4.4–5.7)	(6.0–7.5)
High cholesterol	15.4	15.1	18.8	21.6	4.2	4.2	5.1	6.6
	(13.8–17.1)	(13.5–16.7)	(17.1–20.5)	(19.8–23.4)	(3.5–4.8)	(3.6–4.8)	(4.4–5.8)	(5.8–7.4)
Cancer	17.3	18.5	21.2	25.0	3.9	4.1	5.0	6.5
	(13.8–20.9)	(15.0–21.9)	(17.6–24.9)	(20.9–29.1)	(3.0–4.8)	(3.2–5.0)	(3.9–6.0)	(5.3–7.7)
Arthritis	17.9	18.0	22.6	25.6	4.5	4.7	5.7	7.4
	(16.0–19.8)	(16.1–19.9)	(20.5–24.7)	(23.4–27.8)	(3.8–5.1)	(4.0–5.4)	(4.9–6.5)	(6.5–8.3)
Kidney disease	22.5	24.5	29.1	33.1	5.5	5.4	7.1	9.0
	(17.3–27.7)	(19.6–29.3)	(23.5–34.7)	(27.5–38.8)	(3.5–7.4)	(3.6–7.2)	(5.2–9.1)	(6.7–11.3)
Liver disease	18.1	22.0	25.2	28.0	9.1	12.4	10.8	12.6
	(12.1–24.1)	(15.2–28.8)	(18.1–32.2)	(20.9–35.1)	(3.5–14.7)	(6.1–18.7)	(4.8–16.9)	(6.4–18.9)
Physical inactivity	16.8	17.5	20.9	23.8	4.1	4.2	5.1	6.8
	(15.1–18.5)	(15.8–19.2)	(19.1–22.8)	(21.9–25.7)	(3.4–4.7)	(3.6–4.8)	(4.5–5.8)	(6.0–7.6)
Cardiovascular risk factor profile								
Optimal	10.3	11.4	13.3	14.8	1.6	1.7	2.6	3.3
	(7.5–13.1)	(8.4–14.5)	(10.1–16.6)	(11.5–18.2)	(0.7–2.5)	(0.7–2.6)	(1.3–3.9)	(1.9–4.6)
Average	13.8	13.2	15.6	18.9	2.9	3.0	3.9	5.0
	(11.7–15.8)	(11.2–15.1)	(13.5–17.7)	(16.6–21.1)	(2.3–3.5)	(2.4–3.5)	(3.2–4.5)	(4.2–5.8)
Poor	19.0	19.8	23.9	27.3	5.8	6.0	7.1	9.4
	(16.7–21.4)	(17.5–22.1)	(21.4–26.4)	(24.7–29.9)	(4.7–7.0)	(5.0–7.1)	(5.8–8.3)	(8.0–10.8)
Comorbidities, n								
0	10.8	10.7	11.5	14.0	2.0	2.1	2.3	3.3
	(8.5–13.2)	(8.4–13.1)	(9.0–13.9)	(11.4–16.5)	(1.1–2.8)	(1.2–2.9)	(1.4–3.2)	(2.3–4.3)
1	13.2	13.2	16.5	19.6	2.5	2.5	3.3	4.5
	(10.9–15.4)	(11.0–15.4)	(14.2–18.9)	(17.0–22.1)	(1.8–3.1)	(1.8–3.2)	(2.5–4.1)	(3.5–5.4)
≥2	20.0	20.8	24.9	28.4	5.5	5.7	6.8	8.8
	(17.9–22.1)	(18.8–22.9)	(22.7–27.1)	(26.1–30.7)	(4.6–6.4)	(4.9–6.6)	(5.9–7.8)	(7.7–9.9)

Values indicate weighted percentage (95% CI), unless otherwise indicated. GED indicates general equivalency diploma.

Downloaded from <http://ahajournals.org> by on June 18, 2024

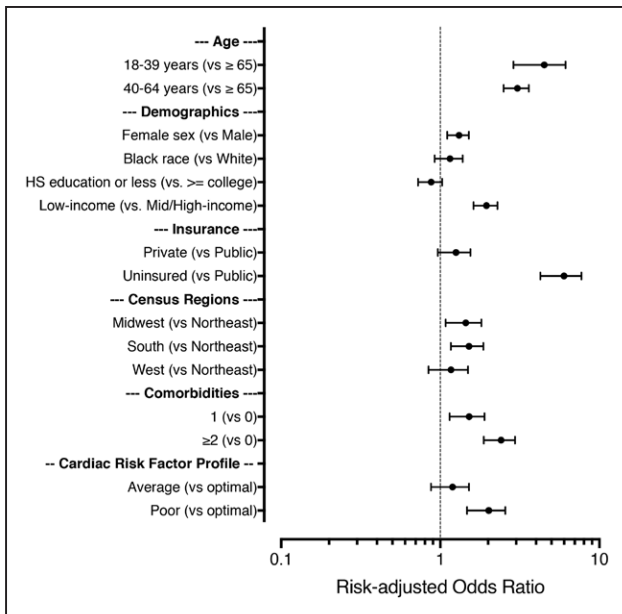


Figure 3. Predictors of cost-related medication nonadherence. HS indicates high school.

it has been addressed in several prior studies.^{21,24} Furthermore, ASCVD is based on self-report, but the rates of self-reported ASCVD in the NHIS are consistent with the national rates¹ and prior published studies from other national databases.³⁴ Last, we are unable to elucidate the whether the nonadherence because of costs has implications for patient outcomes because we do not have information on patient outcomes in the survey. However, several studies have found both financial hardship and poor risk factor control to be independently associated with worse patient outcomes.^{5,19,39–41} The issue of the direct effect of drug costs and CRN as mediators in patient outcomes is an avenue for future research.

CONCLUSIONS

CRN is frequent in many vulnerable Americans with ASCVD. Health policy interventions would need to urgently focus attention on targeting drugs costs as an

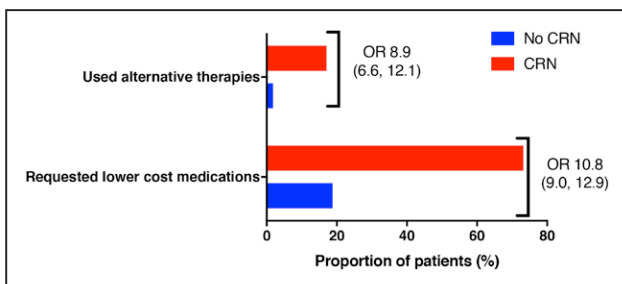


Figure 4. Cost-reducing behaviors with and without cost-related medication nonadherence (CRN). OR indicates odds ratio.

important avenue to improve adherence to medications and to reduce future needs of healthcare services.

ARTICLE INFORMATION

Received May 26, 2019; accepted September 18, 2019.

Guest Editor was Dean Karalis, MD.

The online-only Data Supplement is available with this article at <https://www.ahajournals.org/doi/suppl/10.1161/circulationaha.119.049174>.

Correspondence

Khurram Nasir, MD, MPH, MSc, Houston Methodist DeBakey Heart & Vascular Center & Center for Outcomes Research Houston Methodist, 6550 Fannin St, Suite 1801, Houston, TX 77030. Email knasir@houstonmethodist.org

Affiliations

Division of Cardiology, University of Texas Southwestern Medical Center, Dallas (R.K., S.R.D., J.A.d.L.). Center for Outcomes Research and Evaluation, Yale New Haven Health, CT (J.V.-E., H.M.K.). Division of Cardiology, Department of Medicine, Baylor College of Medicine, Houston, TX (S.S.V.). Center for Outcomes Research, Houston Methodist Research Institute, TX (B.A.K.). School of Public Health, Texas A&M University, College Station (B.A.K.). Section of Cardiovascular Medicine, Department of Medicine, Yale School of Medicine, New Haven, CT (H.M.K.). Department of Health Policy and Management, Yale School of Public Health, New Haven, CT (H.M.K.). Division of Cardiovascular Prevention and Wellness Houston Methodist DeBakey Heart & Vascular Center & Center for Outcomes Research Houston Methodist, Houston, TX (K.N.).

Sources of Funding

Dr Khera is supported by grant UL1TR001105 from the National Center for Advancing Translational Sciences of the National Institutes of Health. The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the article; and decision to submit the article for publication.

Disclosures

Dr de Lemos reports personal fees from Amgen, Regeneron, and Janssen. Dr Krumholz works under contract with the Centers for Medicare & Medicaid Services to develop publicly reported quality measures; was a recipient of a research grant, through Yale, from Medtronic and the US Food and Drug Administration to develop methods for postmarket surveillance of medical devices; is a recipient of a research grant with Medtronic and Johnson & Johnson, through Yale, to develop methods of clinical trial data sharing; was a recipient of a research agreement, through Yale, from the Shenzhen Center for Health Information for work to advance intelligent disease prevention and health promotion; collaborates with the National Center for Cardiovascular Diseases in Beijing; received payment from the Arnold & Porter Law Firm for work related to the Sanofi clopidogrel litigation and from the Ben C. Martin Law Firm for work related to the Cook IVC filter litigation; receives payment from the Siegfried & Jensen Law Firm for work related to Vioxx litigation; chairs a Cardiac Scientific Advisory Board for UnitedHealth; is a participant/participant representative of the IBM Watson Health Life Sciences Board; is a member of the Advisory Board for Element Science, the Advisory Board for Facebook, and the Physician Advisory Board for Aetna; and is the founder of HugoHealth, a personal health information platform, and a cofounder of Refactor Health, an enterprise healthcare artificial intelligence-augmented data management company. The other authors report no conflicts.

REFERENCES

- Benjamin EJ, Virani SS, Callaway CW, Chamberlain AM, Chang AR, Cheng S, Chiuve SE, Cushman M, Delling FN, Deo R, et al; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2018 update: a report from the American Heart Association. *Circulation*. 2018;137:e67–e492. doi: 10.1161/CIR.0000000000000558
- Ford ES, Ajani UA, Croft JB, Critchley JA, Labarthe DR, Kottke TE, Giles WH, Capewell S. Explaining the decrease in U.S. deaths from coronary disease, 1980–2000. *N Engl J Med*. 2007;356:2388–2398. doi: 10.1056/NEJMs053935

3. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005;353:487–497. doi: 10.1056/NEJMra050100
4. Dragomir A, Côté R, White M, Lalonde L, Blais L, Bérard A, Perreault S. Relationship between adherence level to statins, clinical issues and health-care costs in real-life clinical setting. *Value Health*. 2010;13:87–94. doi: 10.1111/j.1524-4733.2009.00583.x
5. Bansilal S, Castellano JM, Garrido E, Wei HG, Freeman A, Spettell C, Garcia-Alonso F, Lizano I, Arnold RJ, Rajda J, et al. Assessing the impact of medication adherence on long-term cardiovascular outcomes. *J Am Coll Cardiol*. 2016;68:789–801. doi: 10.1016/j.jacc.2016.06.005
6. Goldman DP, Joyce GF, Zheng Y. Prescription drug cost sharing: associations with medication and medical utilization and spending and health. *JAMA*. 2007;298:61–69. doi: 10.1001/jama.298.1.61
7. Briesacher BA, Gurwitz JH, Soumerai SB. Patients at-risk for cost-related medication nonadherence: a review of the literature. *J Gen Intern Med*. 2007;22:864–871. doi: 10.1007/s11606-007-0180-x
8. McDonald HP, Garg AX, Haynes RB. Interventions to enhance patient adherence to medication prescriptions: scientific review. *JAMA*. 2002;288:2868–2879. doi: 10.1001/jama.288.22.2868
9. Schumock GT, Vermeulen LC. The rising cost of prescription drugs: causes and solutions. *Pharmacotherapy*. 2017;37:9–11. doi: 10.1002/phar.1873
10. Choudhry NK, Avorn J, Glynn RJ, Antman EM, Schneeweiss S, Toscano M, Reisman L, Fernandes J, Spettell C, Lee JL, et al; Post-Myocardial Infarction Free Rx Event and Economic Evaluation (MI FREEE) Trial. Full coverage for preventive medications after myocardial infarction. *N Engl J Med*. 2011;365:2088–2097. doi: 10.1056/NEJMsa1107913
11. Board of Governors of the Federal Reserve System. Report on the economic well-being of U.S. households in 2017 - May 2018. <https://www.federalreserve.gov/publications/2018-economic-well-being-of-us-households-in-2017-preface.htm>. Accessed September 22, 2019.
12. Centers for Disease Control and Prevention. NHIS data, questionnaires and related documentation. 2018. <https://www.cdc.gov/nchs/nhis/data-questionnaires-documentation.htm>. Accessed September 22, 2019.
13. Khera R, Valero-Elizondo J, Okunrintemi V, Saxena A, Das SR, de Lemos JA, Krumholz HM, Nasir K. Association of out-of-pocket annual health expenditures with financial hardship in low-income adults with atherosclerotic cardiovascular disease in the United States. *JAMA Cardiol*. 2018;3:729–738. doi: 10.1001/jamacardio.2018.1813
14. Kaul S, Avila JC, Mehta HB, Rodriguez AM, Kuo YF, Kirchoff AC. Cost-related medication nonadherence among adolescent and young adult cancer survivors. *Cancer*. 2017;123:2726–2734. doi: 10.1002/ncr.30648
15. Shiroma EJ, Lee IM. Physical activity and cardiovascular health: lessons learned from epidemiological studies across age, gender, and race/ethnicity. *Circulation*. 2010;122:743–752. doi: 10.1161/CIRCULATIONAHA.109.914721
16. Singh J, Valero-Elizondo J, Salami JA, Warraich HJ, Ogunmoroti O, Spatz ES, Desai N, Rana JS, Virani SS, Blankstein R, et al. Favorable modifiable cardiovascular risk profile is associated with lower healthcare costs among cancer patients: the 2012–2013 Medical Expenditure Panel Survey. *J Am Heart Assoc*. 2018;7:e007874.
17. Valero-Elizondo J, Salami JA, Ogunmoroti O, Osondu CU, Aneni EC, Malik R, Spatz ES, Rana JS, Virani SS, Blankstein R, et al. Favorable cardiovascular risk profile is associated with lower healthcare costs and resource utilization: the 2012 Medical Expenditure Panel Survey. *Circ Cardiovasc Qual Outcomes*. 2016;9:143–153. doi: 10.1161/CIRCOUTCOMES.115.002616
18. Bensenor IM, Goulart AC, Santos IS, Bittencourt MS, Pereira AC, Santos RD, Nasir K, Blankstein R, Lotufo PA. Association between a healthy cardiovascular risk factor profile and coronary artery calcium score: results from the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). *Am Heart J*. 2016;174:51–59. doi: 10.1016/j.ahj.2015.12.018
19. Daviglus ML, Stamler J, Pirzada A, Yan LL, Garside DB, Liu K, Wang R, Dyer AR, Lloyd-Jones DM, Greenland P. Favorable cardiovascular risk profile in young women and long-term risk of cardiovascular and all-cause mortality. *JAMA*. 2004;292:1588–1592. doi: 10.1001/jama.292.13.1588
20. Integrated Public Use Microdata Series. National Health Interview Survey, 2019. <https://nhis.ipums.org/nhis/>. Accessed August 19, 2019.
21. Bhuyan SS, Shiyabola O, Kedia S, Chandak A, Wang Y, Isehunwa OO, Anunobi N, Ebuonyi I, Deka P, Ahn S, et al. Does cost-related medication nonadherence among cardiovascular disease patients vary by gender? Evidence from a nationally representative sample. *Womens Health Issues*. 2017;27:108–115. doi: 10.1016/j.whi.2016.10.004
22. Osborn CY, Kripalani S, Goggins KM, Wallston KA. Financial strain is associated with medication nonadherence and worse self-rated health among cardiovascular patients. *J Health Care Poor Underserved*. 2017;28:499–513. doi: 10.1353/hpu.2017.0036
23. Lee M, Khan MM. Gender differences in cost-related medication non-adherence among cancer survivors. *J Cancer Surviv*. 2016;10:384–393. doi: 10.1007/s11764-015-0484-5
24. Zhang JX, Crowe JM, Meltzer DO. The differential rates in cost-related non-adherence to medical care by gender in the US adult population. *J Med Econ*. 2017;20:752–759. doi: 10.1080/13696998.2017.1326383
25. Bureau of Labor Statistics. Labor force statistics from the current population survey, 2019. <https://www.bls.gov/cps/cpsaat03.htm>. Accessed August 3, 2019.
26. Mensah GA, Brown DW. An overview of cardiovascular disease burden in the United States. *Health Aff (Millwood)*. 2007;26:38–48. doi: 10.1377/hlthaff.26.1.38
27. Salami JA, Valero-Elizondo J, Ogunmoroti O, Spatz ES, Rana JS, Virani SS, Blankstein R, Younus A, Arrieta A, Blaha MJ, et al. Association between modifiable risk factors and pharmaceutical expenditures among adults with atherosclerotic cardiovascular disease in the United States: 2012–2013 Medical Expenditures Panel Survey. *J Am Heart Assoc*. 2017;6:e004996.
28. Gerber BS, Cho YI, Arozullah AM, Lee SY. Racial differences in medication adherence: a cross-sectional study of Medicare enrollees. *Am J Geriatr Pharmacother*. 2010;8:136–145. doi: 10.1016/j.amjopharm.2010.03.002
29. Trinacty CM, Adams AS, Soumerai SB, Zhang F, Meigs JB, Piette JD, Ross-Degnan D. Racial differences in long-term adherence to oral anti-diabetic drug therapy: a longitudinal cohort study. *BMC Health Serv Res*. 2009;9:24. doi: 10.1186/1472-6963-9-24
30. Xie Z, St Clair P, Goldman DP, Joyce G. Racial and ethnic disparities in medication adherence among privately insured patients in the United States. *PLoS One*. 2019;14:e0212117. doi: 10.1371/journal.pone.0212117
31. Kronish IM, Ye S. Adherence to cardiovascular medications: lessons learned and future directions. *Prog Cardiovasc Dis*. 2013;55:590–600. doi: 10.1016/j.pcad.2013.02.001
32. Choudhry NK, Denberg TD, Qaseem A; Clinical Guidelines Committee of American College of Physicians. Improving adherence to therapy and clinical outcomes while containing costs: opportunities from the greater use of generic medications: best practice advice from the Clinical Guidelines Committee of the American College of Physicians. *Ann Intern Med*. 2016;164:41–49. doi: 10.7326/M14-2427
33. Gellad WF, Donohue JM, Zhao X, Mor MK, Thorpe CT, Smith J, Good CB, Fine MJ, Morden NE. Brand-name prescription drug use among Veterans Affairs and Medicare Part D patients with diabetes: a national cohort comparison. *Ann Intern Med*. 2013;159:105–114. doi: 10.7326/0003-4819-159-2-201307160-00664
34. Warraich HJ, Salami JA, Khera R, Valero-Elizondo J, Okunrintemi V, Nasir K. Trends in use and expenditures of brand-name atorvastatin after introduction of generic atorvastatin. *JAMA Intern Med*. 2018;178:719–721. doi: 10.1001/jamainternmed.2018.0990
35. Khera R, Valero-Elizondo J, Saxena A, Virani SS, Krumholz HM, Nasir K. National population and cost implications of treatment with icosapentyl ethyl in the United States: an assessment based on the REDUCE-IT trial. *bioRxiv*. 2018:466649.
36. Arrieta A, Hong JC, Khera R, Virani SS, Krumholz HM, Nasir K. Updated cost-effectiveness assessments of PCSK9 inhibitors from the perspectives of the health system and private payers: insights derived from the FOURIER Trial. *JAMA Cardiol*. 2017;2:1369–1374. doi: 10.1001/jamacardio.2017.3655
37. Himmelstein DU, Woolhandler S, Fauke C. U.S. health care in the Trump era: a data update. *Int J Health Serv*. 2019;49:402–411. doi: 10.1177/0020731419840178
38. Khera R, Hong JC, Saxena A, Arrieta A, Virani SS, Blankstein R, de Lemos JA, Krumholz HM, Nasir K. Burden of catastrophic health expenditures for acute myocardial infarction and stroke among uninsured in the United States. *Circulation*. 2018;137:408–410. doi: 10.1161/CIRCULATIONAHA.117.030128
39. Carlsson AC, Starrin B, Gigante B, Leander K, Hellenius ML, de Faire U. Financial stress in late adulthood and diverse risks of incident cardiovascular disease and all-cause mortality in women and men. *BMC Public Health*. 2014;14:17. doi: 10.1186/1471-2458-14-17
40. Daviglus ML, Liu K, Greenland P, Dyer AR, Garside DB, Manheim L, Lowe LP, Rodin M, Lubitz J, Stamler J. Benefit of a favorable cardiovascular risk-factor profile in middle age with respect to Medicare costs. *N Engl J Med*. 1998;339:1122–1129. doi: 10.1056/NEJM199810153391606
41. Pool LR, Burgard SA, Needham BL, Elliott MR, Langa KM, Mendes de Leon CF. Association of a negative wealth shock with all-cause mortality in middle-aged and older adults in the United States. *JAMA*. 2018;319:1341–1350. doi: 10.1001/jama.2018.2055