Effects of Nonadherence With Prescription Drugs Among Older Adults

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Approximately 88% of persons aged ≥60 years in the United States take prescription drugs, usually on a regular basis.[1] The effectiveness of many prescription drugs is seriously impaired by the failure of patients to follow the recommended regimen of medication. Nonadherence rates are as high as 40% to 86% for some conditions and/or patient groups, resulting in preventable visits to emergency departments (EDs) and inpatient stays.[2-6] It is estimated that between 4% and 11.4% of all hospitalizations and 7.6% of all ED visits are related to nonadherence.[7-10] These estimates suggest that increased adherence could significantly improve health and reduce healthcare costs,[6,11] especially among older adults.[12]

The incidence of ED visits among adults increases with age. As adults age, they are more likely to arrive at an ED by ambulance,[13-16] to have longer ED visits,[14-16] and to be admitted from the ED to inpatient care.[13,15,17,18] Those who are admitted to inpatient care are more likely than younger adults to require care in an intensive care unit.[17]

In this article we describe a retrospective, longitudinal study of adherence to prescription drugs in the years 1999-2005 among persons aged ≥60 years who were insured by Medicaid (Arizona Health Care Cost Containment System [AHCCCS]). Each subject had 1 or more of 5 chronic conditions. We compared ED visits among adherent older adults with visits by older adults who were nonadherent.

The benefits of increased adherence appear large in current studies, but these benefits may be understated because they are based on periods of less than 2 years, omitting the longer-term benefits among chronically ill patients. This study contributes information on the longer-term benefits.

METHODS

Subject Population

The subjects include all AHCCCS-insured persons aged ≥60 years at some time during the study period (January 1, 1999–December 31, 2005) with 1 or more of 5 chronic conditions: hypertension, chronic obstructive pulmonary disease (COPD), chronic heart disease (CHD), diabetes, or hypercholesterolemia (high blood cholesterol). The subjects lived in Maricopa County, Arizona, which includes Phoenix, the fifth largest city in the United States. Approximately 127,916 persons met the selection cri-

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Objective: To determine the association between prescription nonadherence and the health of older adults with 1 or more of 5 chronic conditions.

Study Design: Analysis of the correlation between prescription nonadherence and the health of older adults.

Methods: Data were from a 7-year panel with information on healthcare encounters and prescriptions. We used fixed-effects Cox duration regression models and fixed-effects Poisson count regression models to control for time-invariant factors specific to each subject when examining the impact of nonadherence on time to an emergency department (ED) visit (Cox regression) or number of ED visits (Poisson count regression).

Results: Nonadherence was associated with subsequent ED visits for hypertension, chronic heart disease, diabetes, and hypercholesterolemia. No significant short-term effects of nonadherence on chronic obstructive pulmonary disease (COPD) were detected. However, long-term effects of nonadherence (using the count regression model with lagged counts) were detected for COPD, as well as for hypertension, diabetes, and hypercholesterolemia.

Conclusions: Medicinal adherence was important for all 5 conditions analyzed here. A year of nonadherence had the same correlation with ED use as making an older adult 1 year older.

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Take-Away Points

The correlation between emergency department use and adherence with prescription medicine in older adults with chronic conditions (hypertension, chronic heart disease, diabetes, chronic obstructive pulmonary disease, and hypercholesterolemia) was analyzed.

- Older adults with hypertension and high cholesterol had poor outcomes up to 3 years after their period of nonadherence.
- A year of nonadherence had the same correlation with ED use as making an older adult 1 year older.

teria. The AHCCCS data include details of all healthcare encounters; all filled prescriptions; Current Procedural Terminology, *International Classification of Diseases, Ninth Revision*, and National Drug Code (NDC) codes; and patient demographics. Patient characteristics are shown in Table 1.

The number of records in Table 1 exceeded 127,916 because individuals had multiple conditions. Elimination of records with inconsistent or missing values reduced the number of cases that were used in the estimation (row 2 vs row 1 in Table 1).

Measuring Nonadherence

Nonadherence existed when 8 or more days elapsed between the time a prescription was consumed and the time it was refilled, after which we assumed the patient remained nonadherent until the prescription was refilled. We excluded prescriptions that were not refilled within 365 days because we could not know whether this patient was taken off the medicine by a physician, a change in medication was made, or there was simply a long period of nonadherence.

Estimation of Average Number of Pills per Day. The drugs normally prescribed for each condition were identified from the published results of the national Medical Expenditure Panel Survey[19] and associated with their respective NDC. The number of pills consumed per day was estimated by dividing the number of pills refilled by the number of days from the original prescription.

The intended prescription length was estimated by dividing the quantity of pills prescribed by the number of pills consumed per day. The majority of the prescriptions were intended to last 30 days, with a median of 33 days. We assumed that the intended length for estimates from 25 to 38 days was 30 days and reestimated intended lengths. The estimates seemed to be a reasonable approximation of the number of pills per day. Only 5.3% of the 1692 NDCs had estimated values that were not exact multiples of 0.5 or 0.333.

Measuring Emergency Department Visits and Other Variables

We could not identify the primary reason for an ED visit by older persons with chronic conditions. We assumed that our estimates were reasonable for comparing adherent with nonadherent patients since injuries or acute conditions should be distributed more or less equally between adherent and nonadherent patients.

Statistical Analysis

Randomization of treatment and control groups is the gold standard for drug studies, but it is impossible to randomize when analyzing adherence to medications for chronic conditions. There is the moral problem of randomly halting medication for some elderly persons but not for others, as well as forcing control group members to take their medications when they may choose to do otherwise. The inability to randomize makes it difficult for cross-sectional studies to separate the effects of adherence from individual-specific healthy lifestyles and other unobservable personal characteristics.[20] This sample selection problem may result in upward bias of the adherence effects, which appear large in current cross-sectional studies. This bias may be partially offset by the omission of longer term effects in the cross-sectional studies, which typically used sample periods of less than 2 years.

We partially corrected for the problem of unobserved characteristics by using fixed-effects models that identified nonadherence effects for those individuals who changed adherence over time, rather than identifying the effect of nonadherence by using variation between patients at a point in time. While reasons for nonadherence among older persons are not all well known, clear relationships have been found with dose, insurance coverage, complexity of treatment, race, and number of medications.[21-26] Race is of course time invariant, dosage and medications were included in the data, and the persons in the sample had AHCCCS coverage throughout the period and were not subject to copays or deductibles. However, the complexity of treatment was unobserved and changes in complexity could either increase or decrease adherence.

There are other important time-variant but unobservable influences on adherence, including changes in provider-patient relationships, depression, and changes in cognitive impairment,[21,22,27-29] which was a limitation of our study and biased our attempt to estimate the effects of nonadherence. However, regressions of nonadherence on patient and treatment characteristics for AHCCCS patients suggest that our biases might have been relatively small. Medicinal adherence is *higher* for persons over 65 years of age than younger age groups, suggesting that age-related cognitive impairments are probably not an important driver of nonadherence for our sample. Treating physician specialty—which also may change over time for a given patient—is statistically insignificant in explaining adherence. Moreover, comorbidities, which are

Table 1. Sample Population Subsets

Variable	Hypertension (*ICD-9* codes 401.00-401.99)	COPD (*ICD-9* codes 414.00-414.99)	CHD (*ICD-9* codes 490.00-496.99)	Diabetes (*ICD-9* codes 250.00-250.99)	High Blood Cholesterol (*ICD-9* codes 272.00-272.99)
All patients	76,495	42,884	29,743	40,970	41,525
Patients in model[a]	66,781	24,138	26,468	32,820	31,406
Prescriptions[b]	1,930,767	242,433	796,285	678,362	416,387
Mean (SD)					
Male, %	32	35	39	34	33
Age, y	67.97 (10.58)	66.28 (9.93)	68.33 (10.46)	66.61 (9.75)	64.04 (8.22)
White, %	56	68	62	48	51
Hispanic, %	29	21	26	37	35
ED visits, n	2.41 (4.81)	2.84 (5.19)	2.90 (5.34)	2.44 (4.55)	2.04 (3.63)

CHD indicates chronic heart disease; COPD, chronic obstructive pulmonary disease; ED, emergency department; *ICD-9*, *International Classification of Diseases, Ninth Revision*.
[a]Patients for whom an average number of pills per day for at least 1 prescription could be calculated.
[b]Prescriptions for which average number of pills per day was available.

correlates of the complexity of care, were generally statistically insignificant in explaining adherence. In particular, for AHCCCS patients, depression exhibited either a statistically insignificant or quantitatively small effect on adherence. Our fixed-effects models improved on previous estimates but could not control for all potential time-variant but unobservable influences. Our results must be interpreted within those constraints.

We used 2 models—a Cox proportional hazard model and an unconstrained Poisson maximum likelihood model (ie, a count regression model), both with fixed effects for each individual in our sample.

Cox Proportional Hazard Model. The Cox model estimated the correlation between nonadherence and the propensity to use the ED, given the time elapsed since the last ED visit. Each observation consisted of the length of time beginning 7 days after a prescription was estimated to be exhausted until the next ED visit. Also included were a dummy variable recording whether or not the given prescription was filled on time, an age variable, and a censoring variable indicating (before an ED visit) nonadherence durations still in process (ie, not yet completed) when the sample was taken.

$$(1)\ h[t, Noncomp, Age]_i = h_i(t,\alpha_i) \times \exp(\beta_1 Noncomp + \beta_2\, Age)$$

The $h_i(t,\alpha_i)$ function is the baseline hazard function for each individual, including an α_i-effect representing all time-invariant covariates. Each individual had his or her own baseline time between ED visits. The baseline duration was assumed to be proportionally shifted by the "$\exp(\beta_1 Noncomp + \beta_2 Age)$" term. Because of repeated spells on the same patients, the Cox regression partialed out the $h_i(t,\alpha_i)$ term for each individual, controlling for their baseline duration and time-invariant factors (including race, sex, family size, genetic predisposition, motivational and ability factors, and the duration of medication use before each person was initially observed in the sample.

Count Regression Estimates of Nonadherence Effects. The count regression measured the correlation between the number of adherent days and the number of subsequent ED visits. The mean number of ED visits for the subjects was higher (between 2 and 3 visits per year) than the median number.

The count regression model estimated longer term trends by including nonadherent outcomes in prior years. A nonadherent ratio (*N.Adher.Ratio*) for each year in which a patient was continuously enrolled in AHCCCS was calculated as follows:

$$(2)\ N.Adher.Ratio = \frac{(number\ of\ nonadherence\ days)}{(total\ days\ in\ year)}$$

Four dummy variables measured variations in ED use with respect to different levels of nonadherence to capture possible nonlinear effects between number of ED visits and levels of nonadherence:

$N.Adher.Ratio.1 = 1$ if $0 < N.Adher.Ratio \leq .25$
$N.Adher.Ratio.2 = 1$ if $.25 < N.Adher.Ratio \leq .5$
$N.Adher.Ratio.3 = 1$ if $.5 < N.Adher.Ratio \leq .75$
$N.Adher.Ratio.4 = 1$ if $.75 < N.Adher.Ratio \leq 1$

The fixed-effects, unconditional Poisson count regression, estimated for each condition by maximum likelihood, was:

Table 2. Descriptive Means for All Prescription Fills With the Cox Proportional Hazards Model

Variable	Hypertension	COPD	CHD	Diabetes	High Cholesterol
Number of prescriptions filled	1,930,767	242,433	796,285	678,362	416,387
Fraction of prescriptions filled late	0.22	0.29	0.22	0.25	0.27
Fraction of prescriptions not refilled within 1 year	0.19	0.25	0.20	0.22	0.23
Fraction of prescriptions filled on time	0.59	0.46	0.58	0.54	0.51

CHD indicates chronic heart disease; COPD, chronic obstructive pulmonary disease.

$$(3)\ E(ED) = \exp(\varnothing + \alpha_i + \mu_t + NADH_0 x_{t,1} + NADH_1 x_{t-1,i} + NADH_2 x_{2i} + NADH_3 x_{3i})$$

where $E(ED)$ is the expected annual number of ED visits; $\varnothing$ is the overall intercept; α_i is an intercept for each individual; μ_t is an intercept for each time period; and $NADH_T$ is the set of *N.Adher.Ratio* coefficients associated with the 4 nonadherence dummy variables defined above, with the nonadherence ratios extending from the current period to ratios lagged up to 3 years (T = 0-3 years). We used dummy variables to allow for an unrestricted nonlinear response between nonadherence and annual ED visits. The *NADH* coefficients indicate the percent change in number of visits correlated with the respective level of nonadherence compared with patients who were fully adherent, again subject to the potential biases due to our inability to control for unobservable, time-variant factors.

RESULTS

Two sets of results are described. "Time to the next ED visit" effects of nonadherence were estimated as the hazard of using an ED after a period of nonadherence (Table 2, Table 3). We also examined the number of annual ED visits relative to the number of days of adherence using count regressions (Table 4, Table 5). The count regressions modeled the effects of prior years of nonadherence on the current annual use of the ED. The final estimates converted the correlation between nonadherence and ED visits to an equivalent number of additional years of age.

Cox Hazard Rates for Nonadherence

The hazard function measured the instantaneous rate of transition to an ED visit. Consistent with the prior literature,[8-11,30-41] we hypothesized that nonadherence is negatively correlated with health and hence is a positive coefficient in the hazard function: when elderly patients are nonadherent with their medications, the associated duration until their next ED is shorter. We partitioned these Cox regression analyses by chronic condition in Table 3 and reported the estimated factors of proportionality there. Missed refills were associated with a higher hazard of visiting an ED, except for patients with COPD. Our results for COPD patients agree with prior estimates.[41]

The correlation between nonadherence and an ED visit can be expressed in terms of the correlation between an additional year of age and the probability of an ED visit. The correlation between an additional year of age for our older sample and ED use was empirically equivalent to the correlation between being nonadherent for 12 to 18 months and ED use. For example, missing medications for CHD for 12 months had a cumulative impact on the hazard rate of 0.168 (12 × .014), while the effect of growing 1 year older was 0.165. There was no significant change in the results when a covariate was inserted to control for a patient taking multiple medications.

Table 3. Fixed-Effects Cox Regressions: Rates of Transition to Emergency Department Visits Given Nonadherence by Chronic Condition

Variable	Hypertension	COPD	CHD	Diabetes	High Cholesterol
Observations (total durations)	1,531,134	174,639	628,842	521,451	318,449
Nonadherence (SE)	0.012[a] (.003)	0.0109 (.008)	0.014[a] (.004)	0.013[a] (.005)	0.015[b] (.006)
Hazard ratio	1.012	1.011	1.014	1.013	1.015
Age (SE)	0.185[a] (.001)	0.153[a] (.003)	0.165[a] (.002)	0.193[a] (.002)	0.206[a] (.003)
Hazard ratio	1.203	1.166	1.18	1.213	1.229

CHD indicates chronic heart disease; COPD, chronic obstructive pulmonary disease; SE, standard error.
[a]Significant at P <.01.
[b]Significant at P <.05.

Table 4. Descriptive Statistics for Poisson Regression[a]

No. of Lags	Hypertension (n = 66,781/5640)[a]	COPD (n = 24,138/3231)[a]	CHD (n = 26,468/3153)[a]	Diabetes (n = 32,820/3537)[a]	High Cholesterol (n = 31,406/4398)[a]
Current year, %					
N.Adher.Ratio.1	12.71	7.61	12.69	12.47	13.42
N.Adher.Ratio.2	9.04	4.89	10.40	10.43	10.25
N.Adher.Ratio.3	9.95	5.66	7.45	10.35	9.39
N.Adher.Ratio.4	14.98	10.89	16.14	13.94	14.42
Lagged 1 year, %					
N.Adher.Ratio.1	11.37	7.03	11.07	11.93	11.32
N.Adher.Ratio.2	7.78	4.89	8.44	9.56	7.94
N.Adher.Ratio.3	9.29	5.57	7.58	9.22	8.00
N.Adher.Ratio.4	15.57	12.35	16.27	13.68	13.42
Lagged 2 years, %					
N.Adher.Ratio.1	11.65	7.24	11.13	11.96	10.37
N.Adher.Ratio.2	7.98	4.80	8.28	8.91	7.14
N.Adher.Ratio.3	9.01	5.32	7.20	8.79	6.46
N.Adher.Ratio.4	13.37	11.42	14.24	11.08	9.07
Lagged 3 years, %					
N.Adher.Ratio.1	11.60	6.31	10.69	11.42	8.73
N.Adher.Ratio.2	7.66	4.77	7.33	8.14	5.39
N.Adher.Ratio.3	7.68	5.17	7.04	7.04	4.37
N.Adher.Ratio.4	9.06	7.86	9.29	7.27	4.91

CHD indicates chronic heart disease; COPD, chronic obstructive pulmonary disease; *N.Adher.Ratio*, nonadherent ratio (see Methods, Statistical Analysis for details).
[a]Parenthetical values represent original number of observations/number of observations after restriction.

Count Regression Estimates of Nonadherence Effects

The count regression (Poisson regression) measured whether the fraction of nonadherent days was correlated with subsequent ED visits. The analysis was limited to the years 2002-2004 to allow for the lagged covariates (1999-2001). Only persons enrolled in AHCCCS throughout the period were included, to permit the use of fixed-effect models. The year 2005 was omitted because this model's estimation of *N.Adher.Ratio* relies on future years to indicate nonadherence.

The descriptive statistics for the nonadherence ratio dummies in Table 4 indicate that the majority of persons in our sample adhered to their medication. The current year nonadherence ratios for hypertension indicated that a slight majority of the subjects were in adherence with their medication all year round: 53.32% (100%–12.71%–9.04%–9.95%–14.98%). The 2 largest nonadherent categories among hypertensive patients in the current year were those who were nonadherent less than 25% of the time (*N.Adher.Ratio*.1 = 12.71%) and those who were nonadherent 75% or more of the time (*N.Adher.Ratio*.4 = 14.98%).

The positive coefficients in Table 5 imply that nonadherence was correlated with more ED visits, confirming the Cox regression correlations. In every case, there was a strong relationship between nonadherence and increased ED visits in both current and future years.

For example, consider those who were least adherent with their hypertension medications—those in the *N.Adher.Ratio*.4 category (about 15% of those with hypertension prescriptions; see Table 4). The patients with hypertension who were least adherent also had 68% [exp(0.5195) = 1.681] more visits to the ED than those who were fully adherent; this difference is statistically significant at better than the .0001 level. The least adherent patients in lagged year 1—regardless of their level of adherence in the current year—had 42% more ED visits than those who were fully adherent in lagged year 1. Regardless of current and prior year adherence, those who were nonadherent 2 years before the current year also had 23% more ED visits in the current year, although again, this increase may not be casual because of time-variant omitted factors. Similar results were obtained for patients taking medication for diabetes or high cholesterol.

Table 5. Fixed-Effects Poisson Regressions: Annual Emergency Department Visits and Adherence[a]

No. of Lags	Hypertension (n = 5640)	COPD (n = 3231)	CHD (n = 3153)	Diabetes (n = 3537)	High Cholesterol (n = 4398)
Current year					
N.Adher.Ratio.1	**0.696**	**0.833**	**0.598**	**0.623**	**0.588**
P	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**
N.Adher.Ratio.2	**0.689**	**0.650**	**0.612**	**0.657**	**0.425**
P	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**
N.Adher.Ratio.3	**0.511**	**0.585**	**0.6702**	**0.417**	**0.354**
P	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**.0001**
N.Adher.Ratio.4	**0.519**	**0.457**	**0.5491**	**0.574**	**0.422**
P	**<.0001**	**<.0001**	**<.0001**	**<.0001**	**<.0001**
Lagged 1 year					
N.Adher.Ratio.1	**0.205**	**0.319**	0.1262	**0.231**	0.236
P	**.0127**	**.0091**	.2175	**.0126**	.0065
N.Adher.Ratio.2	**0.230**	**–0.001**	0.0786	**0.229**	–0.025
P	**.0106**	**.9927**	.4901	**.0214**	.7995
N.Adher.Ratio.3	**0.349**	**0.038**	0.2704	**0.122**	0.098
P	**<.0001**	**.7807**	.0185	**.2392**	.3130
N.Adher.Ratio.4	**0.351**	**0.248**	0.1532	**0.341**	0.065
P	**<.0001**	**.0097**	.0935	**.0003**	.4900
Lagged 2 years					
N.Adher.Ratio.1	**0.213**	0.100	0.0811	**–0.197**	**0.373**
P	**.0087**	.4334	.4312	**.043**	**<.0001**
N.Adher.Ratio.2	**0.046**	0.046	0.0460	**0.046**	**0.0460**
P	**.2219**	.7555	.9222	**.2336**	**.7627**
N.Adher.Ratio.3	**–0.067**	0.014	0.1535	**0.127**	**0.143**
P	**.4546**	.9248	.2141	**.2295**	**.2158**
N.Adher.Ratio.4	**0.208**	0.174	0.1085	**0.211**	**0.371**
P	**.0119**	.1134	.2654	**.0456**	**.0007**
Lagged 3 years					
N.Adher.Ratio.1	0.115	0.216	–0.0034	–0.041	**0.306**
P	.1376	.0662	.9717	.6528	**.0013**
N.Adher.Ratio.2	0.070	–0.016	–0.0997	0.121	**0.068**
P	.4416	.9123	.3759	.2537	**.5703**
N.Adher.Ratio.3	–0.050	0.011	0.0876	0.001	**–0.083**
P	.5653	.9321	.4265	.9939	**.5409**
N.Adher.Ratio.4	0.138	0.218	–0.0058	0.230	**0.190**
P	.1069	.0611	.9551	.0582	**.1648**

CHD indicates chronic heart disease; COPD, chronic obstructive pulmonary disease; *N.Adher.Ratio*, nonadherent ratio (see Methods, Statistical Analysis for details).
[a]The joint significance of *N.Adher.Ratio*.2 to *N.Adher.Ratio*.4 was also tested with the null hypothesis that: H_o: (*N.Adher.Ratio*.2 + *N.Adher.Ratio*.3 + *N.Adher.Ratio*.4) = 0. Bold formatting is used to denote years for which the null hypothesis was rejected with a confidence level of 95% or greater.

While CHD showed the weakest long-term effects (ie, lagged effects) of nonadherence on ED visits, we note that in lagged 1 year, the coefficient for *N.Adher.Ratio*.3 was both positive and significant and that there were no negatively significant coefficients for this or any other condition (with the exception of the *N.Adher.Ratio*.1 for the diabetes coefficient in lagged year 2).

Though the Cox hazard-rate model indicated that nonadherence may not significantly impact the number of ED visits for patients with COPD, the results in Table 5 indicated both a strong long-term (lagged 1 year) and current-year effect for COPD.

DISCUSSION

Adherence to regimens of care is believed to be correlated with adherence to healthy lifestyles. Where, as in our results, healthy lifestyles were unobservable, there was uncertainty concerning the measured effects of adherence. We partially overcame the problem by measuring changes over time for the same individuals (through fixed-effects models) rather than measuring differences among different individuals at a point in time. Together, our models suggest that risks were associated with nonadherence for any of the chronic conditions studied. We believe our models provide somewhat stronger evidence of relationship between medication nonadherence and increased ED visits in our panel than in the prior literature, as time-invariant effects for *each* individual were controlled for in the analyses. But as is true for all studies in this area, *unobservable time-variant* changes (changes in the provider-patient relationship, the patient's cognitive ability, or depression) might have biased our estimates. Further, our estimates for the elderly in Arizona might not generalize to other regions of the country.

Since no prior studies have attempted to estimate the longer term correlation between nonadherence and health as we did with our count regression models, these results show that for many conditions, this omission may actually lead to an *underestimation* of the costs of nonadherence. Moreover, the very conservative nature of our definition of nonadherence was likely to understate the long-term effects of not maintaining a consistent medication regimen.

Some forms of nonadherence could not be estimated from our data. It has been estimated that as many as one-fifth of all patients never fill their prescriptions and others stop taking the medication before the end of the prescribed period.[17] Therefore, our estimates, although more complete than those in studies of shorter durations, might have understated the effects of nonadherence.

Nonadherence both reduces patients' health and increases healthcare expenditures by reducing the effectiveness of prescription drugs. Increases in adherence to prescribed regimens of care would increase the quality of care while reducing expenditures. Nowhere in the population is the opportunity greater than among older adults with chronic conditions. They are the most intensive users of prescription drugs and their numbers will increase dramatically in the next decade.

If healthcare costs for this portion of the population are to be reduced, it is important that future healthcare systems be structured to increase medication adherence for all patients with the long-term chronic health conditions of hypertension, CHD, COPD, diabetes, and hypercholesterolemia, especially for Medicaid patients such as those examined here. Any decrease in adherence for these conditions can be expected to be associated with an increased number of preventable ED visits.

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REFERENCES

1. **Strange GR, Chen EH, Sanders AB.** Use of emergency departments by elderly patients: projections from a multicenter data base. *Ann Emerg Med.* 1992;21(7):819-824.
2. **Singal BM, Hedges JR, Rousseau EW, et al.** Geriatric patient emergency visits: part 1: comparisons of visits by geriatric and younger patients. *Ann Emerg Med.* 1992;21(7):802-807.
3. **Dickinson ET, Verdile VP, Kostyum CT, et al.** Geriatric use of emergency medical services. *Ann Emerg Med.* 1996;27(2):199-203.
4. **Wong CH, Wang RL, Chang H, et al.** Age related emergency department utilization: a clue of patient demography in disaster medicine. *Ann Disaster Med.* 2003;1:56-68.
5. **Baum SA, Rubenstein LZ.** Old people in the emergency room: age-related differences in emergency department use and care. *J Am Geriatr Soc.* 1987;35(5):398-404.
6. **Naughton BJ, Moran MB, Kadah H, Heman-Ackah Y, Longano J.**

Delirium and other cognitive impairment in older adults in an emergency department. *Ann Emerg Med.* 1995;25(6):751-755.

7. DeVol R, Bedroussian A, Charuworn A, et al; Milliken Institute. *Unhealthy American: The Economic Burden of Chronic Disease—Charting a New Course to Save Lives and Increase Productivity and Economic Growth.* October 2007. http://www.milkeninstitute.org/publications/publications.taf?function=detail&ID=38801018&cat=ResRep. Accessed October 23, 2007.

8. Col N, Fanale JE, Kronholm P. The role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly. *Arch Intern Med.* 1990;150(4):841-845.

9. Grymonpre RE, Mitenko PA, Sitar DS, Aoki FY, Montgomery PR. Drug-associated hospital admissions in older medical patients. *J Am Geriatr Soc.* 1988;36(12):1092-1098.

10. Malhotra S, Karan RS, Pandhi P, Jain S. Drug related medical emergencies in the elderly: role of adverse drug reactions and non-compliance. *Postgrad Med J.* 2001;77(913):703-707.

11. Sullivan SD, Kreling DH, Hazlet TK. Non-compliance with medication regimens and subsequent hospitalizations: a literature analysis and cost of hospitalization estimate. *J Res Pharm Econ.* 1990;2:19-33.

12. Smith C, Cowan C, Heffler S, Catlin A. National health spending in 2004: recent slowdown led by prescription drug spending. *Health Aff (Millwood).* 2006;25(1):186-196.

13. George J, Kong DC, Thoman R, Stewart K. Factors associated with medication nonadherence in patients with COPD. *Chest.* 2005;128(5):3198-3204.

14. Reginster JY, Lecart MP. Treatment of osteoporosis with bisphosphonates—do compliance and persistence matter? *Business Briefing: Long-Term Healthcare.* 2004. www.touchbriefings.com/pdf/886/ACF6111.pdf. Accessed January 19, 2011.

15. McCombs JS, Nichol MB, Newman CM, Sclar DA. The costs of interrupting antihypertensive drug therapy in a Medicaid population. *Med Care.* 1994;32(3): 214-226.

16. Cox ER, Jernigan C, Coons SJ, Draugalis JL. Medicare beneficiaries' management of capped prescription benefits. *Med Care.* 2001;39(3): 296-301.

17. Lichtenberg FR. Do (more and better) drugs keep people out of hospitals? *Am Econ Rev.* 1996;86(2):384-388.

18. Murray MD, Callahan CM. Improving medication use for older adults: an integrated research agenda. *Ann Intern Med.* 2003;139(5 pt 2):425-429.

19. Agency for Healthcare Research and Quality. Medical Expenditure Panel Survey. http://www.meps.ahrq.gov/mepsweb/.

20. Simpson SH, Eurich DT, Majumdar SR, et al. A meta-analysis of the association between adherence to drug therapy and mortality. *BMJ.* 2006;333(7557):15.

21. Balkrishnan R. Predictors of medication adherence in the elderly. *Clin Ther.* 1998;20(4):764-771.

22. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med.* 2005;353(5):487-497.

23. Wang TJ, Vasan RS. Epidemiology of uncontrolled hypertension in the United States. *Circulation.* 2005;112(11):1651-1662.

24. Adams AS, Soumerai SB, Ross-Degnan D. Use of antihypertensive drugs by Medicare enrollees: does type of drug coverage matter? *Health Aff (Millwood).* 2001;20(1):276-286.

25. Blustein J. Drug coverage and drug purchases by Medicare beneficiaries with hypertension. *Health Aff (Millwood).* 2000;19(2):219-230.

26. Committee on Public Health Priorities to Reduce and Control Hypertension in the U.S. Population; Institute of Medicine. *A Population-Based Policy and Systems Change Approach to Prevent and Control Hypertension.* Washington, DC: The National Academies Press; 2010. http://www.nap.edu/catalog.php?record_id=12819. Accessed January 19, 2011.

27. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: a meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med.* 2000;160(14):2101-2107.

28. Safran DG, Taira DA, Rogers WH, Kosinski M, Ware JE, Tarlov AR. Linking primary care performance to outcomes of care. *J Fam Pract.* 1998;47(3):213-220.

29. Martin LR, Williams SL, Haskard KB, DiMatteo MR. The challenge of patient adherence. *Ther Clin Risk Manag.* 2005;1(3):189-199.

30. Huybrechts KF, Ishak KJ, Caro JJ. Assessment of compliance with osteoporosis treatment and its consequences in a managed care population. *Bone.* 2006;38(6):922-928.

31. Levenson T, Grammer LC, Yarnold PR, Patterson R. Cost-effective management of malignant potentially fatal asthma. *Allergy Asthma Proc.* 1997;18(2):73-78.

32. Maronde RF, Chan LS, Larsen FJ, Strandberg LR, Laventurier MF, Sullivan SR. Underutilization of antihypertensive drugs and associated hospitalization. *Med Care.*1989;27(12):1159-1166.

33. Schoen MD, DiDomenico RJ, Connor SE, Dischler JE, Bauman JL. Impact of prescription drugs on clinical outcomes in indigent patients with heart disease. *Pharmacotherapy.* 2001;21(12):1455-1463.

34. Billups SJ, Malone DC, Carter BL. The relationship between drug therapy noncompliance and patient characteristics, health-related quality of life, and health care costs. *Pharmacotherapy.* 2000;20(8): 941-949.

35. Monane M, Bohn RL, Gurwitz JH, Glynn RJ, Levin R, Avorn J. Compliance with antihypertensive therapy among elderly medicaid enrollees: the roles of age, gender, and race. *Am J Public Health.* 1996;86(12):1805-1808.

36. Mojtabai R, Olfson M. Medication costs, adherence, and health outcomes among Medicare beneficiaries. *Health Aff (Millwood).* 2003; 22(4):220-229.

37. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Impact of medication adherence on hospitalization risk and healthcare cost. *Med Care.* 2005;43(6):521-530.

38. Vik SA, Hogan DB, Patten SB, Johnson JA, Romonko-Slack L, Maxwell CJ. Medication nonadherence and subsequent risk of hospitalisation and mortality among older adults. *Drugs Aging.* 2006;23(4): 345-357.

39. Rizzo JA, Simons WR. Variations in compliance among hypertensive patients by drug class: implications for health care costs. *Clin Ther.* 1997;19(6):1446-1457.

40. Weis SE, Foresman B, Matty KJ, et al. Treatment costs of directly observed therapy and traditional therapy for Mycobacterium tuberculosis: a comparative analysis. *Int J Tuberc Lung Dis.* 1999;3(11):976-984.

41. Matuszewski K, Velayudhan P, Flint N, Pierpaoli P. Nonadherence with drug therapy for chronic obstructive pulmonary disease: a risk factor for hospitalization? *Value Health.* 1999;2(6):446-451. ■