Predictors of Adherence With Concomitant Antihypertensive and Lipid-lowering Therapy

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INTRODUCTION

- Cardiovascular disease (CVD) accounts for 931,000 deaths and $368 billion in direct medical costs and lost productivity in the United States each year.[1]
- Hypertension (HTN) and dyslipidemia (DYS) are comorbid conditions in many patients,[2] and the presence of both of these risk factors places patients at substantially greater risk for CVD events than either condition in isolation.[3]
- Numerous clinical trials and meta-analyses have concluded that sustained use of antihypertensive (AH) and lipid-lowering (LL) medications substantially reduces the risk of coronary heart disease (CHD), stroke, and death in patients with cardiovascular risk factors.[4–9]
- In patients with comorbid HTN and DYS, adherence to concomitant AH and LL therapy is especially important.
- In actual practice, however, long-term compliance and persistence are difficult to achieve.[10,11]
- Predictors of adherence to concomitant therapy are not well understood, since previous studies have examined persistence with single-drug classes.

STUDY OBJECTIVE

- To describe the patterns and predictors of adherence with concomitant AH and LL therapy in a US managed care population.

METHODS

Study Design

- Retrospective cohort study in a large US managed care population.

Study Population

- Cohort
  - Patients who initiated both AH and LL therapies within 90 days of each other
  - Required diagnosis of HTN as well as AH medication prescription.
- Inclusion criteria
  - Minimum of 1 year of continuous enrollment in medical and pharmacy plans prior to index date
  - Patients retained in analysis until death, disenrollment, or end of 3 years
  - Follow-up was truncated on April 30, 2001, the last date for which reliable data on mortality were available.

Main Outcomes of Interest

- Percent of patients adherent (PDC ≥80%) and nonadherent (PDC <80%) over time.
- Adherence was measured as the proportion of days covered (PDC) by a given drug class in any interval, based on the quantity dispensed and number of days supplied from each filled prescription.
- Repeated measurement of adherence with AH and LL drugs at 3-month intervals, from treatment initiation until disenrollment from plan or the end of data stream (up to 3 years).
- Dichotomized patients at each interval, based on an 80% adherence threshold.
- Relative odds of being adherent for different levels of potential predictors.

Statistics

- Percent of patients adherent and nonadherent at each interval by AH, LL, and both.
- Multivariate model of adherence with concomitant therapy over time, adjusting for potential predictors.
  - Patient characteristics that predicted adherence were identified using generalized estimating equations, an extension of generalized linear models for correlated repeated measures.
  - A logit-link function and empirical-variance estimators were used in the models.

RESULTS

Study Population (Table 1)

- A total of 8406 concomitant therapy users met the inclusion criteria.
- Almost 75% of patients were in the 45- to 74-year age range.
- Most patients (68%) had no evidence of prior coronary artery disease.
- Over 20% of patients had a history of diabetes mellitus.
- Patients had filled prescriptions for approximately 4 unique medications, on average, in the year prior to starting concomitant therapy.
- Approximately 25% of patients were hospitalized in the previous year.

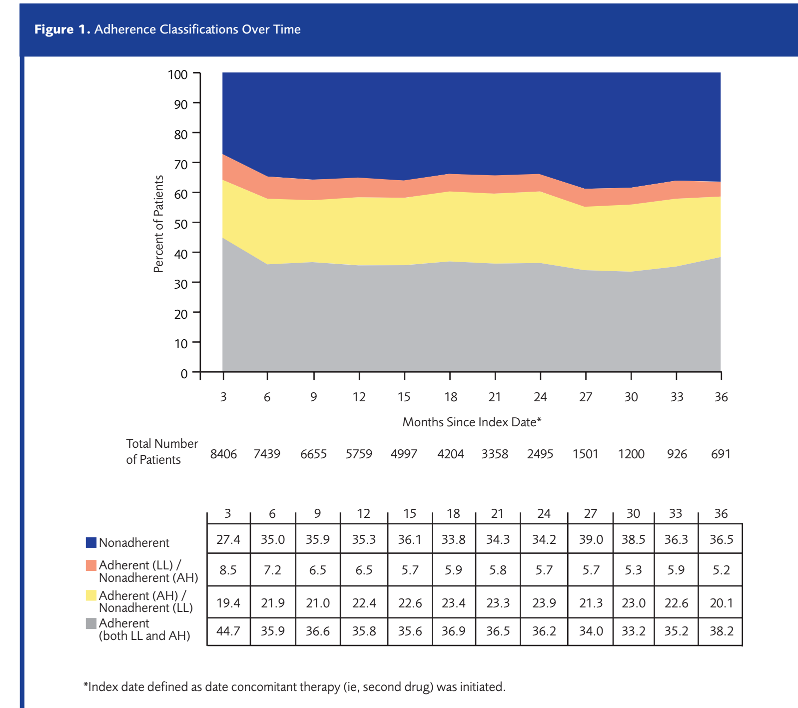
Table 1. Characteristics of Patients Who Initiated Both Lipid-lowering and Antihypertensive Drugs Within 90 Days

Characteristics	% (or mean [SD])
Number of patients	8406
Demographics	
Age, years	
18–24	0.7
25–34	0.9
35–44	6.5
45–54	19.9
55–64	23.8
65–74	30.5
75–84	15.9
≥85	1.8
Gender (% female)	46.9
Clinical history for year prior to index date	
Coronary artery disease	
Level 1 diagnosis (angina or coronary angiography)	2.5
Level 2 diagnosis (PTCA, CABG, or chronic CHD)	18.2
Level 3 diagnosis (acute MI)	11.0
Stroke	9.5
Congestive heart failure	7.5
Depression	5.0
Dementia	1.2
Diabetes mellitus	20.8
Charlson comorbidity index	0.90 (1.26)
Health services in year prior to index date	
Number of prescription medications	3.96 (3.91)
Number of outpatient physician visits	3.89 (4.17)
Hospitalized (%)	24.8

SD, standard deviation; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft; CHD, coronary heart disease; MI, myocardial infarction

Adherence Over Time (Figure 1)

- Six months after treatment initiation, only 36% of patients were adherent with both AH and LL therapies (gray area in Figure 1), a proportion which remained relatively steady over time.
- A similar proportion of the population (35%) did not adhere to either regimen after 6 months (blue area in Figure 1).
- An additional 25%–30% of patients were adherent with either AH or LL therapy, but not both.
- Relatively few patients were adherent with LL therapy while nonadherent with AH therapy.



	3	6	9	12	15	18	21	24	27	30	33	36
Nonadherent	27.4	35.0	35.9	35.3	36.1	33.8	34.3	34.2	39.0	38.5	36.3	36.5
Adherent (LL) / Nonadherent (AH)	8.5	7.2	6.5	6.5	5.7	5.9	5.8	5.7	5.7	5.3	5.9	5.2
Adherent (AH) / Nonadherent (LL)	19.4	21.9	21.0	22.4	22.6	23.4	23.3	23.9	21.3	23.0	22.6	20.1
Adherent (both LL and AH)	44.7	35.9	36.6	35.8	35.6	36.9	36.5	36.2	34.0	33.2	35.2	38.2

*Index date defined as date concomitant therapy (ie, second drug) was initiated.

Figure 1. Adherence Classifications Over Time

Predictors of Adherence (Table 2)

- The strongest predictor of adherence with concomitant AH and LL therapy was the number of other prescription medications taken in the year prior to initiating concomitant therapy. The lower the number of other medications being taken, the higher the likelihood of adherence.
- Age was the second strongest predictor of adherence with concomitant AH and LL therapy. Adherence was greatest among patients 55–64 years of age, followed by those aged 65–74 years and then those aged 45–54 years.
- Time between initiation of AH and LL therapy was the third strongest predictor of adherence; patients who initiated concomitant therapies within 30 days of each other were more likely to be adherent over time.
- Time since initiation of therapy was also a significant predictor of nonadherence, with adjusted odds of adherence declining by 14% for every 1-unit increase in ln (months) following treatment initiation.
- Patients at higher cardiovascular risk at baseline were also more adherent to concomitant therapy than those at lower cardiovascular risk.
- Gender was also a significant predictor of adherence with concomitant therapy; women were less likely to be adherent than men.

Limitations

- Patients were considered adherent if any AH drug was on hand (even if multiple medications were prescribed).
- New fills were assumed to start immediately, rather than serially, after the current supply of drug(s) was exhausted.
- The cohort considered here is from one managed care population and may not be generally applicable to other settings.

Table 2. Associations between Potential Predictors and Adherence to Concomitant Therapy

Variable	Odds Ratio	Adjusted 95% CI	P-value
Days between starts of AH and LL therapy			
0–30 days	1.34	(1.18, 1.52)	<0.0001
31–60 days	1.09	(0.94, 1.27)	0.2534
61–90 days	1.00	–	–
Time since initiation of concomitant therapy			
Ln (months)	0.86	(0.83, 0.89)	<0.0001
Demographics			
Age (years)			
18–44	1.00	–	–
45–54	1.24	(1.05, 1.47)	0.0133
55–64	1.56	(1.32, 1.84)	<.0001
65–74	1.27	(1.08, 1.49)	0.0041
≥75	1.14	(0.96, 1.36)	0.1441
Female	0.91	(0.84, 0.98)	0.0195
Clinical history in baseline year			
Coronary heart disease			
none	1.00	–	–
level 1 (angina or coronary angiography)	0.96	(0.74, 1.24)	0.7316
level 2 (PTCA, CABG, or chronic CHD)	1.20	(1.07, 1.34)	0.0014
level 3 (acute MI)	1.28	(1.09, 1.50)	0.0028
Stroke	1.20	(1.04, 1.39)	0.0150
Congestive heart failure	1.24	(1.06, 1.45)	0.0075
Depression	0.94	(0.78, 1.13)	0.5087
Dementia	0.89	(0.61, 1.30)	0.5504
Diabetes	1.06	(0.96, 1.17)	0.2253
Health services used in baseline year			
Number of other prescription medications			
0	1.96	(1.72, 2.25)	<0.0001
1	1.61	(1.40, 1.84)	<0.0001
2	1.30	(1.14, 1.49)	<0.0001
3–5	1.23	(1.10, 1.38)	0.0004
6+	1.00	–	–
Outpatient physician encounters (all-cause)			
0–1	1.00	–	–
2	0.93	(0.82, 1.05)	0.2218
3–5	1.03	(0.93, 1.14)	0.6040
6+	0.97	(0.87, 1.09)	0.6058
Hospitalized in baseline year	0.83	(0.73, 0.94)	0.0033

CONCLUSIONS

- Adherence was a problem for these patients, with only about 1 in 3 patients classified as adherent to concomitant AH and LL therapy over time.
  - Another third were not adherent with either therapy in each interval
  - The remainder of the population (25%–30%) were adherent with one medication (usually AH therapy) but not the other.
- Age, gender, time since treatment began, and a history of CHD or congestive heart failure were independently associated with the likelihood of being adherent.
- Adherence was better when AH and LL therapies were initiated on or about the same date (within 0–30 days of each other).
- The number of other medications a patient was taking in the pretreatment year was strongly and inversely associated with adherence to concomitant therapy.
- Initiating AH and LL therapy together and keeping the number of other medications to a minimum may improve adherence with concomitant therapy.

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