Medication Utilization Patterns and Hypertension-Related Expenditures among Patients Who Were Switched from Fixed-Dose To Free-Combination Antihypertensive Therapy

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ABSTRACT

Using a retrospective cohort study of medical and pharmacy claims data, we evaluated medication compliance, persistence, and hypertension-related expenditures among patients who were switched from fixed-dose combination (FDC) to free-combination (FC) antihypertensive therapy. An example of a fixed-dose combination product for hypertension would be a valsartan/HCTZ tablet, and a free-combination product would be a valsartan tablet plus a diuretic tablet.

The 7,224 patients identified from January 2003 to December 2005 were matched, in a 1:1 ratio, by propensity scores to controls who remained on their FC antihypertensive medications. Compliance, defined as a medication–possession ratio, was measured over 12 months. Persistence was measured as the percentage of patients who did not experience a lapse in therapy of more than 30 days since their last prescription refill.

The patients continuing with FDC therapy had better persistence (42.5% higher; \( P < 0.002 \)) and compliance (22.1% higher; \( P < 0.001 \)), compared with patients who were switched to FC therapy. The 22.1% higher compliance rate for patients continuing the FDC regimen was associated with significantly lower expenditures for hypertension-related health care (\( P < 0.001 \)) and an estimated 5% reduction in hypertension-related expenditures.

Key words: fixed-dose combinations, antihypertensive therapies, health care costs, compliance, persistence

INTRODUCTION

More than 72 million adults in the U.S. have hypertension, making it the most common cardiovascular disease.\(^1\) If hypertension is not properly managed, it can lead to serious adverse cardiovascular and cerebrovascular events, including myocardial infarction (MI), angina pectoris, stroke, and renal disease.\(^2\) Although lifestyle and diet modifications have the potential to decrease the incidence of hypertension in the general population and improve patients’ blood pressure (BP) control rates, many patients require pharmacological intervention to maintain control of BP.\(^3–5\)

Medications commonly prescribed for hypertension include thiazide-type diuretics such as hydrochlorothiazide (HCTZ), angiotensin-receptor blockers (ARBs), angiotensin-converting enzyme (ACE)–inhibitors, and calcium-channel blockers. These medications are either prescribed as monotherapy (one agent taken as a single tablet or capsule) or as combination therapy (multiple agents taken as a daily regimen of multiple tablets or as a single tablet in a fixed-dose combination (FDC) agent. The evidence suggests that most patients with hypertension require combination therapy to reach target BP.\(^2,6–10\)

For example, the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) states that most patients need two or more drugs to achieve BP control.\(^2\)

Although free-combination (FC) medications are chemically equivalent to FDC products, FC regimens increase the complexity of using and acquiring medications. Simpler regimens can improve medication persistence and compliance for different diseases and age groups.\(^11–15\) Studies specifically comparing single-tablet FDC and FC antihypertensive regimens have demonstrated better persistence and compliance with FDC therapies.\(^16–19\) One study that compared FDC lisinopril/hydrochlorothiazide (HCTZ) with FC lisinopril plus a diuretic, and FDC enalapril/HCTZ versus FC enalapril plus a diuretic, showed a 21.7% and an 18.8% improvement, respectively, in persistence in the FDC arm after 12 months.\(^20\)

Another study examined medication compliance, use of health care resources, and costs in FDC amlopidine besylate/benazepril HCl therapy and a comparable FC component-based therapy.\(^17\) The study demonstrated a 7% absolute increase in the compliance rate in the FDC group. The total

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average annual costs of cardiovascular-related care were $726 for the FDC patients and $1,600 for the two-tablet FC group. In a study by Gerbino et al., better compliance was noted with amlodipine/benazepril than with an ACE-inhibitor plus a dihydropyridine calcium-channel blocker, independent of the number of concomitant medications used.

Therapeutic regimens that improve medication persistence and compliance are more likely to produce better health outcomes and lower health care costs. Several studies have demonstrated the positive correlation between persistence and compliance rates and control of hypertension. In addition to the link between compliance and BP control, studies have shown an inverse relationship between compliance with medication regimens and health care costs in the treatment of hypertension. Inadequate control of BP has been associated with a significant cost burden in treating avoidable complications such as congestive heart failure, coronary heart disease, stroke, and renal disease. Because hypertension is highly prevalent, with estimated direct and indirect costs of $66.4 billion in the U.S. in 2007, improved management of hypertension through better medication compliance has the potential to reduce costs of a disease that generates a significant cost burden in the U.S.

**STUDY OBJECTIVE**

Evidence is limited on the impact of persistence and compliance when patients are switched from FDC to FC antihypertensive regimens. We sought to compare patients who were switched from a FDC to the corresponding free combination of the same medications with patients who continued taking FDC antihypertensive regimens.

We hypothesized that patients continuing with FDC hypertension drugs would be more persistent and compliant than patients who were switched to FC medications. Our second hypothesis was that increased compliance would reduce the use of resources and expenditures for total hypertension-related health care as a result of improved management of hypertension.

**METHODS**

A retrospective cohort study was conducted to compare:

- persistence and compliance with an antihypertensive regimen for patients switching from FDC therapy to FC therapy, consisting of the same compounds, versus patients continuing to take FDC medications.
- hypertension-related utilization of health care resources and expenditures for both cohorts.

All study data were obtained from the Thomson Medstat MarketScan database, which was compliant with HIPAA regulations and contained medical and pharmacy insurance claims obtained from more than 100 health insurance payers.

**Sample Selection**

We evaluated patients who switched from three FDCs: an ARB/HCTZ, an ACE-inhibitor/HCTZ, and an ACE-inhibitor/calcium-channel blocker. To be eligible for enrollment, members of the sample:

- had to have filled prescriptions for an FDC medication for three or more months before the date on which they switched to the FC regimen (the study index date).
- were required to have an index date on or after January 1, 2004.
- had to have had medical and pharmacy coverage for 12 months before the index date and for 12 or more months after the index date.
- had to have a diagnosis of hypertension within 12 months before the index date, according to the International Classification of Diseases-9 (ICD-9-CM 401.XX–404.XX).
- had to have initial prescriptions for each compound of the FC regimen with fill dates within 15 days of each other to identify the switch to the FC regimen.
- had to have two or more prescriptions for each compound after the index date.

Comparable cohorts of patients not switching from FDC medications were identified separately for each of the three combinations according to a propensity-matching algorithm. The nearest-neighbor method was used to match FDC patients to FC patients, in a 1:1 ratio, according to:

- age (younger than 45, 45 to 64, and 65 years and older).
- sex.
- payer type (Medicare or commercial insurance).
- medical comorbidities and risk factors identified from claims diagnoses in the six months prior to the index (i.e., diabetes, tobacco use, time from a prior acute MI, prior heart failure, chronic obstructive pulmonary disease, and lipid disorder).

For each FC patient, the FDC patient with the closest match in propensity score was selected and was assigned an index date so that the duration of FDC therapy prior to the assigned index date matched the length of FDC therapy prior to the index date of the FC match. Like the FC cohort, the selected FDC patients had to have medical and pharmacy coverage 12 months before the index date and 12 months after the index date.

**Measurement of Outcomes**

Using pharmacy claims data, we measured medication persistence by the percentage of patients continuing therapy without a lapse in therapy of more than 30 days from the date of end of supply of the prior prescription during the 12-month follow-up period after the study index date. Thus, FDC patients were classified as “not persistent” after a lapse of more than 30 days without a supply of their FDC medication available.

For example, a patient in the FDC cohort with prescriptions for 30-day supplies of the medication, with each one to be filled on the dates of January 1, 2004, February 15, 2004, March 31, 2004, and none thereafter, would no longer be “persistent” as of April 30, 2004. FC patients were classified as “not persistent” if they had a lapse of more than 30 days without a supply of both medications available each day. Days on which only one drug was available were considered to represent a lapse in therapy.

As an example of persistence within the FC cohort, a patient was taking an ARB plus HCTZ. The patient had prescriptions...
for 30-day supplies for each prescription fill and then filled the ARB prescriptions on January 1, 2004, February 15, 2004, and March 31, 2004. The patient then filled the HCTZ prescriptions on January 1, 2004, February 15, 2004, March 31, 2004, and April 30, 2004 with no further refills. Such a patient was defined as being “no longer persistent” as of April 30, 2004—the day on which both drugs were not available to the patient.

Medication compliance was measured by the medication–possession ratio (MPR) for the one-year follow-up period:

\[
MPR = \frac{\text{days supply of the medication filled during one year}}{365 \times 100}
\]

For patients in the FC cohort, both medications had to be available to the patient on the same day for that day to be included in the numerator of the medication–possession ratio. A drug was considered to be available to the patient on all calendar days from the fill date to end of day’s supply for the prescription fill (e.g., from January 1 through January 30 for a prescription filled on January 1 with a 30-day supply). Thus, for the FC cohort, all calendar days on which both drugs were available to patients were identified and included in the numerator of the medication–possession ratio.

During the 12-month follow-up period, we identified hypertension-related health care services received in a hospital, an emergency department, and physician office settings from medical claims with a primary diagnosis code for hypertension (ICD-9-CM 401.XX–404.XX). For each of the three service settings, we measured hypertension-related utilization of resources as the percentage of patients receiving hypertension-related health care in that setting.

Using total reimbursements from claims data, we created two hypertension-related health care expenditure variables: (1) total health care expenditures over the 12-month follow-up period for services with a primary diagnosis of hypertension, and (2) total expenditures for hypertension-related services and medications (i.e., study drugs and all other hypertension-related agents).

**Statistical Methods**

We used chi-square tests for proportions and \( t \)-tests for means to compare descriptive statistics of outcomes for the FDC and FC cohorts. We estimated the FDC–FC differences in compliance using generalized linear models with the log–link function and gamma distribution,\(^{44,45} \) and we estimated differences in persistence for FDC and FC using logistic regression. All models included patient demographics, medical comorbidities, and risk factors as control variables.

We used multivariate logistic regression models to estimate the effect of improved compliance on the risk of hospitalization, emergency admissions, and physician office use for hypertension-related services, and we used generalized linear models to estimate the effect of improved compliance on expenditures for hypertension-related services and medications.

The log–link function and gamma distribution were used for the generalized linear models to address the skewed distribution of the expenditure data.\(^{44,45} \) The utilization and expenditure models controlled for the patient’s study cohort, demographics, health care expenditures (measured six months prior to the index date), and medical comorbidities and risk factors (measured six months prior to the index date).

To estimate the difference between the FDC and FC cohorts in annual hypertension-related costs associated with the difference in compliance for the cohorts, we computed the product of (1) the percentage point difference in compliance for FDC and FC cohorts estimated in the generalized linear model of compliance, and (2) the change in hypertension-related costs for each percentage point change in compliance estimated in the generalized linear model of hypertension-related expenditures. We also computed similar estimates for the annual risks of hypertension-related hospitalization, emergency admissions, or physician-office visits.

Outcomes were analyzed separately for Medicare beneficiaries, commercially insured patients (“commercial”), and the two groups combined (“total”). Statistical software (Stata and SAS) was used to conduct all analyses.

**RESULTS**

A total of 14,449 patients taking either antihypertensive FDC or FC agents within the same drug classes were enrolled (Table 1, page 660). The sample included 1,216 patients switching from an FDC of an ARB/HCTZ; 1,331 patients switching from an FDC of an ACE-inhibitor/HCTZ; and 4,678 patients switching from an FDC of an ACE-inhibitor/calcium-channel blocker and their respective matched controls (N = 7,224), who continued with their corresponding FDC medications.

Overall, the treatment groups were closely matched between FC and FDC cohorts for all demographic variables and risk factors. This method verified that the propensity score-matching algorithm was successful in selecting cohorts that were balanced on these characteristics.

Of the two cohorts, 8,217 patients were commercially insured and 6,232 patients had Medicare coverage. Mean patient age was 62.06 years (standard deviation [SD] ± 12.67) for the FDC cohort and 62.86 years (SD ± 13.10) for the FC cohort. Women were similarly represented in 56.9% of both cohorts. Prevalence rates for comorbid conditions and risk factors were well matched across the two groups but were relatively low in the overall study population based on the six-month time frame assessed.

**Persistence**

Persistence with therapy declined more rapidly over time for patients who switched from the FDC to the FC regimen. The FDC–FC difference in persistence was greater for Medicare patients than for commercially insured patients (Table 2, page 661).

At the end of the 12 months of follow-up, persistence rates for FDC and FC were 58.3% and 14.9%, respectively (\( P < 0.001 \)) for the total sample; 56.2% and 15.2% for commercial coverage; and 61.2% and 14.4% for Medicare coverage (\( P < 0.001 \)) for all contrasts) (see Table 2 for unadjusted rates).

Multivariate regression-adjusted differences in persistence for FDC, compared with FC regimens, were 42.5% for the total sample, 40.4% for commercial patients, and 45.2% for Medicare patients (\( P < 0.001 \)) for all contrasts) (see Table 2 for regression-adjusted differences).

**Compliance**

Patients who continued taking the FDC regimen also had significantly higher rates of compliance, compared with those

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patients who were switched to FC therapy. The FDC–FC difference was slightly greater for the Medicare patients than for the commercial group (see Table 2). For the total sample, compliance rates were 76.9% for FDC and 54.4% for FC; for commercial coverage, 74.9% for FDC and 55.4% for FC; and for Medicare coverage, 79.4% for FDC and 52.9% for FC ($P<0.001$ for all contrasts) (see Table 2 for unadjusted rates).

Regression-adjusted differences in compliance for FDC, compared with FC, were 22.1% for the total sample, 19.3% for commercial patients, and 25% for Medicare patients ($P<0.001$ for all contrasts) (see Table 2 for regression-adjusted differences).

### Health Care Utilization and Costs

Unadjusted utilization and expenditures for hypertension-related health care were higher for the FC cohorts, although some differences between Medicare cohorts were not significant (Table 3). The percentages of patients receiving health care services for a primary diagnosis of hypertension in the total sample were as follows: for inpatient services, 3.11% with FC and 2.45% with FDC ($P=0.016$); for emergency department visits, 1.72% with FC and 0.27% with FDC ($P<0.001$); and for office visits, 65.81% with FC and 59.39% with FDC ($P=0.001$).

The percentage of patients using hypertension-related services was also higher for FC in the commercial and Medicare samples; however, the difference in rates for inpatient services was not significant in the Medicare sample (see Table 3).

Unadjusted hypertension-related expenditures in the total sample were $657 for FC and $469 for FDC ($P=0.012$) for hypertension-related services and $1,424 for FC and $1,139 for FDC ($P=0.001$) for total hypertension-related health care (services and medications).

Unadjusted hypertension-related expenditures were also significantly higher for FC patients than for FDC patients in the commercial sample, but they were not significantly higher in the Medicare sample (see Table 3).

### Impact of Compliance on Health Care Costs

Regression-adjusted estimates of the relationship between medication compliance and utilization and expenditures for hypertension-related health care show decreased usage as compliance increased (Table 4). All differences between FDC and FC regimens were statistically significant except for the percentage of Medicare patients making a hypertension-related office visit.

The results imply that the higher compliance rates for FDC were associated with lower utilization of and expenditures for hypertension-related services for FDC patients. For instance, in the total sample, each 10-percentage point increase in the compliance rate was associated with a 0.3% reduction in the number of commercially insured patients hospitalized for hypertension (see Table 4) or a 0.03% reduction for each percentage point increase in compliance. Because compliance for
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Table 2 Persistence and Compliance over the 12-Month Study Period with Fixed-Dose Combination (FDC) and Free-Combination (FC) Regimens

<table>
<thead>
<tr>
<th></th>
<th>Total Sample</th>
<th>Unadjusted Rates</th>
<th>Regression-Adjusted Differences: FDC vs. FC§†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted Rates</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>FC</td>
<td>FDC</td>
<td>FC–FDC†</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Persistence at month 12*</td>
<td>58.3%</td>
<td>14.9%</td>
<td>43.4%</td>
</tr>
<tr>
<td>Compliance at month 12†</td>
<td>76.9%</td>
<td>54.4%</td>
<td>22.5%</td>
</tr>
</tbody>
</table>

* Patient must remain on therapy through the month to be considered persistent at that month. Patients are classified as non-persistent if they have a lapse in therapy more than 30 days from the date of the last available day of medication supply from one prescription to the refill date for the next prescription.
† P values less than 0.001 for the FDC–FC difference in rates.
‡ Compliance is measured by the medication–possession ratio (MPR), the percent of the study follow-up period (365 days) for which the patient has a supply of the medication (MPR = [days supply] divided by 365 x100). Days supply is obtained from prescription drug claims data.
§ Regression-adjusted differences were derived from marginal effects of generalized linear models, controlling for cohort, age, sex, comorbidities, and health care expenditures six months prior to index date.
¶ Numbers in parentheses are 95% confidence intervals.

Table 3 Unadjusted Hypertension-Related Health Care Utilization and Costs for Patients Receiving Fixed-Dose Combination (FDC) and Free-Combination (FC) Antihypertensive Medications

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Commercial</th>
<th>Medicare</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>FC</td>
<td>FDC</td>
</tr>
<tr>
<td>Percent with hypertension-related inpatient service</td>
<td>3.11%</td>
<td>2.45%</td>
<td>0.016</td>
</tr>
<tr>
<td>Percent with hypertension-related emergency department visit</td>
<td>1.72%</td>
<td>0.82%</td>
<td>0.0001</td>
</tr>
<tr>
<td>Percent with hypertension-related office visit</td>
<td>65.81%</td>
<td>59.39%</td>
<td>0.0001</td>
</tr>
<tr>
<td>Hypertension-related expenditures for services ($4,013.98)†</td>
<td>$657.16</td>
<td>$468.94</td>
<td>0.012</td>
</tr>
<tr>
<td>Hypertension-related expenditures for services and prescriptions ($5,202.00)†</td>
<td>$1,423.99</td>
<td>$1,138.91</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

* P values are for chi-square tests on FC–FDC differences in percent using a service and for t-tests on FC–FDC differences in mean expenditures.
† Standard deviations for expenditures are in parentheses.

the total number of FDC patients was 22.1 percentage points higher than the total number of FC patients (see Table 2 for regression-adjusted differences), the estimated percentage of total FDC patients hospitalized for hypertension was 0.44% less than the percentage for the total number of FC patients (i.e., –0.03% x 22.1% = –0.06%). This figure represents a 21.3% reduction in the number of patients hospitalized for hypertension, compared with FC patients (based on the 3.11% of the total number of FC patients hospitalized).

When we used the same methodology, the higher compliance for total FDC patients was associated with a 25.7% annual reduction in the number of patients needing emergency visits for hypertension and a 1.3% annual reduction in the number of patients making physician visits for hypertension, compared with FC. Similarly, higher compliance for total FDC patients was associated with a $133 reduction (20%) in annual expenditures for hypertension-related services, and a $73 reduction (5%) in total hypertension-related health care (services and medications). Commercial and Medicare patients experienced similar patterns of lower utilization and expenditures, as reported previously, for the total patient sample except for Medicare office visits.
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Table 4 Effect of Higher Increase in Compliance on Hypertension-Related Utilization and Costs*

<table>
<thead>
<tr>
<th>Utilization and Expenditures</th>
<th>Effect</th>
<th>P Value</th>
<th>Effect</th>
<th>P Value</th>
<th>Effect</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent with hypertension-related inpatient service</td>
<td>–0.3% (–0.4%, –0.2%)†</td>
<td>0.001</td>
<td>–0.2% (–0.4%, –0.2%)</td>
<td>0.001</td>
<td>–0.3% (–0.5%, –0.2%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Percent with hypertension-related emergency department visit</td>
<td>–0.2% (–0.2%, –0.1%)</td>
<td>0.001</td>
<td>–0.2% (–0.3%, –0.1%)</td>
<td>0.001</td>
<td>–0.1% (–0.2%, 0.0%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Percent with hypertension-related office visit</td>
<td>–0.4 (–0.7%, –0.1%)</td>
<td>0.003</td>
<td>–0.6% (–1%, –0.2%)</td>
<td>0.001</td>
<td>–0.2% (–0.6%, 0.2%)</td>
<td>0.337</td>
</tr>
<tr>
<td>Total hypertension-related expenditures (services only)</td>
<td>–$60 (–$64, –$58)</td>
<td>0.001</td>
<td>–$53 (–$56, –$50)</td>
<td>0.001</td>
<td>–$70 (–$75, –$65)</td>
<td>0.001</td>
</tr>
<tr>
<td>Total hypertension-related expenditures (services and prescriptions)</td>
<td>–$33 (–$40, –$26)</td>
<td>0.001</td>
<td>–$25 (–$33, –$17)</td>
<td>0.001</td>
<td>–$48 (–$61, –$36)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* Effect size derived from marginal effects of generalized linear models, controlling for cohort, age, sex, comorbidities, and health care expenditures six months prior to the index date.
† Numbers in parentheses are 95% confidence intervals.

DISCUSSION

Persistence and compliance were significantly higher for patients continuing with fixed-dose combination (FDC) therapy, compared with patients who switched from FDC therapy to free-combination (FC) therapy. This finding supports the hypothesis that simplifying antihypertensive drug regimens may improve persistence and compliance. The results are consistent with a meta-analysis by Bangalore et al., which showed a reduction of 24% in noncompliance when FDC regimens were prescribed instead of FC for treating hypertension.39 Simplifying medication regimens is particularly important, because most patients need more than one antihypertensive agent to reach their BP goal.2,6–10

Patients’ use of and expenses for hypertension-related services decreased as medication compliance increased. Total expenditures for hypertension-related services and medications also decreased as compliance increased, suggesting that the reductions in expenditures for hypertension-related services were greater than the increased medication expenditures associated with higher compliance.

Uncontrolled BP significantly increases the risk of adverse cardiovascular outcomes such as MI, stroke, and mortality.37 Previous studies have demonstrated that improved compliance with antihypertensive medications is associated with improved BP control21–28 and lower health care costs.25,27,28,34,37 Our results showed higher compliance with FDC medications and reduced utilization and costs, attributed to improved compliance; these findings suggest that FDC regimens, when compared with FC regimens, are likely to produce positive health benefits through better control of hypertension and positive economic benefits through lower utilization and expenditures for hypertension-related health care.

Notable are the estimated reductions for FDC, compared with FC, of 21.3% in hypertension-related hospitalizations, 20.2% in expenditures for hypertension-related services, and 5.1% in expenditures for hypertension-related services and medications combined. The relative economic benefits of FDC regimens are likely to extend beyond hypertension-related health care, because improved BP control reduces the incidence and severity of other costly diagnoses such as congestive heart failure, stroke, and renal disease.1,46,47 Thus, estimated reductions in the use of health care resources and costs derived from this study may be conservative estimates of potential impact of FDC regimens on total health care utilization and costs over time.

Our findings and the growing volume of published literature suggest that clinical and formulary design decisions should focus on the complexity of drug regimens and their potential impact on persistence and compliance behaviors of patients, in addition to the costs of medications. Changes based solely on medication costs can have deleterious effects on compliance and patient outcomes.

STUDY LIMITATIONS

The study was limited in several ways. The severity of hypertension could not be assessed and treatment cohorts were nonrandomized groups, thus limiting the internal validity of the study. Persistence and compliance were also measured from medication refill patterns observed within pharmacy claims data and were not based on observations of patients taking their medications. Because most patients incur an out-of-pocket cost for refilling a medication with a copayment and with a time-cost for filling the prescription, purchases are more likely to correspond with actual use, making medication fill rates an accepted measure of persistence and compliance.48–52

Our study did not measure the overall complexity of patients’ drug regimens, the presumed reason for lower compliance and persistence in the FC cohort. Thus, we did not
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estimate the direct effect of regimen complexity on compliance and persistence in this study.

At least one study53 has shown that switching from one statin to another can result in lower compliance and persistence without added complexity in the regimen. However, persistence for patients who switch at 12 months was only 5.9% less than that for non-switchers, a figure that is far less than the 43.4% lower persistence for switchers found in our study. Furthermore, the Thibaud study offered no reasons for the observed differences between switchers and non-switchers.

Although propensity-score matching was used to select FDC and FC samples of patients who were similar on observed factors, patients who switched from FDC to FC may differ from patients who stayed with the FDC regimen in characteristics that were unobserved and that may correlate with compliance. For example, if a change in health insurance coverage prompted the switch from FDC to FC therapy, then changes in plan benefit design, such as prescription copayment rates, could also influence the observed rate of prescription refills and, therefore, persistence and compliance.

Finally, reasons for a patient’s switch from FDC to FC regimens were not available for further stratification.

CONCLUSION

Patients who continued with fixed-dose combination (FDC) antihypertensive therapies showed higher rates of compliance and persistence and had lower utilization and expenditures for hypertension-related health care, compared with patients who switched from FDC to free-combination (FC) therapy. Higher compliance and persistence are likely to produce positive health benefits through better control of hypertension and positive economic benefits through lower expenditures for hypertension-related health care. The possible benefits of FDC therapy should be considered in clinical and formulary decisions on antihypertensive medications.

REFERENCES