# Impact of Patient Financial Incentives on Participation and Outcomes in a Statin Pill-splitting Program

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Objectives: To examine willingness to participate in a pill-splitting program and the impact of pill splitting on patients' adherence and lipid control. Study Design: Nested randomized trial.

Methods: A total of 200 patients who used statins and were candidates for a pill-splitting regimen were identified from a large university-based health plan. Sixty-three percent of study participants were female, 41% were nonwhite, and 94% had at least some college education. Patients were surveyed regarding their willingness to split

pills, and 111 consented to participate in a 6-month trial in which half were randomized to receive a financial incentive to split pills: a 50% reduction in their per-refill copayment. Data on patients' statin refills and lipid control were obtained from

billing and medical records.

Results: Compared with patients unwilling to participate in the program, those agreeing to split pills were more likely to be female and white. After 6 months, most patients in the trial (89%) were willing to continue pill splitting for a 50% copayment reduction. Patients reported few problems with pill splitting and had no noticeable change in their adherence. The financial-incentive group and the control group did not differ significantly with respect to their low-density lipoprotein cholesterol levels after pill splitting: –2.0 mg/dL and –1.2 mg/dL, respectively.

Conclusions: Most patients indicated that at least a 50% copayment reduction would be required to enroll in a pill-splitting program after the study ended. However, in this relatively educated population, financial incentives did not influence patients' adherence, satisfaction, or health outcomes.

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s medication costs continue to escalate, many institutions and managed care organizations are seeking to maximize the cost-effectiveness of individual pharmacotherapy. Pill-splitting programs have been implemented in various settings in an attempt to decrease medication costs. <sup>1-8</sup> However, concerns have been raised that splitting could compromise patient safety due to uneven drug distribution in the split pills and loss of medication potency due to fragmentation. Although these concerns are legitimate for a fraction of the drugs available, for most medications, especially those with a long halflife, small variations due to fragmentation are not clinically important. In a randomized cross-over study, Rindone evaluated the impact of splitting lisinopril pills in 29 patients with hypertension; patients received a full pill for 2 weeks and a split pill for 2 weeks with no significant differences in systolic and diastolic blood pressures.5 Duncan et al evaluated the effects of pill splitting on low-density lipoprotein (LDL) and total cholesterol levels in a retrospective chart review of 125 patients receiving atorvastatin or simvastatin therapy who were switched to pill splitting. The results of that study demonstrated no statistically significant changes in LDL and total cholesterol levels.<sup>3</sup> Another study conducted by Gee et al found that pill splitting of statins had no negative effects on patients' cholesterol profile.6

Concerns also have been raised about patient satisfaction and adherence with pill splitting.<sup>4</sup> The few studies that examined these outcomes have reported variable results. McDevitt et al surveyed 94 patients with hypertension after 10 days of splitting their hydrochlorothiazide pills. Most of the subjects stated a preference for the commercially available lower-strength pills, and 77% reported a willingness to pay more for them.<sup>4</sup> In contrast, Carr-Lopez et al reported that splitting lovastatin pills was easy to do and did not hinder medication adherence in the majority of patients.<sup>1</sup> A study of fosinopril pill splitting reported no significant difference in medication adherence between patients who split pills and those who did not. In fact, the patients splitting fosinopril pills reported positive experiences.<sup>2</sup> In the study by Gee et al, the majority of patients who split statin pills were satisfied and adherent to the new regimen.<sup>6</sup>

Although these prior studies provide some insight, the majority of studies to date were retrospective, were based on very small samples, or evaluated effects after brief periods of

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splitting pills. Finally, it is unclear whether patients who split pills will be more satisfied and adherent to their regimens if they share in the financial benefit associated with this change.

The objectives of this study were (1) to evaluate the impact of pill splitting on clinical measures, patient satisfaction, and acceptance and (2) to determine whether a financial incentive would affect patients' decision to split pills.

## **METHODS**

In the current study, we addressed the previously mentioned issues by using a large survey sample with a nested randomized trial of financial incentives to promote adherence to a pill-splitting statin regimen. First, we recruited patients with hyperlipidemia who were candidates for pill splitting, and we assessed their perceptions about pill splitting. Second, survey respondents were invited to participate in a randomized trial in which they would receive a free pill cutter, would be encouraged to split their lipid-lowering medication, and would have a 50% chance of being randomized to a group who received a reduction in copayment for the split-pill regimen. We compared the characteristics of patients who did and did not consent to participate in the pill-splitting trial. Trial participants were randomized to either pill splitting only or pill splitting plus a 50% reduction in their per-refill copayment. Randomization was done using a blocked randomization and random-number generator with random block sizes of 2, 4, or 6.

After 6 months, we compared patients with and without the copayment reduction in terms of their satisfaction with pill splitting and willingness to continue splitting pills. Finally, we examined pre-post changes in the adherence and lipid levels of patients in the trial to determine whether patients who split pills had any evidence of altered lipid control.

The study was conducted among patients using cholesterol-lowering medications (statins) in a university-based healthcare system. Statin use provides an ideal context in which to evaluate the outcomes of an incentive-based splitting program because these treatments are common, and many patients use brand-name drugs that are expensive to third-party payers. Moreover, hyperlipidemia has a clear, regularly measured physiologic outcome that can be used to quantify any potential negative effects of splitting on patients' health status.

#### **Patient Identification and Recruitment**

This study was approved by the University of Michigan Human Subjects Committee. Potential participants were identified through prescription claims data. Using these data, we identified all patients with 1 or more prescriptions written by a health center physician for atorvastatin, simvastatin, or pravastatin over a 6-month period. Lovastatin was excluded because at the time of the study drug costs varied according to the strength of the tablets. Crestor® was not included because it was not a preferred agent on the formulary. We excluded patients who changed health centers or prescription benefit plans, no longer took 1 of the study drugs, or were deceased. Approval from patients' primary care providers was obtained before patients were contacted regarding the study.

Eligible patients were sent a letter on health system letterhead and signed by the principal investigator. The letter explained the goals of the study and included consent forms, a brief baseline survey, a postage-paid reply envelope, and \$5.00 as an incentive for returning the baseline survey. Patients did not have to agree to pill splitting to participate in the baseline survey.

## **Randomization and Interventions**

Patients who returned the signed consent form and baseline survey by mail indicated whether they would be willing to participate in a randomized trial of copayment reduction associated with pill splitting. All patients agreeing to participate in the trial received a patient education sheet on pill splitting and free pill cutters through the mail. Based on feedback from some of the patients, all patients received 2 different types of pill cutter in the mail to assess which type patients preferred. Their primary care physicians were contacted for a written prescription of the pill-splitting regimen or a verbal order enabling the study investigators to call in the prescription to the patient's pharmacy. The study investigators also called all participants to ensure that the pill cutter was being used properly and to answer questions within 1 month of enrollment in the trial.

Patients randomized to the copayment reduction group received a 50% discount on their copayment for refills of their statin medication, regardless of whether they filled those prescriptions at a university-based or a community-based pharmacy. Because participants differed in their initial copayments, the absolute dollar value of the decrease varied across copayment reduction patients. However, the majority of patients in this group had \$7 or \$5 savings a month depending on whether their prescription was filled at a retail pharmacy or by mail order, respectively. Patients randomized to the comparison group received no discount copayments for pill splitting. Patients were informed of their random assignment within 7 days of enrollment via mail or telephone.

#### Measurement

The baseline survey was used to better understand how patients perceive pill splitting and the characteristics that determine adoption of pill splitting. We also sought to determine whether some patients might not want to participate in research on splitting pills but would be willing to split pills if pill splitting were offered as an established program. The key survey items included demographics, number of medications and cost, health status, adherence, willingness to split pills to save money for the patient or prescription benefit plan, and copayment savings necessary to split pills.

At 6 months postenrollment in the active pill-splitting portion of the study, patients in the trial were mailed an endpoint survey to determine their satisfaction and willingness to continue with the pill splitting after the study was over. Key survey items included willingness to continue pill splitting after the study was completed, copayment savings necessary to continue with pill splitting, perceived effort required to split pills, ease of using the pill cutter, and medication nonadherence due to pill splitting. These survey items were developed specifically for this study. Eight patients who ended the study early (due to discontinuation of study drugs, moving, or refusal to continue) completed the endpoint survey at the time they dropped out. Patients' LDL cholesterol test results were obtained from the lab and compared before and after implementation of pill splitting to determine longitudinal changes in patients' lipid control.

Patients' adherence to statin therapy was measured using medication possession ratios (MPRs). MPR is defined as the sum of the days' supply of medication divided by the number of days between the first pill and the last refill plus the days' supply of the last refill. Days of therapy were based on prescription claims information including the dates of refills and numbers of pills dispensed. For each patient, the MPR was calculated for the 6-month period before and during pill splitting.

# **Statistical Analysis**

All statistical calculations were performed using SAS for Windows 9.1 (SAS Institute Inc, Cary, NC). Using LDL data from the study by Duncan et al,<sup>3</sup> we determined that a sample size of 96 subjects would be required to detect a between-group difference of 9 mg/dL in LDL concentrations with 90% power at P = .05 (2-sided test). We used  $\chi^2$  tests and cross-tabulations to identify variation across demographic groups in the survey sample's perceptions about pill splitting. We used similar statistics to compare the subsets of initial survey respondents who did and did not consent to participate in the financial-incentive trial and outcomes between the groups that did and did not receive the finan-

cial incentive. Pre-post comparisons of patients' adherence and lipid levels were based on either paired Wilcoxon signed rank tests for continuous data or McNemar's test for dichotomous variables. All analyses were conducted on an intent-to-treat basis.

# **RESULTS**

## **Recruitment and Characteristics of the Study Sample**

A total of 302 patients were identified from prescription claims data as taking atorvastatin, simvastatin, or pravastatin. Forty-seven patients were excluded because they had changed health centers or prescription benefit plans, no longer took 1 of the study drugs, or were deceased. Out of 255 eligible patients, 200 patients (78%) completed and returned baseline surveys and informed consent statements. Forty-five patients returned incomplete surveys and were excluded from the current analyses; the remaining 10 patients expressed interest in completing the baseline survey when contacted by the study coordinator but never mailed it back.

#### **Characteristics of the Baseline Survey Sample**

The majority of the 200 patients returning the baseline surveys were age 50 years or older, Caucasian, and had at least some college education. Nearly 80% of respondents rated their own health as very good or good, compared with only 12% who rated their health as excellent and only 8% who rated their health as fair or poor. Most respondents spent \$50 or less per month on their prescriptions, but 5% reported spending more than \$100 per month. Although only 11% reported missing 1 or more medication doses due to cost concerns, 86% of respondents reported being extremely or moderately concerned about the cost of their medications.

Most patients had a positive attitude about splitting pills, with 88% indicating a willingness to split pills in exchange for a reduced medication copayment and 84% willing to split pills to save money for their plan provider. When asked to identify how much money they would need to save per prescription for them to be willing to split pills, only 12% of respondents stated that pill splitting would not be worth any amount of monetary savings, and 59% stated that only a \$5 to \$10 savings per prescription would be needed for them to be willing to split pills. The remaining 57 respondents (29%) indicated that a \$15 to \$20 savings per prescription would be needed.

Baseline characteristics of patients who agreed to participate in the pill-splitting trial were compared with those of respondents who declined trial participation. Patients who participated in the trial were more likely to be more than 50 years old, female, and taking more than 4 medications

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per month. Level of education did not correlate with patients' willingness to participate in the randomized phase of the study. There was no significant difference in health perceptions, amount of money spent on medications, compliance, or concerns about medication costs between trial participants and patients who only completed the baseline survey. However, there was a significant difference between the groups regarding their willingness to split pills to save money.

## **Results of the Randomized Trial**

Of the 111 patients agreeing to participate in the copayment reduction trial, 55 were randomized to the copayment reduction group and 56 to the group with no copayment reduction. Eight patients dropped out during the study, 3 from the copayment reduction group (1 because of a move and 2 because they discontinued the statin) and 5 from the group with no copayment reduction (1 because of myalgia, 1 because of a dosage change, 1 because there was no copayment incentive, and 2 because they did not like splitting pills), leaving the final sample for the randomized trial at 103. A total of 109 (98%) of patients who agreed to participate completed the endpoint survey.

## Satisfaction and Willingness to Split Pills

Overall, 89% of all trial participants expressed a willingness to continue splitting pills for a 50% copayment reduction until the degree of copayment reduction was determined for a future pill-splitting program, with a nonsignificantly larger proportion of those in the copayment reduction group expressing a willingness to continue pill splitting after the study (92.7% vs 85.2%) (Table 1). Responses in the 2 trial groups were generally similar with respect to the perceived effort of splitting pills, and when asked whether they agreed with the statement that the "effort to split pills is no big deal," approximately 80% of trial participants either "strongly agreed" or "agreed." Patients were asked to select how much of a copayment reduction would be necessary for them to participate in a pill-splitting program after the end of the study. Of the 3 possible response categories, 73% reported that they would require a 50% reduction in copayment, 26 (24%) stated that they would need their copayment waived, and 3 (3%) reported that splitting would not be worth the effort regardless of savings. Overall, there were few differences in the required copayment for splitting pills between the group who received a copayment reduction and group who did not.

Patients in the 2 groups had few significant differences in their willingness to continue pill splitting after the trial. Also, individuals willing to continue splitting pills tended to take more medications per month (27% took 7 or more medications per month vs only 8% of those who were not willing to continue splitting pills). Patients willing to split pills also spent more per month out of pocket on their medications, although these differences did not reach statistical significance.

#### Impacts of Pill Splitting on Medication Adherence

Participants in the trial strongly indicated that splitting pills did not negatively affect their adherence. More than 90% either agreed or strongly agreed with the statement that "pill splitting has not affected my willingness to take my medication," and fewer than 5% disagreed or strongly disagreed. Similarly, 90% disagreed or strongly disagreed with the statement that they had "missed more medication doses because of pill splitting." Only 5% reported having 3 or more occasions on which they had to discard pills due to splitting-related problems, compared with 92 (84%) who reported zero such occasions and 12 (11%) who reported only 1-2 such occasions. Self-reported adherence rates were similar for patients with and without the copayment reduction.

A total of 94 trial participants had at least 2 prescription fills identified during the follow-up period, allowing us to calculate MPRs. The mean  $\pm$  SD MPR in the 6 months prior to tablet splitting was 94%  $\pm$  17%. The mean  $\pm$  SD MPR during the pill-splitting period was virtually unchanged at 94%  $\pm$  14%.

# **Impacts on Lipid Profiles**

Overall, lipid profiles did not change significantly over the course of the pill-splitting period in either patients randomized to receive the copayment reduction or those with no copayment reduction (Table 2).

## DISCUSSION

This study is the first prospective randomized trial evaluating the impact of pill-splitting financial incentives on patients' adherence, satisfaction, and health outcomes. It is also unique because the population includes more women and because pretrial and posttrial surveys were used in conjunction with lipid data. With respect to the impact of pill splitting on patients' adherence and health status, our results were very similar to those of other pill-splitting studies. Overall patient satisfaction was high, patients' medication adherence did not change once splitting was initiated, and lipid levels were not negatively affected.

This study provides insight into voluntary pill splitting accompanied by sharing of insurance plan cost savings with

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■ Table 1. Endpoint Survey Responses of Patients Who Did and Did Not Receive a Financial Incentive During the Study

	No. (	(%)		
Endpoint Survey Questions	Copayment Reduction (n = 55)	No Copayment Reduction (n = 54)	P	
Are you willing to continue splitting pills after the study for a 50% copayment reduction?			.21	
Yes	51 (92.7)	46 (85.2)		
What degree of copayment reduction would you require in order to continue splitting?			.79	
A 50% reduction	39 (72.2)	39 (73.6)		
Waive copayment	14 (25.9)	12 (22.6)		
Not worth it	1 (1.9)	2 (3.8)		
Effort to split pills is no big deal			.96	
Strongly agree/agree	44 (80.0)	43 (79.6)		
Pill splitting has not affected my willingness to take my medication			.32	
Strongly agree/agree	48 (87.3)	51 (94.4)		
Missed more medication doses because of pill splitting			.36	
Strongly disagree/disagree	48 (87.3)	50 (92.6)		
Number of pills discarded because of problems with pill splitting			.82	
None	46 (83.6)	46 (85.2)		
Splitting pills with the pill cutter was easy			.60	
Strongly agree/agree	45 (81.8)	42 (77.8)		

patients. The copayment incentive did not influence patient satisfaction, adherence, or cholesterol profiles during the study. Although many participants in the trial reported that they would require a financial incentive to continue splitting pills, the impact of the incentive in the randomized study suggests that in fact such incentives may not influence their willingness to adhere to a split-pill regimen.

Rather than financial incentives, this study identified specific characteristics of a split-pill regimen that can affect patients' acceptance. One of the main reported reasons for dissatisfaction with splitting was difficulty in using the pill cutter for some patients (eg, failure to yield evenly split pills, crushing the tablet). Recognizing the importance of using the proper pill cutter, we provided 2 different types of pill cutters: a small blue splitter without rubber padding and a clear splitter with both rubber padding and a wider cutting area to fit larger pills. Most of the patients preferred the clear splitter, especially those patients taking larger-sized pills. Another reported

reason for dissatisfaction with splitting was difficulty in swallowing split pills due to rough edges and bitter taste (reported by 3 patients).

One of the limitations of our study is that it was conducted at a single university-based health center. It remains to be seen whether pill splitting will be well received and accepted across our whole healthcare system or within health systems treating a more socioeconomically and racially diverse patient population. Compared with some previous pill-splitting trials, our study population was younger and highly educated. Although income data were not collected, such patients may have had relatively high incomes and they may have been less sensitive to the small cost savings associated with pill splitting. Also, we did not distinguish between patients receiving statins for primary versus secondary prevention in our data collection. We found that patients less likely to be interested in pill splitting included those who had more formal education, spent less on medications, and took fewer medications. In conjunction with

■ Table 2. Impact of Pill Splitting on Cholesterol Levels

	Baseline		Post Splitting		Change		
Cholesterol Level	Copayment Reduction	No Copayment Reduction	Copayment Reduction	No Copayment Reduction	Copayment Reduction	No Copayment Reduction	P
Total	180.1 ± 37.8	179.0 ± 30.7	175.6 ± 34.6	179.9 ± 25.4	-4.6 ± 29.9	1.7 ± 24.8	.24
LDL	96.3 ± 29.5	98.1 ± 25.8	$94.3 \pm 27.5$	96.2 ± 24.7	$-2.0 \pm 22.3$	$-1.2 \pm 24.0$	.85
HDL	51.7 ± 13.6	51.0 ± 13.4	49.8 ± 14.1	49.1 ± 14.0	$-1.9 \pm 8.7$	$-1.8 \pm 7.7$	.98
TRIG	165.1 ± 98.0	162.8 ± 95.9	160.9 ± 97.6	171.4 ± 115.9	$-4.2 \pm 76.3$	8.0 ± 79.3	.42

LDL indicates low-density lipoprotein; HDL, high-density lipoprotein; TRIG, triglycerides.

other studies, this result suggests that patients receiving Medicaid or other financially pressed pharmacy insurance programs may be more willing to split pills if the program effectively addresses patients' concerns about using the splitter. Another limitation of this study was its short duration. Our prescription plan allowed for a 3-month supply per refill, providing only 2 opportunities to observe compliance. This may have biased the MPR estimates to reflect overall optimistic adherence levels compared with what would have been observed given a longer follow-up period.

The financial benefits of moving to a split-pill regimen can be enormous. Since this study was completed, we have implemented a pill-splitting program for all university employees through the university pharmacy benefit plan. All patients will be offered a 50% copayment reduction for splitting atorvastatin, pravastatin, and simvastatin, with a free pill cutter provided once a year. Without much marketing effort, 5.3% of statin users were splitting pills within less than 3 months of implementation of the pill-splitting program, yielding \$33 000 savings. Extrapolated annual cost savings of this program would be \$1.3 million if 45% of current statin users started to split pills.

When pill-splitting plans are implemented, only the prescription plan benefits financially unless there is some sharing of cost savings with patients. Although in our study sharing cost savings with patients did not significantly impact their willingness to participate, most patients said that they would expect some financial incentive in order to continue splitting pills. Because there are a variety of patient and product factors involved, voluntary pill-splitting programs seem to be more optimal when some of the financial benefits are shared with patients. This strategy should increase patient participation in a non-

mandatory pill-splitting program. In any program, pill splitting should be implemented with consideration of which pills can be split without compromising clinical outcomes, as well as recognizing that this practice is safe only in patients who are able to cognitively and physically split pills.

## CONCLUSION

The current study found that many patients using lipidlowering therapies, particularly those using a larger number of drugs, were willing to participate in a pill-splitting program. Although patients reported that financial incentives would increase their willingness to split pills, our randomized trial did not indicate that such incentives had influenced patients' adherence, satisfaction with splitting, or lipid levels.

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#### **Take-away Points**

A 50% reduction in patients' per-refill copayment was used to promote adherence to a pill-splitting statin regimen in a randomized trial involving a relatively educated population.

- Pill splitting did not adversely affect cholesterol levels, nor did it hinder compliance with medication therapies.
- During the 6-month trial, the financial incentive did not influence patients' adherence, satisfaction, or health outcomes.
- After the trial, 89% of patients were willing to continue pill splitting for a 50% copayment reduction.

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