

Randomized Controlled Trial of a Dose Consolidation Program

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ABSTRACT

OBJECTIVE: To evaluate the effectiveness and financial impact of a drug dose consolidation (optimization) program using letter intervention.

METHODS: This pilot program in a large, mid-Atlantic health plan utilized a randomized controlled trial research design. A review of adjudicated pharmacy claims records was performed monthly for 3 consecutive months from November 2002 through February 2003 to identify inefficient (i.e., >once-daily) regimens for any one of 68 dosage strengths of 37 single-source maintenance drugs with once-daily dosing recommendations. Prescribers who had prescribed one or more inefficient regimens were identified and randomized to one of the 2 intervention arms or a control arm. Prescribers in both intervention arms were sent personalized letters with information on their patients' inefficient regimens and suggested dose consolidation options. Patients of prescribers in one intervention arm received a complementary, patient-oriented letter. Pharmacy claims for patients in all arms were examined at 180 days after the date of the letter mailing for conversion to an efficient (once-daily) regimen. Financial modeling analysis calculated net savings as changes in pharmacy expenditures minus administrative costs.

RESULTS: A total of 2,614 inefficient regimens, representing 6.7% of claims for the targeted medications, were identified. The rate of consolidation to a suggested dosing option was lower for the Physician Letter arm (7.3%) than for the Physician/Member Letter arm (10.2%) ($P = 0.046$). Both intervention arms had higher consolidation rates than the Control arm (3.9%) ($P = 0.018$ and $P = 0.000$, respectively). Approximately 30% of the regimens in each study arm were never refilled after being targeted. Financial modeling indicated that a dose consolidation intervention could save \$0.03 to \$0.07 per member per month (PMPM) in 2003 dollars with full medication compliance but only \$0.02 to \$0.03 PMPM when savings were calculated with realistic, partial compliance rates. Subanalyses performed at the drug therapy class level revealed few opportunities to justify implementing a dose consolidation program.

CONCLUSIONS: After taking into consideration program administrative costs, high rates of refill discontinuation, and dose consolidation that occurs naturally without intervention, the results indicated that a letter-based dose consolidation program did not appreciably decrease pharmacy expenditures.

KEYWORDS: Dose consolidation, Pharmacy benefit manager, Randomized controlled trial, Cost-effectiveness

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Myriad factors have resulted in increased prescription drug expenditures for health plans since the early 2000s, including increased utilization per patient and price inflation.¹ Pharmacy administrators continue to search for management strategies that will be cost effective, will not restrict access to drugs, and will not alienate prescribers and patients. One such strategy that has received increased attention in recent years is "dose consolidation," also referred to as "dose optimization."²

A dose consolidation program is a drug cost management intervention that examines pharmacy claims to identify patients receiving multiple tablets or capsules of a lower strength dosage of a once-daily, maintenance drug—to convert ("consolidate") the "inefficient" regimen to an equivalent daily dosage of the same drug as a single tablet or capsule.² Single-source maintenance drugs with a once-daily dosing indication that are available in various dosage strengths and have price parity between the dosages are candidates for dose consolidation programs. While physicians may have clinical reasons for prescribing inefficient doses (e.g., tolerability), the belief is that some inefficient doses have inadequate clinical rationale and, thus, could be consolidated. Atorvastatin, a single-source HMG CoA reductase inhibitor, is an example of a candidate drug for a dose consolidation intervention since it is a once-daily maintenance drug available in multiple dosage forms (20, 40, and 80 mg) with "flat" average wholesale prices (AWPs); the 10 mg dose form is 33% lower price.³

While the concept of dose consolidation is appealing to plan sponsors based on the perception that it has a small, negative impact on patients, prescribers, and medication access, its cost-effectiveness has not been demonstrated. Only 1 peer-reviewed article² and 1 study abstract⁴ that evaluated dose consolidation (optimization) programs were identified in a literature search of MEDLINE and HealthStart electronic databases.

The dose consolidation intervention examined by Calabrese and Baldinger² utilized clinical pharmacists in one-on-one and group educational sessions with prescribers and included patient letters to explain the change in dosing regimen. The dose consolidation intervention examined by Wheeler and Buttitta⁴ utilized a letter-based educational program directed to prescribers. While the findings from these studies suggested substantial drug cost savings from a dose consolidation program, these studies had methodological limitations. Both studies utilized nonexperimental study designs that did not account for dose consolidation that would have taken place without the intervention, (e.g., as a result of dose titration). Neither study accounted for administrative costs of the dose consolidation programs that would have offset some of the drug cost savings. Most importantly, neither study took into account that some of

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TABLE 1 Drugs and Strengths Targeted for Dose Consolidation

Therapy Class/ Targeted Drugs	Inefficient Twice-Daily Regimen (mg)	Efficient Once-Daily Regimen (mg)	1-Month Savings (\$)*	Annual Savings (\$)†	Therapy Class/ Targeted Drugs	Inefficient Twice-Daily Regimen (mg)	Efficient Once-Daily Regimen (mg)	1-Month Savings (\$)*	Annual Savings (\$)†
Calcium blockers					Antihyperlipidemics				
Amlodipine	2.5	5	39.68	277.76	Atorvastatin	10	20	29.77	178.62
Amlodipine	5	10	40.48	283.36	Atorvastatin	20	40	96.19	577.14
Felodipine	2.5	5	35.38	247.66	Atorvastatin	40	80	96.19	577.14
Felodipine	5	10	35.38	247.66	Fluvastatin	20	40	48.89	293.34
Isradipine	5	10	23.40	163.80	Fluvastatin	40	80	35.06	210.36
Nisoldipine	10	20	25.47	178.29	Pravastatin	10	20	78.74	472.44
Nisoldipine	20	40	28.47	199.29	Pravastatin	20	40	43.31	259.86
Verapamil	100	200	27.92	195.44	Pravastatin	40	80	119.34	716.04
Antihypertensives					Simvastatin	5	10	34.15	204.90
Benazepril	5	10	28.84	201.88	Simvastatin	10	20	17.72	106.32
Benazepril	10	20	28.84	201.88	Simvastatin	20	40	121.05	726.30
Benazepril	20	40	28.84	201.88	Simvastatin	40	80	121.05	726.30
Fosinopril	10	20	32.62	228.34	Antituberculars				
Fosinopril	20	40	30.33	212.31	Esomeprazole	20	40	112.75	676.50
Moexipril	7.5	15	28.37	198.59	Lansoprazole	15	30	122.24	733.40
Perindopril	2	4	31.94	223.58	Omeprazole‡	10	20	96.45	578.70
Perindopril	4	8	14.90	104.30	Omeprazole‡	20	40	80.58	483.48
Trandolapril	1	2	26.01	182.07	Pantoprazole	20	40	80.53	483.48
Trandolapril	2	4	26.64	186.48	Antidepressants				
Candesartan	4	8	38.19	267.33	Citalopram	10	20	60.82	425.74
Candesartan	8	16	38.19	267.33	Citalopram	20	40	63.31	443.17
Candesartan	16	32	22.61	158.27	Escitalopram	10	20	56.14	392.98
Irbesartan	75	150	37.63	263.41	Fluoxetine§	10	20	92.50	647.50
Irbesartan	150	300	31.10	217.70	Paroxetine	10	20	71.09	497.63
Losartan	25	50	41.86	293.02	Paroxetine	20	40	83.38	583.66
Losartan	50	100	26.70	186.90	Paroxetine CR	12.5	25	71.09	497.63
Telmisartan	20	40	38.99	272.93	Sertraline	25	50	69.88	489.16
Telmisartan	40	80	32.83	229.81	Sertraline	50	100	73.20	512.40
Valsartan	80	160	37.94	265.58	Venlafaxine	37.5	75	59.12	413.84
Valsartan	160	320	32.41	226.87	Venlafaxine	75	150	68.56	479.92
Amlodipine					Anti-inflammatories				
Besylate-Benazepril	2.5-10	5-20	55.05	385.35	Celecoxib	100	200	16.68	66.72
Amlodipine					Rofecoxib	12.5	25	75.92	303.68
Besylate-Benazepril	5-10	10-20	44.29	310.03	Rofecoxib	25	50	40.96	163.84
Benazepril/ Hydrochlorothiazide	5-6.25	10-12.5	28.84	201.88	Valdecoxib	10	20	80.50	322.00
Benazepril/ Hydrochlorothiazide	10-12.5	20-25	28.84	201.88					
Moexipril/ Hydrochlorothiazide	7.5-12.5	15-25	28.47	199.29					
Quinapril/ Hydrochlorothiazide	10-12.5	20-25	29.27	204.89					
Losartan/ Hydrochlorothiazide	50-12.5	100-25	26.70	186.90					

* The difference in discounted average wholesale price (AWP) as of March 2003 between an efficient and inefficient 30-day supply.

† The difference in discounted AWP between an efficient and inefficient 30-day supply multiplied by expected annual refill rate for therapy class (i.e., calcium channel blockers [7], antihypertensives [7], antihyperlipidemics [6], antituberculars [6], antidepressants [7], and antiinflammatories [4]).

‡ Study performed before over-the-counter and generic products were available.

§ Sarafem.

|| Paxil, study performed before generic paroxetine became available.

the funds for dose consolidation programs are spent to modify medication regimens for which the plan subsequently ceases to have financial liability, either due to member plan disenrollment/coverage termination or drug therapy discontinuation.

In this study, the effectiveness and cost-effectiveness of a dose consolidation program for 68 dosage strengths of 37 single-source maintenance drugs were assessed in a large population of commercially insured beneficiaries. The study utilized an experimental study design to examine the (1) "background rate" of dose consolidation (i.e., the degree to which dose consolidation occurs without intervention); (2) effectiveness of a prescriber, letter-based dose consolidation intervention; (3) effectiveness of supplementing prescriber letters with letters to their patients; and (4) financial impact of the program taking into consideration the program costs.

Methods

Population

A health insurer located in the mid-Atlantic region partnered with a pharmacy benefit manager (PBM) to pilot test a dose consolidation program. This health insurer administered a number of health plans, including preferred provider organization and indemnity plan designs. Approximately 50% of the health insurer's members had a 3-tier pharmacy benefit with their average copayments for nonformulary, formulary, and generics being \$30, \$25, and \$10, respectively. Approximately 21% of the health insurer's prescriptions, representing 51.7% of its drug spend, were dispensed through mail-service pharmacy with an average of 2 copayments for a 90-day supply. As of January 2003, the PBM administered the pharmacy benefit for 504,057 of the health insurer's members, who had an average age of 38.6 years and whose mean expenditures for prescription drugs were \$36.72 per member per month (PMPM) in 2003. All of the health insurer's members were eligible to participate in the study. The research was performed under the principles outlined in the Declaration of Helsinki and recently approved Health Insurance Portability and Accountability Act (HIPAA) regulations regarding use of personal health information for program evaluation.

Patient inclusion criteria included (1) a supply on hand for a targeted drug (Table 1) and (2) either 2 or more mail-service pharmacy claims for the targeted drug in the 120 days prior to targeting, or 2 or more community pharmacy claims for the targeted drug for a total of ≥ 60 days of supply in the 120 days prior to targeting. Claims were removed that had incomplete or potentially invalid data such as all zeros in the days supply or quantity fields, duplications, reversals, missing or invalid prescriber identifier (Drug Enforcement Administration [DEA] registration number), and missing or inadequate member or prescriber information. Inefficient regimens were determined by dividing the quantity dispensed by the days supply dispensed for each of the targeted drugs. Values ≥ 1.5 (e.g., twice

daily) were deemed inefficient and suitable for dose consolidation. Values ≥ 2.5 , representing less than 1% of claims for the targeted medications, were not targeted because examination of the claims data suggested that these represented data error in either the quantity dispensed or days supply fields.

Research Design

To mirror real-world pharmacy benefit coverage where beneficiaries may terminate coverage throughout the year, this pilot program was designed as a randomized controlled trial without assurance of continuous coverage (i.e., continuous eligibility was not an inclusion criterion of this study). A review of adjudicated pharmacy claims records was performed monthly for a 3-month intervention period (November 2002 to January 2003). Health plan network prescribers of patients meeting the inclusion criteria and having an inefficient regimen were identified by their DEA numbers. These prescribers were then randomized to either of the 2 intervention arms or a control arm. In order to control for the inadvertent diffusion of the intervention between prescribers, patient subjects were blocked on their prescriber's physical address so that prescribers of inefficient regimens from the same practice were not randomized to different arms. Patient subjects could have inefficient regimens for more than 1 targeted drug. Patient subjects with inconsistent histories (e.g., had claims from physicians in more than 1 arm, used both an efficient and an inefficient regimen within the same therapeutic class during the initial review month, or used 2 different inefficient regimens in the same therapeutic class during the initial review month) were removed from the study. The financial analysis was performed from the perspective of the health insurer (i.e., excluding member cost share).

Intervention

Prescriber subjects in the intervention arms (Physician Letter arm and Physician/Member Letter arm) were sent 1 personalized notification letter that contained (1) a description of dose consolidation with information on potential benefits for the patient and financial savings, (2) individual inefficient dosing drug profiles (suitable for insertion as "chart reminders") for all of the prescriber's subject patients' inefficient drug/strength regimens identified in the calendar month, and (3) suggested dose consolidation options (Table 1). To assess if providing patients with personalized, drug-related information improved the rate of dose consolidation,⁵ patient subjects in the Physician/Member Letter arm received 1 complementary letter per inefficient drug/strength regimen identified over the 3-month intervention period that contained (1) a description of dose consolidation with information on potential benefits, (2) suggested dose consolidation options, and (3) a suggestion that the patient discuss these options with his or her prescriber. Included in the patient letter was a statement that cautioned the patient to continue to take the medication exactly as prescribed

by the physician and to not stop taking or change the way the medication was taken without first talking with the physician. The Control arm prescriber and patient subjects did not receive any intervention, thus providing a measure of the background rate of dose consolidation (i.e., the rate of dose consolidation that would have occurred without any intervention) and cessation of the plan's financial liability for the medication (because of either coverage termination or discontinuation of the drug).

Outcomes

The pharmacy claims for patient subjects in all arms were examined at 180 days after the date of the letter mailing (intervention). For each therapeutic class, each targeted inefficient regimen was classified into one of 7 mutually exclusive groups: (1) discontinuation or disenrollment (i.e., no claim for any drug in the therapy class after the intervention date); (2) at least 1 postintervention claim for the therapeutic class, but none was at an efficient dose; (3) at least 1 postintervention claim with an efficient regimen in the therapeutic class, but the regimen reverted to inefficient dosing before the end of the 180-day period; (4) not consolidated to the suggested efficient regimen, but consolidated from an inefficient to efficient dosing schedule of the original drug and strength (e.g., from 2 tablets per day of amlodipine 2.5 mgs to 1 tablet per day of amlodipine 2.5 mgs); (5) not consolidated to the suggested efficient regimen, but consolidated to an efficient dosing schedule using a new strength of the original drug (e.g., from 2 tablets per day of amlodipine 2.5 mgs to 1 tablet per day of amlodipine 10 mgs); (6) not consolidated to the suggested efficient regimen, but consolidated to an efficient dosing schedule of a different drug within the therapeutic class (e.g., from 2 tablets per day of amlodipine 2.5 mgs to 1 tablet per day of felodipine 5 mgs); and (7) consolidated to the suggested efficient regimen (e.g., from 2 tablets per day of amlodipine 2.5 mgs to 1 tablet per day of amlodipine 5 mgs).

The base-case consolidation scenario was whether the inefficient regimen was in group 7 (i.e., consolidated to the suggested regimen in Table 2). As a sensitivity analysis, an alternative consolidation scenario was whether the inefficient regimen was consolidated to any efficient regimen in the therapy class (i.e., groups 4, 5, 6, or 7 in Table 2). For each arm, the consolidation rate was calculated as the count of efficient regimens divided by the total count of inefficient regimens targeted. One-way analyses of variance with post hoc Bonferroni multiple comparison tests (dose consolidation coded as 0 = No, 1 = Yes) were performed to assess differences in mean number of conversions per targeted inefficient regimen across each of the study arms (e.g., Physician Letter arm versus Control arm, Physician Letter arm versus Physician/Member Letter arm, etc.).

Assessment of the savings attributable to the intervention comprised 4 steps. First, for each consolidated regimen in the 3-month trial, 1-month savings were calculated as the

TABLE 2 Outcomes and Consolidation Rates Across All Therapy Classes After 180 Days

	Physician Letter Arm % (N)	Physician/Member Letter Arm % (N)	Control Arm % (N)
Outcomes			
1. Discontinued/disenrolled: no claim for any drug in the therapy class after the intervention date*	29.5 (260)	29.4 (253)	27.1 (236)
2. Continued with an inefficient regimen	49.7 (438)	46.5 (400)	55.5 (484)
3. Consolidated to an efficient regimen, then reverted to an inefficient regimen	3.9 (34)	3.5 (30)	3.3 (29)
4. Consolidated to an efficient regimen for original drug and strength	3.7 (33)	4.7 (40)	3.2 (28)
5. Consolidated to an efficient regimen for original drug but new strength	1.2 (11)	0.8 (7)	1.1 (10)
6. Consolidated to an efficient regimen for different drug in therapy class	4.8 (42)	4.9 (42)	5.8 (51)
7. Consolidated to the suggested efficient regimen	7.3 (64)	10.2 (88)	3.9 (34)
Total N	882	860	872
Consolidation Rates†			
Consolidated to the suggested efficient regimen	7.3‡ (64)	10.2§ (88)	3.9 (34)
Consolidated to any efficient regimen	17.0 (150)	20.6 (177)	14.1 (123)

* P = 0.445 across arms.
 † Scenarios used to calculate savings.
 ‡ P = 0.046 compared with Physician/Member letter arm and P = 0.018 compared with Control arm.
 § P = 0.000 compared with Control arm.
 || P = 0.001 compared with Control arm.

discounted March 2003 AWP of a 30-day inefficient dose (number of daily tablets times original per-tablet cost times 30) minus the cost of a 30-day efficient dose (number of daily tablets times final per-tablet cost times 30). (To represent a typical health plan's drug acquisition cost, brand and generic drugs were discounted at 88% and 64% of AWP, respectively.) The result represented a first postconsolidation month savings for each conversion. Second, because the program operated for 3 months, the results of step 1 were multiplied by 4. That result represented the savings for the first postconsolidation month for a program run over a 12-month period. Third, to estimate the savings that would accrue for 1-year postconsolidation, the result of step 2 was multiplied by 12 (i.e., 12 refills per efficient regimen). However, since multiplication by 12 assumes an unrealistic 100% compliance by every patient,⁶ sensitivity analysis

APPENDIX Expected Refill Rates

Data were extracted from a 1-year database (2002) constructed for research purposes by Express Scripts, Inc. (ESI). ESI administers pharmacy benefits to more than 50 million persons in approximately 1,300 commercially insured health plans—that is, not Medicare or Medicaid—representing all 50 states and the District of Columbia. The database comprised ambulatory administrative pharmacy claims and eligibility information of a random sample of 3 million commercially insured beneficiaries whose pharmacy benefit was administered by ESI in 2002. The health plan sponsors for these beneficiaries included private- and public-sector employer groups, managed care organizations, third-party administrators, and unions.

There were approximately 100 prescription drug therapy classes (e.g., antidepressants, antihypertensives) in 2002 as defined by Medi-Span (Wolters Kluwer Health, Indianapolis, IN). Prescription claims for all therapy classes were converted to 30-day supply equivalents (i.e., days supply/30). Claims were summed to obtain the total number of 30-day supply equivalents per patient per therapy class per year (*records*). Patients who had had 2 or more claims within a therapy class during the time period (*users*) were selected. Records of users were summed to obtain the total number of 30-day supply equivalents per therapy class per year. The mean of 30-day supply equivalents per user per therapy class per year (i.e., *expected refill rates*) was then calculated.

was performed whereby the result of step 2 was multiplied by a factor representing the expected number of refills over the course of the year. Different refill factors were used for each therapeutic class, including calcium channel blockers (7), anti-hypertensives (7), antihyperlipidemics (6), antiulcers (6), antidepressants (7), and antiinflammatories (4). Factors were based on the PBM's experience with chronic medication therapies (Appendix). Fourth, for each of the intervention arms, savings were offset by \$3 and \$6 per patient intervention in the Physician and Physician/Member Letter arms respectively, to account for program costs (e.g., information systems, programming time, payroll costs for clinical review, and postage and other costs associated with mailing). Finally, for each of the 3 arms, PMPM savings were calculated as total savings divided by one third of the plan's total member-months over a 1-year period (i.e., each arm represented one third of the membership's total inefficient regimens).

Results

A total of 2,675 inefficient regimens, representing 6.9% of the claims for the targeted drugs were identified during the 3 months of interventions. Twenty-five regimens were removed from the analysis because they were for subjects with prescribers in 2 or more study arms. An additional 36 regimens were removed because they represented different strengths of the same drug prescribed in the same month (n = 6), more than 1 medication targeted within the same therapeutic class (n = 13), or were for members whose claims contained missing or invalid data (n = 17). Thus, a total of 2,614 inefficient regimens, representing 6.7% of claims for the targeted drugs during the 3 intervention months, were included in the study. These 2,614 regimens were prescribed to 2,527 subjects (2,442, 83, and 2 subjects were identified with inefficient doses for 1, 2, and 3 unique targeted inefficient regimen drugs and/or strengths, respectively) by 1,521 prescribers. The subjects in the Physician/Letter arm were older, and Physician/Letter arm prescribers had been in practice longer than subjects and prescribers in the other 2 arms (Table 3); however, these differences do not appear to be meaningful either clinically or practically. Overall, subject and prescriber characteristics were comparable across the study arms.

After 180 days of follow-up, approximately 30% of inefficient regimens in all 3 arms (P = 0.445) were discontinued, either because of cessation of therapy or disenrollment (i.e., the member had no postintervention claims for any drug within the therapy class (Table 2). Inefficient regimens in the Physician/Member Letter arm (10.2%) were more likely to have been consolidated to the suggested efficient regimen than inefficient regimens in the Physician Letter arm (7.3%, P = 0.046). Inefficient regimens in both the Physician Letter arm and the Physician/Member Letter arm were more likely to have been consolidated to the suggested efficient regimen than

TABLE 3 Prescriber and Subject Characteristics

Prescriber Characteristics				
Study Arm	Number Randomized	Primary Care* (%)	Female (%)	Years in Practice† (SD)
Physician letter	516	56.8	15.5	25.5 (10.2)§
Physician/Member letter	527	56.7	19.7	23.4 (9.6)
Control	478	59.0	15.1	23.6 (9.4)
Subject Characteristics				
Study Arm Targeted	Number	Mean Age in Years (SD)	Female (%)	Three-Tier Benefit‡ (%)
Physician letter	853	57.1 (15.3)	56.9	49.6
Physician/Member letter	832	55.0 (15.1)	57.1	50.1
Control	842	55.2 (15.1)	56.8	50.5

* Includes family practice, internal medicine, and general practitioners.

† Years since graduation.

‡ Subjects with a 3-tier pharmacy benefit design.

§ P = 0.021 compared with Physician/Member arm.

|| P = 0.017 compared with Physician/Member arm and P = 0.031 compared with Control arm.

inefficient regimens in the Control arm (3.9%, $P = 0.018$).

Assuming full compliance over 12 months and after accounting for administrative costs and background rate (i.e., Control arm) dose consolidation, financial calculations indicated that a dose consolidation intervention could save \$0.03 to \$0.07 PMPM (Table 4). When calculating the savings using the expected therapy class-specific refill rates, savings were reduced to \$0.02 to \$0.03 PMPM. In the sensitivity analysis, whereby consolidation to any efficient regimen would be attributed to the intervention, savings with full compliance were calculated to be \$0.01 to \$0.07. When calculating the savings using the expected therapy class-specific refill rates, savings were reduced to \$0.01 to \$0.03 PMPM. Varying the cost of each intervention letter by \pm \$1 did not appreciably change the PMPM savings under any scenario (data not shown).

The proportion of claims identified as inefficient regimens varied by therapy class: 11.0% of calcium channel blocker, 9.3% of antihypertensive, 1.0% of antihyperlipidemic, 9.8% of antiulcer, 12.0% of antidepressant, and 12.5% of anti-inflammatory regimens were identified as inefficient. Consolidation and discontinuation rates varied across therapy classes (Table 5). The effect of the intervention was most pronounced for calcium channel blocker and antihypertensive regimens. The effect of the member letter was most pronounced for antiulcer regimens. Background rates of consolidation were higher for antihyperlipidemic and antidepressant regimens than for other therapy classes.

Discussion

This is the first experimental-designed study of a dose consolidation program to be reported. This study utilized 2 letter-based interventions along with a control group to determine the effect of intervening with prescribers and patients to make them aware of the benefits of dose consolidation, while simultaneously assessing the rate of dose consolidation that would have occurred without the intervention. A letter-based program was evaluated since it would be a pragmatic, low-cost approach for large and small health plans to implement as an automated program if evidence had been found to support its cost-effectiveness. However, while finding statistically significant improvements in consolidation rates with the prescriber-targeted intervention and yet higher rates when the patient also received an intervention, financial analysis indicated that the impact of the program on PMPM expenditures was negligible with realistic savings amounting to approximately 0.08% of the health insurer's PMPM drug expenditures. Only when savings were calculated under the most favorable scenario did they rise to approximately 0.19% of the health insurer's PMPM drug expenditures. These results did not change substantially when varying the cost of the intervention letter by \pm 33% ($\$3.00 \pm \1.00).

Contrary to our findings, Calabrese and Baldinger² and Wheeler and Buttitta⁴ had reported that a dose consolidation

TABLE 4 Overall Change in Pharmacy Expenditures by Study Arm after 180 Days With Sensitivity Analyses*

Consolidation to the Suggested Efficient Regimen			
Change	Physician Letter Arm	Physician/Member Letter Arm	Control Arm
One month (\pm 95% CI)	-11,526 (388)	-17,653 (602)	-6,714 (227)
Annualized 100% compliance [†] (\pm 95% CI)	-138,317 (4,657)	-211,836 (7,224)	-80,567 (2,728)
PMPM 100% compliance [‡]	-0.07	-0.11	-0.04
Annualized partial (33%-58%) compliance [§] (\pm 95% CI)	-71,173 (2,397)	-106,259 (3,623)	-44,635 (1,512)
PMPM partial compliance	-0.04	-0.05	-0.02
Consolidation to Any Efficient Regimen			
Change	Physician Letter Arm	Physician/Member Letter Arm	Control Arm
One month (\pm 95% CI)	-29,749 (1,002)	-39,974 (1,363)	-28,686 (971)
Annualized 100% compliance [†] (\pm 95% CI)	-356,992 (12,021)	-479,684 (16,357)	-344,227 (11,657)
PMPM 100% compliance [‡]	-0.18	-0.24	-0.17
Annual partial (33%-58%) compliance [§] (\pm 95% CI)	-196,548 (6,618)	-248,078 (8,459)	-188,856 (6,395)
PMPM partial compliance	-0.10	-0.12	-0.09

* Pharmacy expenditures are calculated from the difference in discounted average wholesale price between an efficient and inefficient 30-day supply; intervention arms include administration fee for information systems, programming time, personnel time for clinical review, and mailing costs.

[†] Based on 12 refills per year (100% patient compliance).

[‡] PMPM = per member per month, based on 12 refills per year and 168,019 health plan members per arm.

[§] Based on expected number of monthly refills for each therapy class during a 12-month period (i.e., calcium channel blockers [7 refills, 58%], antihypertensives [7 refills, 58%], antihyperlipidemics [6 refills, 50%], antiulcers [6 refills, 50%], antidepressants [7 refills, 58%], and anti-inflammatories [4 refills, 33%]).

^{||} PMPM = per member per month, based on expected number of refills for each therapy class and 168,019 health plan members per arm.

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TABLE 5 Consolidation Rates After 180 Days by Drug Therapy Class

Therapy Class/Study Arm	No. of Regimens Targeted*	No Post-Intervention Claims† (%)	Consolidation to Suggested Regimen (%)	P Value Physician Letter‡	P Value Physician/Member Letter‡	P Value Control‡
Calcium Channel Blocker						
Physician letter	100	25.0	11.0	–	1.000	0.005
Physician/Member letter	102	24.5	11.8	1.000	–	0.002
Control	114	27.2	0.0	0.005	0.002	–
Antihypertensive						
Physician letter	169	29.6	11.2	–	1.000	0.036
Physician/Member letter	195	27.2	10.8	1.000	–	0.045
Control	185	27.0	3.8	0.036	0.045	–
Antihyperlipidemic						
Physician letter	74	27.0	10.8	–	0.723	1.000
Physician/Member letter	44	31.8	18.2	0.723	–	0.554
Control	45	22.2	8.9	1.000	0.554	–
Antiulcer/Heartburn						
Physician letter	139	30.2	1.4	–	0.001	1.000
Physician/Member letter	105	34.3	10.5	0.001	–	0.000
Control	109	29.4	0.0	1.000	0.000	–
Antidepressant						
Physician letter	283	29.0	6.7	–	0.296	1.000
Physician/Member letter	308	29.9	10.4	0.296	–	0.245
Control	317	26.2	6.6	1.000	0.245	–
Anti-inflammatory						
Physician letter	117	35.0	4.3	–	1.000	1.000
Physician/Member letter	106	31.1	3.8	1.000	–	1.000
Control	102	29.4	2.0	1.000	1.000	–

* Regimens targeted for intervention over 3 months.

† No claim for the targeted drug after the intervention date.

‡ P values for Bonferroni multiple comparisons tests of consolidation rates.

program could realize substantial savings for health plans. Calabrese and Baldinger² estimated annualized drug cost savings of \$1.67 per member per year in 2001 (approximately \$0.15 PMPM in 2003 dollars) with full compliance. This is comparable to the savings we found (\$0.11 PMPM) when savings were calculated based on the preconsolidation to postconsolidation rate to the suggested efficient regimen with full compliance for the Physician/Member Letter arm. Wheeler and Buttitta⁴ did not report PMPM savings, but reported that they found a 60% decrease “in drug spend for prescriptions with an optimized dose in the follow-up period.” While reporting savings attributed to their intervention, these researchers did not take into consideration either the cost of implementing their programs or the expenditure waste that occurs when a plan incurs administrative costs to modify a medication regimen for which the plan subsequently has no financial liability (i.e., for members who either disenroll or discontinue drug treatment). In addition, since neither study utilized a control

group, they could not discern adequately whether consolidation occurred because of their intervention or would have occurred regardless (e.g., dose titration). Furthermore, Calabrese and Baldinger² only speculated on the financial impact of drug therapy discontinuation, while Wheeler and Buttitta⁴ did not address this issue. For example, the decreased drug expenditures observed by Wheeler and Buttitta⁴ could have been the result of noncompliance or member plan disenrollment/coverage termination. These methodological limitations provide a basis for the observed differences between our findings and previous work.

Our study utilized a control group, which allowed for the assessment of the background rates of dose consolidation and cessation of plan financial responsibility for the targeted regimens, and incorporated program costs. While the cost of the intervention had an impact on the PMPM savings difference between intervention and control arms, our findings suggest that substantial drug treatment discontinuation and/or member plan disenrollment, coupled with consolidation naturally

occurring during the course of drug therapy, limited the savings opportunities.

Assessment of the potential for dose consolidation savings at the individual therapy class level revealed few opportunities. While the intervention appeared most successful for calcium channel blocker and antihypertensive regimens, the expenditure difference between inefficient and efficient regimens was minor and the number of potential targets too small to justify implementing such a program. Although the expenditure difference between inefficient and efficient antihyperlipidemic regimens was sizeable, the number of potential targets was small. For classes with substantial savings potential between an inefficient and efficient regimen, the effects of an intervention on the consolidation rate were either minimal (e.g., anti-inflammatory) or the recent availability of generic or over-the-counter versions of drugs in these classes (e.g., antiulcer and antidepressant) may reduce the value of conducting a dose consolidation program.

The study design and financial modeling we employed for this study have limitations. We modeled financial outcomes based upon drug refill patterns observed within the first 6 months after the intervention letters rather than following actual prescription claims utilization for a full year. We did not assess the possible effect of sending more than 1 intervention letter to prescribers. It is unknown whether receiving multiple letters would increase dose consolidation rates as some prescribers become sensitized to the opportunity for dose consolidation or if multiple letters would further disaffect the prescribers who don't appreciate drug therapy suggestions from health plans.

We utilized a definition of an inefficient regimen as a ratio of quantity dispensed to days supply dispensed of ≥ 1.5 . Utilizing fraction ratio values may have resulted in our targeting regimens where patients had been prescribed nonstandard dosages (e.g., a patient receiving 45 of the 30 mg tablets for a 30-day supply may have been instructed to split tablets and take one-and-a-half tablets per day for a 45 mg once-daily dose) and, thus, would not be able to consolidate their dose. In addition, we may have targeted regimens as inefficient where there was a misstatement of days supply by the pharmacist-provider (e.g., due to carelessness, efforts to thwart refill-too-soon edits, or reduce copays for members). If these false-positive inefficient regimens were targeted, this would have led to an underestimate of the consolidation rate; however, any potential bias would have been randomly distributed across arms and not had a noticeable impact on the findings.

Conclusions

A letter-based dose consolidation program is an intuitively attractive management strategy for health plans that desire a cost-savings program for maintenance drugs that does not restrict access to drugs—a criticism of prospective point-of-service quantity management. However, when taking into consideration the cost of administering such a program, high rates of maintenance drugs discontinuation, and background rates of consolidation (without intervention), the results indicated that a letter-based dose consolidation program did not appreciably decrease pharmacy expenditures.

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