

Telephone-Based Cardiovascular Medication Therapy Management in Medicare Part D Enrollees With Diabetes

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ABSTRACT

Objectives: The purpose of this study was to evaluate the impact of pharmacist-delivered medication therapy management (MTM) services via telephone (enhanced MTM intervention) versus the impact of an informative detailed medication letter sent via mail (minimal MTM intervention) on patients' acceptance of guideline-recommended pharmacotherapies, specifically angiotensin-converting enzyme (ACE) inhibitors/angiotensin II receptor blockers (ARBs) and statins.

Study Design: A retrospective database analysis was completed using pharmacy claims and enrollment data from 1 national pharmaceutical benefits manager.

Methods: Medicare Part D beneficiaries with diabetes, managed by 1 pharmacist-based medication management center, received either: 1) a pharmacist's recommendation, delivered via telephone, to add an ACE inhibitor or ARB and/or a statin to existing therapy, or 2) an informative letter detailing current therapies. The primary outcome measure was acceptance of guideline-recommended therapy determined by the presence of at least 1 prescription claim for the target drug in the post-intervention period. Propensity score matching and conditional logistic regression methodologies were used to assess the comparative effectiveness of the interventions.

Results: Patients who received the telephone intervention were 6.33 times more likely to be taking both medications during the postintervention period compared with those who received the letter intervention ($P < .001$). A greater proportion of patients who received the telephone intervention were taking both drugs during the postintervention period, with the greatest difference in those initially receiving a statin to which ACE inhibitor/ARB therapy was added (41.18% vs 7.23%).

Conclusions: Telephone-based MTM services provided to Medicare Part D beneficiaries with diabetes positively impacted acceptance of guideline-recommended ACE inhibitor/ARB and/or statin therapies relative to the letter intervention.

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According to 2014 national estimates provided by the CDC, 29.1 million people in the United States live with diabetes, with 8.1 million of these individuals being undiagnosed.¹ The prevalence of this disease in those 65 years or older is 25.9%, with this age group accounting for more than a third of all individuals with diabetes in the United States.¹ One study projected that by 2050, incident cases of diabetes are expected to almost double and the prevalence will increase to between 21% and 33% of the entire population based on 2010 estimates.²

The economic burden of diabetes has been estimated at \$174 billion, including direct medical costs, reduced productivity, and costs to treat diabetes-related chronic conditions.³ Chronic conditions that have the largest impact on resource consumption in patients with diabetes include cardiovascular disease (CVD), neurological symptoms, and renal complications.³ Behind healthcare expenditures for inpatient hospital stays for general medical conditions, CVD-related inpatient resource consumption is the second largest category of associated costs.³ Moreover, CVD is the leading cause of morbidity and mortality in diabetics, with death from coronary heart disease (CHD) 2 to 3 times higher in patients with diabetes than those without.^{4,5}

Multiple associations have each developed guidelines for the management of CVD risk factors.⁵⁻⁸ The 2010 American Diabetes Association (ADA) guidelines detail current standards of medical care and CVD management in diabetics.⁵ Recommendations for the prevention and management of CVD include blood pressure control, lipid management, use of antiplatelet agents, smoking cessation, and screening for/treatment of CHD.⁴ Hypertension and dyslipidemias remain the most prevalent comorbidities in patients with diabetes. In addition to diet and lifestyle modifications, first-line pharmacotherapy for diabetics with a diagnosis of hypertension include either an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II receptor blocker (ARB). Studies have demonstrated risk reductions in morbidity and mortality associated with cardiac events resultant from primary or secondary prevention interventions.⁹⁻¹² Aggressive lipid management with hydroxymethylglutaryl coenzyme-A

PRACTICAL IMPLICATIONS

- Medication therapy management (MTM) programs and interventions focused on high-risk patients can have significant, critical effects on clinical, economic, and humanistic outcomes.
- This real-world study showed that diabetic Medicare Part D patients receiving a telephonic pharmacist-led MTM intervention to improve adherence to guideline-recommended cardiovascular pharmacotherapies were more than 6 times as likely to have initiated guideline-recommended therapies versus those receiving a letter intervention.
- Interventions that can help facilitate appropriate monitoring and management of complex high-risk patients should be considered for implementation by clinical and policy decision makers to improve patient outcomes; this may also have important economic impacts.

reductase inhibitors (statins), along with diet and lifestyle modifications, is also a first-line recommendation of the ADA. Patients 40 years or older with diabetes and either overt CVD or without overt CVD (but who have 1 other risk factor for CVD regardless of baseline cholesterol levels) are indicated for pharmacotherapy.⁴ The efficacy of statins in primary and secondary prevention of cardiovascular events in patients with diabetes has also been well established.^{10,13-18}

Although the evidence supports the use of these pharmacotherapies for CVD in patients with diabetes, they remain underutilized.¹⁹⁻²³ Medication therapy management (MTM) programs could be one tool used to assist in the initiation and adherence to guideline-recommended therapies. The 2003 Medicare Modernization Act stipulated subsidized drug coverage for Medicare beneficiaries under Medicare Part D, with a mandate for sponsors to establish MTM programs as part of each plan structure.²⁴ Consequently, the potential impact of MTM on subsequent outcomes is the focus of greater study.

MTM services have been delivered in person, via telephone, and/or via mail. It is important to note that although many models and mechanisms of MTM delivery have been implemented over time, in the early phases of implementation, mailed letter interventions often consisted solely of detailed lists of medications intended to provide a tool for future patient-provider discussion during follow-up visits. This model of MTM intervention can be considered a passive intervention for which success is contingent upon the patient remembering to actively contact their physician for follow-up and bringing the medication list to future visits. On the other hand, in-person and telephone-based proactive MTM models allow for 2-way MTM provider-patient communication and greater patient engagement in decision making regarding their treatment. As such, improved outcomes may result from proactive and patient-engaged models of MTM.

Physicians, nurses, and pharmacists have delivered—and continue to deliver—varying models of these services

to patients with a variety of chronic diseases. Diabetes continues to be a priority for MTM, with 96.8% of all programs approved in 2010 indicating diabetes as a core targeted disease.²⁴ Positive clinical and economic outcomes of pharmacist-delivered care have been demonstrated in multiple programs, but most notably in the Asheville Project.^{25,26} A paucity of research in this area remains, but continuous evaluation of the impact

of MTM programs on health outcomes is necessary to investigate potential economic and policy implications for stakeholders. Therefore, an evaluation of the impact of the various types of interventions aimed at increasing adherence to recommended clinical guidelines is warranted.

The purpose of this study was to evaluate the impact of pharmacist-delivered MTM services via telephone (enhanced MTM intervention) versus the impact of an informative detailed medication letter sent via mail (minimal MTM intervention) on patients' acceptance of guideline-recommended pharmacotherapies, specifically ACE inhibitors/ARBs and statins. All patients had diabetes and were enrolled in a Medicare Part D program.

METHODS

Data Source and Patient Population

Claims and enrollment data from January 1, 2006, through June 30, 2007, for patients enrolled in a Medicare Part D plan, administered by 1 national pharmaceutical benefits manager (PBM), were utilized in this retrospective database analysis. The PBM identified probable patients with diabetes via pharmacy claims from January 1, 2006, through October 30, 2006. Patients were included if they: 1) were taking at least 1 medication used in the treatment of diabetes with 2 fills or at least a 60-day supply of medication during the preintervention period, including injectable and oral therapies; or 2) met MTM eligibility requirements, which included at least \$4000 in projected annual prescription drug expenditures, presence of multiple chronic conditions, and taking multiple Medicare Part D medications. Additionally, patients in this analysis had at least 6 months of continuous plan enrollment before and after the intervention and had a documented receipt of either a telephone or letter intervention.

Finally, patients must not have had a prescription for an ACE inhibitor/ARB and/or statin between January 1, 2006, and the time of the intervention, which occurred from November 1, 2006, through December 31, 2006. These

patients may have initially received an ACE inhibitor/ARB but not a statin, a statin but no ACE inhibitor/ARB, or neither an ACE inhibitor/ARB nor statin. All brand, generic, and combination products listed in the Medi-Span Drug Information Database and available in the United States by prescription during the study time period were used to identify whether patients had received 1 of the 3 medication classes. Subjects were excluded from the current analysis if there was invalid member identification, they were recommended for or residing in long-term care facilities, or they were younger than 40 years.

Database management and statistical analyses were performed in SAS version 9.2 (SAS Institute Inc, Cary, North Carolina) and STATA/IC 11 (StataCorp, College Station, Texas). Human subjects approval for this study was obtained from the University of Arizona Institutional Review Board.

Interventions

The telephone intervention, or the enhanced MTM intervention, group consisted of patients who had complete and accurate telephone numbers and were not receiving guideline-recommended ACE inhibitor/ARB and/or statin therapy, as deemed appropriate by a pharmacist review of medications and conditions. These patients were contacted via telephone by a pharmacist who confirmed conditions, recommended the addition of the target medications, and suggested follow-up and discussion with their physician. Afterward, a fax was sent to the patient's physician with the same recommendation, referencing the published ADA treatment guidelines supporting the use of these medications. This study considers the "telephone" intervention group to be those who were contacted by a pharmacist for a 1-on-1 discussion of specific recommendations. In addition, the patient's physician was also contacted via fax with the same recommendations discussed with the patient.

The letter, or minimal, intervention group consisted of all other patients eligible for inclusion for whom telephone contact information was unavailable or inaccurate at the time of outreach and upon review of their medication history were noted as not receiving guideline-recommended ACE inhibitor/ARB and/or statin therapy for inferred conditions. These patients were mailed an informative letter that listed their current prescribed medications and suggested that patients take the list to all medical appointments for discussion with their physicians; however, no specific recommendations were provided regarding any medication and no physician outreach was conducted. This study considers the "letter" intervention group to be those sent a letter with no specific recommendations and no physician outreach.

Outcomes and Covariates

The primary outcome and success of the intervention was defined as the patient having at least 1 prescription claim for both an ACE inhibitor/ARB and statin in the postintervention period. Covariates of interest included patient age at the time of the intervention, gender, total prescription costs, and total number of claims in the preintervention timeframe. As only prescription medication claims were available for analysis, the RxRisk algorithm was used to calculate a risk-adjustment score, with higher scores reflecting a higher number of possible chronic diseases and comorbid conditions.²⁷

Statistical Analyses

To control for possible bias that may have been introduced due to differential selection in this observational study, patients in the telephone intervention group were matched to patients in the letter intervention based on calculated propensity scores.²⁸ To assure an exact match on the preintervention drug group (ie, ACE inhibitor/ARB only, statin only, neither), matches were performed for each subgroup separately, then aggregated for all analyses. In cases where 3 letter intervention patients could not be adequately matched to a telephone intervention recipient, a 2-to-1 match was allowed.

Descriptive statistics were used to characterize the cohort of matched and unmatched patients. To verify that the propensity score matching removed any significant differences between groups, χ^2 tests for categorical variables or Student's *t* tests for continuous variables were performed for the matched and unmatched cohorts.

A conditional logistic regression analysis was performed in the matched cohort to determine the relationship between independent variables of interest and the primary outcome of the presence of target drug-related claims during the postintervention period. The a priori 2-sided level of significance was $P < .05$. Proportions of patients achieving the outcome of interest in each initial drug group (ie, ACE inhibitor/ARB only, statin only, neither) and RxRisk categories within each intervention were reported due to the inability to perform regressions due to sample size limitations. Chi-squared statistics indicating significant differences among these subgroups were also reported.

RESULTS

Baseline characteristics of the unmatched and matched cohorts are delineated in **TABLE 1**. In the unmatched cohort, all but 2 of the covariates were statistically significantly different between the telephone and letter intervention groups. After matching, the intervention groups were

Table 1. Baseline Characteristics of Unmatched and Matched Cohorts

Variables	Unmatched			P ^a	Matched			P ^a
	Telephone (n = 182)	Letter (n = 48,904)	Total (n = 49,086)		Telephone (n = 182)	Letter (n = 535)	Total (n = 717)	
Gender								
Female (%)	123 (67.58)	34,597 (70.74)	34,720 (70.73)	.369	123 (67.58)	339 (63.36)	462 (64.44)	.325
Male	59	14,307	14,366		59	196	255	
Age, years (mean, SD)	65.44 (10.95)	69.26 (13.77)	69.25 (13.76)	<.001	65.44 (10.95)	65.13 (13.10)	65.21 (12.58)	.754
RxRisk score								
Mean (SD)	3.25 (1.21)	3.29 (1.35)	3.29 (1.34)		3.26 (1.21)	3.34 (1.42)	3.32 (1.37)	
Low risk (1-2)	46	14,589	14,635	.320	46	159	205	.366
Intermediate (3-4)	106	25,818	25,924		106	279	385	
High (≥5)	30	8497	8527		30	97	127	
Total cost claims, 2006 US\$ (SD)	4742.47 (3297.44)	7222.37 (6033.56)	7213.17 (6027.58)	<.001	4742.47 (3297.44)	4808.85 (2982.03)	4791.99 (3062.94)	.810
Total number of claims, 2006 (SD)	67.96 (25.09)	99.09 (41.18)	98.97 (41.18)	<.001	67.96 (25.09)	71.67 (29.44)	70.73 (28.42)	.101
Propensity score (SD)	0.0091 (0.014)	0.0037 (0.0056)	0.0037 (0.0056)	<.001	0.0091 (0.0014)	0.0086 (0.011)	0.0087 (0.012)	.619
Initial drug group								
ACE inhibitor/ARB only	39	18,303	18,342	<.001	39	114	153	1.0
Statin only	85	16,737	16,822		85	249	334	
Neither	58	13,864	13,922		58	172	230	

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; SD, standard deviation. ^aStudent's *t* tests were used for continuous variables and χ^2 tests for categorical variables.

similar on all independent variables of interest. All patients in the telephone group (n = 182) were matched to 3 letter intervention patients, except for 11 patients who could be suitably matched to only 2 controls, thus providing 535 letter intervention recipients. RxRisk scores were categorized, with patients receiving a score of 1 or 2 classified in the “low” risk group, those with a score of 3 or 4 classified in the “intermediate” risk group, and those with a score of 5 or higher classified in the “high” risk group. Total costs and number of claims were considerably skewed; thus, a log transformation was employed to achieve normality assumption. As a result, the model fit improved. The matched population (n = 717) was predominantly female, with a mean age of 65.21 years. The mean RxRisk score was 3.32 (standard deviation = ± 1.37), with 54% of patients falling into the intermediate RxRisk category. Untransformed total costs in the 2006 baseline period were approximately \$4792 per patient, or \$399 per member per month, with an average of 71 claims per patient. More than 46.7% of patients were already receiving statin therapy only, 21.4% were receiving an ACE inhibitor/ARB only, and 31.9% were not receiving either guideline-recommended medication.

Results from the conditional logistic regression are displayed in **TABLE 2**. Patients receiving the telephone

intervention were 6.33 times more likely to be taking both medications after the intervention compared with those who received the letter intervention (*P* < .001). Other covariates in the model did not reach statistical significance. Postestimation model checks for this regression indicated good overall model fit.

Outcomes in 2 main subgroups were investigated to explore in which populations these interventions had the least and greatest possible impact. **TABLE 3** presents the proportion of those achieving a successful outcome by intervention type and initial drug group classification. All groups showed a higher percentage of success with the telephone intervention versus the letter intervention, although this difference was greatest in patients initially taking a statin to which an ACE inhibitor/ARB was added (41.18% vs 7.23%, respectively). **TABLE 4** presents those with a successful outcome with each intervention by RxRisk category. Again, a greater proportion of patients in the telephone intervention group had a successful outcome compared with the letter intervention in each of the 3 RxRisk categories. A greater overall percentage of the lowest and intermediate RxRisk groups achieved a successful outcome, regardless of intervention (11.40% and 14.77%, respectively), compared with the highest RxRisk group (7.87%). However, it is important to note that a larger



proportion of patients in the intermediate and highest risk groups who had received the telephone intervention were taking both guideline-recommended medications during the postintervention period.

DISCUSSION

Previous literature has shown the positive impact that pharmacist-delivered MTM and disease management services have on clinical, economic, and humanistic outcomes in the diabetic patient population.^{25,26,29-39}

Overall, based on pharmacy claims, 28% of patients in the unmatched cohort and 32% of patients in the matched cohort were not receiving either guideline-recommended therapy during the period of time under study, thus demonstrating possible underuse of these effective medications in this population. The telephone intervention was statistically significantly more effective than the letter intervention in achieving the successful outcome of patients receiving both guideline-recommended therapies, demonstrating that this model of program and mechanism for intervention delivery was able to educate and engage patients, as well as inform and ultimately influence prescribers about guideline-recommended cardiovascular therapies for patients with diabetes. More patients in the telephone group were successfully taking both medications in all initial drug groups (ie, neither drug, ACE inhibitor/ARB only, statin only) after the intervention than those receiving the letter intervention. The most pronounced difference was in the group of patients who were initially only taking statins (ie, ACE inhibitor/ARB was successfully added): 41.18% of patients were on both medications after telephone intervention compared with 7.23% receiving the letter intervention. The subgroup in which the pharmacist-delivered MTM service did not have a significant impact, compared with the letter intervention, was the group in which patients were initially taking only an ACE inhibitor/ARB.

Results of the current analysis indicate that the patients in the intermediate RxRisk group were slightly more likely to be taking both medications after either intervention, whereas those in the highest RxRisk group were less likely, compared with the lowest RxRisk category. When examining outcomes by RxRisk group and intervention type, it is possible the relative ineffectiveness of the letter intervention in the intermediate and highest RxRisk groups was responsible for the results, as the largest impact of the telephone intervention was in the patients whose RxRisk score indicated higher numbers of chronic conditions.

Results of previous studies concur with the findings of the current program evaluation, showing the effectiveness of clinician-led medication management interventions

Table 2. Conditional Logistic Regression of Matched Cohort^a

Variable	OR	P	95% CI
Telephone intervention	6.33	<.001	3.64-10.90
Age at intervention	0.98	.495	0.92-1.04
Female gender	1.37	.351	0.71-2.64
Log cost	0.56	.505	0.10-3.09
Log number of claims	1.74	.566	0.27-11.30
RxRisk ^b			
Intermediate	1.10	.804	0.51-2.37
High	0.52	.252	0.17-1.61

CI indicates confidence interval; OR, odds ratio.

^aN = 284 (433 observations were dropped due to all positive or all negative outcomes, which are not retained in conditional logistic regression); pseudo-R² = 0.279.

^bBaseline is the "low" RxRisk group.

Table 3. Proportion of Patients Taking Both Drugs Post Intervention by Initial Drug Group

Group ^a	Telephone (n = 182)	Letter (n = 535)	Total (n = 717)	P ^b
ACE inhibitor/ ARB only (%)	6/39 (15.38)	15/114 (13.16)	21/153 (13.73)	.727
Statin only (%)	35/85 (41.18)	18/249 (7.23)	53/334 (15.87)	<.001
Neither (%)	9/49 (18.37)	1/172 (0.05)	10/230 (4.35)	<.001 ^c
Total	50/182 (27.47)	34/535 (6.36)	84/717 (11.72)	<.001

ACE indicates angiotensin-converting enzyme; ARB, angiotensin II receptor blocker.

^aACE inhibitor/ARB only: taking an ACE inhibitor/ARB, but not a statin, before the intervention; statin only: taking a statin, but not an ACE inhibitor/ARB, before the intervention; neither: patient was taking neither an ACE inhibitor/ARB nor statin before the intervention.

^bChi-squared test was used.

^cFisher's exact test was used.

Table 4. Proportion of Patients Taking Both Drugs Post Intervention by RxRisk Group

RxRisk Group ^a	Telephone (n = 182)	Letter (n = 535)	Total (n = 717)	P ^b
Low (%)	10/46 (21.74)	12/147 (8.16)	22/193 (11.40)	.006
Intermediate (%)	33/73 (45.21)	19/279 (6.81)	52/352 (14.77)	<.001
High (%)	7/30 (23.33)	3/97 (3.09)	10/127 (7.87)	<.001
Total	50/182 (27.47)	34/535 (6.36)	84/717 (11.72)	<.001

^aLow: RxRisk score 1-2; intermediate: RxRisk score 3-4; high: RxRisk score ≥5.

^bChi-squared test was used.

in patients with diabetes indicated for treatment with cardiovascular pharmacotherapies, such as ACE inhibitors/ARBs and statins. A retrospective chart review of 75 patients with diabetes in a collaborative care model family medicine clinic determined the influence a pharmacist intervention had

on the use of ADA guideline-recommended ACE inhibitor, ARB, and aspirin use.⁴⁰ At baseline, 59% of these patients were receiving ACE inhibitor or ARB therapy and 34% were receiving aspirin, with postintervention use increased to 90% and 68%, respectively ($P < .0001$). In a similar study, a pharmacist-coordinated diabetic disease management program effectively increased statin use from 35% before pharmacist intervention to 50% post intervention, ACE inhibitor use from 40% to 48%, ARB use from 15% to 19%, and daily aspirin use from 45% to 80%.⁴¹ However, Monte et al, while reporting reductions in primary diabetic and metabolic endpoints, were not able to show that pharmacist-led pharmacotherapy management significantly increased use of aspirin, ACE inhibitors/ARBs, or statins.⁴²

The influence of a nurse care manager–delivered disease management program via telephone on ACE inhibitor, ARB, and statin use, in Medicaid patients with diabetes versus control patients, has also been investigated.⁴³ Those patients not using an ACE inhibitor, ARB, and/or statin at baseline in the care-managed group were more likely to be utilizing these medications 12 months post intervention ($P < .001$). Additionally, patients in the intervention group initially using an ACE inhibitor, ARB, and statin in the year prior to the intervention increased their use in the year post intervention relative to those not receiving the intervention. Finally, a study evaluating MTM program influence on statin prescribing in Medicare Part D enrollees with either coronary artery disease or diabetes reported a 65% higher odds of initiation of statin therapy in those patients whose prescribers received educational materials and a list of their patients who would benefit from statin therapy.⁴⁴

Limitations

Results of these analyses must be considered in light of study limitations. Only patients 40 years or older were included, and it was assumed they had 1 other risk factor for CVD, thus indicated for statin therapy. Additionally, an assumption was made that these patients were indicated for hypertension treatment, with an ACE inhibitor/ARB as first-line therapy, or receiving 1 of these medications for treatment of albuminuria or renal function preservation. However, there may be a contraindication to therapy or previous therapy failure with either ACE inhibitors/ARBs or statins that could not be assessed. Therefore, it could not be determined if these patients had a confirmed diagnosis of type 1 or 2 diabetes, limiting the ability to differentiate outcomes between these 2 subgroups.

Further, as the average age of this population is 65 years, and 90% to 95% of all patients with diabetes in the United States have type 2 diabetes, the results of this study are most

likely generalizable to the population with type 2 diabetes. This study used only pharmacy claims and enrollment data; thus, additional factors that could have influenced results (eg, race, ethnicity, socioeconomic status, clinical factors, patient engagement, physician-related factors, and plan-specific factors) could not be evaluated.

Although propensity score matching was used to reduce potential bias that may be introduced due to the nonrandomized study design, those factors not able to be assessed or controlled for could have introduced bias into the study. For example, those patients not able to be contacted by phone may have additional barriers to receiving healthcare or may not be as engaged and, therefore, may not be as impacted by such interventions. Additionally, the distinct program elements involved in each intervention may have differentially influenced the outcomes. For example, outreach to physicians may have had more impact on initiation of guideline-recommended therapies than patient contact or communication. Intervention success was determined from pharmacy claims with no evaluation of adherence or persistence to therapy during the 6-month postintervention period.

The RxRisk algorithm for risk assessment and adjustment is outdated, which may underestimate the presence of comorbidities. As neither medical records nor claims were available for analysis, this was the only method to control for severity of illness.

CONCLUSIONS

Proactive pharmacist-delivered telephone MTM services provided to diabetic Medicare Part D patients more effectively impacted acceptance of guideline-recommended ACE inhibitor/ARB and statin therapy relative to the passive and/or patient-reactive letter intervention. This study demonstrates the critical roles that these programs, as well as pharmacists, play in ensuring that patients receive therapies that may reduce costs and improve clinical and humanistic outcomes. Future research should focus on long-term clinical outcomes, costs, patient satisfaction, and health-related quality of life for those enrolled in MTM programs, as these factors are of importance to consider for all stakeholders. 

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