Centers for Medicare & Medicaid Services

Center for Medicare and Medicaid Innovation

Evidence Supporting Enhanced Medication Therapy Management

This document summarizes some of the evidence supporting several potential pathways toward achieving the goals of the Part D Enhanced Medication Therapy Management (MTM) model. The information contained in this document is intended to serve as one source of information to aid model applicants as they design proposed interventions. This document is not meant to limit the design or scope of interventions. It is expected that applicants will use various resources and perform additional research to design innovative approaches to improving MTM for their beneficiaries. This document summarizes some of the key findings from literature supporting the MTM model goals. However, the intention is not to imply that this is a complete summary of all evidence supporting improvements in MTM. There may be other relevant information that can be used to support applicants in designing proposed interventions.

A. Improvements in Medication Adherence and Associated Savings

Data from a 2010 retrospective analysis of MA-PD and stand-alone basic PDP plan beneficiaries participating in MTM programs showed that participants with congestive heart failure (CHF), chronic obstructive pulmonary disease (COPD), and diabetes had significantly higher rates of adherence than similarly situated beneficiaries not enrolled in MTM programs (approximately 11-40 percent higher for those with CHF, 11-26 percent higher for those with COPD, and 15-35 percent higher for those with diabetes, compared to the respective control populations).[1] PDP beneficiaries with diabetes or CHF who also received CMR also had decreased utilization and costs for Medicare Parts A and B ($399 and $526 reduction in inpatient costs, respectively, after risk-adjustment), although similar results were not statistically significant for those with COPD or for MTM participants who did not receive a CMR. Another analysis conducted by MedPAC showed similar results, confirming MTM-related improvements in medication adherence and medical expenditures among CHF patients.[2] Both analyses reviewed all-cause savings in total cost of care, meaning that other mechanisms of action beyond improved medication adherence also likely contributed to the demonstrated savings.

Another study among 2,250 beneficiaries of a large employer prescription benefit plan found increased adherence for patients with hypertension and dyslipidemia, and an estimated net cost

[1] Perlroth D, Marrufo G, Montesinos A, et al. *Medication Therapy Management in Chronically Ill Populations: Final Report.* Prepared for CMS by Acumen, LLC and Westat; 2013.
[2] *MedPAC. Measuring the Effects of Medication Adherence for the Medicare Population. In: Report to the Congress: Medicare and the Health Care Delivery System.* Washington, DC: MedPAC, 2014.

savings of $499 overall.[3] The return on investment for this study was 200 percent. Another study showed a relationship between low adherence and higher health-related costs in a hypertensive population, showing excess costs estimated at $3,574 per person, as well as increased chances of cardiovascular disease developing.[4] Another study focusing on medication adherence in Medicaid beneficiaries with congestive heart failure found that increased medication adherence rates resulted in fewer hospitalizations and ED visits, leading to a cost savings of $5,910 per year.[5]

Supporting interventions which complement traditional CMR-based MTM, such as reminder packaging, may represent a simple method for improving adherence that could enhance the effect of traditional MTM;[6] one study among hypertensive patients showed significant improvements in both adherence and persistence.[7]

B. Adverse Drug Events

Other studies have examined the degree to which MTM could prevent adverse drug event-related hospitalizations and other risks to patient safety which result in preventable utilization, which is a mechanism through which significant cost savings can be realized.[8] [9] [10] Adverse drug events are a significant cause of morbidity and mortality in the elderly population. The Institute of Medicine estimates that medication errors cause 1 of 131 outpatient and 1 of 854 inpatient deaths.[11] With nearly 100,000 emergency hospitalizations occurring each year, adverse drug events are an important cause of preventable hospitalizations.[12] In the ambulatory setting, adverse drug events are associated with a significant increase in healthcare costs with nearly half of the increased dollar amount attributable to preventable events.[13] Multifaceted pharmaceutical care provided in a

[3] Moore JM, Shartle D, Faudskar L, Matlin OS, Brennan TA. Impact of a patient-centered pharmacy program and intervention in a high-risk group. *J Manag Care Pharm.* 2013;19(3):228-236.
[4] Dragomir A, Cote R, Roy L, et al. Impact of adherence to antihypertensive agents on clinical outcomes and hospitalization costs. *Med Care.* 2010;48(5):418-425.
[5] Esposito D, Bagchi AD, Verdier JM, Bencio DS, Kim MS. Medicaid beneficiaries with congestive heart failure: association of medication adherence with healthcare use and costs. *The American journal of managed care.* 2009;15(7):437-445.
[6] Mahtani KR, Heneghan CJ, Glasziou PP, Perera R. Reminder packaging for improving adherence to self-administered long-term medications. *The Cochrane database of systematic reviews.* 2011(9):CD005025.
[7] Chrischilles E CB, Voelker M, et al. *Iowa Medicaid Pharmaceutical Case Management Program. Report to the DHS Appropriations Subcommittee.* Iowa March 5 March 5, 2003.
[8] Ibid.
[9] McDonnell PJ, Jacobs MR. Hospital admissions resulting from preventable adverse drug reactions. *Ann Pharmacother.* 2002;36(9):1331-1336.
[10] Senst BL, Achusim LE, Genest RP, et al. Practical approach to determining costs and frequency of adverse drug events in a health care network. *American Journal of Health-System Pharmacy.* 2001;58(12):1126-1132.
[11] *Preventing Medication Errors: an IOM Report.* Washington, DC: Institute of Medicine; July 20 July 20, 2006.
[12] Budnitz DS, Lovegrove MC, Shehab N, Richards CL. Emergency hospitalizations for adverse drug events in older Americans. *The New England journal of medicine.* 2011;365(21):2002-2012.
[13] Field TS, Gilman BH, Subramanian S, Fuller JC, Bates DW, Gurwitz JH. The costs associated with adverse drug events among older adults in the ambulatory setting. *Med Care.* 2005;43(12):1171-1176.

variety of settings has been shown to result in a reduction in inappropriate medication use and adverse drug events significantly (35%) post-intervention.[14]

A handful of medications are responsible for the majority of adverse drug events. Five classes of drugs—insulin, opioid-containing analgesics, anticoagulants, amoxicillin-containing agents, and antihistamines/cold remedies—alone or in combination with other drugs, account for nearly 30% of all adverse drug events, while warfarin, insulin, oral antiplatelet agents, and oral hypoglycemic agents are responsible for nearly 70% of adverse drug events requiring hospitalization.[15] Among post discharge readmissions in patients aged 65 and older, again only a handful of drugs, including several of the same drugs, were involved in the majority of preventable events.[16] Medication self-management programs, including those with pharmacist involvement, appear to improve medicine use, adherence, and clinical outcomes and reduce adverse events and to reduce mortality in people self-managing antithrombotic therapy.[17]

C. Medication Appropriateness and Therapeutic Substitutions

In a prescriber-based intervention that included identifying eligible MA-PD and stand-alone basic PDP plan beneficiaries who had diabetes or coronary artery disease, and who were not currently taking statins but who could benefit from their use, participants had about 65 percent greater uptake of statins than a control group.[18] Using this figure, coupled with estimated reductions in cardiovascular events and factoring in program costs, the authors estimated that for every 220 beneficiaries, one major cardiovascular event and $12,323 in event-associated costs were avoided.

Another study among MA-PD beneficiaries in California examined a different approach to MTM engagement by basing eligibility on targeted medications Results of the study indicate that 57 percent of the drug change recommendations made were implemented and sustained, and the largest category of changes made were therapeutic substitutions[19] made for the purposes of cost reduction. Additionally, after factoring in program costs, the intervention led to $1,797 in plan

[14] Patterson S, Cadogan C, Kerse N, et al. Interventions to improve the appropriate use of polypharmacy for older people. *Cochrane Database of Systematic Reviews* 2014(10):CD008165.
[15] Budnitz, et. al.
[16] Kanaan AO, Donovan JL, Duchin NP, et al. Adverse drug events after hospital discharge in older adults: types, severity, and involvement of Beers Criteria Medications. *Journal of the American Geriatrics Society.* 2013;61(11):1894-1899.
[17] Ryan R, Santesso N, Lowe D, et al. Interventions to improve safe and effective medicines use by consumers: an overview of systematic reviews. *Cochrane Database of Systematic Reviews.* 2014(4):CD007768.
[18] Stockl KM, Tjioe D, Gong S, Stroup J, Harada A, Lew HC. Effect of an intervention to increase statin use in medicare members who qualified for a medication therapy management program. *Journal of managed care pharmacy: JMCP.* 2007;14(6):532-540.
[19] Therapeutic substitutions are exchanges of one drug product for another with a different chemical structure but from the same pharmacological class, and with generally similar therapeutic effects and adverse reaction profiles when administered in therapeutically equivalent doses.

savings (both drug and medical savings) per participant, leading to a return on investment of 1100 percent.[20]

Another study showed that implementing pharmacist-led MTM resulted in better prescribing patterns by physicians, reduced total number of medications taken by patients, and improvement in most clinical outcomes, although these improvements were not always statistically significant, as well as improvement in patient quality of life outcomes.[21]

Medicaid programs using MTM in Iowa, Minnesota, and Connecticut have demonstrated increases in appropriate medication use, resolution of drug problems, and cost savings. In Iowa, operators observed a 12.5 percent increase in the medication appropriateness index, and a 24 percent decrease in use of medications considered inappropriate for the age group.[22] In Minnesota, 789 drug therapy problems were resolved and health care expenditures were reduced by $20 PMPM.[23] The Connecticut program saved an average of $1,123 in drug costs and $472 in medical, hospital, and emergency department charges per patient.[24] Per-person program costs were estimated at $638, resulting in $912 per patient savings and a final return on investment estimate of 150 percent.

D. All-Cause Reductions in Preventable Healthcare Utilization

A randomized trial of telephonic MTM among new Medicare Home Health patients showed a reduction in hospitalizations, but only among beneficiaries in the lowest quartile of risk for hospitalization. These patients were three times less likely to be hospitalized by 60 days post-intervention than similar beneficiaries in the control group.[25] The authors theorize that this may be related to functional status among home health patients, and that MTM may be most effective in those beneficiaries able to act upon recommendations.

The Asheville Project, a study that examined an MTM program for Medicaid patients enrolled in self-insured health plans, showed a decrease in hospitalization to 1.9 percent from 4 percent for asthma patients enrolled in the program, in addition to a decrease in emergency department visits to 1.3 percent from 9 percent, resulting in average direct cost-savings of $725 per year, even after

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[20] Steele S, Gates R. Pharmacoeconomic Outcomes of A Pharmacist-Led Medication Review Program. Paper presented at: CMS 2012 Medicare Prescription Drug Benefit Symposium; March 20-21, 2012; Hunt Valley, MD.

[21] Nkansah N, Mostovetsky O, Yu C, et al. Effect of outpatient pharmacists' non-dispensing roles on patient outcomes and prescribing patterns. *The Cochrane database of systematic reviews.* 2010(7):CD000336.

[22] Chrischilles et. al.

[23] Isetts BJ. *Evaluating Effectiveness of the Minnesota Medication Therapy Management Care Program: Final Report.* December 14, 2007.

[24] Smith M, Giuliano MR, Starkowski MP. In Connecticut: improving patient medication management in primary care. *Health Aff (Millwood).* 2011;30(4):646-654.

[25] Zillich AJ, Snyder ME, Frail CK, et al. A randomized, controlled pragmatic trial of telephonic medication therapy management to reduce hospitalization in home health patients. *Health services research.* 2014;49(5):1537-1554.

accounting for drug costs.[26] The project also observed improvements in markers for cardiovascular disease, around 50 percent decreases in both cardiovascular events and cardiovascular-related ED visits, and cost savings of over $600 per year.[27] Another study of 25 younger Medicaid patients enrolled in an asthma medication therapy management program led to a 76 percent decrease of ER visits (33 to 8) and a 33% reduction in hospitalization related to asthma (3 to 2).[28]

E. All-Cause Reductions in Total Cost of Care

An MTM intervention piloted among people over age 50 in Indiana, in which over half of recipients were Medicare beneficiaries, resulted in increased adherence during the intervention period. Adverse drug events and medication errors combined were 10 percent higher in the control group, and the program resulted in gross savings of $3,165 per beneficiary (net $2,960 once program costs were accounted for), although these results were not statistically significant.[29]

The Pennsylvania Project, which investigated the effect of a community-based pharmacist intervention targeting five major medication classes on overall healthcare costs for several plans offering both commercial and Medicare Part D products, showed significant decreases in overall healthcare costs for patients with diabetes taking oral diabetes medications as well as patients with hyperlipidemia taking statins.[30]

A number of studies conducted among beneficiaries of private plans indicated that MTM interventions were associated with improved adherence and cost savings. One study showed that patients with psychiatric disorders referred to pharmacist-led, comprehensive medication management services resulted in an average savings of nearly $600 per patient, with a return on investment of 280 percent after accounting for the cost of the services.[31]

An evaluation of an innovation project that included a strong MTM management component in several clinics of the Fairview Health System in Minnesota showed that growth in health care spending for beneficiaries seen at the innovation clinics was dramatically lower: 3.7 percent

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[26] Bunting BA, Cranor CW. The Asheville Project: long-term clinical, humanistic, and economic outcomes of a community-based medication therapy management program for asthma. *J Am Pharm Assoc (2003).* 2006;46(2):133-147.

[27] Bunting BA, Smith BH, Sutherland SE. The Asheville Project: clinical and economic outcomes of a community-based long-term medication therapy management program for hypertension and dyslipidemia. *J Am Pharm Assoc (2003).* 2008;48(1):23-31.

[28] Hilsenrath P, Woelfel J, Shek A, Ordanza K. Redefining the role of the pharmacist: medication therapy management. *The Journal of rural health : official journal of the American Rural Health Association and the National Rural Health Care Association.* 2012;28(4):425-430.

[29] Murray MD, Young J, Hoke S, et al. Pharmacist intervention to improve medication adherence in heart failure: a randomized trial. *Annals of internal medicine.* 2007;146(10):714-725.

[30] Pringle JL, Boyer A, Conklin MH, McCullough JW, Aldridge A. The Pennsylvania Project: Pharmacist Intervention Improved Medication Adherence And Reduced Health Care Costs. *Health Affairs.* 2014;33(8):1444-1452.

[31] Cobb CD. Optimizing Medication Use with a Pharmacist Provided Comprehensive Medication Management Service for Patients with Psychiatric Disorders. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy.* 2014;34(12):1336-1340.

between December 2008 and March 2010, compared to 14.7 percent in the control population.[32] In absolute numbers, this equated to an overall savings of $3,768 per beneficiary, and $252 PMPM. Additional studies have indicated an effect of MTM on both estimated[33,34] and actual cost savings of approximately $200-350 per participant annually.[35,36,37]

[32] Isetts BJ, Brummel AR, de Oliveira DR, Moen DW. Managing drug-related morbidity and mortality in the patient-centered medical home. *Medical care.* 2012;50(11):997-1001.
[33] Kilcup M, Schultz D, Carlson J, Wilson B. Postdischarge pharmacist medication reconciliation: impact on readmission rates and financial savings. *Journal of the American Pharmacists Association: JAPhA.* 2013;53(1):78-84.
[34] Ramalho de Oliveira D, Brummel AR, Miller DB. Medication therapy management: 10 years of experience in a large integrated health care system. *J Manag Care Pharm.* 2010;16(3):185-195.
[35] Shimp LA, Kucukarslan SN, Elder J, et al. Employer-based patient-centered medication therapy management program: evidence and recommendations for future programs. *J Am Pharm Assoc (2003).* 2012;52(6):768-776.
[36] Snider M, Carnes C, Grover J, Davis R, Kalbfleisch S. Cost-benefit and cost-savings analyses of antiarrhythmic medication monitoring. *Am J Health Syst Pharm.* 2012;69(18):1569-1573.
[37] Wittayanukorn S, Westrick SC, Hansen RA, et al. Evaluation of medication therapy management services for patients with cardiovascular disease in a self-insured employer health plan. *J Manag Care Pharm.* 2013;19(5):385-395.

Evidence Base – Alphabetical List of Research

Studies/Reports	Summary	Conclusions
Few Medicare Beneficiaries Receive Comprehensive Medication Review Services. Avalere Health Insights. Avalere Health, LLC. August 7, 2014.	Avalere health conducted an analysis of MTM and comprehensive medication review (CMR) participation based on CMS data that was recently made public. The resulting report indicates that half of beneficiaries eligible to receive MTM within the Medicare Part D population receive it and that less than 10% of Part D beneficiaries who take part in MTM receive a comprehensive medication review.	With proper incentives, PDPs may expand MTM services absent changes in MTM eligibility.
Analysis of Pharmacist-Provided Medication Therapy Management (MTM) Services in Community Pharmacies Over 7 Years. Barnett MJ, Frank J, Wehring H, et al. J Manag Care Pharm. 2009;15(1):18-31.	A comprehensive review of MTM programs in 47 states, representing 100,000 MTM claims identified the distribution of reasons for MTM services. The study identifies "Compliance-Underuse" of medication as representing approximately 12 percent of the overall reasons for MTM in 2006.	Medication adherence represents approximately 12% of all medication therapy management (MTM) claims.
Retrospective Analysis of Medication Adherence and Cost Following Medication Therapy Management. Branham A, Moose J, and Ferrari S. Innovation in Pharmacy. 2010;1(1):12.	A retrospective analysis of medication adherence, pre-post comparison study between 2007-2008 shows improved adherence and reduced medication costs as a result of MTM. Patients were adherent to chronic disease-state medication before and after MTM. Overall, change in mean adherence before and after MTM did not change significantly (0.87 and 0.88 respectively). However, patients taking medications for cholesterol management, GERD, thyroid and BPD demonstrated improved adherence following a CMR.	The average total chronic disease state medication costs for participants were reduced from $210.70 to $193.63 after the completion of Comprehensive Medication Reviews (CMRs).
Emergency hospitalizations for adverse drug events in older Americans. Budnitz, D. S., M. C. Lovegrove, N. Shehab, and C. L. Richards. 2011. N Engl J Med 365 (21):2002-12.	Based on adverse event data from 2007-2009, there were nearly an estimated 100,000 emergency hospitalizations for adverse drug events in elderly U.S. adults. Nearly half of these hospitalizations were among adults 80 years of age or older, and two thirds of hospitalizations were due to unintentional overdoses. Four medications or medication classes were implicated alone or in combination in 67.0% (95% CI, 60.0 to 74.1) of hospitalizations: warfarin (33.3%), insulins (13.9%), oral antiplatelet agents (13.3%), and oral hypoglycemic agents (10.7%). High-risk medications were implicated in only 1.2% (95% CI, 0.7 to 1.7) of hospitalizations.	Most emergency hospitalizations for recognized adverse drug events in older adults resulted from a few commonly used medications, and relatively few resulted from medications typically designated as high-risk or inappropriate.

Studies/Reports	Summary	Conclusions
The Asheville Project: clinical and economic outcomes of a community-based long-term medication therapy management program for hypertension and dyslipidemia. Bunting BA, Smith BH, and Sutherland SE. 2008. J Am Pharm Assoc (2003) 48 (1):23-31.	Sufficient data were available for 620 patients in the financial cohort and 565 patients in clinical cohort. Several indicators of cardiovascular health improved over the course of the study: mean systolic blood pressure, from 137.3 to 126.3 mm Hg; mean diastolic blood pressure, from 82.6 to 77.8 mm Hg; percentage of patients at blood pressure goal, from 40.2% to 67.4%; mean low-density lipoprotein (LDL) cholesterol, from 127.2 to 108.3 mg/dL; percentage of patients at LDL cholesterol goal, from 49.9% to 74.6%; mean total cholesterol, from 211.4 to 184.3 mg/dL; and mean serum triglycerides, from 192.8 to 154.4 mg/dL. Mean high-density lipoprotein (HDL) cholesterol decreased from 48 to 46.6 mg/dL. The CV event rate during the historical period, 77 per 1,000 person-years, declined by almost one-half (38 per 1,000 person-years) during the study period. Mean cost per CV event in the study period was $9,931, compared with $14,343 during the historical period. During the study period, CV medication use increased nearly threefold, but CV-related medical costs decreased by 46.5%. CV-related medical costs decreased from 30.6% of total health care costs to 19%. A 53% decrease in risk of a CV event and greater than 50% decrease in risk of a CV-related emergency department (ED)/hospital visit were also observed.	Patients with HTN and/or dyslipidemia who received long term MTM "achieved significant clinical improvements that were sustained for as long as 6 years, a significant increase in the use of CV medications, and a decrease in CV events and related medical costs.
The Asheville Project: long-term clinical, humanistic, and economic outcomes of a community-based medication program for asthma. Bunting BA, Cranor CW. Journal of the American Pharmacists Association. 2006. 46(2):133-147	The quasi-experimental, longitudinal study examined the outcomes associated with a community-based medication program for self-insured patients with asthma. The pharmacists involved with the follow-up were reimbursed for MTM services through the health plans. The program measured changes associated with asthma; severity, symptoms, etc., along with presence of an asthma plan, asthma-related hospital/emergency department events, and costs associated with asthma over time. As a result of the program, the subjective and objective measures of asthma control each improved. Emergency room visits decreased from 9.9% to 1.3% and hospitalizations decreased from 4.0% to 1.9%. Patients were 6 times less likely to be hospitalized after program interventions. While spending on asthma increased, the medical claims associated with asthma decreased and total asthma-related costs were significantly less than projected. Direct cost-savings were an average of $725 per patient per year and indirect cost-savings were an average of $1,230 per patient per year.	MTM and similar programs show the potential for cost-savings through decreased medical claims and hospital/emergency room admissions.

Studies/Reports	Summary	Conclusions
Iowa Medicaid Pharmaceutical Case Management Program. Chrischilles E, Carter B, Voelker M, et al. Report to the DHS Appropriations Subcommittee; March 5, 2003; Iowa.	Iowa Medicaid Pharmaceutical Case Management (PCM) Program was designed to benefit patients taking four or more medications and with a high risk of adverse drug effects. Important findings included that the eligible patients were at a very high risk of adverse drug effects, that the program improved medication safety significantly, and that charges including prescription drugs and Medicaid usage didn't increase. Specifically, PCM was associated with a 12.5% improvement in the Medication Appropriateness Index, and a reduction of inappropriate medications of 24%. There was an increase in health expenditures explained by the increase in drug costs. There were no differences in the number of active medications or charges to Medicaid between study arms after 9 months, and no difference in Medicaid institutional or medical charges even after accounting for $94,170 in program costs.	In cases where they do not accrue savings, MTM pilot and demonstration programs tend to show evidence of quality improvement.
Optimizing medication use with a pharmacist-provided comprehensive medication management service for patients with psychiatric disorders. Cobb CD. Pharmacotherapy. 2014 Dec; 34(12):1336-40.	A study of a pharmacist-led comprehensive medication management intervention showed that patients (n=154) with psychiatric disorders showed reduced drug costs, reduced inpatient admissions, and reduced ED visits, for an average savings of $586.55 per patient over the two-year study period. This resulted in an ROI of 2.8 after accounting for the cost of the services.	MTM services can be effective in reducing both drug and medical costs among psychiatric patients.
Comprehensive Medication Therapy Management: Identifying and Resolving Drug-Related Issues in a Community Pharmacy. Doucette WR, McDonough RP, Klepser D, and McCarthy R. Clinical Therapeutics. 2005;27(7):1104-1111.	A retrospective study which includes the review of 150 Medicaid patients in Iowa. A total of 886 drug-related issues were identified for MTM services and classified into 7 categories: inappropriate adherence (25.9%), needs additional therapy (22.0%), wrong drug (13.2%), unnecessary drug therapy (12.9%), adverse drug reaction (11.1%), dose too low (9.7%), and dose too high (5.3%). Overall, physicians accepted 313 (47.4%) of the 659 recommendations to alter drug therapy made by pharmacists, with the highest rates of agreement to stop or change a medication (50.3% and 50.0%, respectively) and the lowest rate of agreement to start a new medication (41.7%)	Inappropriate medication adherence represents approximately 26% of all drug-related issues leading to medication therapy management (MTM) claims.

Studies/Reports	Summary	Conclusions
Impact of adherence to antihypertensive agents on clinical outcomes and hospitalization costs. Dragomir A, Côté R, Roy L, Blais L, Lalonde L, Bérard A, Perreault S. Medical Care. 2010. 48(5):418-25.	Low antihypertensive medication adherence rates may contribute to higher healthcare costs. This study examines the relationship between low adherence rates to antihypertensive medications (defined as ≥80% or <80%) leading to cardiac outcomes and the healthcare costs related. Within a large cohort (59,647 patients with hypertension), patients with low adherence were more likely to have coronary disease (OR=1.07), cerebrovascular disease (OR=1.13) and chronic heart failure (OR=1.42) within the 3 year follow-up. An increase in cost of $3,574 per person within a 3 year period was involved with low medication adherence (hospitalization in low adherent patients).	There is an association with low medication adherence rates and an increase in healthcare costs.
Real-world impact of reminder packaging on antihypertensive treatment adherence and persistence. Dupclay L, Eaddy M, Jackson J, Raju A, Shim A. Patient preference and adherence. 2012;6:499-507.	Retrospective, propensity score-matched controlled study of reminder packaging among hypertensive patients. Reminder packaging resulted in statistically significant increases in various measures of medication adherence and persistence.	Reminder packaging is an effective method of improving medication adherence and persistence.
Medicaid Beneficiaries With Congestive Heart Failure: Association of Medication Adherence with Healthcare Use and Costs. Esposito D, Bagchi AD, Verdier JM, Bencio DS, Kim MS. American Journal of Managed Care. 2009. 15(7):437-45.	This study examined the association of medication adherence with healthcare use and costs among Medicaid beneficiaries with congestive heart failure (CHF) and to estimate the savings associated with improved medication adherence. Adherence rates were estimated using medication possession ratios (MPR). Adherent participants were hospitalized less (13%) and visited the emergency department less (10%). The total healthcare costs were 23% less per year ($5,910) for adherent participants compared to non-adherent participants. There was a gradient associated with medication adherence and medical costs. Participants with ≥95% adherence had 15% lower healthcare costs compared to participants with ≤80% adherence ($17,665 compared to $20,747).	Medication adherence is associated with healthcare costs. High medication adherence rates are associated with low healthcare costs.

Studies/Reports	Summary	Conclusions
The costs associated with adverse drug events among older adults in the ambulatory setting. Field TS, Gilman BH, Subramanian S, Fuller JC, Bates DW, Gurwitz JH. Med Care. 2005;43(12):1171-1176.	For all adverse drug events, the increase in postevent costs over the preevent period was $1310 (95% confidence interval [CI], $625-$1995) greater for those experiencing an adverse drug event than the comparison group after controlling for age, sex, comorbidity, number of scheduled medications, and having been hospitalized during the preevent period. For preventable adverse drug events, the adjusted increase was $1983 (95% CI, $193-$3773) greater for cases. Based on rates of adverse drug events and these cost estimates, 1000 older adults would have annual costs related to adverse drug events in the ambulatory setting of $65,631 with $27,365 of this associated with preventable events.	The annual cost of preventable ADEs for all Medicare enrollees aged 65 and older. The cost in 2000 per preventable ADE was estimated at $1,983, while national annual costs were estimated at $887 million.
Redefining the role of the pharmacist: medication therapy management. Hilsenrath P, Woelfel J, Shek A, Ordanza K. Journal of Rural Health. 2012. 28:425-430.	A study of 25 Medicaid patients (average age 6.6 years) enrolled in an asthma medication therapy management program led to a 76% decrease of ER visits (33 to 8) and a 33% reduction in hospitalization related to asthma (3 to 2). Due to the size and average age of subjects, this study has a lower applicability to Medicare beneficiaries.	MTM services can be effective in reducing cost of care in a pediatric population.
Preventing Medication Errors: an IOM Report. July 20, 2006. In Quality Chasm Series, edited by Philip Aspden, Julie A. Wolcott, J. Lyle Bootman and Linda R. Cronenwett. Washington, DC: Institute of Medicine.	The aim of this report is developing a national agenda for reducing medication errors-- of which approximately 25% are preventable--based on estimates of the incidence of such errors and evidence on the efficacy of various prevention strategies. In this report, the committee proposes an ambitious agenda for making the use of medications safer.	Medication errors are surprisingly common and costly; this report outlines a comprehensive approach to decreasing the prevalence of these errors. This requires that all stakeholders—patients, providers, payers, industry, and government, working together—commit to preventing medication errors.
Evaluating Effectiveness of the Minnesota Medication Therapy Management Care Program: Final Report. Isetts B. December 14, 2007.	The report is an analysis of the first year of the Medication Therapy Management Care Program in Minnesota. Pharmacists participating were responsible for identifying and resolving drug therapy problems and reimbursed at a flat rate for participation. Based on successful achievement of diabetes health benchmarks, the authors projected estimated savings on diabetes care. There was a slight increase in total health expenditures from pre to post-MTMS intervention with prescription drugs accounting for 24% of the increase.	MTM implementation costs may lead to additional increases in expenditures.

Studies/Reports	Summary	Conclusions
Managing Drug-Related Morbidity and Mortality in the Patient-Centered Medical Home. Isetts BJ, Brummel AR, Ramalho de Oliveira D, Moen DW. Medical Care 2012. 50(11):997-1001.	In 2008, Fairview Health Services implemented a 4-year care model innovation (CMI) initiative to decrease costs through medication therapy management and team-based care within the context of an accountable care organization. Over a span of 4 years, cost spending for the CMI groups increased less than the non-CMI groups. The median per member per month changed from $341 to $354 for the CMI clinics (3.7%), and changed from $366 to $420 in the non-CMI clinic (14.7%). The commercial insurance payer determined this provided sufficient information within the shared incentive agreement that the total cost of care rate of growth was decreasing. Estimates for savings were based only on claims and did not include additional figures for shared savings.	Even in collaborative care settings that offer greater cross-disciplinary care opportunities, there is room for improvement with regard to pharmaceutical management.
Adverse drug events after hospital discharge in older adults: types, severity, and involvement of Beers Criteria Medications. Kanaan, A. O., J. L. Donovan, N. P. Duchin, T. S. Field, J. Tjia, S. L. Cutrona, S. J. Gagne, L. Garber, P. Preusse, L. R. Harrold, and J. H. Gurwitz. 2013. J Am Geriatr Soc 61 (11):1894-9.	Based on discharges from the hospital between August 26, 2010, and December 27, 2010 of individuals aged 65 and older at time, cardiovascular medications, diuretics, opioids, and anticoagulants or antiplatelets were most commonly involved in preventable events. More than half of all ADEs occurred within the first 14 days after hospitalization.	ADEs are common and often preventable in older adults after hospital discharge, underscoring the need to address medication safety during this high-risk period in this vulnerable population.
Post-discharge Pharmacist Medication Reconciliation: Impact on Readmission Rates and Financial Savings. Kilcup M, Schultz D, Carlson J, Wilson B. Journal of the American Pharmacists Association. 2013. 53(1):78-84.	Group Health Cooperative operates 25 primary care medical centers and 5 specialty centers. Group Health followed patients at high risk for readmission. Intervention group consisted of patients who were contacted after discharge by a pharmacist to assess medication therapy and the control group consisted of those who were discharged without a follow-up phone call. The intervention group had lower readmission rates for certain time periods compared to the control group. At one week, the readmission rate for the intervention group was 0.8% compared to 4% for the control group, and at two weeks, the rates were 5% compared to 9 % respectively. Both differences were statistically significant. Based on average cost of admissions, the financial savings were estimated as $35,000 per 100 patients in the intervention group, which accumulates to a potential annual savings of $1.5 million.	MTM and similar interventions after hospital discharge may be especially beneficial for reducing re-hospitalizations and costs.

Studies/Reports	Summary	Conclusions
Reminder packaging for improving adherence to self-administered long-term medications. Mahtani KR, Heneghan CJ, Glasziou PP, Perera R. The Cochrane database of systematic reviews. 2011(9):CD005025.	Reminder packaging significantly decreased diastolic blood pressure and glycated haemoglobin levels. Reminder packaging was preferred by patients with low literacy.	Reminder packing may represent a simple method for improving adherence.
Hospital Admissions Resulting From Preventable Adverse Drug Reactions. McDonnell PJ, Jacobs MR. Annals of Pharmacotherapy. 2002. 36(9):1331-1336.	Adverse Drug Reactions (ADRs) lead to a large number of hospital admissions, and to the extent that ADRs are preventable, these admissions could be considered avoidable. This study assesses the degree to which ADRs encountered at a university hospital during an 11 month period led to hospitalization, and among those that did, it also assesses the individual ADR's causality, severity and preventability. The authors conclude that it was probable that roughly 35% of the ADRs led to hospital admission, and of these probable cases, 62% (96) were preventable. These preventable ADRs led to 595 inpatient days and an average patient stay of 6.1 days per ADR. The authors also assessed reasons for preventability and found that patient non-adherence was the reason for ADRs in a third of cases.	The majority of ADRs that result in hospitalization are preventable, and the frequency with which ADRs occur may diminish with better patient pharmaceutical management.
Measuring the Effects of Medication Adherence for the Medicare Population. MedPAC. In: Report to the Congress: Medicare and the Health Care Delivery System. Washington, DC: MedPAC; 2014:123-139.	This MedPAC report chapter profiles the results of a study MedPAC conducted that assesses the impact that medication adherence has on cost outcomes among Medicare beneficiaries with Congestive Heart Failure (CHF). The study's general finding is that better adherence leads to reduced costs, but the authors caution that this finding is heavily dependent on the way concepts used to estimate savings (e.g. adherence) are defined, the characteristics of the study population, and that adherent beneficiaries with CHF tend to be healthier prior to their diagnosis. The authors also note that the effects of improved adherence diminish over time: the estimation model used in the study notes clear differences in effect size (and sometimes direction) between months 1 to 6 and months 7 to 12.	Although findings indicate that generally, better adherence leads to lower medical costs within the Medicare population, this is dependent on a number of different considerations. As a result, interventions that increase adherence will not necessarily yield cost savings for all PDP plan populations.

Studies/Reports	Summary	Conclusions
Impact of a Patient-Centered Pharmacy Program and Intervention in a High-Risk Group. Moore JM, Shartle D, Faudskar L, Matlin OS, Brennan TA. Journal of Managed Care Pharmacy. 2013. 19(3):228–236.	This MTM pilot looked at a large sample population where the intervention group consisted of those invited and agreed to participate and control group consisted of those who were invited to participate, but declined. Operators measured the pre/post differences in total health care costs, inpatient visits, emergency room visits, total days' supply and medical possession ratios (MPR) for 5 conditions: diabetes, hypertension, dyslipidemia, depression, and asthma. Among the intervention group, plan-paid health care costs decreased by 10.3% or $97, compared to an increase of 0.7% or $6, in costs in the control group. Inpatient visits decreased by 18.6% in the intervention group and visits increased by 24.2% in the control group. Both groups showed decreases in ER visits, but differences were not statistically significant. Average days' supply increased by 72.7 over baseline in the intervention group and decreased by 111.1 days in the control group. The intervention group showed increased MPRs of 2.29% and 2.1% above baseline for hypertension and dyslipidemia, respectively, while the control group showed decreased MPRs of 2.31% and 2.61% for those conditions, respectively. MPRs did not change for asthma, diabetes, and depression. Program costs per patient were estimated at $478 with an ROI of 2.0 in 2009.	MTM has the potential to yield positive cost impacts through reductions in multiple types of care utilization. It also positively impacts medication possession.
Pharmacist Intervention to Improve Medication Adherence in Heart Failure: A Randomized Trial. Murray MD, Young J, Hoke S, et al. Annals of Internal Medicine. 2007. 146(10):714–725.	This article reports on a randomized controlled trial assessing the impact of a pharmacist intervention on medication adherence and other health outcomes for low-income patients with heart failure. The intervention consisted of a 9 month multi-level pharmacist intervention and 3 months of follow-up. A control group had initial contact with pharmacist, but no other pharmacist participation throughout the study. The trial measured medication adherence, total direct costs, quality of life, and participant satisfaction with pharmacy as outcomes. Medication adherence was higher in the intervention group (78.8% compared to 67.9% in the control). During the follow-up period, medication adherence was 70.6% in the intervention group and 66.7% in the control group. After accounting for the cost of implementation and development ($205 per patient), the intervention saved $2,960 per patient.	In general, MTM and similar pharmacist-led interventions can yield improvements in adherence and cost savings. Nevertheless, improvements in beneficiary adherence can vary based on a number of different factors and can be expected to diminish after the conclusion of any intervention.

Studies/Reports	Summary	Conclusions
Interventions for enhancing medication adherence. Nieuwlaat R, Wilczynski N, Navarro T, et al. The Cochrane database of systematic reviews. 2014;11:CD000011.	There is weak & inconsistent evidence from RCTs for improving clinical outcomes and adherence using interventions such as ongoing support from allied health professionals, such as pharmacists, intensive patient education, counseling support services including motivational interviewing or cognitive behavioral therapy, daily treatment support, and additional social support from family or peers.	Current methods of improving medication adherence for chronic health problems are complex so that the full benefits of treatment cannot be realized.
Effect of outpatient pharmacists' non-dispensing roles on patient outcomes and prescribing patterns. Nkansah N, Mostovetsky O, Yu C, et al. The Cochrane database of systematic reviews. 2010(7):CD000336.	Patients who received medication management from a pharmacist showed a significant improvement in systolic blood pressure as compared to those who received usual care from a physician. Pharmacist services reduced the incidence of therapeutic duplication and decreased the total number of medications prescribed. Pharmacist interventions resulted in improvement in most clinical outcomes, although these improvements were not always statistically significant.	The role of pharmacists in medication/therapeutic management resulted in better prescribing patterns by physicians, reduced total number of medications taken by patients, and improvement in most clinical outcomes, although these improvements were not always statistically significant, as well as improvement in patient quality of life outcomes.
Interventions to improve the appropriate use of polypharmacy for older people. Patterson S, Cadogan C, Kerse N, et al. Cochrane Database of Systematic Reviews 2014(10):CD008165.	The interventions included in this review demonstrated a reduction in inappropriate medication use. A mean difference of -6.78 (95%CI -12.34 to -1.22) in the change in Medication Appropriateness Index (MAI) score in favor of the intervention group (four studies). Postintervention pooled data (five studies) showed a mean reduction of -3.88 (95% CI -5.40 to -2.35) in the summated MAI score and a mean reduction of -0.06 (95% CI -0.16 to 0.04) in the number of drugs per patient (three studies). Evidence of the effect of the interventions on hospital admissions (four studies) was conflicting.	Most interventions were complex, multifaceted pharmaceutical care provided in a variety of settings, resulting in reduction in inappropriate medication use and ADEs reduced significantly (35%) post-intervention; however it is not clear if this always results in clinical improvements.

Studies/Reports	Summary	Conclusions
Medication Therapy Management in Chronically Ill Populations: Final Report. Perlroth D, Marrufo G, Montesinos A, et al. Prepared for CMS by Acumen, LLC and Westat; 2013.	This report covers an evaluation of MTM in chronically ill Medicare beneficiaries enrolled in stand-alone prescription drug plans (PDP) or managed care drug plans (M-PD). Results were compared to a similarly situated control population, and were compared separately for those who underwent CMR and those who did not. There was improved medication adherence for the targeted conditions (CHF, COPD, Diabetes), but less of an effect on non-targeted conditions. Adherence to evidence based medications were estimated to be approximately 11-40% higher for those with CHF, 11-26% higher for those with COPD, and 15-35% higher for those with diabetes, compared to the respective control populations. Decreased costs and hospital utilization were associated with CHF and Diabetes participants who underwent a CMR. All-cause hospitalization costs for diabetes participants who underwent a CMR were about $399 less, and for CHF participants were about $526 less than controls. Overall, the results also indicated that conducting MTM without a CMR was associated with increased in costs, but conducting it with a CMR was associated with decreases.	The impact MTM has on adherence, care utilization, and costs is dependent not only on patient and plan characteristics, but on what services plans provide as part of a MTM intervention. Effective MTM requires targeting the right patients with the right services.
The Pennsylvania Project: pharmacist intervention improved medication adherence and reduced health care costs. Pringle JL, Boyer A, Conklin MH, McCullough JW, Aldridge A. Health Affairs. 2014. 33(8):1444-52.	The Pennsylvania Project is a large-scaled community pharmacy study that evaluated a pharmacy based intervention and its impact on medication adherence within 5 chronic medication classes. An intervention group of 283 pharmacists (working for a national community pharmacy chain) screened 29,042 patients for low adherence risk and provided patients, with an elevated risk, brief consultations. The control group, of 295 pharmacists, screened 30,454 patients, but offered no guidance. The intervention group showed a significant increase in medication adherence and there was a significant decrease in health care spending per patient compared to the control group ($241 for patients taking statins, $341 in patients taking oral diabetes medications).	MTM with pharmacist intervention shows the potential for cost-savings through medication adherence.

Studies/Reports	Summary	Conclusions
Medication Therapy Management: 10 Years of Experience in a Large Integrated Health Care System. Ramalho de Oliveira, D, Brummel AR, Miller DB. Journal of Managed Care Pharmacy. 2010, 16(3):185–195.	This article reports on a retrospective study assessing the clinical, economic and humanistic outcomes of MTM in the past 10 years in the Fairview Health Services health care delivery system. The authors documented 9,068 patients with a total of 38,631 drug therapy problems identified and addressed by MTM pharmacists. The authors observed that the major drug therapy problem in this population was the underutilization of effective medications. Based on assumptions of reduced physician visits due to MTM, the pharmacist-estimated costs avoided savings was $2,913,850 ($86 per encounter) whereas the cost of MTM was $2,258,302 ($67 per encounter), for an estimated ROI of $1.29 per $1 spent in MTM costs. Actual healthcare costs for program participants were not examined.	In addition to healthcare savings, MTM programs may improve quality by supporting increased update of evidence-based regimens.
Medication Adherence Leads to Lower Health Care Use and Costs Despite Increased Drug Spending. Roebuck MC, Liberman JN, Gemmill-Toyama M, Brennan TA. Health Affairs. 2011. 30(1):91-99.	This article assesses the extent to which greater medication adherence directly leads to (causes) lower spending, specifically with respect to four conditions: congestive heart failure, hypertension, diabetes, and dyslipidemia. The authors find evidence that for all four conditions tracked, higher adherence led to increased drug spending that was more than offset by decreased medical costs. Combining pharmaceutical cost increases with medical cost decreases, the observed benefit-cost ratio for adherence was 8.4:1 for congestive heart failure, 10.1:1 for hypertension, 6.7:1 for diabetes, and 3.1:1 for dyslipidemia.	Greater medication adherence directly leads to lower health care use and costs, despite increases in pharmaceutical expenditures.
Interventions to improve safe and effective medicines use by consumers: an overview of systematic reviews. Ryan R, Santesso N, Lowe D, et al. Cochrane Database of Systematic Reviews. 2014(4):CD007768.	Promising interventions to improve adherence and other key medicines-use outcomes include: simplified dosing regimens with positive effects on adherence; interventions involving pharmacists in medicines management, such as medicines reviews (with positive effects on adherence and use, medicines problems and clinical outcomes) and pharmaceutical care services (consultation between pharmacist and patient to resolve medicines problems, develop a care plan and provide follow-up; with positive effects on adherence and knowledge).	Medication self-management programs appear to improve medicine use, adherence, and clinical outcomes and reduce adverse events and to reduce mortality in people self-managing antithrombotic therapy.

Studies/Reports	Summary	Conclusions
Practical approach to determining costs and frequency of adverse drug events in a healthcare network. Senst BL, Achuism LE, Genest RP, et al. American Journal of Health – System Pharmacy. 2001. 58(12):1126-32.	Adverse drug events (ADEs) were studied during a 53-day case-control study within a four-hospital integrated academic health network. ADEs were evaluated through random patient sampling, computerized flagging, and self-reporting. The results showed that 3.2% of hospital admissions were ADE-related, and the ADE rate during hospitalization was 4.2 events per 100 admissions. The cost involved with hospital admissions was $6,685 and the cost for ADEs during hospitalization was $2,162. Of hospital ADEs, 15% were considered preventable and as well as 76% of admission due to ADEs. The calculated annual cost of ADEs during hospitalization was $1.7 million and the cost of preventable ADEs was $260,000. The projected cost of preventable ADEs causing admissions was $3.8 million. An additional finding explained that 71% of serious medication errors occurred in the prescribing of medication stage.	ADEs in the hospital setting are associated with higher healthcare costs and a majority of the ADEs are preventable. The frequency with which ADEs occur may diminish with better provider pharmaceutical management.
Employer-Based Patient-Centered Medication Therapy Management Program: Evidence and Recommendations for Future Programs. Shimp LA, Kucukarslan S N, Elder J, et al. Journal of the American Pharmacists Association. 2012. 52(6): 768–776.	MHealthy Focus on Medicine (FOM) is a MTM intervention that the University of Michigan offered to all qualifying beneficiaries starting in 2007. This article describes FOM program specifics, eligibility, patient feedback and reasons for participation, and discusses program results, and their potential implications for other MTM interventions. Although FOM had a low participation rate, it was found that the majority of beneficiaries who chose to enroll in MTM were retirees, that their reasons for participation in MTM are quite diverse, and that those who chose to participate were satisfied with the program. FOM also yielded prescription drug savings for both individuals and the University, although not all savings estimates were statistically significant.	MTM has the potential to yield positive cost impacts for both payers and employers who sponsor coverage.
In Connecticut: Improving Patient Medication Management in Primary Care. Smith M, Giuliano MR, Starkowski MP. Health Affairs. 2011. 30(4): 646–654.	This article profiles a MTM intervention that was provided to a small number of patients with chronic conditions who receive primary care at a group of Federally Qualified Health Centers in Connecticut. The intervention differed from Part D MTM programs in that it was offered within the context of Patient-Centered Medical Home offering collaborative care, and all participating pharmacists had access to patients' electronic medical records to assist with patient counseling and recommendations. Through the intervention, pharmacists were able to resolve eighty percent of the drug therapy problems they identified, and after accounting for program costs, the program led to an estimated average reduction of $957 in per-patient per-year medical and drug spending.	MTM can lead to improved outcomes and cost savings even in care environments that already stress collaboration.

Studies/Reports	Summary	Conclusions
Cost-Benefit and Cost-Savings Analyses of Antiarrhythmic Medication Monitoring. Snider M, Carnes C, Grover J, et al. American Journal of Health-System Pharmacy. 2012. 69(18): 1569–1573.	The Electrophysiology Program (EP) at The Ohio State University Heart Hospital has offered an outpatient antiarrhythmic monitoring clinic run by pharmacists for a number of years. In the clinic, pharmacists provide cardiac medication-specific services to patients similar to those provided to Part D MTM beneficiaries. The authors of this article model the cost benefit of operating the clinic, and estimate cost savings generated. Under three profit models, results indicate that the clinic generates profit for the EP. The authors also conduct a crossover analysis among a small subset of patients and conclude that in addition to generating profit, the clinic saves the EP money compared to usual (physician) care, though the results were not statistically significant.	MTM and similar programs present a viable business case for the pharmacists who provide it, and for hospitals that provide testing needed to monitor pharmaceutical use.
Impact of Medication Adherence on Hospitalization Risk and Healthcare Cost. Sokol MC, McGuigan KA, Verbrugge RR, Epstein RS. Medical Care. 2005. 43(6):521-530.	This study attempts to quantify whether increased adherence leads to reduced medical care costs. More specifically, the authors examine adherence's impact on hospitalization risk and all-cause and disease specific medical and pharmaceutical costs for beneficiaries under the age of 65 with diabetes, hypertension, hypercholesterolemia, and congestive heart failure. Using claims from 1997-1999, they find that for all four conditions, hospitalization rates were significantly lower among high adherers than among other groups but that high adherence was only associated with lower disease related costs for diabetes and hypercholesterolemia. All-cause medical costs were reduced due to high adherence for patients with diabetes, hypercholesterolemia, and hypertension.	The effect that adherence has on medical costs varies by condition.
Pharmacoeconomic Outcomes of A Pharmacist-Led Medication Review Program. Steele S, Gates R. Presentation presented at: CMS 2012 Medicare Prescription Drug Benefit Symposium; March 20-21, 2012 Hunt Valley, MD.	This presentation profiles a pharmacist-led intervention offered to a small group of MAPD beneficiaries in California. The goals of the intervention included reducing drug costs for the plan and for beneficiaries, and reducing the number of beneficiaries who fell into the Part D "doughnut hole." In contrast to similar interventions, eligibility was restricted to beneficiaries taking targeted medications and who received care through a targeted primary care provider. Results of the study indicate that 57% of the drug change recommendations made were implemented and sustained, and that the largest category of changes made were therapeutic substitutions made for the purposes of cost reduction. Additionally, after factoring in program costs, the intervention led to $1797 in plan savings per participant and realized a ROI of 1100%. Beneficiaries themselves also realized substantial savings through copayment reductions.	Changing the allowable MTM targeting criteria under Part D may lead to plans changing their targeted MTM populations, and could lead to savings independent of other CMS efforts to realign MTM plan incentives.

Studies/Reports	Summary	Conclusions
Effect of an Intervention to Increase Statin Use in Medicare Members Who Qualified for a Medication Therapy Management Program. Stockl KM, Tjioe D, Gong S, Stroup J, Harada ASM, Lew HC. Journal of Managed Care Pharmacy. 2008 14(6):532–540.	Statin therapy has been shown to significantly lower the risk of cardiovascular events among patients with Diabetes and Cardiovascular Disease. In this study, PDP and MAPD beneficiaries with these two conditions who were not receiving Statin therapy were invited to take part in a MTM program. The study evaluated the likelihood of the beneficiary receiving Statin therapy, the number of MTM interventions that were required to prevent one major cardiovascular event, and the savings associated with avoiding this event. The likelihood of receiving Statin therapy increased for beneficiaries receiving MTM, and authors estimated that as a result, one major cardiovascular event was avoided for every 220 beneficiaries who received MTM, saving $12,323 per event. After factoring in the cost of the intervention, this still represented a cost savings.	MTM increases the likelihood that beneficiaries will receive beneficial drug therapies and can lead to fewer hospitalization events.
Increasing Medicare Part D Enrollment in Medication Therapy Management Could Improve Health and Lower Costs. Stuart BM, Loh E, Roberto P, Miller LM. Health Affairs. 2013. 32(7):1212-1220.	Research shows MTM can be associated with increased medication adherence, and that medication adherence can be associated with reduced costs. However, research on MTM has not assessed how changes in adherence due to MTM affect costs directly. This article shows how medication adherence within the PDP population impacts cost of care for beneficiaries with three chronic conditions. Overall findings indicate that within both the PDP and MTM-eligible population, lower adherence leads to greater average beneficiary medical costs. Findings also indicate that in most cases, beneficiaries who take prescribed medication on an episodic basis are more costly than those who take it on a consistently low basis, and that lack of adherence is more costly for beneficiaries eligible to receive MTM than among those who are not.	On an individual beneficiary level, increasing the percentage of currently eligible PDP beneficiaries who take part in MTM will yield greater savings than expanding MTM eligibility criteria.

Studies/Reports	Summary	Conclusions
Medication Therapy Management Interventions In Outpatient Settings (Comparative Effectiveness Review No. 14(15)-EHC037-EF). Viswanathan M, Kahwati, L, Golin C, et al. Rockville, MD: Agency for Healthcare Research and Quality. 2014.	This was a comparative effectiveness review of medication therapy management. The authors evaluated 44 studies (including 21 randomized controlled trials) and concluded that the evidence was insufficient on the effect of MTM on most outcomes. However they concluded that there was evidence for improvement for some measures of medication adherence and appropriateness, medication dosing, health plan expenditures on medication costs, and, for patients with diabetes, the proportion and costs of hospitalization. Reviewed studies frequently measured number of drug problems identified and number of drug problems resolved as primary outcomes. With further research, it will be important to find a better understanding of which MTM components are effective. While the studies were inconclusive on certain aspects of MTM, future research is needed to further assess the relationship MTM can have with various outcomes.	Although the literature contains some evidence for MTM effectiveness, many knowledge gaps currently exist. Therefore, the average strength of evidence must be considered when projecting cost savings from published estimates.
Medication Therapy Management Interventions in Outpatient Settings: A Systematic Review and Meta-analysis. Viswanathan M, Kahwati LC, Golin CE, et al. JAMA internal medicine. 2015;175(1):76-87.	MTM interventions improved medication appropriateness (4.9 vs 0.9 points on the medication appropriateness index, P < .001), adherence (approximately 4.6%), and percentage of patients achieving a threshold adherence level (odds ratios [ORs] ranged from 0.99 to 5.98) and reduced medication dosing (mean difference, -2.2 doses; 95% CI, -3.738 to -0.662). Medication therapy management interventions reduced health plan expenditures on medication costs. For patients with diabetes mellitus or heart failure, MTM interventions lowered the odds of hospitalization (diabetes: OR, 0.91 to 0.93 based on type of insurance; adjusted hazard rate for heart failure: 0.55; 95% CI, 0.39 to 0.77) and hospitalization costs (mean differences ranged from -$363.45 to -$398.98).	Medication therapy management interventions may reduce the frequency of some medication-related problems, including non-adherence, and lower some health care use and costs, but the evidence is insufficient to support its role in overall improvement in health outcomes.
Evaluation of Medication Therapy Management Services for Patients with Cardiovascular Disease in a Self-Insured Employer Health Plan. Wittayanukorn S, Westrick SC, Hansen R, et al. Journal of Managed Care Pharmacy. 2013. 19(5):385–395.	This study assessed the effect that MTM had on costs of care and clinical indicators among beneficiaries of a self-insured public university who had cardiovascular disease. In the study, patients who received MTM were matched with similar patients who did not, and intervention costs were also taken into consideration in the overall analysis. The study found that although MTM did not impact clinical indicators, it did have a significant impact on costs: over the course of the study both pharmaceutical and medical costs simultaneously lowered for the MTM group and raised for the match group. This represented a savings, even considering the cost of the intervention.	MTM has the potential to yield savings for self-insured employers as well as other groups.

Studies/Reports	Summary	Conclusions
A Randomized, Controlled Pragmatic Trial of Telephonic Medication Therapy Management to Reduce Hospitalization in Home Health Patients. Zillich AJ, Snyder ME, Frail CK, et al. Health Services Research. 2014. 49(5): 1537–1554.	This study assessed the effect of a telephone-based MTM intervention on the rate of preventable hospital admission among new Medicare Home Health patients. The MTM intervention consisted of a prescription verification phone call, a medication review, and at least one additional follow-up pharmacist call (within a subsequent 30 day period). In general, MTM did not significantly impact overall hospitalization, time to first hospitalization, or odds of unplanned hospitalization. However, patients in the lowest risk quartile who received MTM experienced significantly fewer hospitalizations and significantly increased their expected time to first hospitalization. The authors theorize that this may be because among home health patients, those in the lowest risk quartile have the highest functional capacity and require the least assistance. The study also found that among all patients, MTM led to the resolution of 90% of drug therapy problems.	The effectiveness of MTM may vary depending upon an individual's functional capacity and their ability to act upon recommendations.

If there are questions related to the Part D Enhanced MTM model, please visit our website at http://innovation.cms.gov/initiatives/enhancedmtm/ or email EnhancedMTM@cms.hhs.gov.