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Adherence to Medications to Treat Diabetes, Hypertension, and Hypercholesterolemia among Medicare Part D Beneficiaries

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Adherence to Medications to Treat Diabetes, Hypertension, and Hypercholesterolemia among Medicare Part D Beneficiaries

A dissertation submitted in partial satisfaction of the requirements for the degree of Doctor in Philosophy in Public Health (Epidemiology)

by

Richard Scott Leslie

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2015
The Dissertation of Richard Scott Leslie is approved and it is acceptable in quality and form for publication on microfilm and electronically:

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University of California, San Diego, 2015

San Diego State University, 2015

Chair
DEDICATION

This dissertation is dedicated to my family (parents, wife and children) for always supporting my academic pursuits throughout my life. All of whom demonstrated encouragement and patience during years of coursework, studying for exams and completing this dissertation.
EPIGRAPH

“Increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments”

Haynes RB. Interventions for helping patients to follow prescriptions for medications. Cochrane Database of Systematic Reviews, 2001.
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<tr>
<td>ANOVA</td>
<td>Analysis of Covariance</td>
</tr>
<tr>
<td>CHOL</td>
<td>Cholesterol</td>
</tr>
<tr>
<td>CMS</td>
<td>Center for Medicare and Medicaid Services</td>
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<tr>
<td>DID</td>
<td>Difference in Difference</td>
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<tr>
<td>DM</td>
<td>Diabetes</td>
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<td>HTN</td>
<td>Hypertension</td>
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<tr>
<td>MA-PD</td>
<td>Medicare Advantage Prescription Drug</td>
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<tr>
<td>MCC</td>
<td>Multiple Chronic Conditions</td>
</tr>
<tr>
<td>NCQA</td>
<td>National Committee of Quality Assurance</td>
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<tr>
<td>OR</td>
<td>Odds Ratio</td>
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<tr>
<td>PDP</td>
<td>Prescription Drug Plan</td>
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<tr>
<td>PQA</td>
<td>Pharmacy Quality Alliance</td>
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<td>URAC</td>
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Chapter 2, in full, has been published of the materials as it may appear. Leslie RS, Tirado B, Patel BV, Rein PJ. Evaluation of an Integrated Adherence Program Aimed to Increase Medicare Part D Star Rating Measures. Journal of Managed Care & Specialty Pharmacy. 2014;20(12):1193-1203. The dissertation author was the primary investigator and author of this paper.
Chapter 3, in full, is currently being prepared for submission for publication of the materials as it may appear. Leslie RS, Gilmer TJ. Natarajan L, Hovell M. A Multi-Channel Medication Adherence Intervention Influences Patient and Prescriber Behavior. The dissertation author was the primary investigator and author of this paper.

Chapter 4 is currently being prepared for submission for publication of the materials as it may appear. Leslie RS, Hovell MF. Measuring Adherence to Maintenance Medications among Older Adults: A Critical Review. The dissertation author was the primary investigator and author of this paper of this material.
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ABSTRACT OF THE DISSERTATION

Adherence to Medications to Treat Diabetes, Hypertension, and Hypercholesterolemia among Medicare Part D Beneficiaries

by

Richard Scott Leslie

Doctor of Philosophy in Public Health (Epidemiology)

University of California, San Diego, 2015
San Diego State University, 2015

Professor Todd Gilmer, Chair

Background: Poor adherence to medication is associated with significant increased morbidity, mortality and health care utilization. Older adults are more vulnerable to medication nonadherence because this population utilizes more medications and has lower health literacy rates than younger adults. The purpose of this dissertation is to examine adherence to pharmacologic therapies used to treat diabetes, hypertension, and hyperlipidemia among Medicare Part D beneficiaries. Specific objectives are 1) to evaluate the effectiveness of a coordinated patient-directed medication adherence
intervention on adherence rates and a Medicare-Advantage Prescription Drug (MAPD) plan’s CMS Part D star ratings, 2) to assess the impact of a quasi-experimental multi-channel adherence intervention on beneficiaries’ medication adherence and health plan quality performance measures among two MAPD plans, and 3) to critically review recently published adherence interventions with specific focus on measurement methods and theoretical fidelity.

Methods: To address the first two objectives, two quasi-experimental interventions (a daily prescriber-directed 90-day program and a patient-directed counseling program), were assessed by using pharmacy claims and member eligibility data. Pre-post changes in adherence were adjusted for demographics, comorbid conditions and secular adherence trends. To address the remaining objective, articles of adherence interventions in the past five years identified by a systematic review were examined and scored based on quality of measurement method and use of a behavioral theoretical framework.

Results: For the patient-directed intervention, pre-post adherence rates increased an average 20.7 percentage points ($P < .001$). For the prescriber-directed program, adherence for the intervention group increased 2.0 ($P < .001$) and 1.8 percentage points ($P < .001$) for antihypertensives and antihyperlipidemics, respectively, relative to control. In both interventions, naïve to treatment and younger age were risk factors for nonadherence. Subjective indirect measurement methods (e.g., self-reports and electronic monitoring) are mostly used in randomized clinical trials whereas objective indirect methods (e.g., pharmacy claims) are employed in observational studies. Few interventions identified a behavioral model.
Conclusions: Large scale interventions may offer an effective approach for health plans to address common adherence barriers and improve both adherence and quality performance ratings. Future clinical trials addressing medication adherence should incorporate theoretical frameworks to address the complexity of medication use behavior.
CHAPTER 1

BACKGROUND AND RESEARCH OBJECTIVES
Poor adherence to medication continues to be a worldwide problem despite decades of research, numerous multi-modal interventions and nationwide promotional campaigns.\textsuperscript{1,2,3} Nearly one-third of all prescriptions are never filled and 25\% of filled prescriptions are followed incorrectly.\textsuperscript{4} The World Health Organization (WHO) estimates adherence to long-term pharmacotherapy for chronic diseases at 50\% in developed countries.\textsuperscript{5} Specific to antihypertensive therapy, 16\% to 50\% of patients new to therapy discontinue within the first year of treatment\textsuperscript{6} and rates of discontinuation vary between 50\% and 70\%.\textsuperscript{7} Despite large associations between adherence and glycemic control, adherence to oral antidiabetics in two longitudinal cohort studies of elderly patients was reported to average 75\%\textsuperscript{8} and be as low as 65\%.\textsuperscript{9} Within medications to treat cardiovascular disease, a cohort study found only 40\% of participants continued therapy within 2 years after a hospitalization for acute coronary syndrome and adherence rates were 25.4\% in those participants with coronary artery disease but not hospitalized.\textsuperscript{10} A systematic review and meta-analysis of 67 observational studies assessing statin medication adherence concluded that only 49.0\% of patients were considered adherent after 1-year of follow-up.\textsuperscript{11}

Cost estimates due to nonadherence are estimated at $177 billion per year.\textsuperscript{12} Poor adherence and discontinuation of therapy leads to increased frequency and severity of disease symptoms and is associated with decreased quality of life, unnecessary progression of disease, poor outcomes and increased medical utilization.\textsuperscript{4,13,14,15} Nonadherence to statin therapy has been associated with 12\%-15\% increased mortality in patients with a history of myocardial infarction hospitalizations.\textsuperscript{16} Additionally, poor statin adherence was associated with higher cholesterol (17.23 mg/dl) in nonadherent
participants of a cohort study of Medicare beneficiaries. Specific to cardioprotective medications, nonadherence has been linked with 10% to 40% relative increases in cardiovascular hospitalizations and 50% to 80% relative increase in mortality risk. Associations between poor adherence and poor outcomes are especially pertinent to elderly populations because two of three elders are now estimated to have two or more chronic physical or behavioral health conditions. The burden of nonadherence is projected to rise with the expected increase in rates of chronic disease and longer life expectancy.

Barriers to medication adherence include, but are not limited to, cost, forgetfulness, motivation, health literacy, religion, self-efficacy, provider relationships and severity of side effects. The WHO categorizes possible reasons for nonadherence into 5 groups; 1) patient-related, 2) disease condition, 3) health system-related, 4) therapy-related and 5) social-economic. These factors involve several interactions between the patient, provider and health system therefore interventions aimed at improving adherence are multifactorial. Systematic reviews and meta-analyses report patient self-efficacy, patient-provider relationships, and belief in medication as key moderators for success. Additional systematic reviews and meta-analyses emphasize the need for interventions to identify and follow a specified behavioral theory.

Interventions to improve adherence in populations affected by hypertension, hypercholesterolemia and diabetes have used a variety of techniques (educational programs, patient interviewing, motivational strategies, monitoring and feedback) to influence the multiple contributors (patient, provider, pharmacist, family members) of
medication adherence.\textsuperscript{3,23,25} Empirical evidence demonstrate short-term (less than one year) effectiveness of adherence interventions; however, study of long-term effectiveness is warranted to address chronic nature of these disease conditions. Behavioral interventions demonstrating the most success have been conducted in patients with AIDS, asthma or rheumatoid arthritis where symptoms and disease progress rapidly when not taking medication.\textsuperscript{26,27} In disease conditions that are relatively asymptomatic in nature, such as hypertension, hypercholesterolemia, and diabetes, it is hypothesized that a main contributor to nonadherence is the lack of perceived benefit when one consumes medication.\textsuperscript{16,22}

Heightened awareness of nonadherence has led national organizations to implement campaigns to inform providers and the public on the significance of adhering to prescribed medication.\textsuperscript{28} In 2008, the National Consumers League launched “Script Your Future”, a multi-year public education effort, which focuses on diabetes, respiratory disease, and cardiovascular disease.\textsuperscript{2} In 2011, the Department of Health and Human Services announced the Million Hearts Initiative which aims to prevent 1 million cardiovascular events within the next 5 years.\textsuperscript{29} Two of the four indicators used to achieve the initiative’s goal are blood pressure control and cholesterol management.

Medication adherence is vital to both these indicators.

\textit{Federal Policy Perspective}

The Centers for Medicare and Medicaid Services (CMS) developed the Medicare Plan Quality Star Ratings Program to evaluate quality performance and allow beneficiaries to compare cost and quality of available Medicare Advantage Prescription
Drug (MAPD) plans and Prescription Drug Plans (PDPs). Each year Medicare Part D plans with 500 beneficiaries or greater receive an overall “Star Rating” which is a weighted average of a Part C domain summary rating (33 performance measures) and a Part D domain summary rating (13 measures). Star Ratings are released on Medicare’s Plan Finder website each October before Medicare’s annual open enrollment period and are linked with increased enrollment and Medicare reimbursements. Of the 18 total 2013 Part D domain measures, the three Patient Safety measures; Medication Adherence for Oral Diabetes Medications (D16), Medication Adherence for Hypertension (D17), and Medication Adherence for Cholesterol (D18) carry triple the weight of other process measures and therefore contribute 11.7% of a plan’s overall Star Rating and 31% of its Part D rating.⁴⁰

In November 2010, CMS implemented a demonstration project in provision with the 2010 Patient Protection and Affordable Care Act that tied quality bonus payments to overall Star Ratings as incentives promote quality among Medicare Part D contracts. Health plans receiving ratings of 3 or more stars (1 = lowest and 5 = highest ranking) are eligible to receive a 5% bonus payment per year, a potential multi-million dollar payment that is based contract benchmark payment methodology.⁴¹ The highest rated plans (5 Stars) are able to enroll members outside of the customary enrollment period (Oct 15 - Dec.7) and receive a “high performing icon” on the Medicare Plan Finder website used by beneficiaries to research plan offerings.

Adherence Interventions among Medicare Part D Beneficiaries
As a way to improve medication adherence and quality performance ratings, MA-PDs and PDPs have implemented adherence interventions. These interventions vary by mode of delivery (e.g., mail, phone, in-person, etc.), frequency of administration and target audience (e.g., patient or provider). Published findings of randomized controlled trials provide evidence of intervention effectiveness among small, select populations\textsuperscript{32,33} and quasi-experimental studies have demonstrated usefulness of pharmacy-based interventions limited to populations utilizing select pharmacies\textsuperscript{34} or intervention among members enrolled in Medication Therapy Management programs\textsuperscript{35}; however, there is insufficient research describing effects of adherence interventions targeting chronic medications applied to entire health plan populations. Evidence of population-level adherence interventions within usual, routine clinical care settings can guide pharmacy directors and managed care professionals on possible methods to increase medication adherence within entire memberships.

Definition of Medication Adherence

The World Health Organization defined adherence in general terms as, “the extent to which a person's behavior - taking medication, following a diet, and/or executing lifestyle changes - corresponds with agreed recommendations from a health care provider”.\textsuperscript{5} One limitation of this definition is that it assumes an agreement between patient and provider when most studies are not able to determine whether such an agreement has ever occurred. More specific to medication use, the special interest group of the International Society of Pharmacoeconomics and Outcomes Research in 2007
defined adherence as “the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen”.36

Measurement of Medication Adherence

Adherence measurement methods are commonly grouped as objective or subjective and direct or indirect. Subjective methods include validated self-reporting tools (e.g., Morisky scale), non-validated self-report tools (e.g., patient interview) and pill counts. Objective, indirect methods include electronic medication event monitoring systems and pharmacy claims. Medication adherence in large populations is most often measured using pharmacy claims because administrative records are readily available and recorded daily. The most common technique using pharmacy claims identifies patients within a specified time period and calculates the Proportion of Days Covered (PDC) by medication over a cross-sectional review period (usually one-year).37 First introduced in 2002, PDC is now used in quality improvement initiatives by national organizations such as National Quality Forum (NQF), Pharmacy Quality Alliance (PQA) and NCQA. CMS uses PDC as their method of choice when evaluating health plan performance as part of the Medicare Part D Star Ratings program.

Specific calculation of PDC uses fill dates and days’ supply of pharmacy claims to calculate the number of days a patient is covered by medication over a review period. According to CMS technical specifications, a patient’s review period is the number of days from treatment initiation (index date) to end of a measurement period or disenrollment. PDC is a continuous variable ranging from 1–100%, but adherence reporting uses thresholds to categorize patients as “adherent”. Although little literature
supports the use of one fixed threshold, the mostly widely used threshold is 80% for maintenance medications. Adherence rates for populations can be estimated using patients’ adherence rates. CMS uses a member-years adjustment for calculating adherence rates for health plans. Member-years is the time a member is enrolled in a measurement year and the health plan rate is a summation of member-years for adherent patients divided by the summation of member-years for all patients.

Figure 1.1 presents a patient’s medication fill pattern over a 1-year review period. PDC is measured from first claim in the measurement period (index date) to end of the measurement period or member disenrollment. Days of medication coverage is calculated using fill dates and day supply elements of prescription claims within each member’s measurement period. In this example a patient had 11 refills, all of which are 30 days of supply, and the PDC is 90.1% (320 days covered by medication / 355 review days). Patients commonly refill medications before exhausting their current fill as seen in claim 7 of this example. In circumstances when days’ supply of two claims overlap, the latter refill claim is shifted forward by the number of overlapping days to account for medication completion before next refill. Conversely, prescription claims that extended beyond the follow-up period are truncated in order to prevent overestimating medication adherence.

Another common measure related to medication behavior is persistence which is defined as, “the duration of time from initiation to discontinuation of therapy”. Persistence is generally expressed in days on therapy versus a percentage. In light of this, both measures are highly, positively correlated with one another. The key advantage of PDC over other adherence methods, e.g. Medication Possession Ratio (MPR), is the
measurement of medication coverage for each day during a period of time. Knowledge of daily medication coverage not only determines the exact days of coverage but allows for accurate measurement of gaps in therapy which are used in calculating persistence for many NCQA HEDIS measures. Additionally, PDC is advantageous when assessing patient’s medication adherence to multiple medications. Daily medication coverage can be estimated to show when and how often patients are covered by both medications at the same time.  

This is useful for therapy regimens that benefit most from concomitant use (e.g., diabetes medications with statin). Figure 1.2 describes how PDC can measure and report adherence for individual therapies A and B (both are 67%) and adherence to both therapies simultaneously (40%).

**Conceptual Model and Research Objectives**

Figure 1.3 is a conceptual model of medication adherence to chronic therapies based on frameworks outlined by the WHO adherence group. The timeline at the bottom of the model depicts the act of initializing therapy or receiving first fill of medication (“primary adherence”) followed by subsequent refilling of medication over a prescribed period (“adherence”). During the treatment period patients have numerous interactions with health care professionals (e.g., pharmacists and doctors) and medication use behavior can discontinue at any time due to a multitude of reasons. These reasons can be influenced by macro-level contingencies, such as health care policies and collective societal perceptions of medication consumption, or micro contingencies, such as patients’ environments and those involved in patients’ everyday routines. Incorporating the Principles of Behavior, positive experiences after consuming medication can be
positively reinforcing. Likewise, poor experiences can be punishing and result in discontinuation of therapy. Adhering to medications is positively associated with health outcomes and hence this model describes long-term outcomes as reliant on the latency periods of diabetes, hypertension and hyperlipidemia.

Extending the WHO classification criteria, factors affecting adherence can be grouped further as modifiable (e.g., access, out of pocket costs) and non-modifiable (e.g., age, sex). This dissertation evaluates interventions that address modifiable factors by 1) improving patient access to medications via increased supply and provider education, 2) educating providers of 90-day pharmacy benefits, 3) addressing patients’ forgetfulness via refill reminders, and 4) counseling patients on barriers to medication adherence. The purpose of this dissertation is to examine adherence to pharmacologic therapies used to treat diabetes, hypertension, and hyperlipidemia among Medicare Part D beneficiaries. The specific objectives are,

1) To evaluate the effectiveness of a coordinated patient-directed medication adherence intervention on a Medicare-Advantage Prescription Drug plan’s adherence rates and CMS Part D star ratings.

2) To assess the impact of a quasi-experimental multi-channel adherence intervention on beneficiaries’ adherence and health plan quality performance measures among two Medicare-Advantage Prescription Drug plans.

3) To critically review recently published adherence interventions with specific focus on measurement methods and operational and theoretical fidelity.
Figure 1.1: Prescription Fill Pattern and Medication Coverage
Figure 1.2: Proportion of Days Covered for Concomitant Therapy
Figure 1.3: Conceptual Framework of Medication Adherence to Long-term Therapies
References


CHAPTER 2

EVALUATION OF AN INTEGRATED ADHERENCE PROGRAM AIMED TO INCREASE MEDICARE PART D STAR RATING MEASURES
Abstract

**Background:** The Centers for Medicare and Medicaid Services (CMS) Plan Quality and Performance Program, or Star Ratings Program, allows Medicare beneficiaries to compare quality of care among available Medicare Advantage Prescription Drug plans (MAPDs) and stand-alone Prescription Drug Plans (PDPs). Health plans have increased intervention efforts and applied existing care management infrastructure as an approach to improving member medication adherence and subsequent Part D Star Rating performance. Independent Care Health Plan (iCare), a MAPD plan, MedImpact Healthcare Systems, Inc. (MedImpact) a pharmacy benefits manager, and US MED, a mail order pharmacy, partnered to engage and enroll iCare’s dual-eligible special needs population in an intervention designed to improve patient medication adherence and health plan performance for three Part D Patient Safety outcome measures: Medication Adherence for Oral Diabetes Medications (ODM), Medication Adherence for Hypertension (HTN) and Medication Adherence for Cholesterol (CHOL).

**Objectives:** To (a) assess the effectiveness of a coordinated member-directed medication adherence intervention and (b) determine the overall impact of the intervention on adherence rates and CMS Part D Star Rating adherence measures.

**Methods:** Administrative pharmacy claims and health plan eligibility data from MedImpact’s databases were used to identify members using three target medication classes. Adherence was estimated by the proportion of days covered (PDC) for all members. Those members considered at high-risk for nonadherence were prioritized for care management services. Risk factors were based on members’ use of more than one target medication class, newly started therapy, and suboptimal adherence (PDC<80%) in
the most recent 6-month period. Data files listing member adherence rates and contact information were formatted and loaded monthly into iCare’s care management system that triggered an alert for care coordinators to counsel members on the importance of adherence and offer the member an option for monthly 30-day supply medication delivery via US MED. Member adherence rates were calculated 9 months pre- and post-implementation for all members and adjusted by length of member enrollment based on CMS technical specifications. Regression analysis assessed pre-post changes in rates by intervention group, a) members receiving iCare counseling only (iCare-only), and b) members receiving counseling and medication delivery (iCare+US MED). To evaluate the overall impact of the intervention, iCare’s adherence rates and iCare’s measure-specific Star Ratings for the 2011 and 2012 calendar years (CMS measurement years) were compared to both the national MAPD contract average and to a health plan similar in member characteristics but without adherence intervention exposure.

**Results:** A total 2,700 members were initially targeted for referral to iCare care management and US MED customer service specialist teams. Between April 2012 (implementation date) and January 2013, a total 1,302 (48.2%) members enrolled in the US MED component of the intervention. Seventy-six percent of identified members were non-adherent (PDC < 80%) to one of the three target medication classes and 32% of members were non-adherent to more than one target medication class. Pre-post absolute average adherence rates increased for both the iCare-only group (ODM=15.1, HTN=10.1, CHOL=13.6) and the iCare-US MED group (ODM=30.9, HTN=25.5, CHOL=29.4). From 2011 to 2012, iCare adherence rates increased by absolute differences of 15.2, 9.2 and 10.1 percentage points for diabetes, hypertension, and cholesterol measures.
respectively, compared to the average MAPD contract differences (1.1, 2.1 and 2.5) and the comparator health plan differences (-2.7, -1.4, -4.1). Increases in iCare’s adherence rates were associated with significant increases in iCare’s 2014 adherence measure Star Ratings (1 Star to 3 Stars for ODM and CHOL, 1 Star to 2 Stars for HTN) which contributed to increases in the Drug Plan Quality Improvement measure (2 Stars to 4 Stars) and iCare’s overall Part D Star Rating (3 to 3.5 Stars).

**Conclusions:** Members in this MAPD dual-eligible population benefited from multiple points of contact to achieve increased adherence. Health plans can use network pharmacies, care management staff, and their pharmacy benefits manager to collaborate and implement interventions aimed to improve members’ adherence to targeted maintenance medications and overall health plan quality performance and Star Ratings.

**What is already known about this subject**

- National agencies, such as Centers for Medicare and Medicaid Services, Pharmacy Quality Alliance, National Committee for Quality Assurance, National Quality Forum and URAC (formerly named as the Utilization Review Accreditation Commission) recognize nonadherence as a prevalent public health problem.
- Medicare plans continue to search for effective and novel approaches to improve quality of care and performance in CMS Star Ratings.
- Little research demonstrates effectiveness of quasi-experimental adherence interventions.
• Special Needs Plans (SNPs) experience lower adherence rates and lower Star Ratings than other MAPD plans. Enrolling a special needs population in health care behavior interventions can be challenging.

What this study adds

• An integrated and targeted intervention can drive positive changes in medication adherence patterns and CMS Star Ratings.
• Results show a persistent intervention increased a plan’s Star Ratings for the three medication adherence Patient Safety measures by 2 Stars (Diabetes Medications and Cholesterol) and 1 Star (Hypertension).
• Partnerships between health plans, pharmacy benefits managers, and network pharmacies can effectively engage members of SNPs to improve adherence to maintenance medications.

Background

Medication nonadherence continues to be a pandemic problem despite decades of exploratory research, multi-modal interventions and nationwide promotional campaigns.1,2,3,4 Among Medicare Part D beneficiaries, the Centers for Medicare and Medicaid Services (CMS) reported 2012 adherence rates to medication classes used to treat three highly prevalent disease conditions (diabetes, hypertension and hyperlipidemia) as significantly lower (75%, 77% and 71%, respectively) than the most commonly recommended and published adherence threshold of 80%.5 For beneficiaries
receiving low income subsidy (LIS), adherence rates are five to seven percentage points lower compared to non-LIS beneficiaries.\textsuperscript{6}

The consequences of poor adherence include unnecessary morbidity and mortality, lost quality of life, increased medical utilization and poor health outcomes.\textsuperscript{1,2,7,13} Health care costs attributable to sub-optimal adherence are estimated at $177 billion per year.\textsuperscript{2} Several national organizations committed to improving quality of care, namely Centers for Medicare and Medicaid Services (CMS), National Committee for Quality Assurance (NCQA), Pharmacy Quality Alliance (PQA), and National Quality Forum (NQF), recognize poor adherence as a major public health problem. The CMS Plan Quality and Performance Program, or Star Ratings Program, which measures health plan performance and allows members to compare the quality of available Medicare Advantage Prescription Drug plans (MAPDs) and stand-alone Prescription Drug Plans (PDPs), increased the weighting of three Part D Patient Safety medication adherence measures (Medication Adherence for Oral Diabetes Medications, Medication Adherence for Hypertension, and Medication Adherence for Cholesterol) to three times that of other Part D measures.\textsuperscript{14} For the 2014 Plan Star Ratings, these three Part D measures contributed to approximately 11\% of a MAPD contract’s overall Star Rating and 32\% of the Part D Star Rating.\textsuperscript{14}

As an approach to improving medication adherence and subsequently Star Ratings, many Medicare plans have increased the use of broad member-directed or provider-directed interventions. Independent Care Health Plan (iCare), a MAPD plan with a dual-eligible special needs population, received the lowest Star Rating (1 Star) for each of the three adherence Patient Safety measures for both the 2010 and 2011
performance measurement years, which represent the 2012 and 2013 Plan Ratings respectively. The demographic make-up of iCare includes members that are often transient, receive low-income subsidies and may be affected by mental illness and substance addiction. These issues present many challenges with contacting and counseling members about medication adherence. Previous intervention attempts directed at prescribers to inform them of potential member nonadherence issues were not comprehensive and demonstrated little effectiveness. Therefore, MedImpact Healthcare Systems, Inc., a pharmacy benefit manager, iCare and US MED, a mail order pharmacy, collaborated to design a member-directed adherence intervention aimed to improve quality of care, member adherence and plan performance for the three medication adherence Part D Patient Safety measures. The purpose of this research was to assess the effectiveness of this member-directed intervention by measuring changes in members’ adherence rates and iCare’s Star Ratings.

Methods

Study Design and Study Population

This research is a retrospective analysis of a quasi-experimental intervention using the administrative pharmacy claims and health plan eligibility data from the MedImpact research database. The study population comprised of enrolled members of iCare, a dual-eligible Special Needs Plan (SNP) based in southeast Wisconsin (mainly Milwaukee metropolitan area), during the calendar years of 2011, 2012, and 2013. Members 18 years of age and older with at least one pharmacy claim for one of three target medication classes between October 2011 and March 2012 were identified for the
intervention beginning April 2012 (Figure 1). Subsequent monthly queries of pharmacy
claims using similar inclusion criteria identified additional members for intervention
during the remaining months of 2012. Members were categorized as iCare-only enrollees
or iCare+USMED enrollees based on their participation in the US MED component of
the intervention. Medication adherence to the three medication classes was measured 9-
months pre and post implementation for all members and stratified by participation
calendar years (CMS measurement periods) were used to evaluate the intervention effects
on iCare’s Star Ratings.

**Intervention**

This coordinated medication adherence intervention used existing care
management infrastructure to create a member-focused program for members utilizing
medications in the three CMS targeted therapeutic classes. Starting in April of 2012,
monthly analyses of pharmacy claims data over 6-month review periods were used to
identify members who were non-adherent to therapy as calculated by the proportion of
days covered (PDC < 80%). Data files containing member contact and demographic
information (e.g., phone, address, age, gender), provider and pharmacy contact
information (e.g., name, phone), calculated adherence rates, known risk factors for
nonadherence (such as non-adherent to more than one targeted medication class and
therapy-naïve), were prepared and loaded into the care management system used by
iCare, called TruCare™. Approximately 29 care managers and care coordinators from
iCare’s care management department received monthly alerts presented in the form of a
“task” that triggered them to call their members to address medication nonadherence and review recent prescription fill history. Care coordinators and managers, most of who were experienced in human and social services, were trained on the importance of medication adherence and common reasons for nonadherence. Calls permitted an open conversation between the care coordinator/care manager and iCare member. No particular call script was followed; however, a typical question after review of the member’s pharmacy fill history would be “I see you have not filled your high blood pressure medicine in a while – do you still take that medicine?” If the member indicated that he/she is currently taking the medication, follow-up questions could be “How often do you forget to take your medicine?” or “Do you have trouble getting to the pharmacy to get your medicine?” All members were also provided an option for monthly scheduled, auto home delivery of 30-day supply for target medications provided by US MED. In addition, members interested in this option were referred to US MED and received customized outbound calls from US MED Pharmacy’s customer service specialists. Members opting into the home delivery program (iCare+US MED group) received enrollment materials consisting of a co-branded introductory letter from the health plan and pharmacy, a printed application, and a US MED Welcome Guide. A web-based tool allowed real-time communication between iCare’s care management team and the pharmacy’s customer service team to facilitate member enrollment and update member contact information. Members contact information was verified and corrected by the care management teams, physician office visits, online databases, and the National Change of Address database in order to maintain member enrollment. The US MED team sent weekly emails to iCare care management staff to inform the care management team about
any difficulties obtaining new prescriptions (e.g., member needing an appointment or incorrect prescriber information provided). Satisfaction surveys were provided to enrollees throughout 2012 and members could opt-out of the program at any time. Survey questions used a 5-point Likert-type scale to ask members to rank their overall satisfaction with the pharmacy, satisfaction with friendliness and professionalism of the pharmacy contact person, likelihood to use the pharmacy in the future, and likelihood of referring friends and family. Members not enrolling in the US MED component (iCare-only group) were called monthly and those contacted were counseled by the iCare care management team. Each month member and medication adherence data files were sent to iCare to identify new members for intervention and to update existing members’ adherence rates for continued counseling. The care management team’s goal was to contact all members identified as nonadherent (~ 900 tasks per month) within 30 days of receiving a task. Members identified as non-adherent in consecutive months were contacted multiple times over the study period.

Initial evaluation of the intervention in September of 2012 identified a large proportion of members that could technically reach the adherence threshold (PDC ≥ 80% as used by CMS) by end of the measurement year with additional medication supply. In other words, members’ prescription claims for the January through September 2012 time period were used to estimate members’ current PDC for the 2012 measurement year and forecast the worst and best case PDC performance scenarios for each member’s year-end PDC, assuming days' supply was available for the remaining days in the year. These additional prioritized member files were provided twice by MedImpact to iCare in October and late November of 2012. Two iCare Pharmacy Services Representatives
(PSRs) used the files to determine the calling order of members based on members’ last date of medication fill and anticipated end of supply. For example, a member that last filled his/her lisinopril on 10/7/2012 was called on or near 11/7/2012 if the member had not filled prior. If the PSRs were not able to reach the member, the pharmacy was called and the pharmacist or pharmacy technician was asked to contact the member regarding a refill of the target medication.

The adherence intervention was augmented in January of 2013 with a refill reminder component. This program component used interactive voice response (IVR) technology to conduct telephonic outreach to members 7 days late in refilling medications for each of the three target classes. Upon member authentication, target members received a customized message reminding them to refill their medication and were asked if they intended to refill. Those members responding “No” to this introductory question were asked to select one of five options that best fit their reason for not planning to refill. The five options were cost, doctor said stop, don’t believe they need the medication, don’t understand instructions and medication side effects. The evaluation of this refill reminder component allowed an assessment of self-reported reasons for nonadherence and was used to improve the intervention in 2013. Detailed IVR program reports were provided weekly and reviewed by iCare Pharmacy Services. For members self-reporting a barrier to adherence that iCare considered clinical in nature (i.e., don’t believe they need the medication, don’t understand instructions, or side effects), the information was referred to an iCare nurse for follow-up.
Study Measures

Total number of members identified for the intervention was measured for the initial cohort and for each medication class for the 2012 calendar year. To gauge member enrollment in the US MED component of the intervention, the enrollment rate was calculated as the proportion of identified members that consented to participate in the US MED program.

The main outcomes of interest were member adherence rates and health plan adherence rates. Member adherence rates were calculated as the proportion of days covered (PDC) for three medication classes as defined by specifications from the CMS Medicare Health & Drug Plan Quality and Performance Ratings 2013 Part C & Part D Technical Notes (released 10/10/2012) and Acumen, LLC (CMS contractor) Patient Safety Analysis Report User Guide. Specifically, for members aged 18 years and older with at least 2 claims for the target medication measure, PDC was measured from first claim in the measurement period (index date) to end of the measurement period or member disenrollment. Days of medication coverage to at least one medication in the class was calculated using fill dates and day supply elements of prescription claims within each patient’s measurement period. Health plan adherence rates were calculated by using members’ adherence rates while adjusting for length of member enrollment, or member-years. Member-years were calculated as number of months enrolled divided by months eligible in each measurement period. Health plan adherence rates were calculated as the sum of member-years for adherent members divided by the sum of members-years for all members. Validation of methodology and calculations were done by comparing estimated adherence rates to published CMS performance measure values.
for the calendar year of 2011. Estimated adherence rates using our methodology were within one-tenth to a half percentage points of CMS published rates. Differences between our calculated rates and published rates by CMS were most likely due to the CMS adjustment for inpatient hospital stays, which CMS estimates at 0.4 – 0.6 percentage points\textsuperscript{14}, and slight variations in our respective NDC medication lists.

Published CMS adherence rates and Star Ratings for the 2011 and 2012 measurement years were used to assess the impact of the program on the plan’s Star Ratings. These publicly available files obtained from CMS include adherence rates and Star Ratings for all MAPD contracts.\textsuperscript{14} Changes in adherence rates and Star Ratings between the 2011 and 2012 measurement years for iCare were calculated and compared to calculated changes for the national MAPD contract average (the average for all contract types). Furthermore, changes in rates were compared to another dual-eligible SNP that did not implement an adherence intervention in 2012. This comparator plan was selected among MedImpact health plans similar in membership size and demographics (dual-eligible SNP, 100% of members receiving low income subsidy).

Lastly, January 2014 Patient Safety Reports published by Acumen were used to assess possible sustained effects of the program on the 2013 measurement period.

To evaluate changes in members’ adherence rates post implementation, prescription claims were used to calculate adherence rates for 9-month pre- and post-implementation periods. Changes in pre-post period rates for each intervention group were compared to assess differences between intervention components (iCare-only and iCare+US MED). To assess the effectiveness of the member priority file component of the intervention, year-to-date adherence was measured for the health plan for the last 5
months of 2012. Changes in rates from the prior month period (e.g., Jan-Oct vs. Jan-Sep) were calculated and compared to published national MAPD rates for similar time periods to detect differences in adherence as the measurement period progressed. To assess the refill reminder component of the program, the number of authenticated calls out of the total placed calls was used to calculate member contact rates. Survey response rates were calculated and the number and percent of members providing self-reported reasons for not refilling medication were summarized.

**Additional Study Measures**

Member demographics and health plan enrollment status were ascertained from member eligibility files. Age was determined as of intervention start date. Baseline adherence to each medication class was calculated for the 6-month period prior to intervention start date (10/1/11 to 3/31/12). Members were classified as naïve to therapy if they had a negative history of a claim for the medication class in this baseline period. Baseline medication use was measured by the number of distinct medications (as determined by generic name). Comorbidities were estimated using members’ prescription claims in the calendar year 2012. The First DataBank™ therapeutic classification system was used to identify specific medication use by National Drug Code (NDC) and comorbid conditions were measured using Medicaid Rx, a pharmacy-based risk adjustment model used to adjust capitated payments for Medicaid health plans. This risk adjuster, which uses NDCs to create indicator variables for 45 disease states, was selected due to the nature of the dual-eligible study population. The provider specialty of
the prescriber for each member was determined by the prescriber’s first-listed specialty using the Health Market Science (HMS) Prescriber MasterFile™.

**Statistical Analysis**

Descriptive statistics for all independent and outcome variables were tabulated for the total intervention population and stratified by medication class. Multivariate logistic regression was used to identify risk factors for nonadherence in the baseline period by modeling the probability of a member being non-adherent (dependent variable) in the six months before intervention start date. The cut point used by CMS, PDC ≥ 80%, was used to categorize members as adherent or non-adherent. Independent variables included age group, gender, new to therapy, number of target medication classes used and number of comorbid conditions (based on the Medicaid Rx categories). For the member-level pre-post intervention assessment, analysis of covariance (ANCOVA)\(^{18,19}\) was used to compare mean pre-post differences in adherence rates between participant groups while controlling for baseline adherence and members’ age, gender and comorbidity. Interactions and correlation diagnostics were assessed in the final models. A 0.05 (two tail) level of significance was used to determine covariate significance. All analyses were conducted by medication class to understand potential adherence differences between medication classes. To assess the influence of the intervention on the overall health plan population performance, differences in adherence rates and Star Ratings from 2011 to 2012 measurement years were calculated for the health plan and compared to differences calculated for the MAPD contract average and the comparator health plan. All analyses were performed using SAS (SAS Institute Inc., Cary, NC) Version 9.3.
Results

Patient Identification and Enrollment

An initial cohort of 2,700 members was identified for intervention in April 2012 (Figure 1). Subsequent monthly analyses of prescription claims identified an average 2,763 members per month that represented a total of 3,429 distinct members identified for intervention during the 2012 calendar year. By January of 2013, 845 (31.3%) of the initial cohort and 1,302 (38.0%) of the total identified members enrolled in the US MED program component (iCare+US MED group). The remaining members, 1,855 (68.7%) of the initial cohort (2,700 members), were enrolled in the iCare-only group. One hundred and thirty members of the total iCare-US MED enrollees chose to opt out of the US MED component. Members opting out of the program were not different than participating members with respect to age, gender, number of comorbidities and baseline adherence. Out of 1,400 surveys mailed to members who enrolled in the US MED component, 233 (16.6%) were returned. A large majority of responders indicated overall satisfaction (84% very satisfied), likely to use the pharmacy in the future (87%), and likely to refer US MED to family and friends (72.2%).

Member Characteristics and Risk Factors for Poor Adherence

Of the total 2,700 distinct members initially identified for intervention, a respective 659, 2,005 and 1,777 members were identified by the three medication classes: medications for oral diabetes (ODM), medications for hypertension (HTN), and medications for cholesterol (CHOL) (Table 1). Members identified for intervention by more than one medication class were advised on adherence to all targeted medication
classes. The number and percent of non-adherent members at baseline by class were 186 (28.2%), 630 (31.4%) and 622 (35.0%), respectively, for ODM, HTN and CHOL. Fifty-two percent of members utilized more than 1 class (e.g., prescription claims for ODM and HTN) and 72.6% of members were non-adherent to one or more target medication classes. The intervention study population was 67.0% female and the average member age was 60.5. The proportion of members new to therapy ranged from 17.8% for ODM to 20.1% for CHOL. The most common comorbidity outside of the target medication classes was pain management (ranging from 66.6% to 70.6%). The proportion of members filling medications to treat asthma or chronic obstructive pulmonary disease (COPD) ranged from 42.1% to 43.7%. Characteristics of members identified for intervention during subsequent monthly identification were similar to the initial cohort.

Table 2 provides results of logistic regression identifying risk factors associated with nonadherence in the baseline period. Risk factors were similar by medication class. Overall, younger members were more likely to be nonadherent. Compared to members aged 75 and older, members aged less than 54 were 1.39 (95% CI = 0.77 – 2.58), 1.87 (95% CI = 1.34 – 2.61) and 1.64 (95% CI = 1.18 – 2.27) times more likely to be nonadherent to ODM, HTN and CHOL, respectively. Members new to antihypertensive therapy had increased odds of nonadherence (OR= 1.51 95% CI = 1.18 – 1.93). The factor most associated with nonadherence was number of target medication classes. Members identified for intervention by only one of the three target classes were 3.6 times more likely to be non-adherent to ODM (OR = 3.60 95% CI = 2.13 – 6.10) and 1.8 times more likely to be non-adherent to HTN (OR = 1.87 95% CI = 1.38 – 2.54), compared to members identified by all three measures. No association between number of target
medication classes used and adherence was found in the CHOL group. Associations between comorbidity and nonadherence were mixed. Increased comorbidity was slightly associated with nonadherence for members identified by ODM, but indicated decreased risk among members identified by HTN.

Adherence Rates and Star Ratings

Adherence increased for both intervention groups post-implementation. The iCare-only group increased 15.1, 10.1 and 13.6 percentage points, respectively, for the diabetes, hypertension and cholesterol measure in the 9-month post-period (Table 3). The average change in adherence for the iCare+US MED group was a respective 30.9, 25.5 and 29.4 percentage points for ODM, HTN and CHOL. The adjusted change in adherence rates for iCare+US MED enrollees were significantly greater than iCare-only enrollees for each measure. Adjusting for age, gender, comorbidity and baseline adherence, absolute post-period PDC differences between means for iCare+US MED enrollees compared to iCare-only enrollees was +17.4 ($P < .001$), +15.6 ($P < .001$) and +16.3 ($P < .001$) for ODM, HTN, and CHOL, respectively. The proportion of members reaching the adherence threshold (PDC ≥ 80%) for ODM, HTN, and CHOL increased for iCare in the post-period was a respective, 49.7%, 49.3% and 57.3% (data not shown). These rates were greater than those observed with the comparator group in the same 9-month time period; 38.9%, 46.4% and 41.4%.

Plan-level adherence rates increased for all three measures in the two months after the member priority list implementation in November 2012. For the cholesterol measure, health plan year-to-date adherence rates increased 0.9 and 1.2 percentage points during
November and December compared to a decrease of 1.2 and 1.0 percentage points for the national MAPD contract average for the same time periods (Figure 2). This trend was also observed for ODM and HTN; health plan adherence rates increased 0.3 and 0.5 percentage points for ODM where the MAPD contract average decreased 1.1 and 0.2 percentage points, and for HTN, health plan adherence rates increased 0.4 and 0.2 percentage points where the MAPD contract average decreased 1.0 and 0.7 percentage points.

Comparing the CMS-published adherence rates and Star Ratings for the 2011 and 2012 measurement periods, iCare’s adherence rates increased 15.2, 9.2 and 10.1 percentage points for the ODM, HTN, and CHOL measures, respectively, from 2011 to 2012 (Figure 3). Plan adherence rate increases were considerably higher for iCare compared to average MAPD contract rate changes (1.1%, 2.1%, 2.5%) and the comparator health plan (-2.7%, -1.4%, -4.1%). Final adherence rates and Star Ratings for the 2012 measurement period (2014 Star Ratings) for iCare were 72.5% (3 Stars), 68.5% (2 Stars), and 68.4% (3 Stars) for the ODM, HTN and CHOL measures, respectively (Figure 4). Adherence rates continued to improve during the 2013 measurement period. Through November of 2013, iCare rates were 3.4, 1.2 and 2.7 percentage points greater than the same 11-month period in 2012 (data not shown).

**IVR Refill Reminder Component**

From January 9th, 2013 (IVR implementation date) to August 23, 2013, a total 4,767 distinct late refill instances (member- drug combinations) were identified (results not shown). Approximately 1,278 (26.8%) of instances were authenticated by members.
Among these members that authenticated and responded to individual questions, 1,207 (94%) responded yes to the question “do you plan to refill your medication”. For the 129 members that responded no to this question, 99 members provided a response. The most common response of the five choices was “doctor recommended stopping the medication” (45.5%), followed by “don’t believe you need it” (26.3%), “problems with side effects” (15.2%), “cost of medications keeps you from refilling medication” (8.1%) and “did not understand doctor’s instructions on how to take their medication” (5.1%). A total 949 of 1,036 (91.6%) members responded yes to the concluding survey question, “was the call helpful”.

Discussion

Evaluation of this innovative adherence program found that member and health plan adherence rates to all three medication classes increased significantly after program implementation. Changes in health plan adherence rates from 2011 to 2012, which approximates the pre-post program implementation periods, were much higher for iCare as compared to changes observed with the national MAPD contract average and a comparable dual-eligible special needs plan. The pre-post member-level analysis found increased adherence post-implementation for all three medication classes for both participation groups (iCare-only and iCare+US MED), with greater increases observed for members participating in the iCare+US MED component after adjusting for patient demographics, comorbidity and baseline adherence. Findings from our assessment are particularly meaningful given this intervention was conducted on a dual-eligible, low-income subsidy population that previously proved to be difficult to contact and engage.
Our results of intervention effectiveness are greater than available findings of interventions directed at these therapeutic classes; however, nearly all published interventions are clinical trials conducted in small, controlled study populations for short durations (3 to 6 months). The objective of this intervention was to improve adherence over longer periods of time a more appropriate, goal given the chronic prognosis of diabetes, hypertension, and hyperlipidemia. With the introduction of the CMS Star Ratings program and national campaigns promoting adherence, many health plans have employed adherence interventions to improve quality of care and adherence rates. Therefore we used the national MAPD contract average and a health plan similar in member characteristics as adequate comparators in our assessment of effect size. The national MAPD contract average includes a mix of health plans that likely perform a variety of adherence interventions. Our results are similar in direction to studies describing multi-component approaches as more effective than a single approach in changing medication adherence behavior. Jing et al. found messaging both providers and patients was effective at improving antihypertensive and antidiabetic adherence in a Medicare population.

The rapid enrollment of members in the first few months after implementation demonstrated the effectiveness of the enrollment process into the iCare+US MED program component. By January 2013, thirty-eight percent (1,302) of 3,429 referred members enrolled in the iCare+US MED program. The low disenrollment rate, 8.7% (113 of 1,302 enrolled members), suggests the intervention was effective at maintaining member care. The convenience of medication delivery is a likely reason for initial and sustained enrollment in the iCare+US MED component. Monthly member and pharmacy
claims data files supplied the care management team with visibility to specific member adherence issues. The web-based application allowed both US MED and iCare personnel to update member information to sustain enrollment in the intervention and also allowed fast communication that facilitated member engagement.

We expected members with higher baseline adherence rates would be more likely to participate in the US MED component and therefore thought members would self-select into the iCare+US MED group; however, we observed similar baseline adherence for both iCare+US MED and iCare-only members. We also anticipated iCare+US MED enrollees to demonstrate greater adherence improvements in the post period because they received continual medication supply via mail and were counseled by both the care management team of iCare and pharmacy service teams from US MED, in contrast with the iCare-only members that received counseling from only the iCare team. After implementation, the iCare+US MED group did demonstrate significantly greater improvements compared to iCare-only enrollees, but both groups experienced meaningful improvements that subsequently increased iCare’s adherence rates.

The increased adherence rates gained during the 2012 measurement year translated into higher Star Ratings for all measures targeted by the intervention. iCare’s performance ratings went from 1 to 3 stars for the Medication Adherence for Diabetes Medications and Medication Adherence for Cholesterol measures and 1 to 2 stars for the Medication Adherence for Hypertension measure. The adherence rates for iCare had a significant net relative increase compared to the national MAPD contract average, which observed a slight improvement, and the comparator health plan, which observed a slight decline in adherence. Increases in the adherence measures for each of the three
medication classes provided an additional impact to iCare’s overall Part D Star Rating by increasing the Drug Plan Quality Improvement measure from 2 stars to 4 stars. Overall, iCare’s Part D Star Rating increased from 3 to 3.5 Stars from the 2013 Star Ratings (CY 2011 measurement period) to the 2014 Star Rating (CY 2012 measurement period). Furthermore, adherence rates reported for 2013 measurement year are higher than 2012 demonstrating positive sustained effects of the program.

The value of increased Star Ratings to health plans include incentive payments (i.e., quality bonus payments and greater rebate percentage), as well as increased membership through exposure to publicly reported ratings on Medicare Plan Finder, the CMS website available to members to compare health plans. A recent study evaluating the association between Star Ratings and enrollment decisions quantified the average value of increased ratings. Reid et al. found that an increase in 1 star was associated with a 9.5% increased likelihood to enroll new enrollees. Among members switching plans, for every 1-star increase there was a 4.4% increased likelihood to enroll. For MAPDs with consecutive low Star Ratings, increases in performance ratings will prevent a “Low Performing Icon” (LPI). In 2011, CMS began labeling plans with the LPI on the Medicare Plan Finder website if consecutive plan performance was less than 3 stars for either the Part D or Part C rating for the last three measurement years.

MAPD plans continue to search for novel approaches to increasing appropriate and persistent use of medications. This intervention demonstrated an effective collaboration between a MAPD plan, pharmacy benefit manager and pharmacy to engage members in an adherence intervention. The increased adherence rates observed in our study may be due to the ability of care coordinators to address some of these barriers by
1) improving medication access, 2) counseling members on when to take medication, and 3) scheduling provider visits. The large proportion (31%) of members electing the mail order option suggests that members of this dual-eligible population may have had difficulty with medication access that could be resolved with this convenience. Although mail order does not completely ensure full consumption of medications, members with limited access to pharmacies may have benefited from ongoing medication delivered to their home. We believe this benefit of home delivery, which was restricted to a 30-day supply (considerably less than most mail-based 90-day fill programs), outweighs the potential waste and mismanagement of these medications because there is low potential for abuse of medications in these classes.

Limitations

We acknowledge the following limitations to our evaluation. First, we recognize actual adherence may differ from our estimated adherence rates that used administrative pharmacy claims data. Although this is a limitation of the measurement method, the PDC methodology is the selected method used by CMS in Part D performance ratings and was used consistently for all intervention groups and comparators. The use of pharmacy claims as an estimate of adherence to maintenance medications has been well validated in integrated health systems.\textsuperscript{24-25} In the case that actual adherence is lower than our estimated adherence, associations between the intervention and adherence may be overestimated. Additionally, members may have appropriately discontinued therapy per provider recommendations due to medication side effects or changes in disease status. Data from the IVR intervention component was leveraged to identify members reporting
side effects and lack of understanding of medication regimens. Members self-reporting medication side effects or those reporting trouble with provider instructions were called by iCare coordinators. These members were included in our analysis and therefore may be falsely classified as nonadherent which would lead to a biased underestimation of the effectiveness of the intervention. Conversely, members may have received medication from other sources (e.g., samples, family members). These members may be falsely identified as non-adherent if the member is taking their medication as prescribed. The above limitations would apply similarly to the intervention and comparator group and is not felt to substantially influence the results observed.

Second, in our member level sub-analysis that compared member participation groups, we understand that iCare+US MED enrollees received medication by mail that provides a convenience advantage over members that obtain medications at retail pharmacies. Mail delivery of medication ensures close to full medication coverage, as measured by the PDC method, therefore estimated adherence rates for iCare+US MED enrollees were expected to be greater than iCare-only enrollees. We did find adherence improvement for both groups substantiating the overall effectiveness of the program. Additionally, adherent members may exhibit better overall health behavior patterns\textsuperscript{26}, which may bias results in favor of one of the participation groups. Given the unavailability of overall measure of one’s health behavior, we addressed this potential participation bias by accounting for member characteristics, baseline adherence and pharmacy utilization in the modeling stage of the analysis.

Third, this intervention was implemented within a single health plan and may not be representative of other MAPD plan experiences. However, our findings of positive
effectiveness are consistent with evaluations of hypertension and diabetes adherence interventions in Medicare populations.\textsuperscript{20} The intervention population consisted of dual-eligible members which have more comorbid conditions and more complex medication regimens than non-SNP MAPD plans.\textsuperscript{27} Application of this intervention in non-SNP populations may provide equal or greater effectiveness.

Fourth, communications between members and iCare care coordinators would have allowed better evaluation of the effectiveness of the entire program. Data on time and frequency of member contact by care management staff was not available and therefore limited any detailed comparison of differential program component effects.

**Conclusions**

Members in this Medicare special needs population benefited from an integrated communication program aimed to increase medication adherence to treat three highly prevalent disease conditions. The large, positive increases in medication adherence for all three targeted classes post-implementation are substantial because of the study population’s previous poor adherence record and relative improvements compared to the national MAPD contract benchmark and a comparator plan that did not implement an adherence intervention. Adherence rates continued to improve in the 2013 measurement year indicating continuing effectiveness of the intervention. Health plans, including their pharmacy and care management teams, can effectively utilize pharmacy benefit managers and pharmacy partners to offer novel methods to improve member and overall health plan medication adherence.
Acknowledgements

Chapter 2, in full, has been published of the materials as it may appear. Leslie RS, Tirado B, Patel BV, Rein PJ. Evaluation of an Integrated Adherence Program Aimed to Increase Medicare Part D Star Rating Measures. Journal of Managed Care & Specialty Pharmacy. 2014;20(12):1193-1203. The dissertation author was the primary investigator and author of this paper.
Members of iCare, a dual-eligible Medicare Prescription Drug Plan
Approximately 5,000 members

Members aged ≥18 years with at least 1 prescription claim for 1 of 3 target medication classes (oral antidiabetics, antihypertensives, or statins) during October 1, 2011, to March 31, 2012
2,700 members

Initial Intervention Cohort
2,700 members

Diabetes
(n=659)

Cholesterol
(n=1,777)

Hypertension
(n=2,005)

Member and claim data files sent to iCare care management team and US MED pharmacy’s customer service specialists.

Footnotes:
4Prescription claims for target medication classes were identified using NDC lists accessed from CMS Technical Notes.
5Members could be identified for intervention by more than 1 medication class.
CMS = Centers for Medicare & Medicaid Services; iCare = Independent Care Health Plan; NDC = National Drug Code.

Figure 2.1: Selection Diagram of Initial Intervention Cohort
Table 2.1: Characteristics of the Initial Intervention Cohort (N=2,700)

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<th>Hypertension (HTN)</th>
<th>Cholesterol (CHOL)</th>
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<td>1,777</td>
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<td>60.8 (12.6)</td>
<td>61.7 (11.7)</td>
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<td>&lt; 54</td>
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<td>621 (31.0)</td>
<td>513 (29.9)</td>
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<td>55-64</td>
<td>183 (27.6)</td>
<td>549 (27.4)</td>
<td>473 (27.6)</td>
</tr>
<tr>
<td>65-74</td>
<td>193 (29.3)</td>
<td>567 (29.3)</td>
<td>533 (30.9)</td>
</tr>
<tr>
<td>75+</td>
<td>80 (12.1)</td>
<td>268 (13.4)</td>
<td>258 (14.5)</td>
</tr>
<tr>
<td>Baseline adherence status, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adherent, PDC ≥80%</td>
<td>473 (71.8)</td>
<td>1,375 (68.6)</td>
<td>1,155 (65.0)</td>
</tr>
<tr>
<td>Nonadherent, PDC &lt;80%</td>
<td>186 (28.2)</td>
<td>630 (31.4)</td>
<td>622 (35.0)</td>
</tr>
<tr>
<td>Identified by ≥1 medication class, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New to therapy</td>
<td>117 (17.8)</td>
<td>360 (18.0)</td>
<td>357 (20.1)</td>
</tr>
<tr>
<td>History of therapy</td>
<td>542 (82.2)</td>
<td>1,645 (82.0)</td>
<td>1,420 (79.9)</td>
</tr>
<tr>
<td>Pre-index medication count mean (SD)</td>
<td>13.3 (6.1)</td>
<td>13.0 (6.5)</td>
<td>13.4 (6.6)</td>
</tr>
<tr>
<td>Comorbidity count, mean (SD)</td>
<td>4.5 (2.3)</td>
<td>4.4 (2.3)</td>
<td>4.4 (2.4)</td>
</tr>
<tr>
<td>Comorbidity, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma/COPD</td>
<td>42.1</td>
<td>43.6</td>
<td>43.7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>87.1</td>
<td>65.6</td>
<td>86.8</td>
</tr>
<tr>
<td>Depression/anxiety</td>
<td>25.3</td>
<td>25.3</td>
<td>27.2</td>
</tr>
<tr>
<td>Diabetes</td>
<td>90.8</td>
<td>45.0</td>
<td>46.8</td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>41.8</td>
<td>45.7</td>
<td>46.8</td>
</tr>
<tr>
<td>Infections</td>
<td>42.7</td>
<td>44.0</td>
<td>46.0</td>
</tr>
<tr>
<td>Inflammatory/autoimmune</td>
<td>42.1</td>
<td>23.9</td>
<td>25.3</td>
</tr>
<tr>
<td>Multiple sclerosis/paralysis</td>
<td>23.8</td>
<td>24.1</td>
<td>24.0</td>
</tr>
<tr>
<td>Pain management</td>
<td>66.6</td>
<td>70.6</td>
<td>70.2</td>
</tr>
<tr>
<td>Seizure disorders</td>
<td>22.6</td>
<td>25.4</td>
<td>27.0</td>
</tr>
<tr>
<td>Prescriber specialty, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiology</td>
<td>5.2</td>
<td>6.4</td>
<td>12.1</td>
</tr>
<tr>
<td>Endocrinology</td>
<td>12.7</td>
<td>6.7</td>
<td>6.7</td>
</tr>
<tr>
<td>Family practice</td>
<td>31.5</td>
<td>33.5</td>
<td>33.5</td>
</tr>
<tr>
<td>Internal medicine</td>
<td>36.8</td>
<td>34.3</td>
<td>31.5</td>
</tr>
<tr>
<td>Nurse practitioner</td>
<td>8.7</td>
<td>8.7</td>
<td>5.7</td>
</tr>
<tr>
<td>Physician assistant</td>
<td>3.4</td>
<td>3.4</td>
<td>3.4</td>
</tr>
<tr>
<td>Other specialty</td>
<td>4.5</td>
<td>4.6</td>
<td>4.5</td>
</tr>
</tbody>
</table>

*Members could be identified for intervention by more than 1 medication class.
*New to therapy if absence of a prescription in the 280-day baseline period.
*Comorbidity measured by Medicaid Rx. Reported for categories where prevalence was >20%.
*COPD = chronic obstructive pulmonary disease; PDC = proportion of days covered; SD = standard deviation.
### Table 2.2: Risk Factors for Nonadherence (PDC <80%) in Baseline Period

<table>
<thead>
<tr>
<th></th>
<th>Diabetes, n=659</th>
<th>Hypertension, n=2,065</th>
<th>Cholesterol, n=1,777</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio&lt;sup&gt;a&lt;/sup&gt; 93% CI</td>
<td>Odds Ratio&lt;sup&gt;a&lt;/sup&gt; 93% CI</td>
<td>Odds Ratio&lt;sup&gt;a&lt;/sup&gt; 93% CI</td>
</tr>
<tr>
<td>Age group (reference: 75+)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;54</td>
<td>1.39 (0.77-2.58)</td>
<td>1.87 (1.34-2.61)</td>
<td>1.64 (1.18-2.27)</td>
</tr>
<tr>
<td>55-64</td>
<td>1.08 (0.59-2.03)</td>
<td>1.42 (1.01-2.00)</td>
<td>1.15 (0.62-1.60)</td>
</tr>
<tr>
<td>65-74</td>
<td>0.90 (0.42-1.82)</td>
<td>1.26 (0.90-1.77)</td>
<td>1.17 (0.65-1.61)</td>
</tr>
<tr>
<td>Male (reference: female)</td>
<td>1.07 (0.73-1.56)</td>
<td>1.06 (0.87-1.30)</td>
<td>0.95 (0.77-1.17)</td>
</tr>
<tr>
<td>New to therapy (reference: history of therapy)</td>
<td>1.32 (0.84-2.07)</td>
<td>1.51 (1.16-1.93)</td>
<td>1.19 (0.92-1.55)</td>
</tr>
<tr>
<td>Number of target medication classes&lt;sup&gt;b&lt;/sup&gt; (reference: 2 classes)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3.60 (2.13-6.10)</td>
<td>1.87 (1.38-2.54)</td>
<td>0.92 (0.74-1.14)</td>
</tr>
<tr>
<td>2</td>
<td>1.50 (1.02-2.22)</td>
<td>1.51 (1.12-2.00)</td>
<td>1.07 (0.62-1.74)</td>
</tr>
<tr>
<td>Comorbidity count&lt;sup&gt;c&lt;/sup&gt; (reference: &lt;4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-6</td>
<td>1.14 (0.74-1.67)</td>
<td>0.79 (0.64-0.98)</td>
<td>0.87 (0.70-1.09)</td>
</tr>
<tr>
<td>7+</td>
<td>1.03 (0.62-1.71)</td>
<td>0.96 (0.72-1.37)</td>
<td>1.02 (0.76-1.37)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Odds ratios estimated using multivariate logistic regression.

<sup>b</sup>Number of target medication classes utilized by member (diabetes, hypertension, cholesterol).

<sup>c</sup>Comorbidity count estimated by Medicaid R.E.

CI = confidence interval; PDC = proportion of days covered.
Table 2.3: Member Demographics and Adherence Change by Participation Group

<table>
<thead>
<tr>
<th></th>
<th>Diabetes</th>
<th>Hypertension</th>
<th>Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>iCare-only Enrollees</td>
<td>iCare + US MED Enrollees</td>
<td>P Value</td>
</tr>
<tr>
<td>Age, mean</td>
<td>60.3</td>
<td>58.8</td>
<td>0.422</td>
</tr>
<tr>
<td>Female, %</td>
<td>66.3</td>
<td>65.0</td>
<td>0.860</td>
</tr>
<tr>
<td>Number of comorbid conditions, n</td>
<td>4.7</td>
<td>4.3</td>
<td>0.314</td>
</tr>
<tr>
<td>Baseline period PDC, mean</td>
<td>53.9</td>
<td>54.8</td>
<td>0.709</td>
</tr>
<tr>
<td>Postperiod PDC, mean</td>
<td>69.1</td>
<td>85.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unadjusted PDC change (pre-post), mean</td>
<td>35.1</td>
<td>30.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjusted mean difference in postperiod PDC&lt;sup&gt;a&lt;/sup&gt;</td>
<td>174</td>
<td>&lt;0.001</td>
<td>15.6</td>
</tr>
</tbody>
</table>

<sup>a</sup> Difference in postperiod adherence between iCare-only versus iCare + US MED member groups. Adjusted for baseline adherence, age, gender, and comorbidity. P values for adjusted mean difference in postperiod PDC were estimated by analysis of covariance. P values for age, gender, baseline period PDC, and postperiod PDC were determined by individual sample t-tests.

iCare = Independent Care Health Plans; PDC = proportion of days covered.
Figure 2.2: Change in Year-to-Date Adherence Rates for last 5 months of 2012 Measurement Period
Figure 2.3: Percentage Point Change in Adherence Rates from 2011 to 2012 Measurement Periods
Figure 2.4: iCare Adherence Rates and Star Ratings\textsuperscript{a} by Year and Measure

\textsuperscript{a}CMS started rounding to whole numbers with 2014 star ratings.

CMS = Centers for Medicare & Medicaid; iCare = Independent Care Health Plan
References


10. Jha AK, Aubert RE, Jianying YJ, Teagargen JR, Epstein RS. Greater adherence to diabetes drugs is linked to less hospital use and could save nearly $5 billion annually. Health Affairs. 2012;31(8):1836-46.


CHAPTER 3

A MULTI-CHANNEL MEDICATION ADHERENCE INTERVENTION

INFLUENCES PATIENT AND PRESCRIBER BEHAVIOR
Abstract

**Background:** The Centers for Medicare and Medicaid Services (CMS) Medicare Health Plan Quality and Performance Ratings program, or “Star Ratings” program, includes three medication adherence outcomes measures (Medication Adherence for Diabetes Medications, Medication Adherence for Hypertension, and Medication Adherence for Cholesterol) which contribute to approximately 31% of a Medicare Advantage Prescription Drug (MA-PD) contract’s Part D summary rating and 12% of its overall star rating (a weighted summary of a contract’s Part C and Part D rating). MAPD plans have been increasing their adherence intervention efforts as an approach to improving beneficiaries’ medication adherence and their quality performance ratings. However, little is known about the effect of these interventions on medication adherence and performance ratings.

**Objectives:** To assess the impact of a quasi-experimental multi-channel adherence intervention on beneficiaries’ medication adherence and health plan quality performance measures among two MA-PD plans. The intervention included a daily prescriber-directed, retail-based 90-day refill component and a weekly member-directed refill reminder component.

**Methods:** Members filling one or more medications assessed by the three CMS star ratings adherence measures (oral antidiabetics [DM], antihypertensives [HTN], and statins [CHOL]) were identified for a two component intervention starting in April 2013. The retail-based 90-day refill component sent pre-populated 90-day prescription letters via fax to prescribers of any member whom filled a 30-day prescription. One fax per member-medication instance was sent and included the option to fax approval of a new
90-day prescription. Upon prescriber approval, members were notified that a 90-day supply refill was available at their retail pharmacy. The refill reminder component used weekly scans of pharmacy claims to identify members’ refill patterns. Reminder letters were sent to members seven days late to refill. An intent-to-treat approach was used to assess intervention effectiveness. Administrative pharmacy claims and health plan eligibility data were used to calculate adherence among patients enrolled one-year pre and post intervention start (April 2013) for the intervention group and a comparator group which consisted of four MA-PD plans not implementing an adherence intervention. Adherence was estimated by the proportion of days covered (PDC) and generalized linear models were fit to calculate difference-in-difference (DID) estimators to control for demographics, comorbid conditions and changes in adherence over time. Post hoc analyses assessed effects of the intervention on a subgroup of beneficiaries targeted for the 90-day intervention component. To estimate the impact of the intervention on plan quality performance, 2013 and 2014 CMS Star Ratings (2012 and 2013 measurement years) were compared for the intervention group.

Results: During the first year of the intervention, 1,344 prescribers representing 6,701 members, were faxed 15,284 pre-populated prescription letters. Prescriber response rate was 53.7% from which approval rate was 47.3%. An average of 539 refill reminder letters were sent per month. DID estimators showed positive influence of the intervention on adherence to antihypertensives and statins, but insignificant effectiveness on oral antidiabetic adherence. For the intervention group, adherence increased 2.0 percentage points ($P < .001$) for HTN and 1.8 percentage points ($P < .001$) for CHOL, relative to the control group. The odds of achieving adherence (PDC $\geq 80\%$) was greater
in the intervention group compared to control for HTN (ratio of odds ratio [ROR] =1.334; 95% CI=1.203-1.479) and CHOL (ROR=1.247; 95%CI=1.051-1.132). For the two plans implementing the intervention, CMS-published adherence rates increased from 2012 to 2013 by an average 5.5, 6 and 7 percentage points, respectively, for DM, HTN and CHOL compared to the control group.

**Conclusions:** This study found increases in adherence to antihypertensives and statins in two MA-PDs implementing a combined prescriber and patient-directed intervention. MA-PDs can use broad multi-channel interventions to address common adherence barriers and improving both members’ adherence to maintenance medications and health plan quality performance ratings.
What is already known about this subject

- Providing better quality at lower costs are main goals of the Centers for Medicare and Medicaid Services (CMS) and 2010 Patient Protection and Affordable Care Act.
- The CMS Plan Quality Star Ratings Program incentivizes Medicare Advantage-Prescription Drug plans (MA-PDs) to increase medication adherence in their populations.
- MA-PDs implement interventions to improve medication adherence and quality performance ratings.
- Systematic literature reviews and medication adherence advisory committees recommend that additional research assess interventions in large routine care patient populations.

What this study adds

- A broad, multi-channel medication adherence intervention can address common adherence barriers, such as forgetfulness and access, and effectively increase adherence rates among entire memberships.
- Health plans can implement broad interventions to influence a health plan’s quality performance ratings.
- A prescriber-directed retail 90-day intervention can effectively influence prescribing patterns of maintenance medications.
Background

The prevalence of diabetes, hypertension and hyperlipidemia in the elderly are 25.9%, 69.7% and 58.2% respectively.\textsuperscript{1,2,3} The incidence of these diseases are projected to rise with the aging of the baby boom generation.\textsuperscript{4,5} Pharmacologic treatment is fundamental to the management of these conditions, and suboptimal adherence to prescribed therapies threatens treatment effectiveness. Consequences of poor adherence include increased healthcare utilization and costs and poorer clinical outcomes.\textsuperscript{6-11} Among Medicare beneficiaries in 2013, adherence rates for medication classes used to treat diabetes, hypertension and hyperlipidemia were lower (77%, 79% and 74%, respectively) than the most commonly recommended and published adherence threshold of 80%.\textsuperscript{12}

The Centers for Medicare and Medicaid Services (CMS) developed the Medicare Plan Quality Star Ratings Program to evaluate quality performance and allow beneficiaries to compare cost and quality of available Medicare Advantage Prescription Drug (MA-PD) plans and Prescription Drug Plans (PDPs). Each year Medicare Part D plans with greater than 500 beneficiaries receive an overall star rating which is a weighted average of a Part C domain summary rating (33 performance measures) and a Part D domain summary rating (13 measures). Star ratings are released on Medicare’s Plan Finder website each October before Medicare’s annual open enrollment period and are linked with increased enrollment and Medicare reimbursements. A 2012 study quantified the average value of increased star ratings and found that a one overall star increase was associated with 9.5% increased likelihood to enroll new enrollees.\textsuperscript{13} In November 2010, CMS implemented a demonstration project in provision with the 2010
Patient Protection and Affordable Care Act that tied quality bonus payments to overall Star Ratings as incentives promote quality among Medicare Part D contracts. In 2012, quality bonus payments totaled was $3.1 billion. Of the 13 Part D domain star rating measures, three patient safety outcome measures; Medication Adherence for Diabetes Medications (D11), Medication Adherence for Hypertension (D12), and Medication Adherence for Cholesterol (D13) carry triple the weight of other process measures and therefore can contribute up to 12% of a health plan contract’s overall Star Rating and 31% of its Part D rating.

MA-PDs and PDPs have implemented adherence interventions to improve their quality ratings. These interventions vary by mode of delivery, frequency of administration and target audience (e.g., patient or provider). Published findings of randomized controlled trials provide evidence of intervention effectiveness among small, select populations and quasi-experimental studies have demonstrated usefulness of pharmacy-based interventions limited to populations utilizing select pharmacies or intervention among members enrolled in Medication Therapy Management programs; however, there is insufficient research describing effects of adherence interventions targeting chronic medications applied to entire health plan populations. Evidence of population-level adherence interventions within usual, routine clinical care settings can guide pharmacy directors and managed care professionals on possible methods to increase medication adherence within entire memberships.

In April 2013, two MA-PDs under contract with MedImpact implemented a multi-channel medication adherence intervention to increase member adherence to the three medication classes characterized by the CMS plan performance ratings. The two
component adherence intervention included a prescriber-directed, retail-based, 90-day prescription program and a member-directed, refill reminder program intervention. The objective of this research was to assess the effectiveness of this intervention among Medicare beneficiaries treated for diabetes, hypertension and high cholesterol. We hypothesized that adherence rates would increase among beneficiaries enrolled in these health plans relative to a comparison group of beneficiaries enrolled in health plans that were not conducting any form of adherence intervention. Evidence of effectiveness could assist MA-PD plans when deciding on potential interventions based on their quality performance goals and available resources.

Methods

Intervention Description

The multi-channel medication adherence intervention identified members filling medications included in the CMS quality performance adherence ratings. Specifically, these medications comprise of non-insulin hypoglycemic agents (biguanides, thiazolidinediones, sulfonylureas, DPP-IV inhibitors, incretin mimetics, metglitinides), renin–angiotensin system (RAS) antagonists (a subset of antihypertensives consisting of angiotensin ACE inhibitors, ARBs and direct renin inhibitors), and antihyperlipidemics (statins). The intervention included two components starting in April 2013: a 90-day fill component and a refill reminder component. The 90-day fill component was a prescriber-directed, daily fax program that identified members whom filled at least one prescription of 30 days’ supply for any of the targeted medications in the previous 3 month-period. Prescribers of the most recent prescription for each targeted medication
were faxed a letter containing a pre-populated 90-day prescription for members eligible for 90-day refills at retail pharmacies. One letter fax per member-medication combination was sent to the prescriber therefore prescribers could receive more than one letter for a member (Figure 1). Prescribers were asked to respond via fax. For those prescribers that approved of the prescription, the new 90-day prescription was sent to the pharmacy for automatic processing on date of the members’ next scheduled refill. Members were then notified by letter that their prescription was changed to a 90-day supply and would be available at their retail pharmacy. Prescribers were retargeted if their patients refilled a 30-day fill instead of the proposed 90-day prescription. Prescribers that did not respond within 21 days were faxed a second letter. Prescribers whom denied the prescription were not retargeted for the specific member-medication occurrence.

The refill reminder component was a member-directed, letter program. Weekly scans and analysis of prescription claims data identified members late in refilling one or more of the three target medication classes (Figure 2). The fill date and corresponding days’ supply data fields for members’ most recent claim were used to calculate the end of medication supply and potential days late to refill. CMS-approved refill reminder letters were sent to members late in refilling by 7 days. Letters explained the importance of medication adherence and listed medication name and last fill date. Members received a letter for each late refill instance.

**Study Design and Population**
This is a retrospective, quasi-experimental evaluation of the multi-channel medication adherence intervention. The study population comprised of enrolled beneficiaries of six MA-PD contracts (health plans) utilizing the three medication classes of interest in the 2-year study period (April 2012 to March 2014). The intervention group was comprised of beneficiaries in two health plans with a combined membership approximately 24,000 members that were exposed to the refill reminder and 90-day refill programs. The comparison group was comprised of beneficiaries in four health plans with a combined membership of approximately 75,000 members that were not conducting any adherence interventions during the study period. Health plan account teams and pharmacy directors were contacted to rule out possible interventions conducted by the health plans selected for the comparison group.

**Study Measures**

**Outcomes**

The primary outcomes for this evaluation were member and health plan-level adherence rates. Member adherence rates were calculated as the proportion of days covered (PDC) by medication using specifications from the CMS Medicare Health & Drug Plan Quality and Performance Ratings 2014 Part C & Part D Technical Notes\(^{22}\) (released 09/27/2013) and Acumen, LLC (CMS contractor) Patient Safety Analysis Report User Guide.\(^{23}\) Members aged 18 years and older with 2 or more prescription claims covering at least 91 days for the target medication class were included in the analysis. In accordance with CMS measurement specifications, members with a prescription claim for insulin were excluded from the diabetes adherence assessment.
PDC was measured from first claim in the measurement period (index date) to end of the measurement period or member disenrollment. Days of medication coverage was calculated using fill dates and day supply elements of prescription claims within each member’s measurement period. Adherence for each medication class was calculated both as a continuous variable, ranging from 1-100% and a binary measure, based on the adherence threshold used by CMS: PDC ≥80%. For scenarios where refills occurred before members exhausted their current supply, the overlapping days’ supply between fills was carried forward. Medication coverage occurring after the measurement year was not counted in the PDC denominator. Adherence was measured for the one year prior (Apr-12 to Mar-13) and first year after (Apr-13 to Mar-14) intervention start date (Apr-13).

CMS-published performance ratings were used to assess change in health plan quality performance. Changes in rates were calculated as the difference between the rates for the 2012 and 2013 measurement years (corresponding 2014 and 2015 Star Ratings) which approximates the pre-post intervention period.

Additional Study Measures

Socio-demographic covariates (age, sex and low-income subsidy status) were ascertained from member eligibility files. Age was calculated from the date of the first claim in the baseline period. An indicator variable was created to identify members whom received low income subsidy (LIS) at any time during the study period. This covariate is pertinent because published CMS adherence rates are lower for this subgroup of the Medicare population. Previous studies have demonstrated a larger number of
comorbid conditions among LIS beneficiaries vs. non-LIS beneficiaries.\textsuperscript{25,26} Higher illness burden is a risk factor for poor adherence and CMS is currently assessing the potential influence of LIS and socioeconomic status on quality performance measures.\textsuperscript{27}

Additional control variables included indicators variables for being new to therapy receiving 90 refills in the pre period, and categorical variables measuring the number of comorbidities in the pre period and the number of specific conditions targeted by the intervention. Members were identified as new to therapy if they had no history of a prescription claim for the respective medication class in the six months prior to index date. Members were identified as receiving 90 refills if they filled one or more prescriptions for a 90 days’ supply in the pre period.

Comorbidities were identified using the Medicaid Rx model. Medicaid Rx is a pharmacy-based classification system used to risk adjust capitated payments for Medicaid health plans.\textsuperscript{28} The model uses prescription claims to identify 45 disease states based on National Drug Codes (NDCs). This risk adjuster was selected over other pharmacy-based risk adjusters because a large proportion of the study population comprised of dual-eligible Medicare and Medicaid beneficiaries. A categorical variable was created to identify the number of comorbidities: <3, 3-4, 5-6, 7-8, 9+. A second categorical variable identified the number of targeted conditions. This variable was created to account for patients receiving multiple exposures, since members could be identified for the intervention for up to three medication classes.

\textbf{Statistical Methods}
All data analyses were performed using SAS® version 9.4 (SAS Institute, Cary, North Carolina). Descriptive statistics were calculated for all independent and outcome variables and tabulated by treatment group. Estimations of group differences were evaluated by t-tests for continuous variables and chi-square tests for categorical variables. Cross-tabulations showing between-group differences in baseline measurements were used to identify potential confounders. Univariate, bivariate and multivariate analyses were performed using two-sided hypothesis tests and a 0.05 level of significance.

Adherence rates and proportion of adherent members were measured in 1-year periods before and after intervention start date (April 13). The pre-period spanned from April 2012 to March 2013 and the post period spanned April 2013 to March 2014. The analysis included only those members with values in both the pre- and post-intervention periods. Change in adherence rates (continuous outcome) and proportion of adherent members (binary outcome) from pre to post-intervention were calculated. Unadjusted differences in the changes in adherence between groups were compared and assessed for statistical significance.

Changes in medication adherence associated with the multi-channel medication adherence intervention were examined using intent-to-treat, difference-in-difference (DID) design (i.e. pre-post study design with a contemporaneous control group). This approach mitigates the risk of attributing a confounded change in the secular trends to the intervention. Secular trends in medication adherence may arise due to several adherence-promoting campaigns initiated by national organizations over the last five years.29-33 These programs and the addition of the three adherence-related performance measures to the CMS star ratings program in 2010 may have increased patient, prescriber and
pharmacist awareness and knowledge of medication adherence over the study period. A main assumption of the DID approach is the parallel trend assumption which fails if factors other than the intervention affected adherence in groups differentially. To test this assumption, adherence to another maintenance medication class, antidepressants, was measured across the study period to assess possible differences in underlying trends between groups.

For the dichotomous outcome (PDC ≥80%) the GENMOD procedure in SAS® was used to fit logit models for each medication class. Generalized estimating equations were used to account for correlated repeated measures data (pre and post-period measurements per member) and clustering effects (potential treatment similarities of patients within a health plan) of members within health plans. For each medication class, logistic regressions modeled the probability of achieving adherence using the following equation,

\[
P(\text{Adherence}) = \beta_0 + \beta_1 \text{Group}_i + \beta_2 \text{Time}_i + \beta_3 (\text{Group} \ast \text{Time})_i + \beta_k X_{ki} + \varepsilon \ast \text{Time}_i
\]

where adherence to therapy (PDC ≥80%), the dependent variable, was modeled by a treatment group indicator (Group), a time indicator (Time), a Group * Time interaction term and the following available variables known to affect adherence (\(X_k\)), age, sex, new to therapy, number of medication classes targeted for intervention, number of comorbid conditions, filling a prescription of 90-days’ supply in the pre period, and low-income subsidy status. The DID estimator assesses the intervention effect as the difference in medication adherence between the intervention and control groups during the intervention, adjusting for the difference between treatment groups before the
intervention and accounting for natural adherence trends during the 2 year study period. A positive, significant coefficient on $\beta_3$ indicates a positive intervention effect. In logistic models, odds ratios are calculated as the exponential of parameter estimates. The exponent of the DID parameter is a ratio of odds ratios, where the odds of achieving adherence in the post period vs. pre period for the treatment group is divided by the odds of adherence in the post vs. pre periods for the control group. For ease of interpretation separate models were fit to calculate the odds of adherence in the post period relative to the pre period for the treatment and control groups separately.

Similar models were fit using the continuous adherence outcome. PDC distributions are commonly non-normal with a large proportion of patients with high PDC measurements and less patients with low PDC values. The GLMMIX procedure was used to fit generalized linear mixed models that accounted for this non-normal distribution and nesting of patients within health plans.³⁶

As part of a post-hoc analysis, we ran models on a subgroup of members targeted by the 90-day intervention component. To avoid targeting members beginning therapy, the 90-day component required members to have filled at least one 30 days’ supply prescription before their prescriber was sent a prescription letter, therefore only members without a 90-day fill were targeted. Models were fit for this patient subgroup to examine differential effects of the intervention within this targeted subgroup.

Results

Intervention Activity
During the first year of the 90-day program (April 2013 to March 2014), a total 1,344 prescribers, representing 6,701 members, were faxed 15,284 pre-populated prescription letters. This total letter volume represented 9,544 unique prescriber-patient-medications combinations. Prescriber response rate was 53.7%. The percentage of prescribers approving of new 90-day prescriptions (approval rate) was 47.3%. During this same period, the Refill Reminder program sent a total 28,008 reminder letters to 9,938 members, an average of 539 letters per week.

**Study Population**

Our analysis included a total 28,924 unique members filling prescriptions for one or more of the three medication classes: diabetes (DM), hypertension (HTN), and cholesterol (CHOL) (Table 1). Members of the intervention group were slightly younger (DM, 71.3% vs. 73.7%, \( P < .001 \); HTN, 71.8% vs. 74.6%, \( P < .001 \); CHOL, 71.3% vs. 73.8%, \( P < .001 \)), less likely to be female (DM, 51.8% vs. 53.9%, \( P < .001 \); HTN, 53.6% vs. 56.9%, \( P < .001 \); CHOL, 51.8% vs. 54.9%, \( P < .001 \)), and more likely to receive low income subsidy (DM, 41.4% vs. 18.9%, \( P < .001 \); HTN, 34.6% vs. 15.9%, \( P < .001 \); CHOL, 32.7% vs. 16.2%, \( P < .001 \)) compared to members of the control group. The proportion of members new to therapy was similar between groups, but slightly higher among the intervention group for the CHOL class (21.8% vs.19.4%, \( P < .001 \)). Use of 90 days’ supply in the pre period was more prevalent in the control group for all three targeted classes (DM, 70.0% vs. 59.6%, \( P < .001 \); HTN, 71.6% vs. 64.4%, \( P < .001 \); CHOL, 72.8% vs. 65.7%, \( P < .001 \)). Members of as the DM class had the largest
prevalence of the other two target medication classes; 47.1% of the intervention group and 52.6% of the control group also filled HTN and CHOL medications.

**Unadjusted Changes in Adherence**

Changes in adherence rates for HTN and CHOL for the treatment group were significantly greater than the control group (Table 2). For HTN and CHOL respectively, the average difference in pre-post PDC percentage points were greater in the treatment group compared to the control group (1.4 vs. -0.6, \( P < .001 \); 1.3 vs. -0.5 \( P < .001 \)). The percent of beneficiaries who were identified as being adherent to HTN and CHOL was also greater in the intervention group than the control group (HTN, 2.6 vs. -1.3 points, \( P < .001 \); CHOL: 2.8 vs. -0.8 points, \( P < .001 \)). There was not a statistically significant difference in the pre-post changes in DM adherence between the treatment group and control group.

**Adjusted Adherence Rates**

Table 3 shows results of difference-in-difference regressions for both continuous and dichotomous outcomes. These results show that adherence to HTN and CHOL increased in the intervention group relative to the control group when accounting for correlated data due to repeated measures and controlling for patient characteristics and time trends. As observed in the unadjusted analyses, there was not a statistically significant difference in the pre-post changes in DM adherence between the treatment group and control group. Across all models, receipt of a 90-day refill in the pre period
was associated with increased adherence, and being new to therapy was associated with reduced adherence.

Adherence to HTN increased 2.0 percentage points ($P < .001$) in the intervention group relative to the control group. For the binary adherence outcome model, the DID coefficient was positive and statistically significant (.288, $P < .001$). The exponential of this estimate was 1.334 (95% CI = 1.203-1.479). The intervention group had a 12.5% increased odds of achieving adherence in the post period compared to the year before the intervention (OR =1.125, 95% CI = 1.028-1.231) whereas the control group had 15.6% lower odds of being adherent in the post compared to before the intervention (OR =0.844, 95% CI = 0.797-0.892) (data not shown).

Adherence for cholesterol increased 1.80 percentage points ($P < .001$) for the intervention group relative to the control group. For PDC $\geq 80\%$, the DID coefficient was positive and significant (.221, $P < .001$) translating to a ratio of odds ratio of 1.247 (95% CI = 1.051 – 1.132). The intervention group had an 11.3% increased odds of achieving adherence in the post period compared to the year before the intervention (OR =1.113, 95% CI = 1.022-1.213) whereas the control group had 10.7% lower odds of being adherent in the post compared to before the intervention (OR =0.893, 95% CI = 0.849-0.938).

For the two plans implementing the intervention, CMS-published adherence rates increased from 2012 to 2013 by an average 5.5, 6.0 and 7.0 percentage points, respectively, for the adherence Part D measures: Medication Adherence for Diabetes, Medication Adherence for Hypertension, and Medication Adherence for Cholesterol.
These increases were greater than the average changes among plans in the control group (3.5, 2.0 and 1.8 percentage points).

**Post Hoc Analysis**

Differences in adherence rates between groups were greater when restricting our analysis to members without a 90 day prescription in the pre period. For the intervention group, adherence increased 2.27 percentage points ($P = .020$) for DM, 2.72 percentage points ($P < .001$) for HTN and 3.25 percentage points ($P < .001$) for CHOL, relative to the control group (data not shown). For PDC $\geq 80\%$, results were similar in direction but higher in magnitude than the unrestricted population models; DID coefficients for DM, HTN and CHOL were .231 ($P = .085$), .225 ($P < .001$) and .315 ($P < .001$), respectively.

**Discussion**

Evaluation of this multi-channel adherence intervention found greater increases in adherence to antihypertensives and statins for two health plans implementing the intervention compared to a group of health plans not employing adherence programs. Adherence to antidiabetics was similar between treatment groups for the primary analysis but was greater for the intervention group when restricting the analysis to a subgroup of members with no history of 90-day prescriptions. For the continuous adherence outcome, average adherence rates to medications prescribe for diabetes (DM), hypertension (HTN) and cholesterol (CHOL) increased an average 0.57, 2.0 and 1.8 percentage points for plans implementing the intervention. For the dichotomous adherence outcome, the intervention group had 10.7%, 12.5%, 11.3% increased odds of achieving adherence in
the post period for DM, HTN, CHOL, respectively. Assessing the continuous and dichotomous adherence outcome provides useful information to health plans. The PDC ≥80% binary outcome describes the ability of the intervention to increase the proportion of members reaching the adherence threshold as used by CMS in performance ratings; the continuous PDC outcome provides estimates of potential absolute adherence gain. Both outcomes can aide health plans in understanding potential increases given their current adherence levels. Measuring both outcomes also served as a robustness check of results.

Our results are similar in direction and magnitude to an observational study that observed greater effectiveness when using a multi-component approach compared to a single level intervention. Jing et al. found messaging both providers and patients improved antihypertensive and antidiabetic adherence by 1.8 percentage points in a Medicare population.\(^37\) Our findings of slightly greater adherence rates older age groups and among men are similar to a study of 447,285 Medicare members by Cuoto et al that found men more adherent than females.\(^38\) We feel our analysis was more robust than previous research because we controlled for secular adherence trends attributable to possible increased patients’ and prescribers’ awareness of the CMS star ratings and national adherence-promoting campaigns.\(^29\)\(^-\)\(^33\) As a result of the CMS Star Ratings program and national campaigns promoting adherence, many health plans have employed adherence interventions to improve quality of care and adherence rates; however, published findings of broad interventions applied within entire health plan populations is scarce. The large majority of published adherence interventions are clinical trials conducted within small, controlled study populations and for durations of 3 to 6
months. Hence our evaluation adds to the small amount of observational studies reporting empirical evidence of adherence interventions.

The adherence increases we observed are most likely attributable to the high prescriber response and acceptance rates for the 90-day component. In the first year of the intervention, prescribers replied to 53.7% of faxes (member/prescriber/medication events) and 47.3% of the total 90-day prescription letters were approved by prescribers. For members switching to 90-day prescriptions, the additional medication supply translates into higher PDC and greater measured adherence. 90-day claim volume for the three target classes increased pre-post intervention by an average 52.2% for the intervention group compared to 30.8% in the control group. This indicates that the intervention was effective at switching members to 90-day prescriptions. It is also possible that prescribers may not have known of 90-day benefit eligibility in which informing prescribers of the 90-day benefit may have increased 90-day prescribing for patients not targeted by the program. From the member perspective, the refill reminder letters may have reminded and encouraged members to refill their medications and/or schedule needed provider appointments. Likewise prescriber-directed faxes may have prompted providers and staff to schedule office visits for their patients. Either of the above scenarios would lead to increased patient care management which is a positive consequence on any intervention.

The similar antidiabetic adherence rates observed between treatment groups may be explained by the smaller proportion of 90-day claims filled for this medication class (47.8%) compared to antihypertensives (51.5%) and statins (55.6%). This difference in fulfillment indicates that the intervention was less effective at switching members to 90-
day supply for antidiabetics. Because medication regimens often require more than one medication to control HbA1c, antidiabetic adherence is measured by coverage to any of several subclasses of antidiabetics. Another reason for the little difference between treatment and control groups could be due to the difficulty and complexity of managing diabetes. Diet and exercise recommended for all three conditions, but diabetes self-management includes foot care, scheduled doctor visits. It may be more complex to manage than hypertension and therefore adherence is more difficult. Differences in prescribing patterns and higher rates of discontinuation are also possible reasons for differences between classes. There were no differences in prescriber approval and denial rates across classes so medication intolerance may be a reason for this difference. According to systematic reviews, intolerance rates for antihypertensives range from 5-25%. Statins are estimated at 18% and antidiabetic intolerance rates are 12%. Based on these findings, members taking antidiabetics may benefit from adding behavioral or motivational interviewing approaches.

Additional post-hoc analyses revealed greater intervention effects within a subgroup of patients with no prior 90-day use. The 90-day intervention excluded members with a history of a 90-day claim to avoid targeting new starts. Restricting the analysis to members without a 90-day fill in the baseline period found positive and larger effects of the intervention for all three medication classes. This suggests the intervention was more effective for members with 30-day prescription history. Our evaluation also demonstrated greater effectiveness among members using more than one targeted medication class (e.g., filling an antidiabetic and antihypertensive). Adherence improvements were greater in members using two of three classes (range = 0.8 - 2.1
percentage points) and greatest in members utilizing all three classes (range = 1.4 - 3.2 percentage points) which may be due to these members receiving multiple exposures; multiple prescriber letters to in the case of the 90-day component, or multiple refill reminders in the case of the refill reminder program.

The purpose of this evaluation was to understand the overall effect of the intervention from the health plan perspective using an intent-to-treat approach; however, we also gauged possible effects of the intervention on the health plan’s CMS quality performance ratings. Changes in rates between the measurement years of 2012 and 2013 were larger year-to-year increases (5.5 to 7.0 percentage points) than observed in our 1-year pre-post analysis (0.6 to 2.0 percentage points). CMS measures adherence for all members utilizing medications in the calendar year where our pre-post analysis was restricted to members continuously eligible both before and during the intervention periods that straddled two calendar years. After a review of membership records, we found member enrollment increased significantly (53%) from 2012 to 2013 for the plans implementing the intervention. Thus a probably explanation for the large differences between CMS calendar year rates and our findings is due to reporting on different populations. The large increase in CMS-reported rates suggest that the intervention positively influenced new 2013 enrollees, a large group which were not captured in pre-post analysis selection criteria. Further evaluation using a with-in subject analysis tracking adherence before and after receipt of the intervention would distinguish individual patient’s response. Such analysis could also provide information for targeted intervention efforts. Additional analysis could also distinguish differences between the two intervention components to understand which was more or less effective in certain
subsets of the targeted population. For instance, the refill reminder letter may be more effective among certain age groups.

Our findings support the use of broad, multimodal interventions as an effective means of improving population-level adherence rates. This intervention can be applied to large populations with relatively minimal resources and training compared to more intense behavioral or motivational interviewing approaches that require trained individuals to contact members. The intervention was relatively quick to implement because it leveraged existing prescription adjudication processes and administrative pharmacy claims databases to identify targeted prescribers and members. The benefits of retail 90-day supply from the patient perspective are increased medication access, the opportunity to synchronize maintenance medications, reduces (fewer required pharmacy visits) and decreased out-of-pocket costs (copays for 90 days’ supply prescriptions equal that of two 30-day copays). From the health plan perspective, increased 90-day prescription volume lends to less costs with extended medication supply. Increased supply of medication also offers providers additional ways to help patients maintain therapy. This intervention can also be adjunct to existing interventions as part of large multifactorial approaches (e.g., behavioral counseling) to improve adherence as recommended by systematic reviews of published work.6

The value of increased adherence to patients, their associated health plans and society include avoidable health care utilization and costs. A 2011 study by Roebuck et al. associated adherence with less inpatient hospital days per year (3.14, 3.41 and 1.88) and fewer annual total health care costs ($5,824, $5,170 and $1,847) for hypertension, diabetes and dyslipidemia respectively, among patients over age 65.44
The benefits of increased quality performance to health plans include publicized performance ratings on Medicare’s Plan Finder website and greater possibility for monetary and enrollment incentives. Performance ratings for the previous measurement period are posted at the beginning of Medicare’s Open Enrollment period each fall. CMS developed this site to allow members to compare health plans in hopes of driving enrollment to better performing plans. A recent study by Reid et al. quantified the average value of increased ratings by finding that an increase in 1 star was associated with 9.5% increased likelihood to enroll new enrollees. The current CMS demonstration project gives quality bonus payments to plans receiving an overall rating of 4+ stars and 2012 bonus payments totaled $3.1 billion.

Limitations

The following considerations should be regarded when interpreting our findings. First, the observed adherence improvements may be related to unmeasured factors or progressive adherence trends over the two year study period. We addressed natural time trends by using a difference-in-difference approach that estimated a treatment group effect while controlling for time effects. To examine the parallel trend assumption, the main assumption of the difference-in-difference approach, we measured antidepressant adherence during the study period and found no differential trends between the intervention and comparator group (0.7 vs. 0.6 percentage points). Models also included covariates traditionally associated with adherence to control for possible confounding in estimating intervention effects. Second, we acknowledge that medication adherence is a series of behaviors influenced by multiple health system and patient-related factors.
This intervention aimed to influence two of the commonly reported adherence barriers; medication access and patient forgetfulness. Adherence barriers reported in studies of elderly populations but not measured in this analysis, include cost, regimen complexity, and coordination of care. Third, actual adherence may differ from our estimated rates that used pharmacy claims to calculate proportion of days covered by medication. This objective, indirect measurement method assumes members consume and refill medications as prescribed, but possession may not equate consumption. If actual adherence is lower than observed adherence, associations between the intervention and adherence may be overestimated. Conversely, patients may receive medication from sources outside of pharmacies covered by the health plan’s pharmacy benefit (e.g., samples from providers or international pharmacies). This uncaptured utilization, although believed to be minimal, would result in underestimated adherence rates. PDC may also misrepresent actual adherence in scenarios where discontinuation of therapy is deemed appropriate by one’s provider or in the case where members don’t tolerate medication. Appropriate discontinuation of therapy due to side effects or based on provider recommendations is another scenario where measurement by pharmacy claims may misrepresent actual adherence. We believe the above scenarios likely affect both treatment groups, therefore would not differentially bias estimates of adherence for the intervention and comparator groups. Despite the known limitations, the PDC methodology is endorsed by the Pharmacy Quality Alliance and National Quality Forum and is used by CMS in their Medicare Star Ratings. Additionally several studies have used pharmacy claims data as a proxy for medication adherence. Ideally an additional adherence measurement method to validate PDC would strengthen the assessment of
members’ medication adherence; however, subjective (e.g., patient self-reports) or other objective measures (e.g., biomarkers) were not available in this large study population. Fourth, we acknowledge that PDC is positively associated with extended supply of medication, which was an aim of the intervention. To improve estimates of the intervention effect while accounting for 90-day prescriptions, models included a control variable indicating the presence of 90-day refill in the baseline and intervention period. Finally, this intervention was implemented within two health plans. Findings may not be generalizable to other MAPD plans; however, our findings of positive effectiveness are consistent with evaluations of adherence interventions similar in modality within Medicare populations. Replication of findings in similar populations would strengthen the generalizability of results.

Conclusions

This study found adherence improvements to antihypertensives and statins, but modest change to antidiabetics, in two MAPDs implementing a prescriber and patient-directed intervention while adjusting for natural adherence trends and members’ clinical and demographic characteristics. MAPDs can use broad multi-channel interventions to address common adherence barriers and improve members’ adherence to maintenance medications and health plan quality performance ratings.
Acknowledgements

Chapter 3, in full, is currently being prepared for submission for publication of the materials as it may appear. Leslie RS, Gilmer TJ, Natarajan L, Hovell M. A Multi-Channel Medication Adherence Intervention Influences Patient and Prescriber Behavior. The dissertation author was the primary investigator and author of this paper.
Figure 3.1: 90-day Fill Sequence of Communications
**Figure 3.2.** Refill Reminder Sequence of Communications
| Table 3.1: Member Demographics and Clinical Characteristics |
|---------------------------------|------------------|----------------|----------------|----------------|
|                                 | Interventions    | Control        | P              | Interventions  | Control        | P              | Interventions  | Control        | P              |
| Member Count, n                 | 1,277            | 4,144          |               | 4,787          | 14,733         |               | 4,382          | 14,862         |               |
| Female, %                       | 51.8             | 53.9           | .180          | 53.6           | 56.9           | <.001          | 51.8           | 54.9           | <.001          |
| New to therapy^a, %             | 21.5             | 22.4           | .484          | 20.9           | 20.0           | .155           | 21.8           | 19.4           | <.001          |
| 90-day Refill, %                | 59.6             | 70.0           | <.001         | 64.4           | 71.6           | <.001          | 65.7           | 72.8           | <.001          |
| Low Income Subsidy, %           | 41.4             | 18.9           | <.001         | 34.6           | 15.9           | <.001          | 32.7           | 16.2           | <.001          |
| Age, mean (SD), years           | 71.3 (8.8)       | 73.7 (8.7)     | <.001         | 71.8 (9.2)     | 74.6 (8.7)     | <.001          | 71.3 (8.5)     | 73.8 (8.5)     | <.001          |
| Age Group, %                    |                 |                | <.001         |                |                | <.001          |                |                | <.001          |
| < 54                            | 4.6              | 3.0            |               | 4.8            | 2.2            |               | 3.7            | 2.5            |               |
| 55-64                           | 12.9             | 6.8            |               | 12.0           | 5.5            |               | 11.9           | 5.4            |               |
| 65-74                           | 53.6             | 49.8           |               | 51.5           | 47.9           |               | 54.1           | 48.9           |               |
| 75+                             | 28.9             | 40.4           |               | 31.6           | 44.4           |               | 30.4           | 43.2           |               |
| Number of target medication     | .640             |                |               | <.001          |                |               | .090           |                |               |
| classes^b, %                    | 1                | 13.7           | 12.1          | 41.2           | 34.6           |               | 38.5           | 36.0           |               |
|                                 | 2                | 39.2           | 35.3          | 45.4           | 50.0           |               | 47.0           | 48.5           |               |
|                                 | 3                | 47.1           | 52.6          | 13.4           | 15.3           |               | 14.5           | 15.4           |               |
| Comorbidity Count^c, %          | .161             |                |               | .008           |                |               | .078           |                |               |
| < 3                             | 29.8             | 30.9           | 41.7           | 42.1           | 45.6           | 44.2           |
| 3-4                             | 40.5             | 40.6           | 35.3           | 35.9           | 31.9           | 34.2           |
| 5-6                             | 20.8             | 20.5           | 16.7           | 16.0           | 16.1           | 15.4           |
| 7-8                             | 6.6              | 6.5            | 4.8            | 4.8            | 5.0            | 4.9            |
| 9+                              | 2.3              | 1.5            | 1.5            | 1.2            | 1.6            | 1.3            |

^a New to therapy defined as absence of prescription claim for targeted medication class in 1-year baseline period.

^b Members could be identified for intervention by more than one medication class.

^c Comorbidity Count estimated by Medicaid Rx.

SD = standard deviation.
### Table 3.2: Unadjusted Changes in Adherence by Treatment Group

<table>
<thead>
<tr>
<th></th>
<th>Diabetes (DM)</th>
<th>Hypertension (HTN)</th>
<th>Cholesterol (CHOL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention n = 1,277</td>
<td>Control n = 4,144</td>
<td>Intervention n = 4,787</td>
</tr>
<tr>
<td>PDC, mean</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre Period</td>
<td>87.6</td>
<td>89.5</td>
<td>88.5</td>
</tr>
<tr>
<td>Post Period</td>
<td>89.1</td>
<td>90.3</td>
<td>89.9</td>
</tr>
<tr>
<td>Difference</td>
<td>1.5</td>
<td>0.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Difference-in-Difference</td>
<td>+0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDC ≥80, %</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Pre Period</td>
<td>78.6</td>
<td>80.3</td>
<td>80.2</td>
</tr>
<tr>
<td>Post Period</td>
<td>81.7</td>
<td>83.6</td>
<td>82.8</td>
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<tr>
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<td>3.1</td>
<td>3.3</td>
<td>2.6</td>
</tr>
<tr>
<td>Difference-in-Difference</td>
<td>-0.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*PDC = Proportion of Days Covered*

*Pre Period = Apr-12 to Mar-13*

*Post Period = Apr-13 to Mar-14*

*Difference = Post Period - Pre Period*

*Difference-in-Difference = Difference (intervention) – Difference (control)*

*t-tests used to assess statistical difference between treatment groups*
Table 3.3: Intervention Effects on Adherence Outcomes (Diabetes)

<table>
<thead>
<tr>
<th>Variable</th>
<th>PDC (Continuous)</th>
<th></th>
<th>PDC ≥80% (Binary)</th>
<th></th>
<th></th>
<th>OR</th>
<th>95% CI</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coefficient</td>
<td>SE</td>
<td>P</td>
<td>Coefficient</td>
<td>SE</td>
<td>OR</td>
<td>95% CI</td>
<td>P</td>
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<td></td>
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<tr>
<td>Intercept</td>
<td>0.805</td>
<td>0.012</td>
<td>&lt;.0001</td>
<td>0.563</td>
<td>0.187</td>
<td>1.756</td>
<td>1.217</td>
<td>2.534</td>
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<tr>
<td>Female</td>
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<td>-0.039</td>
<td>0.059</td>
<td>0.961</td>
<td>0.857</td>
<td>1.079</td>
<td>0.505</td>
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</tr>
<tr>
<td>Age Group (reference: &lt;55 y)</td>
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<td></td>
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<td>55-64</td>
<td>0.034</td>
<td>0.012</td>
<td>0.004</td>
<td>0.312</td>
<td>0.190</td>
<td>1.366</td>
<td>0.941</td>
<td>1.982</td>
<td>0.101</td>
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<td>65-74</td>
<td>0.029</td>
<td>0.011</td>
<td>0.006</td>
<td>0.191</td>
<td>0.170</td>
<td>1.210</td>
<td>0.866</td>
<td>1.690</td>
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<td>75+</td>
<td>0.029</td>
<td>0.011</td>
<td>0.006</td>
<td>0.207</td>
<td>0.171</td>
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<td>0.880</td>
<td>1.719</td>
<td>0.225</td>
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<tr>
<td>Comorbidity Count (reference: &lt;3)</td>
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<td></td>
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<td></td>
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<td></td>
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<td>3-4</td>
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<td>0.003</td>
<td>0.078</td>
<td>0.100</td>
<td>0.060</td>
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<td>0.984</td>
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<td>5-6</td>
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<td>0.004</td>
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<td>0.118</td>
<td>0.076</td>
<td>1.125</td>
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<td>7-8</td>
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<td>0.006</td>
<td>0.758</td>
<td>0.063</td>
<td>0.114</td>
<td>1.065</td>
<td>0.852</td>
<td>1.332</td>
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<td>9+</td>
<td>-0.001</td>
<td>0.012</td>
<td>0.963</td>
<td>0.193</td>
<td>0.220</td>
<td>1.213</td>
<td>0.788</td>
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<td>New to therapy</td>
<td>-0.019</td>
<td>0.004</td>
<td>&lt;.0001</td>
<td>-0.458</td>
<td>0.070</td>
<td>0.633</td>
<td>0.552</td>
<td>0.725</td>
<td>&lt;.0001</td>
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<tr>
<td>90-day Refill</td>
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<td>0.004</td>
<td>&lt;.0001</td>
<td>0.706</td>
<td>0.062</td>
<td>2.026</td>
<td>1.796</td>
<td>2.286</td>
<td>&lt;.0001</td>
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<tr>
<td>Number of target medication classes (reference: 1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>0.021</td>
<td>0.005</td>
<td>&lt;.0001</td>
<td>0.212</td>
<td>0.085</td>
<td>1.236</td>
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<td>&lt;.0001</td>
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<td>1.280</td>
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<td>0.990</td>
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<tr>
<td>Time (reference: pre period)</td>
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<td>0.003</td>
<td>0.97</td>
<td>0.135</td>
<td>0.051</td>
<td>1.144</td>
<td>1.035</td>
<td>1.265</td>
<td>0.009</td>
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<tr>
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<td>0.005</td>
<td>0.081</td>
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<td>0.967</td>
<td>0.798</td>
<td>1.172</td>
<td>0.734</td>
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</tr>
</tbody>
</table>

PDC=Proportion of Days Covered, OR=Odds ratio, CI=Confidence Interval
Pre Period = Apr-12 to Mar-13
Post Period = Apr-13 to Mar-14
Difference = Post Period – Pre Period
Group X Time Interaction Variable is Difference-in-Difference estimator
Generalized linear models used to assess statistical difference between treatment groups. Logistic regression used for PDC ≥80% outcome.
Table 3.4: Intervention Effects on Adherence Outcomes (Hypertension)

<table>
<thead>
<tr>
<th>Variable</th>
<th>PDC (Continuous)</th>
<th>PDC ≥80% (Binary)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Coefficient</td>
<td>SE</td>
</tr>
<tr>
<td>Intercept</td>
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</tr>
<tr>
<td>Female</td>
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<td>0.002</td>
</tr>
<tr>
<td>Age Group (reference: &lt;55 y)</td>
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<td></td>
</tr>
<tr>
<td>55-64</td>
<td>0.022</td>
<td>0.006</td>
</tr>
<tr>
<td>65-74</td>
<td>0.035</td>
<td>0.006</td>
</tr>
<tr>
<td>75+</td>
<td>0.035</td>
<td>0.006</td>
</tr>
<tr>
<td>Comorbidity Count (reference: &lt;3)</td>
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<td></td>
</tr>
<tr>
<td>3-4</td>
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<td>0.002</td>
</tr>
<tr>
<td>5-6</td>
<td>-0.009</td>
<td>0.002</td>
</tr>
<tr>
<td>7-8</td>
<td>-0.019</td>
<td>0.004</td>
</tr>
<tr>
<td>9+</td>
<td>-0.034</td>
<td>0.007</td>
</tr>
<tr>
<td>New to therapy</td>
<td>-0.013</td>
<td>0.002</td>
</tr>
<tr>
<td>90-day Refill</td>
<td>0.053</td>
<td>0.002</td>
</tr>
<tr>
<td>Number of target medication classes</td>
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<td></td>
</tr>
<tr>
<td>(reference: 1)</td>
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<tr>
<td>2</td>
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<td>0.002</td>
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<tr>
<td>3</td>
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<tr>
<td>Low Income Subsidy</td>
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<td>0.002</td>
</tr>
<tr>
<td>Time (reference: pre period)</td>
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<td>0.001</td>
</tr>
<tr>
<td>Group (reference: Control)</td>
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<td>0.002</td>
</tr>
<tr>
<td>Group X Time Interaction</td>
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<td>0.003</td>
</tr>
</tbody>
</table>

PDC=Proportion of Days Covered, OR=Odds ratio, CI=Confidence Interval
Pre Period = Apr-12 to Mar-13
Post Period = Apr-13 to Mar-14
Difference = Post Period – Pre Period
Group X Time Interaction Variable is Difference-in-Difference estimator
Generalized linear models used to assess statistical difference between treatment groups. Logistic regression used for PDC ≥80% outcome.
Table 3.5: Intervention Effects on Adherence Outcomes (Hypertension)

<table>
<thead>
<tr>
<th>Variable</th>
<th>PDC (Continuous)</th>
<th>PDC ≥80% (Binary)</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Coefficient</td>
<td>SE</td>
</tr>
<tr>
<td>Intercept</td>
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</tr>
<tr>
<td>Female</td>
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<td>0.002</td>
</tr>
<tr>
<td>Age Group (reference: &lt;55 y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>55-64</td>
<td>0.026</td>
<td>0.007</td>
</tr>
<tr>
<td>65-74</td>
<td>0.029</td>
<td>0.006</td>
</tr>
<tr>
<td>75+</td>
<td>0.030</td>
<td>0.006</td>
</tr>
<tr>
<td>Comorbidity Count (reference: &lt;3)</td>
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<td></td>
</tr>
<tr>
<td>3-4</td>
<td>0.000</td>
<td>0.002</td>
</tr>
<tr>
<td>5-6</td>
<td>-0.005</td>
<td>0.002</td>
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<tr>
<td>7-8</td>
<td>-0.006</td>
<td>0.004</td>
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<tr>
<td>9+</td>
<td>-0.010</td>
<td>0.007</td>
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<tr>
<td>New to therapy</td>
<td>-0.014</td>
<td>0.002</td>
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<td>90-day Refill</td>
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<td>Number of target medication classes (reference: 1)</td>
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<tr>
<td>2</td>
<td>0.008</td>
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<tr>
<td>3</td>
<td>0.014</td>
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<td>Low Income Subsidy</td>
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<td>Time (reference: pre period)</td>
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<tr>
<td>Group (reference: Control)</td>
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<td>0.003</td>
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<tr>
<td>Group X Time Interaction</td>
<td>0.018</td>
<td>0.003</td>
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</tbody>
</table>

PDC = Proportion of Days Covered, OR = Odds ratio, CI = Confidence Interval
Pre Period = Apr-12 to Mar-13
Post Period = Apr-13 to Mar-14
Difference = Post Period – Pre Period
Group X Time Interaction Variable is Difference-in-Difference estimator
Generalized linear models used to assess statistical difference between treatment groups. Logistic regression used for PDC ≥80% outcome.
References


CHAPTER 4

MEASURING ADHERENCE TO MAINTENANCE MEDICATIONS AMONG OLDER ADULTS: A CRITICAL REVIEW
Abstract

**Background:** Adherence to medication is a complex behavior involving several patient, health systems, disease condition and provider-related factors that is best measured using a combination of self-report and objective measures. Increased comorbidity, decreased cognition and lower health literacy render older adults susceptible to medication nonadherence. This critical review evaluated interventions designed to modify medication adherence behavior in elderly populations with special focus on measurement methods and operational and theoretical fidelity.

**Methods:** Articles published between March 2010 and February 2015 assessing adherence to therapies to treat diabetes, hypertension or hyperlipidemia were reviewed and evaluated on study design, choice of measurement method and application of behavioral theory.

**Results:** Twenty-two studies designed to modify adherence were reviewed. The most commonly used measurement method was self-report (n=11) followed by pharmacy claims (4), pill counts (4) and electronic medication-event monitor systems (4). Eight studies did not designate a theoretical framework. The average overall quality score was 12. The average quality assessment scores was 5.5 (min=2, max=8). Fifteen studies found positive intervention effects reporting an average 8% increase among treatment compared to control groups.

**Conclusion:** Few papers met the review inclusion criteria. There was no consensus on measurement method and those utilized were developed decades ago. Use of more than one method could increase internal validity and increase understanding of the complex behavior of consuming medication. Few interventions propose behavioral
theories to address a multi-faceted behavior. Future designs should employ behavioral theories that address the macro and micro-environments in which older adults consume medication.
Background

Prescription medication is a vital component of disease management. Compromised delivery and consumption of medication threatens public health because suboptimal adherence is associated with decreased treatment effectiveness, progression of disease, increased utilization, increased costs and decreased quality of life.\textsuperscript{1-3} Medication adherence is especially relevant to elderly populations for several reasons. First, a higher proportion of elders have multiple chronic conditions (MCC) compared to populations under 65 years of age.\textsuperscript{4} Elders consume more medications\textsuperscript{5} to tackle this greater comorbidity and this complicates the medication regimen, which demands greater attention to adherence in order to insure full adherence to all medications. Second, elders have lower health literacy and more likely to experience decreased cognition both of which are associated with adherence, morbidity and mortality.\textsuperscript{6} A study by Baker et al. found total annual health care costs for Medicare patients with low health literacy were 4 times greater than costs for patients with high health literacy.\textsuperscript{7} The elderly population is forecasted to total 72 million, which is nearly 20 percent of the total U.S. population, by 2030.\textsuperscript{8} Lastly, there are health policy implications. Center for Medicare and Medicaid Services (CMS), Pharmacy Quality Alliance (PQA) and the National Committee of Quality Assurance (NCQA) monitor and report adherence as quality performance measures or standards for accreditation.\textsuperscript{9-11} These standards, implicitly, should reflect the state of the art behavioral science for insuring adherence to medications, even as the prescriptions become more complex and the patient less capable of self-management.

The most common objective method for measuring adherence is the use of pharmacy records. Administrative pharmacy claims contain the data needed to quickly
calculate possession of a patients’ medication; but, assume that possession equals consumption. Thus the main disadvantage of this method is the potential for misclassification of patients as adherent in circumstances where patients fill medications but do not consume them reliably, by taking too few medications, too many medications, the wrong medications or with or without meals, etc. However, this approach can be used to calculate adherence in large populations and offers a crude but efficient means of identifying the subset that do not attain the prescriptions in the first place. Despite its wide use by CMS, NCQA, and PQA for quality performance measures and health plan accreditation purposes, this type of measure falls short of adequate assessment or medication adherence and there is no common standard for measuring adherence or uniform terminology for describing adherence.\textsuperscript{12–14}

In 2003 the World Health Organization published a landmark report on adherence to long-term therapies.\textsuperscript{15} This landmark study identified five domains of medication adherence; patient, therapy, social economic, health system, and disease condition. A key conclusion of the report was little published evidence on effective interventions that address these factors. Despite this call for action, nearly a decade later, a 2011 systematic review describing barriers to adherence in the elderly concluded that there is a scarcity of research in this age group and recommended standardizing adherence measurements.\textsuperscript{16} A 2013 review of methods by Raebel et al concluded inconsistent definitions across studies using electronic databases to measure adherence inhibits comparative effectiveness of studies.\textsuperscript{12}

Interventions used to promote adherence vary by approach, purveyor of information, frequency and delivery method. They range from patient refill reminders,
prescriber messaging, increasing convenience and packaging strategies (such as combination pills and increased day supply), patient counseling, information materials and behavioral support. These interventions imply a relatively shallow conceptual model to explain the full adherence to medication or the failure to do so. Most assume the patient does not know how to take the correct medications, context or conditions under which to do so and that they forget even when they do know. Despite the decades of research, several systematic reviews summon need for more research on successful intervention characteristics.\textsuperscript{2,3,17,18,19}

The World Health Organization adherence report, among select systematic reviews, also described medication adherence as a multifaceted behavior that warrants more application of behavioral theory in the design and implementation of adherence interventions.\textsuperscript{1,13,17} Among older adults, a 2008 systematic review of interventions by Banning et al concluded that few studies offered a theoretical basis for interventions.\textsuperscript{20} The purpose of this research is to critically review interventions designed to modify medication adherence behavior in elderly populations with special focus on measurement methods and operational and theoretical fidelity. The quality of randomized controlled trials published in the last five years were assessed to understand the merits and limitations of current methods, application of behavioral theory in intervention design, and recommend potential approaches that could contribute to the advancement of adherence-related science.

**Methods**

**Literature Inclusion Criteria**
Our critical review targeted articles that met the following criteria: the study design was a randomized controlled trial (RCT), at least one of the study outcomes was medication adherence, the article was published in the last 5 years (April 2010-March 2014), was published in English, the study sample was > 65 years of age or consisted of Medicare beneficiaries, and aimed to modify medication adherence behavior to chronic medications administered orally to treat diabetes, hypertension, or hyperlipidemia. We narrowed our literature search to these conditions because they have similar attributes; they are therapies that treat chronic conditions, are orally self-administered, are prescribed as adjunct therapy to recommended lifestyle modifications (such as physical activity, healthy diet and proper sleep), have a long latency period and consumption of medications are generally not perceived by the patient to improve immediate or short-term health gains.

**Search Strategy**

Our literature search included PubMed and PyscINFO. We used the following Medical Subject Heading (MeSH) terms and keywords in our PubMed search; "behavior therapy", "behavioral intervention”, "Medication Adherence", "medication nonadherence”, "diabetes mellitus, type 2", "type 2 diabetes mellitus”, "hypertension", "high blood pressure", "hyperlipidaemia", "hyperlipidemia". The PyschINFO search included the following terms; (hypertension OR diabetes OR hyperlipidemia) AND (behavioral intervention) AND ((medication OR drug) adherence OR patient compliance)) AND age.exact("Very Old (85 Yrs & Older)" OR "Aged (65 Yrs & Older)”).
Additional relevant articles (systematic reviews and seminal articles before the identification period) were identified from the reference lists of the identified articles. Specific journal searches were conducted to include articles that reported explicit theory and possibly higher operational fidelity, including the rough rank of the journal, *Patient Preference and Adherence*. This journal is described as an “international, peer reviewed, open access journal that focuses on the growing importance of patient preference and adherence throughout the therapeutic continuum”. Mendeley®, a reference manager, was used to organize and manage all references.

**Study Selection**

Initial article assessment reviewed abstracts for meeting our inclusion criteria; disease states of interest, study design and study population. The following items were recorded during the review; authors name, study name, year of publication, study design, study setting, disease state, sample size, intervention, adherence measurement method, identification of behavioral theory, results and conclusion. To align with the objective of this critical review, specific attention was given to the adherence measurement method, the number of measurement methods used, the length of adherence assessment (review) period, and the identification and explanation of theory used in the intervention.

**Evaluation Criteria**

To assess the overall quality of the study we used the most recent Consolidated Standards of Reporting Trials (CONSORT) guidelines which provides guidance for reporting of randomized, controlled trials with focus on individually randomized, 2-
group, parallel trials. The CONSORT 2010 statement includes a 25 item checklist and a flow diagram recommended when reporting and publishing RCTs. Based on further explanation of these guidelines, we assessed the overall quality of each study using 15 of the 25 items that have been associated with greater bias. Selection of these 15 items is a method used in reporting quality of RCTs in pain management and clinical decision support meta-analyses. Table 1 describes the items used to score articles identified by our search. To address the purpose of this critical review, we rated studies on four criteria crucial to our research question; operational definition of adherence, measurement method, length of treatment period, and theoretical fidelity (Table 2).

Knowing that medication adherence has been studied for decades and has resulted in several measurement methods we assessed studies based on their adequacy of explanation of adherence in the context of the study and description of the measurement method utilized. We believed length of the period in which adherence was assessed, or review period, was important in order to address the nature of these chronic conditions and because most interventions assess adherence in a short review period. Theoretical fidelity was chosen as a standard because adherence is a multi-factorial behavior, and most studies don’t identify, much less describe, a theoretical framework of medication adherence. A review by Munro, described that few interventions that address long-term adherence use theories of health behavior.

The measurement method and length of review period standards were adapted from a 1999 critical review of medication adherence methods, A Critical Evaluation of the Methodology of the Literature on Medication Compliance. Their evaluation aimed to provide a means for researchers to evaluate the large number of medication adherence
articles (“Compliance” was the term most commonly used before year 2000) being published at the time. Their article evaluation tool contains eight standards over three aspects (design, disease and adherence) and has been used in previous studies.\(^{30}\)

For the overall quality assessment, each of the 15 CONSORT quality items was assigned a score of 1 if the article included the item, and zero if absent. For the specific quality assessment, the adherence measurement method item was the highest weighted attribute and ranged from 6 to 0. The maximum score for an article that comprised of all attributes assessed (adherence definition, theoretical fidelity, study duration, measurement method) was 12 and the lowest possible score was 0.

**Results**

Our literature search identified 138 articles (Figure 1). The abstract review step excluded 104 articles where medication adherence was not a study outcome, were duplicates or the article was not a randomized trial. Thirty four citations met the inclusion criteria and were reviewed in full text. After excluding articles published before 2009, and studies that were quasi-experimental design, 22 met our standards for detailed review. During our search we found two adherence interventions conducted in heart failure. We considered these studies similar in disease condition and study population and therefore included in the review. We also found articles with study populations less than our designated 65 year old search criteria. We included these studies since they included older adults.

Table 3 lists select characteristics of each article. Articles were published between March 2010 and February of 2015. The studies enrolled sample sizes that ranged
from 15 to 5855 participants. Approximately half of studies reviewed were conducted in the United States (n=13), with the remainder in Europe (n=4), Australia (n=2), New Zealand (n=1), Nigeria (n=1), and Canada (n=1). Only 2 studies used more than one adherence measurement method. Four studies were part of larger clinical trials to assess health outcomes. Interventions varied by disease condition; nine addressed hypertension, five addressed diabetes, two hypercholesterolemia and the remaining interventions aimed to increase adherence to all three medication classes (n=4) or cardiovascular disease (n=2).

Interventions included behavioral counseling (live counseling, motivational interviewing, behavioral coaching or identification of medication goals), education and Informational materials (guideline-based treatment recommendations, medication instruction cards, web based information to get patient understanding of their condition, refill reminder postcards or illustrated medication schedules) and medication packaging that increased convenience by combining pills in a blister pack. The interventions were delivered by a nurses, trained care managers, physicians, and pharmacists. Adherence measurement methods ranged from objective to subjective. Indirect methods included validated self-reporting tools (e.g., Morisky scale), non-validated self-report tool (e.g., patient interview), pill counts, electronic monitoring systems, pharmacy claims and blood pressure. Two studies used direct methods (urine assay and measured level in the blood). Four studies used more than one measurement method and four studies were part of larger clinical trials to assess health outcomes. Eight studies lacked a theoretical framework. Of the 14 articles that mentioned a theory there was little discussion of the theory in the interpretation of results. Theoretical frameworks listed by authors included
the Transtheoretical model, Health Decision Model, Levanthal’s self-regulation theory and modified Health Belief Model. No trials used a mixed model (quantitative and qualitative) approach.

The average overall trial score was 12. The specific quality assessment scores ranged from 2 to 8 with the average score of 5.5. For the specific methods quality assessment, scores ranged from 2 to 8 with the average score of 5.5. Eight studies included an adherence definition and criteria. The average rating for the measurement method was low because of the large amount of self-reported methods. Twelve studies used a 1-year treatment period. The theoretical fidelity score was low because 8 studies lacked any mention of theory. Fifteen of the 22 studies found positive intervention effects. The percent increase ranged from 6% to 8% point increases for intervention groups compared to control groups. The largest effectiveness was observed in interventions that used combination pills and behavioral counseling. Seven trials did not show differences between groups. There was no specific trend by intervention type or by measurement method (2 self-report, 2 objective measures, 3 pill counts and 1 used pharmacy claims).

**Discussion**

This article critically reviews recent interventions aimed at influencing adherence to medications to treat diabetes, hypertension and hyperlipidemia among older adults. Articles published in the last 5 years assessing adherence to maintenance medications in elderly populations were reviewed and evaluated on overall study quality, measurement methods and use of behavioral theory during the design, implementation and evaluation
of findings. Restricting our analysis to RCTs identified the highest empirical evidence. A scoring algorithm was developed to meet the special focus of this critical review by combining standards of existing tools and guidelines. As a result of our review of recent clinical trials, we found that current measurement methods warrant critique. Studies lacked development of novel methods. The most common measurement method of adherence was self-reported tools. Similar to findings by Hardeman et al, overall behavioral theory was underspecified. Eight studies did not mention a theoretical framework and the remaining fourteen studies lacked discussion of the theory involvement in the intervention. Theoretical frameworks are important because it provides a reference for additional research. It gives a basis from which to improve methods and advance the science. It also helps understand the reasons for the effectiveness, or lack therefore, of an intervention. Misclassifying a theory could lead to attributing findings incorrectly which can misguide future research. We found variable evidence that interventions increased health outcomes. This is concordant with a 2012 systematic review of adherence interventions that found 18 of 62 articles found improved adherence.

**Potential measurement methods**

Alternative methods of measuring adherence could improve precision of measuring actual medication consumption. One option could be to survey a random sample of patients as done by CMS when using the CAPHS survey in quality performance measures (e.g., patient satisfaction measures). Another option is the assessment of biomarkers or obtaining urine assays to validate self-report as has been
done in tuberculosis adherence in adolescents. Several smartphone applications act as cues and reminders to take medications. These devices could also be used to observe medication consumption as done with direct observed therapy to treat tuberculosis and HIV/AIDS. Financial incentives also offer a method to increase adherence.

**Future directions for research**

The results of our review suggest considerable need to advance the science of measuring medication adherence. Objective, moderately valid measures via pharmacy claims uses accessible data to calculate and trend adherence measures within large populations fairly easily. Self-reported measures within routine care are non-invasive and allow providers to address at the point-of-care, but such methods are suspect to recall bias and social desirability biases.

Although medication adherence is a complex behavior, medication consumption is a binary outcome (did one ingest medication or not) that is easier to interpret and measure compared to other complex health behaviors (e.g., exercising, following diet.) Future research should use more than one measurement method to validate measurements and employ technological advancements to detect ingestion of medicine. Adherence research should also use theory-driven approaches, or incorporate the Principles of Behavior to address countervailing contingencies confronting patients as they consume medication. As mentioned by Steiner, patients are required to make hundreds of adherence decisions, ranging from provider visits to taking medication, per year.

**Limitations**
Our findings should be interpreted in the context of the following limitations. First, although we used a systematic approach, our search may have excluded published articles relevant to medication adherence measurement methods. We acknowledge the vast amount of observational and quasi-experimental adherence studies; but, we chose evaluations of randomized controlled trials because they offer the highest quality of empirical evidence. Common to any literature review, studies with null or negative results are less likely to be published in peer-reviewed literature. Second, our results found significant heterogeneity of studies which limited grouping studies. Third, we acknowledge that the article scoring tool used in this critical review was adapted from sources plus additional criteria that have not been published in peer review. Studies could be scored based on additional criteria; however, the specific aim of this review was to assess measurement methods. Finally, adherence was one of a few outcomes for several studies and understanding effects of individual intervention aspects is difficult when interpreting multifaceted interventions.

**Conclusions**

Results from our examination of articles conclude the necessity for improved methods to measure adherence to chronic therapies to treat diabetes, hypertension and hyperlipidemia among elderly populations. Current methods are dominated by subjective measurements using patient self-reports and objective measurements using pharmacy refills data. Use of multiple measurement methods would increase study internal validity and understanding of the complex behavior of consuming medication. Additional qualitative work that addresses the macro and micro-environment in which older adults
consume medication would identify factors that influence the multi-faceted behavior of medication adherence.
Acknowledgements

Chapter 4 is currently being prepared for submission for publication of the materials as it may appear. Leslie RS, Hovell MF. Measuring Adherence to Maintenance Medications Among Older Adults: A Critical Review. The dissertation author is the primary investigator and author of this paper of this material.
Figure 4.1: Flow Chart Summary of Literature Search
**Table 4.1: Items and Descriptions Used in Overall Study Quality Rating**

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<thead>
<tr>
<th>Item*</th>
<th>Item No</th>
<th>Item Description</th>
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<td>Title and abstract</td>
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<td>Identification as a randomized trial in the title. Structured summary of trial design, methods, results, and conclusions.</td>
</tr>
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<td>Background</td>
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<td>Specific objectives or hypotheses</td>
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<td><strong>Methods</strong></td>
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<td>Eligibility criteria for participants. Settings and locations where the data were collected.</td>
</tr>
<tr>
<td>Interventions</td>
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<td>The interventions for each group with sufficient details to allow replication, including how and when they were actually administered</td>
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<td>Outcomes</td>
<td>6</td>
<td>Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed</td>
</tr>
<tr>
<td>Sample size</td>
<td>7</td>
<td>How sample size was determined. When applicable, explanation of any interim analyses and stopping guidelines</td>
</tr>
<tr>
<td>Randomization: Sequence generation</td>
<td>8</td>
<td>Method used to generate the random allocation sequence. Type of randomization; details of any restriction (such as blocking and block size)</td>
</tr>
<tr>
<td>Randomization: Implementation</td>
<td>9</td>
<td>Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions</td>
</tr>
<tr>
<td>Statistical methods</td>
<td>10</td>
<td>Statistical methods used to compare groups for primary and secondary outcomes. Methods for additional analyses, such as subgroup analyses and adjusted analyses</td>
</tr>
<tr>
<td><strong>Results</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participant flow (a diagram is strongly recommended)</td>
<td>11</td>
<td>For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome. For each group, losses and exclusions after randomization, together with reasons.</td>
</tr>
<tr>
<td>Recruitment</td>
<td>12</td>
<td>Dates defining the periods of recruitment and follow-up. Why the trial ended or was stopped</td>
</tr>
<tr>
<td>Baseline data</td>
<td>13</td>
<td>A table showing baseline demographic and clinical characteristics for each group</td>
</tr>
<tr>
<td>Outcomes and estimation</td>
<td>14</td>
<td>For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval). For binary outcomes, presentation of both absolute and relative effect sizes is recommended</td>
</tr>
<tr>
<td>Harms</td>
<td>15</td>
<td>All important harms or unintended effects in each group</td>
</tr>
</tbody>
</table>

*Subset of CONSORT 2010 checklist of information to include when reporting a randomized trial \[22,32\]
Table 4.2: Items and Descriptions Used in Specific Study Rating

<table>
<thead>
<tr>
<th>Standard</th>
<th>Points</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition of Adherence</strong>*</td>
<td>2</td>
<td>Adherence criteria explicitly stated</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Criteria stated, without description of measurements; or measurements stated without description of criteria</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>No definition</td>
</tr>
<tr>
<td><strong>Adherence Measurement Method</strong>*</td>
<td>6</td>
<td>nonscheduled measurement of <strong>one</strong> of the following:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>blood concentration of drug, urine tracer, other physical and biologic measurements</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>plus</strong> one of the following measurements:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pill count, prescription refill, medication event monitoring (electronic chips)</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>nonscheduled measurement of one of the following <strong>alone</strong>:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>blood concentration of drug, urine tracer, other physical and biologic measurements</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>or</strong> scheduled measurement of one of the following:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>blood concentration of drug, urine tracer, other physical and biologic measurements</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>plus</strong> one of the following measurements:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pill count, prescription refill, medication event monitoring (electronic chips)</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>scheduled measurement of one of the following alone:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>blood concentration of drug, urine tracer, other physical and biologic measurements</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>nonscheduled measurement of:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pill count, prescription refill, medication event monitoring (electronic chips)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>scheduled measurement of:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pill count, prescription refill, medication event monitoring (electronic chips)</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>validated self-reported compliance measurement (e.g., Morisky scale)</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>not stated or not validated compliance measurement (e.g., interview of patient, patient’s family, clinician, or chart review)</td>
</tr>
<tr>
<td><strong>Study Duration</strong></td>
<td>2</td>
<td>≥ 1 year follow-up period</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>&lt; 1 year follow-up period</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>Not stated</td>
</tr>
<tr>
<td><strong>Theoretical fidelity</strong></td>
<td>2</td>
<td>Identified and followed a behavioral theory during design, implementation and analysis</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Theory named but underspecified and underreported</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>Behavioral theory framework not named</td>
</tr>
</tbody>
</table>

* Adapted from Nichol et al., Annals of Pharmacology, 1999**
### Table 4.3: Characteristics of Reviewed Articles

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Condition</th>
<th>Population/Setting</th>
<th>Sample size</th>
<th>Intervention</th>
<th>Adherence Measurement Method</th>
<th>Theoretical Framework</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adeyemo et al(^{35}), 2013</td>
<td>Hypertension</td>
<td>Nigeria</td>
<td>544</td>
<td>Clinic-based treatment administered by trained nurses</td>
<td>Pill counts and biological assay with a urinary riboflavin tracer</td>
<td>None stated</td>
</tr>
<tr>
<td>Bosworth et al(^{37}), 2008</td>
<td>Hypertension</td>
<td>North Carolina, 2 clinics</td>
<td>636</td>
<td>Nurse-administered behavioral intervention or usual care</td>
<td>Self-report, Morisky Medication Adherence Scale (4 item)</td>
<td>Transtheoretical model and Health decision model</td>
</tr>
<tr>
<td>Broekhuizen et al(^{38}), 2012</td>
<td>Hypercholesterolemia</td>
<td>Dutch screening program</td>
<td>340</td>
<td>Web-based tailored lifestyle advice and face-to-face counselling with telephone booster</td>
<td>Self-report, Medication Adherence Report Scale (MARS-5)</td>
<td>I- Change model= behavioral change</td>
</tr>
<tr>
<td>Choudhry(^{39}), 2011</td>
<td>HTN, DM, CHOL</td>
<td>USA</td>
<td>5855</td>
<td>Full prescription coverage (waived copay) or usual prescription coverage</td>
<td>Pharmacy claims</td>
<td>None stated</td>
</tr>
<tr>
<td>Criswell(^{40}), 2010</td>
<td>Hypertension</td>
<td>11 US university-affiliated primary care clinics</td>
<td>584</td>
<td>Intensified hypertension management and drug adherence counseling by pharmacists</td>
<td>Morisky self-reported adherence questionnaire</td>
<td>None stated</td>
</tr>
<tr>
<td>Evans(^{41}), 2010</td>
<td>Hypercholesterolemia</td>
<td>Primary clinic in Canada</td>
<td>176</td>
<td>Pharmacist counseling, Follow up group and single contact</td>
<td>Pharmacy claims</td>
<td>None stated</td>
</tr>
<tr>
<td>Study, Year</td>
<td>Condition</td>
<td>Population/Setting</td>
<td>Sample size</td>
<td>Intervention</td>
<td>Adherence Measurement Method</td>
<td>Theoretical Framework</td>
</tr>
<tr>
<td>------------------</td>
<td>----------------------------</td>
<td>---------------------------------------------</td>
<td>-------------</td>
<td>-------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Granger37, 2015</td>
<td>Heart Failure</td>
<td>North Carolina clinics</td>
<td>86</td>
<td>Nurse conducted self-management training</td>
<td>Morisky Medication Adherence Scale 8-item and pill counts</td>
<td>None stated</td>
</tr>
<tr>
<td>Griffin44, 2014</td>
<td>Diabetes</td>
<td>34 general practices in Eastern England</td>
<td>478</td>
<td>Intensive treatment plus a theory-based behavior change led by a facilitator</td>
<td>Objective, plasma concentration levels using liquid-chromatography–mass-spectrometry</td>
<td>None stated</td>
</tr>
<tr>
<td>Keyserling45, 2014</td>
<td>Coronary Heart Disease</td>
<td>5 diverse family medicine practices in North Carolina</td>
<td>385</td>
<td>Counselor-delivered or web-based format, each including 4 intensive and 3 maintenance sessions</td>
<td>Self-report by Morisky scale (4-item)</td>
<td>None stated, assume behavioral counseling</td>
</tr>
<tr>
<td>Kripalani6, 2012</td>
<td>Cardiovascular</td>
<td>New York City, African American inner city</td>
<td>435</td>
<td>4 arms: refill reminder postcards, illustrated med schedules, both, or usual care</td>
<td>Pharmacy claims, measured Cumulative Medication Gap</td>
<td>None stated</td>
</tr>
<tr>
<td>Lee47, 2006</td>
<td>several, at least 4 chronic medications</td>
<td>Elderly military with at least 4 chronic medications, Walter Reed Medical Facility</td>
<td>200</td>
<td>2 arms patient education and an adherence aid (medications custom packaged in blister packs)</td>
<td>Pharmacy claims, Proportion of Days Covered</td>
<td>None stated</td>
</tr>
</tbody>
</table>
### Table 4.3: Characteristics of Reviewed Articles, cont.

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Condition</th>
<th>Population/Setting</th>
<th>Sample Size</th>
<th>Intervention</th>
<th>Adherence Measurement Method</th>
<th>Theoretical Framework</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migneault, 2012</td>
<td>Hypertension</td>
<td>African Americans, New York</td>
<td>337</td>
<td>8-month automated, multi-behavior intervention or to an education-only control</td>
<td>Self-report, Morisky Medication Adherence Scale (8 item)</td>
<td>None stated</td>
</tr>
<tr>
<td>Ogedegbe, 2014</td>
<td>Hypertension</td>
<td>New York City, African Americans</td>
<td>256</td>
<td>Patient education, home BP monitoring, and monthly lifestyle counseling</td>
<td>Pill count</td>
<td>None stated</td>
</tr>
<tr>
<td>Peterson et al., 2013</td>
<td>Hypertension</td>
<td>African Americans, New York</td>
<td>756</td>
<td>Patient education plus positive affect induction and self-affirmation and positive affect induction</td>
<td>Electric cap monitor (Medic-eCap)</td>
<td>Positive affect and self-affirmation</td>
</tr>
<tr>
<td>Rubak, 2011</td>
<td>Diabetes</td>
<td>Denmark, general practitioners</td>
<td>628</td>
<td>Motivational interviewing</td>
<td>Pill count</td>
<td>None stated</td>
</tr>
<tr>
<td>Ruppar, 2010</td>
<td>Hypertension</td>
<td>USA, convenience sample from Midwest senior centers</td>
<td>15</td>
<td>Intervention-group participants received biweekly MA and BP feedback, habit counseling, medication and disease education, a medication instruction card</td>
<td>Electric cap monitor, Medication Event Monitoring System.</td>
<td>Leventhal's self-regulation</td>
</tr>
<tr>
<td>Salek, 2011</td>
<td>CVD</td>
<td>New Zealand</td>
<td>600</td>
<td>Combination pill burden</td>
<td>Self-report, patient interview</td>
<td>Decrease pill burden</td>
</tr>
</tbody>
</table>
Table 4.3: Characteristics of Reviewed Articles, cont.

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Condition</th>
<th>Population/Setting</th>
<th>Sample size</th>
<th>Intervention</th>
<th>Adherence Measurement Method</th>
<th>Theoretical Framework</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stuart⁵, 2015</td>
<td>Hypertension</td>
<td>Pharmacies in Australia</td>
<td>395</td>
<td>Package comprising BP monitor; training on BP self-monitoring; motivational interviewing; medication use review; prescription refill reminders.</td>
<td>Self-report, Morisky scale</td>
<td>None stated</td>
</tr>
<tr>
<td>Thorn⁵, 2015</td>
<td>CVD</td>
<td>Europe and India</td>
<td>2004</td>
<td>Combining pills into fixed-does combination product</td>
<td>Self-reported patient interview</td>
<td>None stated</td>
</tr>
<tr>
<td>Williams⁶, 2012</td>
<td>Diabetes</td>
<td>Diabetes clinics of Australian hospital</td>
<td>75</td>
<td>Self-monitoring of blood pressure, individualized medication review, a 20-minute DVD, and motivational interviewing follow-up telephone contact</td>
<td>Manual pill count, self-report and surrogate biochemical markers of disease control</td>
<td>Modified Health Belief Model</td>
</tr>
</tbody>
</table>
References


51. Rubak S, Sandbæk A, Lauritzen T, Borch-Johnsen K, Christensen B. Effect of “motivational interviewing” on quality of care measures in screen detected type 2


CHAPTER 5
OVERALL CONCLUSIONS AND DISCUSSION
Diabetes, hypertension and hyperlipidemia are highly prevalent diseases among the elderly. The Centers for Disease Control and Prevention (CDC) estimates prevalence in this population for these three diseases at 26.9%, 70% and 58%, respectively.\textsuperscript{1,2,3} These rates are projected to rise as the proportion of the population aged 65 and greater increases; the elderly population is forecasted to total 72 million, nearly 20 percent of the total U.S. population, by 2030.\textsuperscript{4}

Pharmacologic treatment is core to treating these diseases therefore suboptimal adherence threatens disease management. Suboptimal adherence decreases effectiveness of treatment (i.e., medicines doesn’t have a chance to work if not consumed) and may also signal nonadherence to other non-pharmacologic treatment regimens. The World Health Organization states that “adherence is the single most important modifiable factor that compromises treatment outcome.”\textsuperscript{5} In the first volume of *Interventions for Helping Patients to Follow Prescriptions for Medications*, Haynes et al. on behalf of the Cochrane Review, stated that “increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments.”\textsuperscript{6}

The elderly population is especially vulnerable to suboptimal adherence for several reasons. First, a higher proportion of elders have multiple chronic conditions (MCC)\textsuperscript{7} compared to populations under 65 years of age. Elders consume more medications\textsuperscript{8} to tackle this greater comorbidity and this increased medication use compounds medication regimen complexity demanding greater medication use behavior of patients. Second, adherence becomes progressively complicated with increased medication regimens that require more instructions, visits to providers and pharmacies.
Third, elders also have lower health literacy and more likely to experience decreased cognition both of which are associated with utilization and mortality.9

The purpose of this dissertation was to examine adherence to pharmacologic therapies used to treat diabetes, hypertension, and hyperlipidemia among Medicare Part D beneficiaries. The first two specific objectives of this dissertation were addressed by evaluating interventions that aimed to modify adherence risk factors by 1) improving patient access to medications via increased supply, 2) educating providers of 90-day pharmacy benefits, 3) addressing patients’ forgetfulness via refill reminders, and 4) counseling patients on barriers to medication adherence. The third chapter of this dissertation reviewed empirical evidence from randomized controlled trials designed to modify medication adherence in order to comprehend the breadth of measurement methods and extent of behavioral theories specified during intervention design, implementation and interpretation of results.

Chapter 2 demonstrated the effectiveness of a coordinated patient-directed medication adherence intervention that leveraged a partnership between a health plan, pharmacy benefits manager and network pharmacy. The observed increases in adherence rates may be due to the ability of care coordinators to address adherence barriers by 1) improving medication access, 2) counseling members on when to take medication, and 3) scheduling provider visits. The large proportion (31%) of members electing the mail order option suggests that members of this dual-eligible population may have had difficulty with medication access that could be resolved with this convenience. The large, positive increases in medication adherence for all three targeted classes post-implementation were especially compelling because of the study population’s previous
poor adherence record and high proportion of members suffering from mental disabilities and low access to care.

Chapter 3 assessed the impact of a quasi-experimental multi-channel adherence intervention on beneficiaries’ adherence and health plan quality performance measures among two Medicare-Advantage Prescription Drug plans. Adherence to antihypertensives and statins increased in two health plans implementing a prescriber and patient-directed intervention when compared to similar plans that did not implement an intervention. The observed increases in adherence rates were most likely attributable to increased access via informing prescribers of a 90-day benefit. Results of this work demonstrate that a broad intervention can address common patient-related adherence barriers, such as forgetfulness and access, and effectively increase adherence rates among entire memberships. It also demonstrated that a prescriber-directed retail 90-day intervention can effectively influence prescribing patterns of maintenance medications. The benefits of 90-day prescriptions include decreased out-of-pocket and transportation costs for the patient, decreased costs to the health plan that accompanies decreased generic costs, fewer refills for providers and added convenience to patients (less trips to the pharmacy).

As demonstrated in both evaluations, large scale interventions offer ways to increase population-level adherence rates to medications indicated for highly prevalent chronic conditions. Broad interventions can potentially reach all members (with the target disease condition) within a health plan population while simultaneously addressing several common patient-related adherence barriers (e.g., access, forgetfulness, and cost). Stratification of members can identify subsets of members with multiple adherence issues
for more intense intervention strategies (e.g., counseling). Physician-directed campaigns can be used to increase awareness and provide fulfillment options that facilitate member convenience.

Chapter 4 critically reviewed recently published adherence interventions with specific focus on measurement methods and operational and theoretical fidelity. The aim was to investigate current tools used to measure adherence and understand if and how theoretical frameworks were incorporated in recently randomized controlled trials. None of the trials reviewed used directly observed therapy (DOT), considered the ideal method for ensuring consumption, and all studies used measurement methods that were developed decades ago. Subjective self-reporting and objective measurements using pharmacy claims were the most common methods. Use of pharmacy claims to estimate consumption provides a quick, objective measurement in large populations when gathering self-reports is not feasible. Hence CMS uses this method for their Health Plan Quality Ratings System which requires measures of adherence for millions of beneficiaries each year. However, observed medication use may not constitute actual consumption which may lead to misclassification and misrepresentation of health plan performance. Self-reports are useful in routine clinical care allowing providers to inform patients of the risks of poor adherence plus offer tools to increase appropriate use; however, this method is hard to scale in large populations and is exposed to social desirability and recall biases. Electronic monitoring devices, such as MEMS® (Medication Event Monitoring System), can record time and frequency of dosing as indicated by the opening of a prescription bottle cap. However this method may be limited to the extent patients manipulate the bottle (open but don’t consume). Special
bottles also require special handling for refills, resulting in an expense to patients and sponsoring organizations, and can sometimes act as an intervention in itself. Ultimately, a combination of subjective and feasible objective measures would offer better measurement of behavior than single approaches. The choice of method often depends on the study population size and intervention purpose and circumstances.

Among the twenty-two reviewed studies, eight did not mention a theoretical framework and the remaining fourteen studies that did name a theory lacked a discussion of the theory. Theoretical frameworks are important because it provides a reference a basis from which to improve methods and advance the science. It also helps understand the reasons for the effectiveness, or lack therefore, of an intervention. Misclassifying a theory could lead to incorrectly attributing findings to a theory which can misguide future research. Future interventions should use theory-driven approaches, or incorporate the Principles of Behavior to address countervailing contingencies confronting patients as they consume medication.

**Future Directions**

Mobile, real-time technology offers ways to improve existing measurement methods. Smartphone and tablets can be utilized to measure adherence via photography or videos, as currently done with directly observed therapy in tuberculosis and HIV/AIDS, plus act as intervention mediums to remind patients of refills, instruct patients on guidelines, and provide feedback when patient consume properly. Future trials addressing medication adherence would also benefit from establishing and describing detailed theoretical frameworks a priori to improve the context and constructs
of medication use. Additional qualitative work that addresses the macro and micro-environment in which older adults consume medication could identify contingencies that influence adhering to medication this multi-faceted behavior. This includes studying patients’ everyday routines, previous medication experiences (first-hand experienced or observed), and the potential immediate and long-term consequences of using medication.

Medication adherence is in the best interest of patients, providers, health systems and government agencies. Greater adherence is associated with better health outcomes which is a main goal of the Patient Protection and Affordability Act of 2010. Improving measurement and understanding the theoretical underpinnings of this complex behavior would advance adherence-related science and increase the validity of quality performance measurements used by government and national quality organizations.
References


